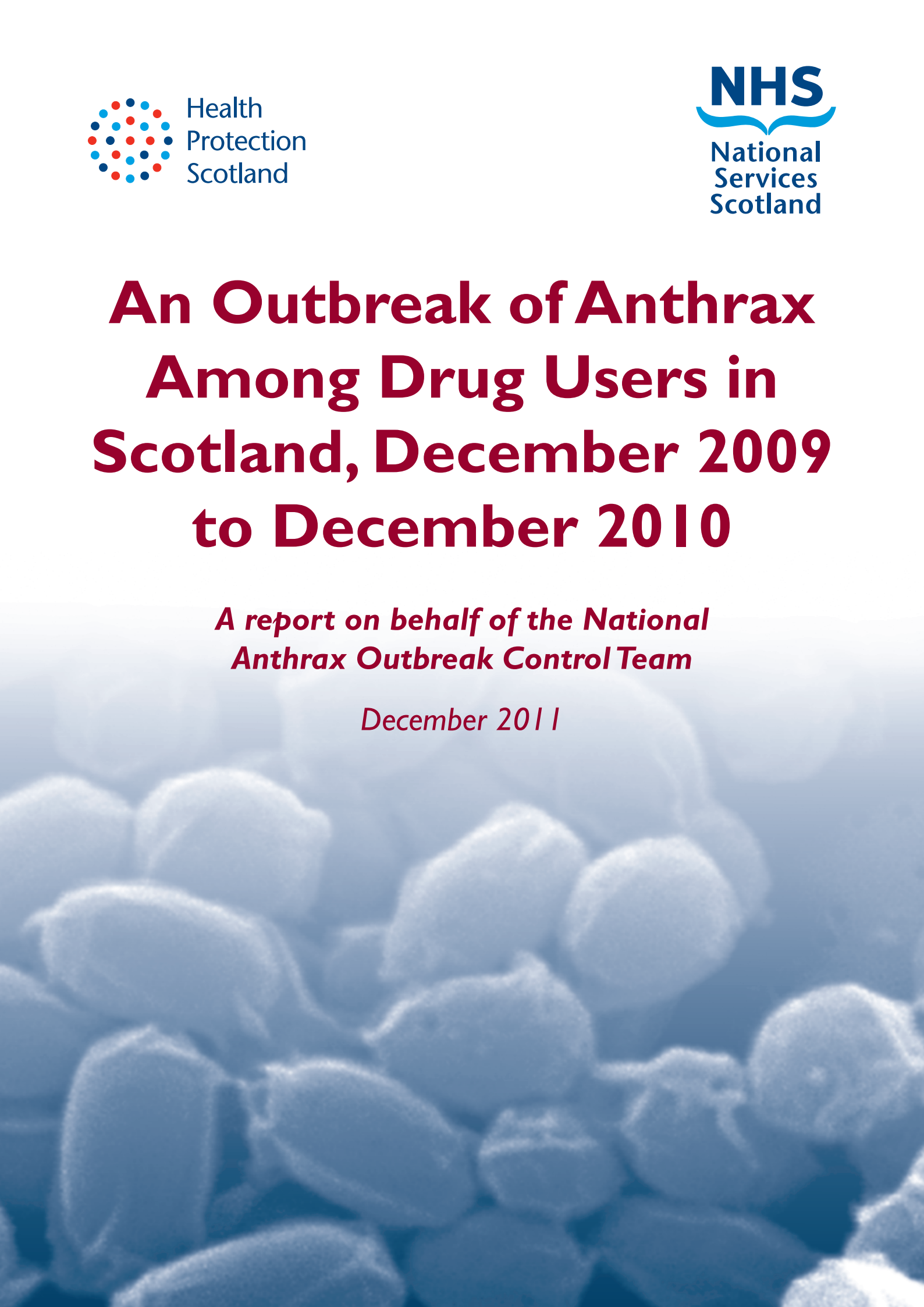
Health Protection Scotland

NHS National Services Scotland

An Outbreak of Anthrax Among Drug Users in Scotland, December 2009 to December 2010

A report on behalf of the National Anthrax Outbreak Control Team

December 2011



Health Protection Scotland is a division of NHS National Services Scotland.

Health Protection Scotland website: http://www.hps.scot.nhs.uk

Published by Health Protection Scotland, NHS National Services Scotland, Meridian Court, 5 Cadogan Street, Glasgow G2 6QE.

First published December 2011

Reference this report as:
National Anthrax Outbreak Control Team. An Outbreak of Anthrax Among Drug Users in Scotland, December 2009 to December 2010. Health Protection Scotland, 2011.

Health Protection Scotland
NHS National Services Scotland
Meridian Court
5 Cadogan Street
Glasgow G2 6QE

Tel: +44 (0) 141 300 1100

Email: NSS.HPSEnquiries@nhs.net

Designed and typeset by:
Graphics Team, Health Protection Scotland

Table of Contents

List of Tables

List of Figures

Abbrevations

A&E	Accident and Emergency
ACN	Anthrax Clinical Network
AIGIV	Anthrax Immune Globulin – Intravenous
B. anthracis	*Bacillus anthracis*
C. novii	*Clostridium Novii*
CBRN	Chemical, Biological, Radiation and Nuclear
CDC	US Centres for Disease Control and Prevention
CMO	Chief Medical Officer
COPFS	Crown Office Procurator Fiscal Service
ECDC	European Centre for Disease Prevention and Control
FAI	Fatal Accident Inquiry
HHS	Health and Human Services
HPA	Health Protection Agency
HPA CFI	Health Protection Agency, Centre for Infection
HPA-NDPL	Health Protection Agency, Novel and Dangerous Pathogens Laboratory
HPN	Health Protection Network
HPS	Health Protection Scotland
HPTs	Health Protection Teams
ID	Infectious Disease
IgG	Immunoglobulin G
IM	Intramuscular
IV	Intravenous
ITU	Intensive Therapy Unit
NAOCT	National Anthrax Outbreak Control Team
NAU	Northern Arizona University
NHS	National Health Service
NHS GG&C	NHS Greater Glasgow and Clyde
NSS	National Services Scotland
OCT	Outbreak Control Team
PCR	Polymerised Chain Reaction
SC	Sub-cutaneous
SDF	Scottish Drugs Forum
SDMD	Scottish Drug Misuse Database
SGHD	Scottish Government Health Directorate
SMF	Scottish Microbiology Forum
SNP	(Canonical) Single Nucleotide Polymorphism
SSTI	Serious soft tissue infection
TEA	Trans-Eurasian
TGen	Translational Genomics Research Institute

Foreword

This report summarises the events associated with the investigation and management of the anthrax outbreak involving drug users in Scotland between December 2009 and December 2010. The report describes the investigations; the epidemiology of the outbreak; action taken and the lessons identified; from the challenges of diagnosis and clinical management of a new presentation of anthrax, to managing effective communication with a hard-to-access vulnerable group of drug users.

A large number of agencies and individuals were involved in the investigation, both members of the National Anthrax Outbreak Control Team (NAOCT) and other collaborators, who all provided essential advice, expertise and support. The contributions of all the members of the NAOCT and others over the prolonged duration of the investigation are gratefully acknowledged.

This is the first documented outbreak of anthrax involving heroin users and proved to be the largest single common source outbreak of human anthrax in the UK in over 50 years. Associated cases also occurred in England and Germany in the same period, making this a European as well as a UK outbreak. The outbreak presented many unique challenges, not least in working with the population primarily affected, namely users of illicit drugs. The investigation was further complicated by finding that contaminated (illicit) heroin was implicated as the primary vehicle for transmitting anthrax infection and that, as an illegal substance supplied via a criminal dealer network, the opportunities to apply conventional methods of outbreak investigation and management were restricted. Drug users (and dealers) were less amenable to normal public health methods of enquiry and persuasion, via risk communication, to reduce their personal risks of infection or to limit the risk of exposing others. Close collaboration between public health agencies, police and procurator fiscal (judicial) services in Scotland and equivalent across the UK, especially the Health Protection Agency (HPA), was therefore an essential feature of the investigation. International collaboration was also prominent with a significant input from colleagues from the US Centres for Disease Control and Prevention (CDC) and the Northern Arizona University (NAU).

As long as there is an illicit drug trade, the risk of further such outbreaks will continue; opportunities for their primary prevention are likely to remain limited. Hopefully the experience and lessons from this investigation may assist in improving the planning, preparation and response to any such future challenge.

Dr Colin N. Ramsay

Chair of the National Anthrax Outbreak Control Team

Consultant Epidemiologist
Health Protection Scotland

December 2011

Summary

Outbreak Characteristics

- An outbreak of anthrax was identified starting in Glasgow in December 2009, when cases of serious soft tissue infection (SSTI) among drug users were confirmed as being due to infection with *Bacillus anthracis*, the first such outbreak formally recorded. A local outbreak investigation began, which became a national investigation in January 2010, co-ordinated by Health Protection Scotland (HPS), when cases were identified in multiple NHS board areas.

- The clinical presentations of anthrax were atypical; cases did not have typical cutaneous anthrax lesions but presented with serious localised soft tissue infections accompanied by disproportionate tissue swelling (oedema), often with less pain than seen in other serious soft tissue infections (SSTIs) (e.g. necrotising fasciitis). Fever was not a prominent feature. Not all cases had localised injection related lesions; some cases, especially the more seriously ill patients (and some that died very rapidly), presented with features more typical of systemic anthrax infection and toxaemia, with manifestations including haemorrhagic meningitis, multi-organ failure and bleeding diathesis.

- Cases were treated with conventional multi-antimicrobial and supportive therapy; some required extensive reconstructive surgery following surgical debridement of wounds and destroyed tissue. In addition, 14 patients were treated with Anthrax Immune Globulin - Intravenous (AIGIV) donated by the US Government via the US Centres for Disease Control and Prevention (CDC).

- The outbreak was declared as ended in December 2010, by which time 208 initially suspected cases had been formally investigated; 119 patients were ultimately classed as anthrax cases, classified further as: 47 confirmed cases; 35 probable cases; and 37 possible cases based on the strength of microbiological evidence, provided by the Health Protection Agency, Novel and Dangerous Pathogens Laboratory (HPA-NDPL) at Porton Down; the remaining 89 initially suspected cases were finally classed as not having anthrax (anthrax negative). Fourteen anthrax cases died (13 confirmed, 1 probable).

- Most of the cases occurred between December 2009 and March 2010. The last case to be confirmed in Scotland had symptoms in July 2010; however, the last suspected case was investigated in October 2010, indicating that the risk of infection to drug users in Scotland persisted for almost a year.

- There were twice as many male as female cases. The cases ranged in age from 18 to 55 years; the average age for all cases was 34 years.

- The outbreak cases lived in 10 of 14 NHS board areas in Scotland with most cases resident in the Glasgow/Lanarkshire/Central Scotland conurbation. Significant clusters also occurred in Dundee and Dumfries. Lothian and Grampian NHS Board areas by contrast, despite having significant heroin using populations, had few cases; Highland and the Island areas had no cases. Attack rates (incidence per thousand estimated drug users) were highest in Dumfries and Dundee.

- All cases were heroin users, taking the drug by multiple methods including injection (IV, IM) and smoking. Unlike earlier drug user infection outbreaks, deliberate muscle injecting (muscle-popping) was not a more prominent risk factor.
- Although taking heroin by any route was identified as carrying a risk, evidence from a retrospective case-control study (not available to the NAOCT at the time) suggested that injecting heroin may have carried an increased risk compared to *only* smoking heroin.
- Cases were also investigated over the same period in England and Germany, with five anthrax cases confirmed in England and two in Germany.
- Genotyping identified that all the isolates from Scottish cases (as well as those from cases in England and Germany) were of a single, indistinguishable, novel strain of anthrax not previously seen in the UK or elsewhere. The closest strains to this novel variant were from anthrax infected goats identified previously in Turkey.
- No anthrax was found in samples of heroin itself; however, the epidemiological evidence implicating heroin as the vehicle for spore transmission was very strong.
- There were many parallels to the outbreak of *C. novii* infection in 2000 which also affected heroin users predominantly in West Central Scotland; that also had an international dimension and was also attributed to the importation of a batch of spore contaminated heroin.

Control Measures

- The illicit nature of the heroin supply considered responsible for transmitting the infection, together with the illegal drug trafficking trade, limited the options for intervention and made control of the outbreak very difficult. Conventional options normally available to an outbreak control team to enforce eradication of a contaminant at source, or to remove contaminated material from supply, were not available in this situation.
- Police action focussed on identifying and disrupting heroin distribution networks and dealer activities and confiscating heroin supplies where possible.
- Public health action focussed on alerting heroin users to seek urgent attention if unwell and providing advice that all heroin circulating at the time had to be considered as potentially contaminated; that drug users should therefore avoid all use of heroin and should seek treatment from drug addiction services (e.g. for opioid substitution therapy).
- Guidance was also provided on preventing secondary infection to healthcare professionals in the NHS, police and other staff in settings where personal contact with cases, heroin and heroin contaminated property was likely.
- Additional control measures such as the use of vaccination against anthrax and the use of antibiotic prophylaxis for heroin users were assessed as being impractical as outbreak control measures. Some external parties proposed that approved non-street (prescribed) heroin should be made available to drug users during the outbreak. The NAOCT determined that advising on supplying (prescribed) heroin to users, as a risk control measure, was beyond the NAOCT remit and therefore did not express an opinion on the proposal.

Conclusions

The epidemiological and microbiological evidence supports a conclusion that heroin was the vehicle for transmission of anthrax spores and that exposure was by a variety of routes, particularly by injection but also by smoking (inhalation). The mechanism and the location of spore contamination are not known. Genotyping evidence strongly suggests that infection was due to a single, novel, anthrax strain related to Trans-Eurasian (TEA) anthrax strains previously identified in goats, in Turkey. This and other intelligence on the heroin trafficking trade supports a conclusion that the contaminated heroin imported to Scotland was from a single batch contaminated with anthrax spores via contact with a single infected animal (or contaminated hide), somewhere in transit between Afghanistan/Pakistan and Scotland, probably in Turkey.

There remains a risk that at any time, pathogen contaminated heroin could be imported to the UK again, causing another outbreak of anthrax or similar infection. A set of good practice points have been identified, based on the collective experience of this outbreak. Recommendations involving more substantive work have also been made on the planning, preparedness and response to any such future outbreaks.

Good Practice Points

Planning and Preparedness for Anthrax Outbreaks

- Local NHS boards Health Protection Teams (HPTs) should encourage early alerting by local clinicians (particularly A&E & ITU) of any unusual patterns of infection among drug users including suspected anthrax. Other sectors involved in drug service provision could also have a role in early alerting (e.g. injection paraphernalia providers). *(Attention of NHS boards).*

- Clinicians (A&E physicians, ITU staff and surgeons etc.) should be reminded periodically about the signs and symptoms of anthrax infection (classical and atypical anthrax presentations) and the need to take blood samples for blood cultures, before antibiotic treatment is commenced for any suspected anthrax infection. *(Attention of Scottish Government, HPS, NHS boards, Scottish Microbiology Forum (SMF)).*

- NHS Scotland microbiologists should be reminded periodically of the microbiological features of anthrax and the protocols for its identification via appropriate professional channels. *(Attention of HPS, SMF).*

- The protocols for sending microbiological and pathology samples for *Bacillus anthracis* testing at HPA-NDPL should be clarified to differentiate clearly between samples that require urgent investigation to exclude anthrax in highly clinically suspicious cases, compared to samples of a less urgent nature. *(Attention of HPS, HPA, SMF).*

- Local NHS board HPTs, statutory and voluntary drug services and local police forces should develop plans for collaborative working and joint public health and police investigations, particularly for future incidents involving the use of contaminated street drugs. *(Attention of NHS boards, police forces and Scottish Drugs Forum (SDF)).*

- HPS should incorporate lessons from the outbreak relating to preparedness, responsibilities and resources into internal plans for managing National outbreaks of drug related infections, including anthrax. *(Attention of HPS).*

- A teleconference based Clinical Forum, as developed in this outbreak, should be considered as a useful mechanism for obtaining broadly based clinical input to any future OCT. *(Attention NHS boards, HPS).*

Outbreak Investigation and Management

- Epidemiological investigation questionnaires for use in the investigation of cases of anthrax should be refined to facilitate improved data collection on a range of potential environmental anthrax exposures, including details of drug use practices associated with possible anthrax exposure. *(Attention of HPS, HPA).*

- In any future drug related outbreaks, NHS boards should consider the potential role of appropriately experienced drug service workers in assisting in the collection of detailed information on drug use behaviours. *(Attention of NHS boards, HPS, SDF).*

Risk Assessment

- The risk assessment and other guidance material on infection control and occupational exposure risks developed during this outbreak should remain available for future use and should be refined further to provide generic guidance for use in future anthrax exposure and infection incidents. *(Attention of HPS, Health Protection Network (HPN)).*

Risk Management (Control Measures)

- Drug addiction and treatment services should take opportunities to advise drug users of the risks of infection from a variety of pathogens including anthrax, associated with using heroin or other uncontrolled street drugs by any method. *(Attention of NHS Scotland, SDF, local drug service providers).*

Risk Communication

- In any future drug use related incident, NHS board HPTs should seek early involvement of local drug addiction services, to assist with the rapid dissemination of information and advice to drug users. *(Attention of NHS boards, local drug service providers).*

Recommendations

The recommendations are derived from the lessons identified and could apply equally well to other parts of the UK and more widely.

Planning and Preparedness

1. Further consideration should be given to the practicability of options for enhancing microbiology capability to identify and confirm *Bacillus anthracis* within Scotland. *(Action by HPS, HPA, SMF).*

Risk Management (Control Measures)

2. Further discussion could usefully be held between health protection services and Government departments with respect to the best ways of engaging drug treatment, care and recovery services during outbreak situations. In addition, the extent, if any, to which emergency outbreak control considerations should influence clinical decisions about the prescribing of a controlled drug such as diamorphine could usefully be clarified, with the aim of providing guidance to future OCTs and addiction services. *(Action by HPS, Scottish Government Health Directorate, HPA, UK Government Department of Health).*

Risk Communication

3. In the event of a future outbreak involving anthrax contaminated heroin, advice to drug users should emphasise that any form of taking heroin (via injection routes or smoking), could result in a fatal anthrax infection and that injecting by any route (IV, IM or SC) is likely to carry a higher risk. Advice should however avoid suggesting that smoking (or snorting) heroin is a risk free alternative to injection. *(Attention of NHS boards, local drug service providers).*

Knowledge Sharing

4. Maximum use should be made of the data collected during this outbreak to ensure effective knowledge management of new learning obtained on anthrax infection, its diagnosis, treatment and prevention, and to identify opportunities for further research. *(Action HPS, Scottish Government).*

Future Research

5. Options for research aimed at investigating unresolved questions associated with this event, including the reasons for the preponderance of significant and unusual outbreaks of infection among drug users particularly in West Central Scotland, should be explored. *(Action by HPS, NHS boards, Scottish Government, SDF).*

International Aspects

6. In the light of the findings of this outbreak investigation, options for proposing a review of the current European Centre for Disease Prevention and Control (ECDC) case definitions for anthrax should be explored. *(Action by HPS, HPA).*

Economic Aspects

7. The benefits of carrying out a detailed economic appraisal of the costs of the outbreak should be considered further. *(Action by HPS, Scottish Government).*

This page has been intentionally left blank

1. Aims and Objectives of the Report

This report describes the response to the outbreak of anthrax affecting drug users in Scotland between December 2009 and December 2010. The report records the results of the investigations carried out by Health Protection Scotland (HPS) and the NHS board Health Protection Teams (HPTs), supported by Strathclyde Police Force, the Crown Office Procurator Fiscal Service (COPFS) and other members of the National Anthrax Outbreak Control Team (NAOCT). The report addresses:

- the chronology of the outbreak;
- the public health and multi-agency response;
- who was affected (the descriptive epidemiology);
- the possible causes of the outbreak;
- lessons identified and good practice points;
- conclusions and recommendations.

Additional supporting material is provided in the appendices.

2. Introduction and Background

2.1. Introduction

In December 2009, an injecting drug user living in Glasgow presented to hospital with a severe soft tissue infection (SSTI). Cases of soft tissue infection in drug users are not unusual and are caused by a wide variety of bacteria. Around 34% to 37% of injecting drug users develop an infection annually (Hope et al, 2008; Hope et al, 2010). Outbreaks of bacterial infection had also occurred before in the drug using populations of West Central Scotland and elsewhere, notably with spore forming organisms including: *Clostridium novii* in 2000 (McGuigan et al, 2002; Taylor et al, 2005), tetanus and a variety of bacillus organisms over the years (Brett et al, 2005).

A few days after admission to hospital the infection in the Glasgow drug user was confirmed as being due to *Bacillus anthracis* (anthrax), an extremely unusual event. Anthrax is a very rare disease now in the UK, occurring as isolated sporadic cases associated with occupational or recreational risk factors. Only one case of anthrax in a drug user had ever been reported previously; a heroin user in Norway in 2000 (Ringertz et al, 2000).

Over the following weeks more cases of severe soft tissue infection (SSTI) were identified in drug users in Glasgow and neighbouring areas, also confirmed as being due to anthrax. All these cases shared a common factor; the recent use of illicit (street bought) heroin. This incident became the first documented non-occupational common source human anthrax outbreak in the UK since 1960, when official (non-occupational) case reporting began. Although there have been anecdotal accounts of anthrax outbreaks among drug users in Iran and elsewhere, this was the first documented outbreak associated with heroin use in the UK or anywhere else. During the same period, cases of anthrax occurred among heroin users in England and in Germany, who were later found to be infected with an indistinguishable strain of *B. anthracis*, making this both the first UK and the first European outbreak linked to heroin use as a common source of anthrax. This outbreak was therefore an exceptional event that provided many challenges in terms of investigation and control.

2.2. Background

Anthrax is a highly infectious (zoonotic) disease caused by *B. anthracis* a gram positive, encapsulated, spore forming, non-motile rod shaped bacterium. Anthrax primarily affects herbivorous animals. Humans are susceptible to infection following exposure to anthrax spores originating directly from infected animals or via their by-products (Hugh-Jones et al, 2002).

2.2.1. Anthrax In Animals

Anthrax is thought to have originated in sub-Saharan African wildlife some thousands of years ago and then progressively spread to domesticated animals in Africa, Eurasia, North America and Australia, as rearing of domestic livestock evolved (Smith et al, 2000; Hugh-Jones et al, 2002; Keim et al, 2002). Anthrax was a major cause of livestock mortality worldwide in the 19th

and early 20th centuries until the development and use of animal vaccines by Pasteur in 1881 and Sterne in the 1930's. Anthrax is now uncommon among livestock in the UK, Western Europe, North America and Australia (Prince, 2003) but still occurs in animal populations of Africa, Central and Southern America, Southern and Eastern Europe, Eurasia including Turkey, the Middle East, and Central Asia (Afghanistan, Pakistan).

Anthrax organisms cause a lethal illness in animals and survive via consequent environmental contamination as anthrax spores. Herbivorous animals are usually exposed to spores via grazing on vegetation or by drinking water contaminated with anthrax originating from the blood and body fluids of previously infected and deceased animals. When exposed to air, anthrax bacteria in these fluids sporulate producing the highly robust form that remains viable for many years, awaiting ingestion or contact with another animal host (or human) to initiate another life-cycle.

2.2.2. Anthrax in Humans

Human anthrax infection is normally acquired through direct contact with infected animals or via spore contaminated animal products. Human anthrax is more common where infection occurs among livestock, e.g. in Africa, Central and Southern Asia (WHO, 2008). Where the disease is uncommon in livestock (e.g. Europe, North America) it is also rare in humans. In the UK and other industrialised countries, human anthrax is regarded as mainly an occupational disease. Historically, those at greatest risk worked in industries processing animal products (meat, hides, hair, wool and bones). The disease was traditionally associated with textile industries in the UK (wool-sorters disease) and elsewhere (rag-pickers disease in Germany and Austria) (Fee et al, 2002). However, even occupationally acquired anthrax infection is now extremely rare in the UK.

An outbreak of anthrax in the former Soviet Union in 1979 was eventually identified as being due to the accidental release of a Soviet bio-weapon strain from a secret facility in Sverdlovsk and resulted in at least 79 cases and many deaths due to airborne spread and inhalation of spores (Meselson et al, 1994). The deliberate dispersal of anthrax spores via the US mail system in 2001 resulted in 22 known cases of anthrax, and was traced eventually to a laboratory strain of anthrax originating from within the US (Jernigan et al, 2002; US Dept. of Justice, 2010).

More recently human infection in the UK and US has been associated with unconventional occupational and/or leisure activities; e.g. contact with spore contaminated goat skins while making or using traditional drums from West Africa and elsewhere (CDC 1974; CDC 2006; Riley, 2007).

Anthrax in humans normally occurs as one of three classical presentations: (a) cutaneous, (b) gastro-intestinal and (c) respiratory anthrax. Additional presentations (anthrax meningitis) are also sometimes described.

a. Cutaneous anthrax

This form accounts for around 95% of human cases of infection worldwide and is usually non-lethal. Generally, contact between *B. anthracis* spores and broken skin is necessary, although exceptions do occur (WHO, 2008). Spores inoculated via abrasions or cuts gain access to sub-epidermal tissue where they germinate, releasing vegetative (reproducing) bacteria. After approximately 2-3 days a small papule (or pimple) develops at the inoculation site, which ulcerates, developing the characteristic painless black crusted lesion known as an *eschar*. Anthrax reputedly derives its name from the black eschar characteristically associated with cutaneous infection

(*anthrax* being ancient Greek for *charcoal*). Symptoms at this point may include low grade fever and headache. However, most cutaneous anthrax cases resolve with or without anti-bacterial (antibiotic) treatment. If not treated with antibiotics, disease can progress to a more severe and potentially fatal illness with generalised (systemic) symptoms. Anthrax bacteria liberate toxins, which cause localised cell damage and necrosis. If the toxins spread via the bloodstream (toxaemia), these may cause an overwhelming illness by inhibiting the normal immune system response, enabling further bacterial proliferation and causing cellular damage with widespread cell death in vital organs including the brain. Systematic symptoms progress with high fever; low blood pressure; localised lymph-node swelling (regional lymphadenopathy), meningitis (severe headache, cerebral irritation, changes in mental state and altered consciousness); blood clotting abnormalities and organ failure; leading to collapse, coma and death.

b. Gastro-intestinal (Ingestion) anthrax

Ingestion of anthrax spores (e.g. from eating infected meat) can lead to two forms of disease involving the gastro-intestinal tract (GI tract): *oropharangeal* anthrax (involving only the upper GI tract) and *gastro-intestinal* anthrax (involving tissue beyond the oropharynx).

Oropharangeal anthrax is less common and causes lesions in the oral cavity or pharynx. Extensive swelling of the neck and chest may occur resulting in breathing difficulty. Severe systemic toxaemic illness may follow.

Gastro-intestinal anthrax more often affects the GI tract beyond the oropharynx. Multiple lesions may occur anywhere in the alimentary tract giving symptoms including: nausea; vomiting; diarrhoea; fever; and headache, followed by abdominal pain, bloody diarrhoea; signs of an *acute abdomen* (abdominal pain and swelling) may occur. Lesions may ulcerate causing potentially fatal haemorrhage. Severe generalised (toxaemic) illness may also occur. From symptom onset to death in this form may take from 2-5 days, although not all GI anthrax cases are fatal.

c. Respiratory (pulmonary or inhalational) anthrax

Respiratory anthrax results from anthrax spores being inhaled into deep lung tissues (alveoli). Inhaled spores are ingested by local immune defence cells (macrophages), which migrate to regional lymph-nodes where the spores germinate and vegetative bacteria reproduce. These organisms then release increasing quantities of toxins that kill the host macrophages, then spread via the bloodstream to the vital organs. Inhalational anthrax can present as a bi-phasic illness, lasting 3-5 days; initial signs and symptoms may be non-specific and unremarkable: e.g. flu-like illness with general malaise. Initial symptoms may be followed by a short respite, then a rapidly fatal deterioration occurs. Typically, there may be some tightness or pain in the central chest, due to bleeding into and swelling of chest lymph-nodes. As toxaemia progresses, signs and symptoms of cerebral and meningeal involvement (haemorrhagic meningitis) may develop, with multi-organ failure presaging a rapid deterioration and fatal outcome.

The incubation period for inhalation anthrax varies and may be short (a few days) to much longer; evidence from the outbreak associated with the accidental release of a Soviet bio-weapon strain at Sverdlovsk suggested that the incubation could be 60 days or more (Jackson et al, 1998).

d. Anthrax meningitis

Meningitis may occur as a complication of any of the classical anthrax illnesses after spores gain entry via cutaneous, gastro-intestinal or inhalation routes. However, there have been incidences reported where anthrax meningitis developed in the absence of any cutaneous, gastro-intestinal or inhalation/respiratory disease (Sejvar et al, 2005). Presenting symptoms include a severe headache, neck pain, altered mental state, vomiting and fever; leading to loss of consciousness, coma and ultimately death, with or without other clinical evidence of infection.

e. Injectional anthrax

Sub-cutaneous anthrax was reportedly induced experimentally by injection in chimpanzees (Berdjis et al, 1964). Anthrax was also reported in India possibly associated with injection of contaminated antibiotics (Lalitha et al, 1988).

Prior to this outbreak, a single case of (atypical) anthrax was reported in a 49 year old drug user in Norway, who had a four day history of infection in his right buttock, following injection of heroin (Ringertz et al, 2000). The patient was not initially systemically ill and did not have a high temperature. Anthrax was not suspected and he was treated with conventional antibiotics and sent home. Three days later he was admitted to hospital in a coma and with evidence of a severe soft tissue infection (SSTI) in his right buttock. Lumbar puncture identified purulent blood stained cerebrospinal fluid (CSF); gram positive rod-like bacteria were later grown, identified as *B. anthracis*. His condition deteriorated leading to death.

The authors of the case report described the patient as being a "skin-popper" (someone who injects heroin into the skin). The authors consequently proposed the novel term "injectional" anthrax on the grounds that this presentation was not classical cutaneous anthrax but was caused by non-accidental sub-cutaneous inoculation of anthrax spores.

2.2.3. Anthrax in Scotland and the UK

a. In animals

Anthrax spores remain viable for many decades in the environment and may be carried on animal products. Anthrax spores were formerly imported into the UK via meat and bone meal, untreated skins, hair (wool) and hides. Meat and bone meal used to be included in livestock feed until this was banned due to BSE. Spores on skins and hides washed off during tanning processes could be dispersed in waste-water, resulting in contamination of pasture land and potentially infecting animals subsequently grazing on the land. Anthrax is now however, rare in UK domestic livestock; cattle remain the most frequently affected animals, with occasional outbreaks affecting pigs. In Scotland the last confirmed livestock case involved a cow in 1997; the last confirmed livestock cases elsewhere in the UK occurred in 2006 in Wales, where 2 cows died (DEFRA, 2011).

b. In humans

Anthrax became a notifiable industrial disease in the UK under the Factories Act in 1895, and became a notifiable disease under Public Health legislation in 1960. Data on human cases of the disease in the general population are therefore available only since 1961. Notification data are based on a clinical suspicion, not on microbiological confirmation, and have minimal detail on the nature of the exposure or illness; there is therefore a degree of uncertainty in the accuracy of the data. Anthrax cases reported in Scotland (1968-2009) are detailed in Table 1.

The last fatal human case of anthrax reported in Scotland occurred in 2006 (Riley, 2007). A musician/wood-worker living in the Scottish Borders died after a short illness diagnosed originally as a possible sub-arachnoid haemorrhage or haemorrhagic meningitis but was later confirmed (via post-mortem microbiology tests) as having died from an atypical inhalation anthrax infection. He had been exposed to goatskin drum-heads on West African Djembe drums, subsequently shown to be contaminated with anthrax spores of an indistinguishable strain. Locations where the incriminated drums were used and stored were subsequently found to have evidence of environmental contamination with spores, confirming their capacity to spread from an original source of contamination. Contaminated premises were decontaminated to eliminate the risk of further exposures and infections.

The last reported human case in the UK occurred in 2008 in England, also involving a man whose main risk factor was contact with goat-skin hides used in drum making. Environmental contamination also occurred in that case.

Table 1: Human Anthrax Cases Reported in Scotland 1968–2009

Year	Sex	Age (years)	Infection Presentation and Primary Infection Site	Risk Factor Reported
1968	M	46	Cutaneous Neck lesion	Tannery worker
1969	M	42	Cutaneous Neck swab	Tannery worker
1969	M	30	Cutaneous Pustule on arm	Worked in bone meal factory
1969	M	57	Cutaneous Pustule on neck	Gardener – used bone meal
1970	M	52	Cutaneous Neck abscess	Gardener – used bone meal
1971	F	8	Cutaneous Pustule	Worked near farm/bowling green
1977	F	(adult)	No Information	Wool-spinner
1978	M	50	No Information	Wool-worker
1987	F	3	Cutaneous Leg lesion	(Presumed from playing in garden)
1990	M	?	No information	No information
1991	F	27	Cutaneous Lesion on arm	Reported through RIDDOR, wool-worker
2006	M	50	Respiratory Anthrax (atypical) presenting as haemorrhagic meningitis	Spore inhalation following contact with contaminated West African Djembe drums

Data compiled from official notifications, RIDDOR and additional sources of information.

3. Outbreak Investigation, Methods and Management

3.1. Outbreak Detection

On 7 December 2009, a heroin user living in South East Glasgow (Case 1) presented to the Victoria Infirmary in Glasgow with a serious soft tissue infection (SSTI); was admitted and treated for a suspected drug-injection related wound infection. The type of soft tissue wound infection was not considered particularly unusual for an injecting drug user; many of whom present for medical treatment with such infections in any year.

Initial blood cultures (bacterial cultures of blood samples) from Case 1 grew a *Bacillus* species organism of uncertain type. Discussions between the local Microbiologist and a colleague at Glasgow Royal Infirmary concluded that this isolate could be *Bacillus cereus*, most probably an insignificant skin contaminant. *B. anthracis* infection was considered but only as an outside possibility. The isolates were sent to the Health Protection Agency (HPA) Bacillus Reference Laboratory at the Centre for Infection (CfI) Colindale, London, to identify the type of *Bacillus* species.

By the 17 December, initial testing of blood and tissue samples from Case 1 at HPA CfI had grown a *Bacillus* species presumed to be anthrax; the samples were then sent to the HPA Novel and Dangerous Pathogens Laboratory (HPA-NDPL) at Porton Down, Wiltshire for further confirmation.

The original case had been reported to NHS Greater Glasgow and Clyde Board (NHS GG&C) Health Protection Team (HPT) who initiated a public health investigation and ascertained that three other drug users had been admitted to hospitals across Glasgow around the same time, with signs and symptoms of serious soft tissue infections (SSTI). It was concluded that an outbreak of infection among drug users could already be in progress in Glasgow; consequently NHS GG&C HPT established an Outbreak Control Team (OCT), which first met on the 17 December. The NHS GG&C OCT comprised staff from NHS GG&C HPT, local microbiologists, Health Protection Scotland (HPS), the Health Protection Agency (HPA), and representatives of the Scottish Government Health Directorate (SGHD) (as observers). Given that heroin (an illegal drug) was involved, Strathclyde Police and the Crown Office and Procurator Fiscal Service (COPFS) also joined the NHS GG&C OCT.

On the 18 December, the HPA-NDPL confirmed that the organisms from Case 1 were *B. anthracis,* making this the first ever confirmation of an anthrax infection involving an injecting heroin user in the UK.

By the 21 December, two more drug users with infections living in the Glasgow area had been confirmed as having anthrax by HPA-NDPL, with five other possible cases identified, one of whom lived in Lanarkshire. The initial confirmed cases of anthrax were all drug users who injected heroin prior to developing illness.

3.2. Initial Outbreak Investigation and Management

The initial hypothesis formed by NHS GG&C OCT was that anthrax infection was associated with exposure to illicit drugs, specifically heroin, contaminated with anthrax spores; that the heroin may have been contaminated via mixing with contaminated materials (e.g. paracetamol or other unknown materials) added to dilute ("cut") the heroin purity; and/or via contaminated drug paraphernalia used to prepare heroin for injection (e.g. needles, syringes, water, citric acid etc.) or that the heroin was contaminated at some other point in the distribution network in the UK or beyond. The scale of possible heroin contamination was unknown and hence the potential scale of the outbreak was uncertain but assumed to be potentially large.

The investigation by NHS GG&C HPT was focussed on the population in West Central Scotland: drug users; local drug dealers; anyone having any form of contact with heroin users (socially, casually or occupationally) and the physical environments where local drug users were living. Work related to: assessing the scale of the situation; developing further possible hypotheses to explain the outbreak; assessing the risks to the public and professionals involved in case management; and identifying the means to ensure dissemination of risk communication messages to drug users and others. The initial risk communication priorities included:

- Alerting drug users to the risk of anthrax infection using a variety of routes, including via press releases and broadcast media;
- Alerting local health care providers (General Practitioners, hospital clinicians), and drug service providers, to the identification of anthrax in a drug user;
- Advising clinicians on how to identify other possible cases;
- Providing guidance to clinicians on appropriate microbiological investigations in suspect cases, including blood cultures and giving recommendations on antibiotic treatment;
- Raising awareness among NHS staff and other professional groups of appropriate infection control precautions;
- Alerting other NHS board HPTs across Scotland to the situation.

In the following weeks, more patients with signs and symptoms of possible anthrax infection were identified in NHS GG&C hospitals and in neighbouring and other areas: Lanarkshire, Tayside (Dundee) and Forth Valley. The original NHS GG&C (local) OCT was expanded with representatives from other NHS board areas affected. Representatives of the US Centers for Disease Control and Prevention (CDC) were invited to join the OCT to provide additional advice. In addition, at the request of Dr. Tim Brooks, HPA-NDPL, CDC facilitated access to the US Government supply of anthrax anti-toxin (Anthrax Immune Globulin – Intravenous (AIGIV)) for the treatment of patients in Scotland. In late December 2009, CDC staff were deployed from the US to Glasgow to supervise the initial use of anti-toxin (AIGIV).

By early January 2010, 12 cases of anthrax had been microbiologically confirmed involving drug users living in multiple NHS board areas. In accordance with Scottish Government guidelines, a National Anthrax Outbreak Control Team (NAOCT) was then established, led by HPS, to co-ordinate the investigation and the management of the outbreak across the country.

3.3. National Anthrax Outbreak Control Team (NAOCT) (Scotland)

3.3.1. Aims and Objectives of the NAOCT

The NAOCT met first on 6 January 2010 and included representatives from: NHS boards; Strathclyde Police; COPFS; the Scottish Drugs Forum (SDF); HPA; CDC; and others (Appendix A). SGHD representatives attended the NAOCT meetings (as observers) and provided support throughout the investigation. The objectives of the NAOCT were to:

- Co-ordinate the surveillance and investigation of suspected anthrax cases and obtain detailed epidemiological and other information;
- Collate and analyse data to quantify the scale of the outbreak and track it's spread and development;
- Interpret case data to identify risk factors associated with infection (descriptive epidemiology);
- Test potential outbreak hypotheses using analytical epidemiological methods where practical;
- Provide information to NHS clinical services to assist the management of cases;
- Assess the risks of infection to drug users; their social contacts; occupational groups involved in the investigations including drug service staff, police, prison officers and others; and risks to the general public;
- Co-ordinate action with police and COPFS on control measures;
- Ensure co-ordinated communication of information on risk reduction options to appropriate parties;
- Monitor the effectiveness of control measures (risk management) and risk communication efforts;
- Identify lessons and disseminate new learning.

3.3.2. NAOCT Activities

The activities of the members of the NAOCT were co-ordinated in a number of work streams:

- Case detection, investigation, reporting and data management was carried out primarily by the NHS board HPTs and HPS Anthrax Investigation Team;
- Police and COPFS conducted their own investigations but co-ordinated these with the public health investigations via HPS;
- Risk assessment and risk management were discussed and progressed by HPS working with relevant experts then agreed at the NAOCT meetings;
- Information and risk communications were co-ordinated by HPS via respective agency and government media staff;
- Advice and guidance was developed via a separate sub-group.

The Advice and Guidance sub-group developed protocols (e.g. investigation algorithms) for NHS clinicians, health care and other occupations for infection risk management; a Communications sub-group co-ordinated key messages for drug users, drug services and others. An Anthrax Clinical Network (ACN) was also established to provide a (teleconference based) forum for hospital clinicians across Scotland to enable the exchange of information, lessons and experience gained in the clinical management of anthrax cases.

3.4. National Outbreak Investigation

3.4.1. Case Detection, Reporting and Investigation

Hospital clinicians and General Practitioners across Scotland were alerted to the signs and symptoms of anthrax and asked to report any suspect cases to the local NHS board HPT.

a. NHS board epidemiological investigations

A standard epidemiological investigation questionnaire was developed from questionnaires used in past drug related infection episodes and circulated for use by NHS board staff. This sought information on personal and medical details: the circumstances leading to the onset of illness; drugs used including heroin and how drugs were taken. Patients were asked about recent changes in their drug buying patterns; in the colour, consistency or quality of the drugs, bought prior to developing illness (Appendix B).

Case finding included investigation of recent sudden deaths among drug users, looking for evidence suggesting possible occult anthrax infection.

b. Police and COPFS investigations

The Lord Advocate for Scotland agreed that the COPFS and Strathclyde Police investigations would focus on assisting the public health investigation, rather than pursuing the prosecution of drug users themselves. Police officers conducted investigations using standard police interview methods in parallel to the public health investigations.

3.4.2. Data Confidentiality Issues

The NAOCT sought advice (via the SGHD representatives), from the Chief Medical Officer (CMO) for Scotland on the appropriateness of the data sharing procedures being used to enable the joint public health and police investigations. The CMO provided a letter which advised that; due to the circumstances of the outbreak the controlled sharing of data with the police was justified as part of the efforts to control a significant threat to public health in Scotland, with a high risk of mortality. This advice was distributed to NHS boards and clinicians (Appendix C).

3.4.3. Data Management

HPS co-ordinated case data management using a line listing system to track daily case status and a dedicated database to collate the data provided by local HP teams. Regular updates were provided on the progress of the outbreak to the NAOCT members and SGHD.

Public health and the police investigation data were compared to identify gaps and inconsistencies in the data and efforts were made to resolve any by re-interviewing cases. A final reconciled case record was created for each case and used in the data analysis.

3.4.4. Epidemiological Investigation

Case data were analysed to determine if there were characteristic factors associated with those drug users who developed infection, which might help to identify potential control measures. However, the variable quality and completeness of case data made it difficult to draw satisfactory conclusions, at the time.

A (prospective) case-control study to investigate hypotheses relating to the risk associated with specific heroin preparation techniques or methods of heroin taking (via injection, inhalation, snorting etc) was proposed. Due to a variety of practical problems, this study could not be carried out (e.g. controls would need to be recruited from the drug user population who were difficult to access and the ethics of such a study were questioned on the basis of the low likelihood of being able to confirm a specific hypothesis). A retrospective case-control study was ultimately carried out using routinely collect data on drug users via NHS Scotland data systems but was not completed until after the outbreak ended.

Additional work was initiated to try to identify whether exposure to anthrax spores had occurred among drug users before the detection of the first clinical case in November 2009, using serological testing of stored blood samples from drug users. This work is still in progress.

In view of the unique nature of the outbreak and the need to document the presentation of cases for future reference, enhanced clinical data was collected to help inform future clinical understanding of anthrax infection acquired via drug use. This exercise was actively assisted by the secondment in September 2010, of a dedicated field epidemiology team from CDC.

3.4.5. Microbiological Investigations

Initial microbiological investigations of blood, body fluid, wound and tissue samples to screen for anthrax organisms were carried out at local NHS board Hospital Microbiology Laboratories. *B. anthracis* is considered to be a dangerous pathogen *(Hazard Group 3)* and may only be handled in appropriately designated laboratories. When local testing identified possible anthrax bacteria, the samples were therefore sent for further confirmation testing to the HPA-NDPL at Porton Down using methods including:

- Culture, isolation of *B. anthracis* and subsequent morphological assessment to identify consistency with *B. anthracis* characteristics;
- DNA based methods using Polymerised Chain Reaction (PCR) technology to detect DNA fragments indicating the presence of anthrax bacteria;
- Anthrax toxin testing;
- Anti-toxin antibody testing.

Strathclyde Police also sent samples of confiscated heroin to HPA-NDPL to test for *B. anthracis* contamination.

3.5. Risk Assessment, Control and Risk Management Activities

3.5.1. Risk Assessment

The risk assessments for professional groups and the general public were influenced by the early evidence that anthrax infection apparently involved exclusively heroin users who had recent exposure to heroin. No early (or subsequent) cases of infection were identified in people who had not deliberately taken heroin. The primary risk factor for anthrax infection therefore appeared to be taking heroin for recreational purposes, not any other form of heroin or other exposure.

a. Risks to drug users

The natural history of anthrax suggested that taking anthrax spore contaminated heroin by any route (injection, inhalation or ingestion) could pose an infection risk. The information from cases supported this conclusion. The NAOCT therefore concluded that no method of heroin taking could be safely considered as being risk free. New cases continued to be reported from an increasing number of locations across Scotland. The continuing spread of the outbreak and the absence of accurate data on the quantity of potentially contaminated heroin in supply led the NAOCT to conclude, and to advise, that all heroin circulating in Scotland at the time had to be considered as posing an anthrax infection risk. Heroin users were therefore advised that the best way to minimise the risk of anthrax infection was to avoid taking (illicit) heroin at all.

b. Risks associated with non-recreational exposure to heroin

Many non-drug users had exposure to potentially contaminated heroin including: drug dealers; household, social and family contacts of cases; police and prison staff; hospital and laboratory staff etc. Anthrax was not identified affecting any of these individuals; the NAOCT therefore concluded that non-recreational exposure to heroin posed a minimal risk of anthrax infection and issued advice accordingly.

c. Risks to health care workers and other occupational groups

Despite extensive close physical contact with early cases, no healthcare or other individuals developed symptoms of anthrax. The NAOCT therefore assessed that the risk of acquiring anthrax infection following contact with clinically ill patients was probably very low. However, the group identified a potential risk of exposure to anthrax bacteria associated with splashing or aerosolisation of blood or blood contaminated (sero-sanguinous) fluids. There was also a potential risk of exposure to anthrax spores from dried body fluids and tissues. Advice was therefore provided to health care staff to highlight these risks.

There was concern about the potential risk from spore contaminated heroin, based on the evidence of environmental dispersion of spores, especially from recent respiratory anthrax cases in the UK and US. The NAOCT considered that contaminated heroin could pose an infection risk via cutaneous contact or if it became airborne, inhaled spores could cause respiratory anthrax. Advice was therefore issued by the NAOCT on the need to reduce opportunities for heroin becoming airborne, targeted particularly at police, prison officers, social and health care staff who might all encounter potentially contaminated heroin while handling cases' possessions or searching drug users' (or dealers) premises. Although the risk was not considered sufficient to warrant recommending the use of full body protection (CBRN protection suits) in all circumstances, appropriate respiratory protection was recommended for situations where the risk of exposure to (airborne) heroin could not be minimised by other means.

d. Risk to the general public

Although some people (family members etc.) had contact with clinically ill patients and had accidental (non-recreational) contact with heroin that had a high probability of being contaminated, none developed clinical anthrax infection. The NAOCT therefore advised that for the general public, the risk of contracting anthrax from casual non-parenteral (non IV/IM) contact with heroin, or from clinical cases or their personal effects, was minimal.

3.5.2. Control and Risk Management Measures

The NAOCT considered various potential measures to try to reduce the incidence of further cases and control the outbreak.

a. Provision of prophylactic antibiotic treatment to try to prevent anthrax infection in heroin users

Antibiotic prophylaxis can be used to reduce the risk of infection to individuals exposed to anthrax spores. Anthrax spores may lie dormant in tissues (e.g. the lung) for extended periods before germinating. Antibiotics need to be taken daily for a continuous period while the hazard exists and for up to 3 months after the elimination of the hazard, in order to cover the incubation period. However, it was not possible to estimate for how long contaminated heroin might remain in circulation. The NAOCT was concerned that heroin users could have difficulty maintaining the strict daily regime required, for an indeterminately long period, to ensure continuing protection. There was also concern that antibiotic prophylaxis could generate a false sense of security, and might encourage heroin users to continue using potentially contaminated heroin on the assumption that they were completely protected. The NAOCT therefore concluded that mass antibiotic prophylaxis for all heroin users in Scotland would not be a practical outbreak control option and did not pursue this.

b. Provision of anthrax vaccination

The NAOCT considered offering vaccination to drug users as a possible control measure as an early stage of the outbreak. Anthrax vaccination is normally only available in the UK where there is a high occupational risk of exposure to anthrax. Immunisation with the vaccine requires four doses over a year to give effective long lasting protection, followed by annual boosters. The NAOCT considered that in this outbreak situation, the four dose schedule would take too long to provide effective protection. Vaccination was not therefore pursued as a practical control measure during the outbreak.

c. Provision of alternatives to illegal heroin

The substitution of illicit (street bought) heroin with officially supplied (or prescribed) heroin was suggested as a control option. The NAOCT recognised that this was a controversial proposal and that it would be highly complicated from legal, ethical, practical and logistic perspectives and would involve policy decision at Government level. The group therefore decided that consideration of such a measure was outside its remit and expressed no view on its merits or otherwise.

d. Alerting heroin users to high risk types of heroin

Some early cases reported that there were distinctive features associated with the heroin they had used before becoming ill, in terms of unusual colour, consistency, potency etc. However, this evidence proved to be inconsistent and unreliable. It was not therefore possible to provide evidence based advice on what type of heroin might carry a higher risk.

e. Elimination of contaminated street heroin supplies

Strathclyde Police advised that large quantities of heroin are regularly imported into the UK and Scotland. The police had intelligence on heroin supply routes generally but the information was not specific enough to determine the likely quantity of potentially contaminated heroin in circulation at the time, nor to identify the exact distribution. It was therefore not practical to eliminate all potentially contaminated heroin from Scotland. In effect, all heroin illegally imported from late November 2009 had to be considered as potentially contaminated.

f. Interruption of heroin distribution networks

The police concluded that targeting the suppliers of heroin used most recently by anthrax cases and in turn, their suppliers, was likely to be the most useful method of reducing the amount of potentially contaminated heroin in circulation and would assist to identify the more distant elements of the supply chain. Strathclyde and other police forces across the UK therefore focussed on reducing heroin users' access to supplies of potentially contaminated heroin by:

- Encouraging drug user cases (and non-cases) and their associates (family, friends etc.) to surrender any remaining heroin, samples of which were sent to HPA-NDPL for testing;
- Tracing drug dealers who supplied heroin to cases prior to them developing illness; seizing these drug dealers' supplies and preventing their further drug trading;
- Disruption of wider drug supply networks across the UK by tracing links between local dealers and traffickers importing bulk heroin supplies from intermediate dealers in Europe and beyond;
- International collaboration to identify supply chains as far back as opium source countries (Afghanistan and Pakistan).

3.5.3. Risk Communication

The Scottish Drug Forum (SDF) representatives advised the NAOCT that the drug user population was difficult to access and were less likely to use conventional press or mass media as sources of information. In collaboration with the SDF, specific materials were developed for distribution via drug service networks, hostels and other locations where drug users were likely to congregate. This material provided advice to drug users to stop using illegal heroin, to seek help via drug treatment programmes and to consider taking heroin substitutes (e.g. methadone) (Appendix D). Scottish Government and NHS boards alerted drug service providers to the potential for increased service demand resulting from this advice.

The NAOCT also provided advice to professional and occupational groups, service providers and others, to ensure awareness of infection control precautions to reduce the risk of secondary infection associated with cases or with exposure to contaminated heroin.

The HPS microsite was regularly updated with the latest information on case numbers and locations, as well as advice and guidance materials. Media statements were issued; radio and television interviews were carried out.

Information was shared with the Health Protection Agency (HPA) in England who distributed similar advice to the public and professionals in England and Wales. HPA also acted as the link with the European Centre for Disease Control (ECDC) regarding the outbreak.

3.6. Termination of the Outbreak Investigation

In Scotland, the last cases later classed as confirmed and probable cases, were identified in July 2010; suspected cases however, continued to be identified into October 2010. In England, suspect cases continued to be identified and confirmed until November 2010.

By mid December 2010, no more suspected cases had been reported in Scotland for at least eight weeks, beyond the outer limit of the anticipated incubation period. By then 208 suspected cases had been investigated in Scotland with cases identified in 10 of 14 NHS board areas.

A final NAOCT meeting was held on 21 December 2010. The NAOCT concluded that on the basis of the likely incubation period, sufficient time had elapsed to be reasonably confident that the risk of infection had abated and it was formally agreed that the outbreak should be declared over. The meeting concluded with a debriefing to draw conclusions, identify lessons and suggest recommendations on preparedness, planning and response for future outbreaks.

A press release was circulated to advise that the outbreak response was being terminated. The NAOCT advised that there remained a continuing risk, at any time, that illicit (street bought) heroin could be contaminated with a variety of human pathogens, including anthrax. The NAOCT also recommended that anthrax should continue to be included in the differential diagnosis of illness in any heroin user with symptoms of serious soft tissue infection (SSTI) or any other of the typical clinical features identified during this outbreak.

3.7. UK and European Anthrax Case Investigation

Anthrax was also confirmed in five heroin users in England and two in Germany during the same period (December 2009 to December 2010). This was therefore a UK and a European outbreak. The first German case had symptoms in December at the same time as the first cases emerged in Glasgow.

Anthrax cases in England

Five cases of anthrax among drug users (all heroin users) were confirmed across England during 2010; in London, Leicester, Blackpool and Kent. Two cases had onsets in January, followed by single cases in February, August and November. The age and sex distribution of the cases were similar to those in Scotland: the age range was 27-43 years; three males and two females. All presented with severe soft tissue infections (SSTI), and four of the five cases died. Other than having the common risk factor of using illegal (street bought) heroin, investigations into possible links between the cases within England and between England and Scotland did not identify any links.

Anthrax cases in Germany

Two confirmed cases were identified in Germany over the same period. The first case, a resident of the Aachen region near the German/Dutch Border had a symptom onset date in early December 2009 (around the time of the first cases in Scotland). The second case identified soon afterwards also had connections to Aachen. In July 2010, a person from Bavaria was retrospectively identified as having been infected with anthrax by serological tests (therefore not meeting the current case definition of the German surveillance system for a confirmed case of anthrax). The onset of disease in this person was probably in March 2010 and a link to the German/Dutch border area could not be excluded. Despite extensive investigation by police and public health agencies, other than the common factor of taking illicit (street bought) heroin, there was no evidence of any direct links between the cases in Germany, in Scotland or in England.

4. Investigation Findings

The results of the microbiological, epidemiological police and fiscal investigations are described.

4.1. Case Definitions

The European Centre for Disease Control (ECDC) defines official criteria for reporting anthrax cases in Europe (Appendix E). These specify case categories as follows:

a. *Possible Case* – not applicable.

b. *Probable Case* – any person meeting the clinical criteria with an epidemiological link.

c. *Confirmed Case* – any person meeting the clinical and the laboratory criteria.

The ECDC case definitions did not however allow for the possibility of exposure via drug use and did not include all the clinical features identified in this novel outbreak. The ECDC laboratory criteria did not include the detection of anthrax toxins or the detection of anthrax anti-toxin (anti-bodies to anthrax toxins); methods which were used in this outbreak to detect evidence of anthrax infection.

The NAOCT therefore agreed an enhanced set of case definitions for the outbreak, which included additional criteria (Appendix F) and with final amendments (Appendix G):

a. *Clinical criteria*: evidence of serious soft tissue infection (SSTI) or other clinical evidence compatible with anthrax infection;

b. *Epidemiological criteria*: use of illicit drugs by any route prior to symptom onset and;

c. *Microbiological criteria*: detection of *B. anthracis* (evidence of organisms or nucleic acid) or anthrax toxins or specific anti-toxin to the organism consistent with recent infection.

The final outbreak case classification was as follows:

a. *Possible Case* – clinical evidence and epidemiological evidence consistent with anthrax infection and microbiological evidence that was equivocal.

b. *Probable Case* – clinical and epidemiological evidence consistent with anthrax infection and positive microbiological evidence short of confirmation.

c. *Confirmed Case* – clinical and epidemiological evidence consistent with anthrax infection and unequivocal microbiological evidence.

d. *Non-anthrax case* – clinical and epidemiological evidence of suspected anthrax infection with negative results on microbiological testing for anthrax and/or evidence of an alternative microbiological agent that could explain their clinical illness.

The outbreak *confirmed case* definition was consistent with the ECDC *confirmed case* definition but included microbiological confirmation using serological testing in the laboratory criteria (specifically detection of anthrax toxins or a rising titre of anti-bodies (IgG) to anthrax toxins, in a paired set of clinical samples).

The outbreak *probable case* definition was stricter than the respective ECDC *probable case* definition in requiring microbiological evidence as well as clinical and epidemiological evidence. The distinction between an outbreak *probable case* and outbreak *confirmed case* was that probable cases only had a single positive serological test, rather than a paired set.

The ECDC do not define a *p*ossible case of anthrax. However, the NAOCT agreed that a possible category was required to differentiate cases where microbiological evidence fell short of that required for a confirmed or probable case classification. The possible case outbreak category also meets the ECDC *probable case* definition criteria. Hence, for this outbreak all *possible, probable and confirmed cases* have been counted as *outbreak cases*.

4.2. Data Quality Issues

The nature of the patient group, their use of illicit heroin and in some cases the severity of their illness, made it difficult to collect complete epidemiological information on all of them. In some NHS areas, especially where many new suspected cases were reported in a short period, HPS was sent only minimal data for the daily line listing; the local HPT did not complete the full anthrax outbreak questionnaire initially but waited until microbiological evidence was obtained that resulted in a case designation as a *probable* or a *confirmed case.* Consequently, information on *possible cases* was often incomplete whereas *data on confirmed* and *probable cases* was usually more complete. This impacted on the scope for subsequent data analysis.

4.3. Final Outbreak Case Designations and Totals

There was some early concern that if the clinical diagnostic criteria adopted for the investigation were too inclusive, this might require clinicians to report every single case of soft tissue infection among drug users to their local HPT as a suspected anthrax case. The clinical criteria for reporting suspected cases were therefore set to balance sensitivity (the ability to detect cases that had anthrax) and specificity (the ability to exclude cases that did not have anthrax). Subsequent data analysis suggests that an appropriate balance was achieved.

Between December 2009 and December 2010 in Scotland, a total of 208 patients were reported to HPS initially as suspected cases; 89 of these were subsequently excluded as non-anthrax (anthrax negative) cases and 119 were classed as anthrax cases, further classified as:

- 47 *confirmed anthrax cases* (34 survived, 13 died);
- 35 *probable anthrax cases* (34 survived, 1 died);
- 37 *possible anthrax cases* (37 survived).

During the outbreak period, samples were sent to HPA-NDPL from another 153 patients (not officially reported to HPS as suspected anthrax cases) to exclude the possibility of anthrax infection. Local clinicians and microbiologists did not apparently consider that these patients met the clinical criteria for a suspected case, yet they sought to exclude anthrax by microbiological testing. If included, this would bring the number of patients investigated to 361. However, none of these other patients had microbiological evidence of anthrax infection (and would have therefore been classed as anthrax negative), suggesting that the clinical diagnostic criteria set for a suspect case were sufficiently sensitive and specific to ensure that the true anthrax cases were identified and included in the official outbreak investigation.

4.4. Microbiological Investigation Results

4.4.1. Results by Case Designation

A large number of tests were carried out at HPA-NDPL on each clinical sample, generating a suite of results that required expert interpretation to arrive at a final laboratory case designation. The laboratory results were reported using separate laboratory criteria which were then translated to the equivalent epidemiological case classification (Appendix F, Appendix G). This occasionally gave rise to confusion over a case's status.

Testing by HPA-NDPL included anthrax anti-toxin testing using methods previously applied routinely to detect the presence of anti-toxin antibodies following anthrax vaccination. This was the first large scale use of anti-toxin testing in human clinical cases as part of an outbreak investigation in the UK. The interpretation of serology results in particular, required expert judgement by HPA-NDPL staff.

The NAOCT decided that a single positive result from a serology test was not sufficient evidence to classify a case as confirmed; hence two sequential (paired) serology tests, which demonstrated a rising antibody titre to anthrax toxin (immunoglobulin G (IgG)) were required for serological confirmation. Cases with only a single positive serology result, or where the antibody levels did not rise in a paired set, were classed as probable rather than confirmed cases.

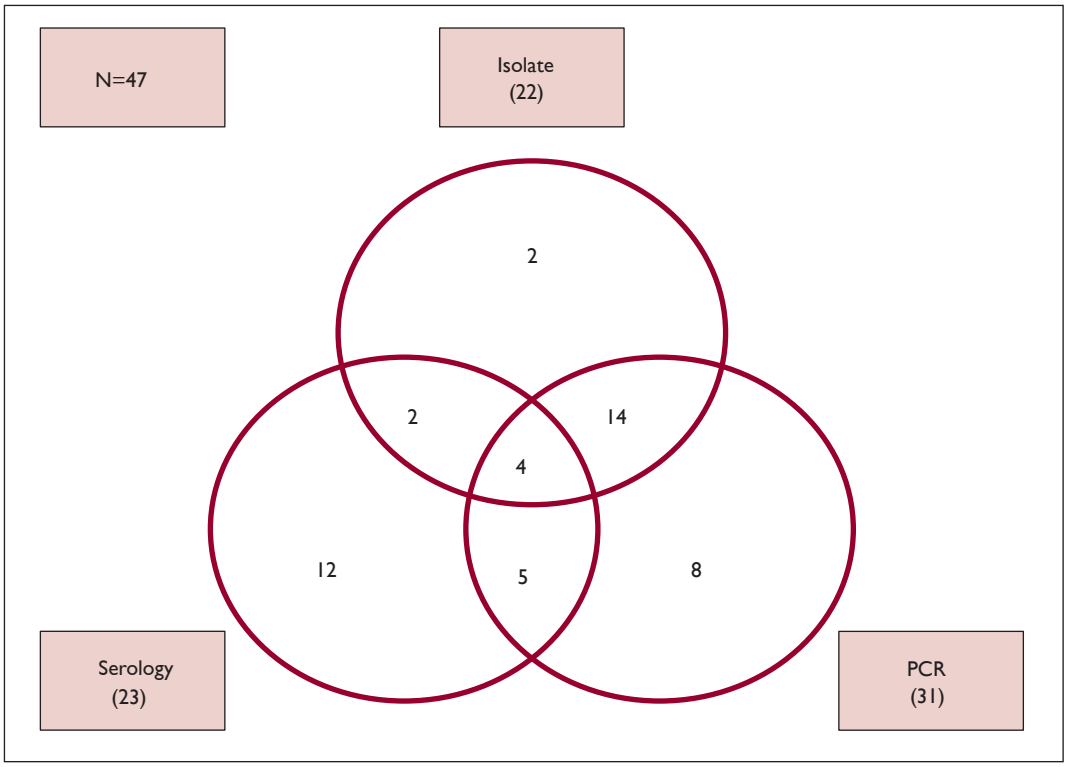
The results of HPA-NDPL microbiological investigations are detailed in Table 2 and Figure 1.

Table 2: Microbiological results by epidemiological case designation

Positive Microbiology Results	Confirmed Cases (N=47)	Probable Cases (N=35)	Possible Cases (N=37)
Isolate	22	0	0
PCR	31	(1 equivocal)	0
Serology (anti-toxin) - single positive result	0	29	(37 equivocal)
Serology (anti-toxin) - paired positive results	23	5 paired positive but non-rising titres	0
Toxin	11 (+10 equivocal)	(1 equivocal)	0

None of the confirmed cases were positive on all of the test methods but four were positive for all of isolation, PCR and serology (paired titres) (Figure 1). Of the 47 confirmed cases 35 were positive on the basis of bacterial isolation and/or positive PCR; an additional 12 were confirmed on the basis of (only) a rising serology titre in paired sera.

Figure 1: Venn diagram of microbiology results for confirmed cases



4.4.2. Genotyping of the *B. anthracis* Outbreak Strain

To characterize the particular strain (or strains) isolated from the outbreak cases, genotyping of *B. anthracis* isolates was carried out at the HPA-NDPL and by Professor Paul S. Keim of the Northern Arizona University (NAU), Translational Genomics Research Institute (TGen), USA.

B. anthracis is considered to be a relatively new organism in that its low genetic diversity implies that all strains existing now can be traced back to a common ancestor, evolving some thousands of years ago from its close relative *Bacillus cereus*. For that reason *B. anthracis* is considered to be a recently emerged pathogen. The nature of the *B. anthracis* organism allows genotyping analysis (known colloquially as DNA fingerprinting) to be used to compare and categorize an unknown or new strain into previously known genetic groups. These groupings sometimes have characteristic distribution patterns in time and place. This technical approach is helpful in excluding infective sources and, sometimes, indentifies possible sources of a particular strain. This organism is "clonally propagated", which means that new strains evolve and change over time by mutations of its genome (the DNA sequence of the bacteria). Evolutionary analysis of these mutations enables the construction of a family tree, which allows any newly identified strain to be compared to its nearest related strains.

Genotyping of strains worldwide (based on collections of isolates held at NAU and elsewhere), has identified two highly successful branches to the anthrax family tree: a Western-North American branch and a Trans-Eurasian (TEA) branch. The Western-North American strains are exclusively found in North America. In contrast, the Trans-Eurasian strains are more generally distributed in Europe, Asia and Africa. There is a strong tendency for strains identified in any individual anthrax focus or country to show genotype similarities. The TEA strains are highly similar to each other, however with complete genome sequencing it has been possible to differentiate amongst them and to identify three major sub-branches or "clades", each having distinctive further branching of related strains.

The initial genotyping technique used to identify a particular strain is known as Canonical Single Nucleotide Polymorphism (SNP). Using this SNP technique, some 1100 distinct *B. anthracis* isolates have been identified and catalogued at NAU. The SNP technique was used to analyse isolates from the heroin-associated outbreak cases from Scotland. This technique allows the exclusion of a new strain sequentially from specific branches of the phylogenetic (family) tree. By successive exclusions, a new strain can be located sequentially into further sub-branches. This process allowed elimination of possible strains of particular concern in the Scottish anthrax outbreak. Genotyping therefore enabled conclusive exclusion of the possibility that the Scottish strain was related to the former Soviet Union bio-weapons (Sverdlovsk) strain; Vollum (the former British bio-weapons strain); and the Ames strain, which was associated with the USA anthrax bioterrorism attacks of 2001, causing an outbreak of respiratory and cutaneous anthrax.

The elimination of the outbreak isolates from the Vollum branches was particularly important because these strains are found commonly in Afghanistan and Pakistan. This particular exclusion was significant in that intelligence on the sources for heroin trafficking into the UK and Scotland indicated that Afghanistan and Pakistan were the most likely countries of origin. Had the heroin used by the outbreak cases been contaminated in one of these source countries (e.g. during raw heroin production), it would more likely have been of a Vollum strain type.

Exclusionary conclusions are very strong and there is therefore great confidence that the outbreak strain is not a common laboratory strain or a previously known United Kingdom variant.

Progressive sequential genotype comparisons excluded more strains, until there were only two previously identified anthrax strains that showed a closely related phylogenetic SNP profile to the outbreak variant. Both of these strains originated from animals (goats) dying of anthrax in central Turkey. Further testing using additional techniques supported this conclusion. The approximate location of these two earlier animal cases is shown on Figure 2.

In order to determine if all the heroin-associated outbreak cases were infected with heroin from a common source, an additional highly specific genotyping procedure was developed for the outbreak strain. This was accomplished by the complete sequencing of the genome (DNA sequence) of one outbreak isolate at TGen. This genome sequence was compared to other previously completed anthrax genomes to identify SNPs that could be strain specific. Screening a set of three SNPs revealed that they differentiated the outbreak strain from the two Turkish strains and all other known *B. anthracis* strains (~2,000). In addition, the SNPs grouped all the outbreak isolates together. This strongly suggests that all the heroin-associated outbreak isolates are of a single strain, emanating from a single infective source, perhaps even a single infected animal.

The overall conclusion from this work is therefore that the isolates of *B. anthracis* grown from the heroin associated anthrax outbreak cases in Scotland were most closely related to strains

Figure 2: Geographic location of two strains most closely related to the Scottish outbreak strain

previously found in infected animals in Turkey. This finding provides additional support for the favoured outbreak hypothesis; that the heroin implicated as the vehicle for transmitting the anthrax identified in Scottish drug users, was probably contaminated in transit between the source country (probably Afghanistan or Pakistan) and final destination (Europe/UK/Scotland) and that a likely locus of this contamination was in Turkey, possibly via contact with a contaminated animal, carcass or hide.

Police intelligence also supports the plausibility of such a link in that Turkey is a known staging post in the distribution of illegal heroin, between Afghanistan and Pakistan and the UK.

Although evidence from the genotyping data linking the outbreak strain to the Turkish strains is not conclusive, it is highly significant and supportive of the favoured outbreak hypothesis. It is also consistent with anecdotal evidence obtained from several sources; that animal skins (particularly goat skins) are used in the transport of illegal heroin. Contamination with anthrax spores from a goat skin is therefore a plausible explanation for the origin of the anthrax spores, imported via heroin to Scotland.

To date all the isolates from the Scottish cases have been characterised as an indistinguishable novel strain, not isolated from human anthrax cases previously. The fact that all the strains identified to date are indistinguishable suggests that they are a very closely related clonal population and that they had a single common origin from one infected animal. The strains identified from cases in England and Germany similarly show that these are indistinguishable from the Scottish strains and therefore are highly likely to have shared a common single source.

The considerable additional work carried out by HPA-NDPL and by NAU, TGen has been invaluable in supporting the outbreak investigation and in providing scientific evidence of the anthrax spore's likely origins.

Based on this evidence, it seems reasonable to conclude that contamination of heroin occurred well before the implicated batch reached the individual drug dealers or users within the UK. On that basis, alternative theories on how heroin might have been contaminated more locally within the UK or Scotland can be rejected as lacking supporting evidence.

4.5. Epidemiological Findings

4.5.1. Descriptive Epidemiology

a. Age and sex characteristics

The age range, mean age and sex distribution of all suspected cases investigated during the outbreak are given by case category (Tables 3, 4 and Figure 3).

Table 3: Age and sex of cases by case type

Case type	Case Numbers	Minimum age (years)	Maximum age (years)	Mean age (years)	M:F ratio
Confirmed (a)					
Males	33	25	55	36	
Females	14	26	42	32	
Total	47	25	55	35	2.4:1
Probable (b)					
Males	25	21	50	35	
Females	10	21	41	30	
Total	35	21	50	34	2.5:1
Possible (c)					
Males	23	20	53	34	
Females	13	18	44	29	
Total	(1nk) 37	18	53	32	1.8:1
All outbreak cases (a+b+c)					
Males	81	20	55	35	
Females	37	18	44	31	
Total	(1nk) 119	18	55	34	2.2:1
Non-anthrax (negative) patients					
Males	52	21	53	37	
Females	32	18	44	30	
Total	(1nk) 89	18	53	34	1.6:1

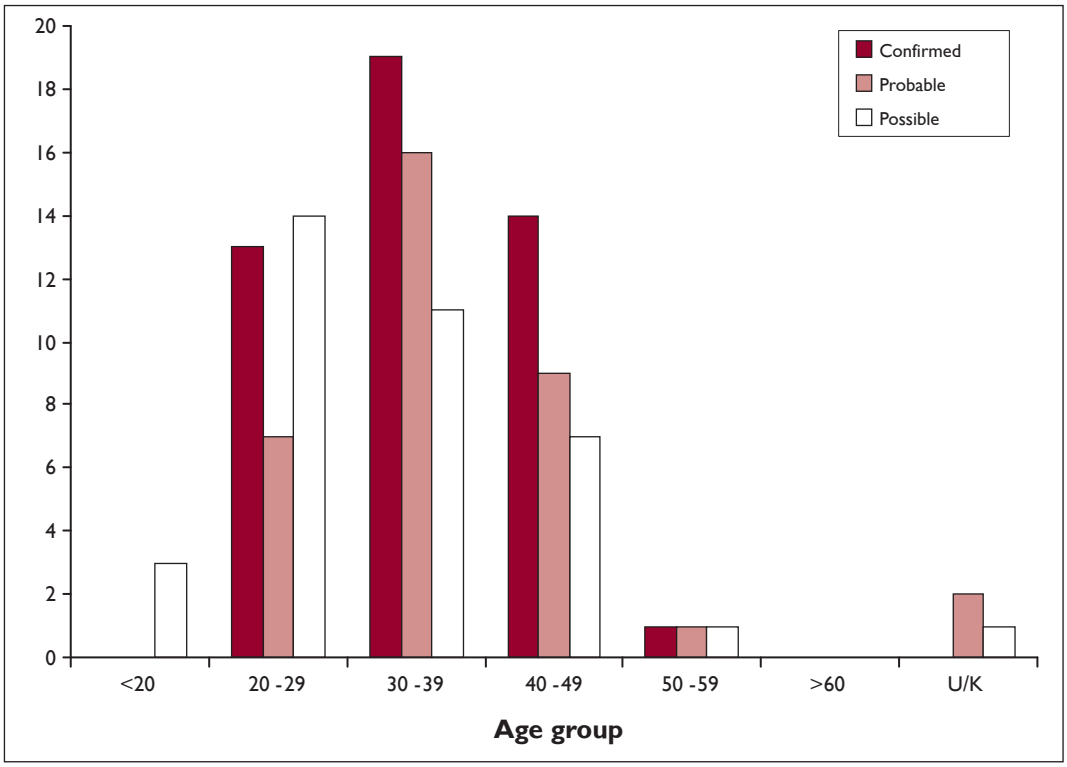
nk = not known

Table 4: Age distribution of cases by case type

Age range (years)	Confirmed (%)		Probable (%)		Possible (%)		All Cases (%)		Non-anthrax (negative) (%)	
<20	0	(0%)	0	(0%)	3	(8.1%)	3	(2.5%)	2	(2.3%)
20-29	13	(27.7%)	7	(20%)	14	(37.8%)	34	(28.6%)	23	(25.8%)
30-39	19	(40.4%)	16	(45.7%)	11	(29.7%)	46	(38.7%)	39	(43.8%)
40-49	14	(29.8%)	9	(25.7%)	7	(18.9%)	30	(25.2%)	18	(20.2%)
50-59	1	(2.1%)	1	(2.9%)	1	(2.7%)	3	(2.5%)	2	(2.3%)
>60	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Unknown	0	(0%)	2	(5.7%)	1	(2.7%)	3	(2.5%)	5	(5.6%)
Total	**47**	**(100%)**	**35**	**(100%)**	**37**	**(100%)**	**119**	**(100%)**	**89**	**(100%)**
Min. age	25		21		18		18		18	
Max. age	55		50		53		55		53	
Mean age	35		34		32		34		34	

There were more males than females in all case categories. There was little difference in the age profiles of cases whether confirmed, probable or possible; cases ranged in age from 18 to 55 years, with a mean of 34 years, indicating that drug users were probably all from the same source population. Confirmed and probable cases had a mean age slightly but not significantly older than possible cases. The modal age group was 30 to 39 years, except for possible cases (20 to 29 years). The non-anthrax (negative) patients were not significantly different from the outbreak cases in age, although there were relatively more female drug users in this category.

Figure 3: Age distribution of anthrax outbreak cases by case type



The age distribution of confirmed cases by infection outcome is summarised in Table 5; there was only one death among probable cases.

Table 5: Age distribution of confirmed cases by final outcome

Age range (years)	Died	Survived	Total	Case Fatality Ratio Deaths: total
<20	0	0	0	-
20-29	3	10	13	1:4.33
30-39	6	13	19	1:3.17
40-49	3	11	14	1:4.67
50-59	1	0	1	1:1
>60	0	0	0	-
Unknown	0	0	0	-
Min. age	25	25	25	-
Max. age	55	55	55	-
Mean age	30	35	35	-
Total cases	**13**	**34**	**47**	**1:3.61**

b. Cases by NHS board of residence

Cases by NHS board of residence are given in Table 6. The highest number of cases lived in Tayside, which had relatively more possible cases; then Greater Glasgow & Clyde where the outbreak began. Lanarkshire had the third highest number in total. Tayside also had the highest number of anthrax negative (non-anthrax) patients; this may suggest that Tayside were reporting proportionately more suspected anthrax cases from among drug users with infections than other areas.

Table 6: Cases (and deaths) by NHS board of residence and case type

NHS board		Confirmed (deaths)		Probable (deaths)		Possible	Total Cases (deaths)		Negative (deaths)	
Ayrshire & Arran	(AA)	1		0		0	1		0	
Borders	(BR)	0		0		1	1		0	
Dumfries & Galloway	(DG)	5		2		0	7		1	
Fife	(FF)	5	(1)	1		0	6	(1)	2	(1)
Forth Valley	(FV)	2	(1)	3		4	9	(1)	5	
Greater Glasgow & Clyde	(GGC)	19	(7)	16	(1)	5	35	(8)	20	(1)
Grampian	(GR)	0		1		0	1		1	
Highland	(HI)	0		0		0	0		1	
Lanarkshire	(LN)	7	(2)	5		6	18	(2)	20	
Lothian	(LO)	2		0		2	4		10	
Orkney	(OR)	0		0		0	0		0	
Shetland	(SH)	0		0		0	0		0	
Tayside	(TY)	6	(2)	7		19	37	(2)	29	
Western Isles	(WI)	0		0		0	0		0	
Scotland		**47**	**(13)**	**35**	**(1)**	**37**	**119**	**(14)**	**89**	**(1)**

Table 7 gives cases by NHS board of residence (home location) and sex. Males predominated in all areas in all case categories except for possible cases in Glasgow and Clyde area.

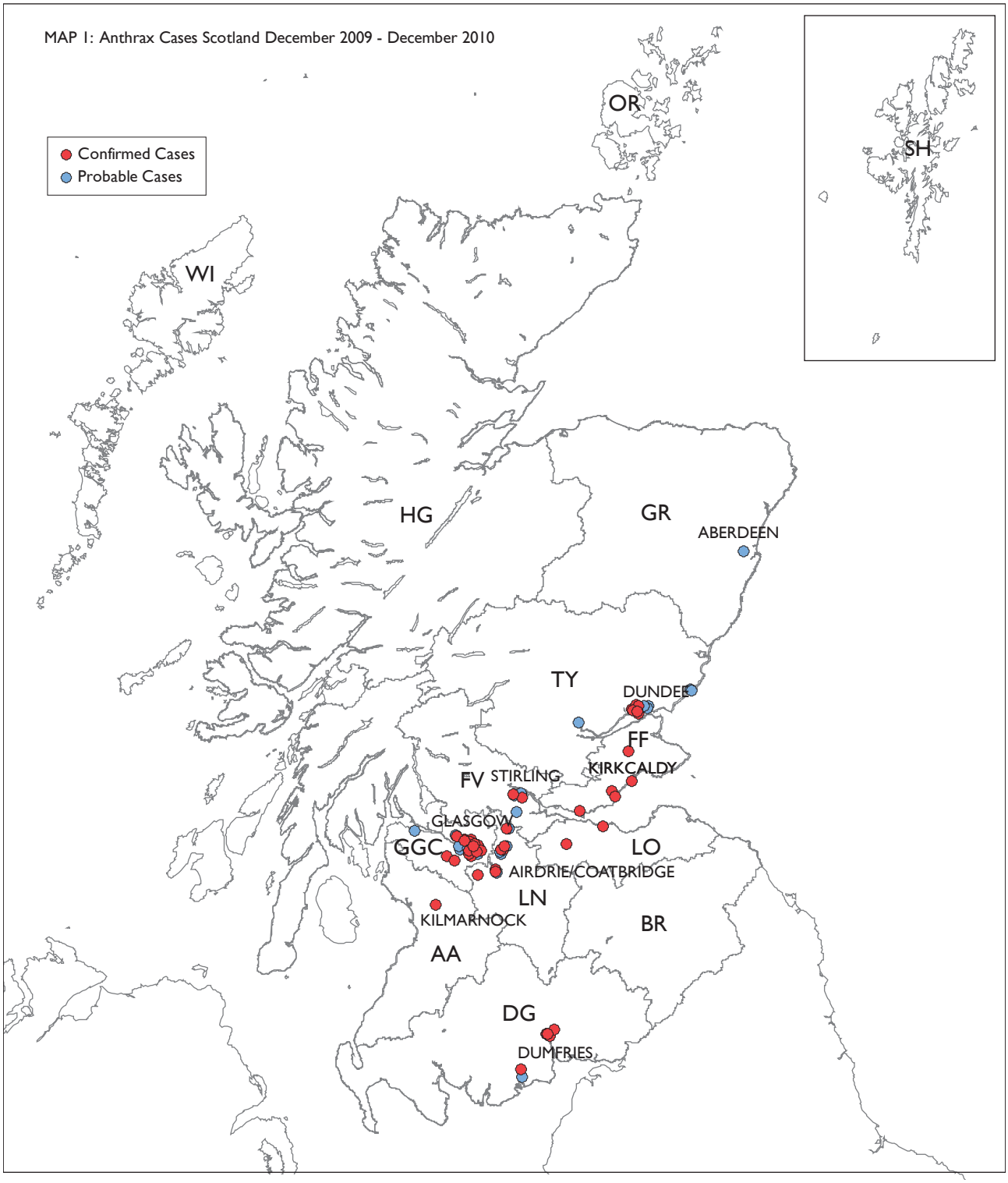
Table 7: Cases by NHS board of residence by case type and sex

NHS board area	Confirmed			Probable			Possible		
	Total	**M**	**F**	**Total**	**M**	**F**	**Total**	**M**	**F**
AA	**1**	1	0	**0**	0	0	**0**	0	0
BR	**0**	0	0	**0**	0	0	**1**	1	0
DG	**5**	4	1	**2**	1	1	**0**	0	0
FF	**5**	3	2	**1**	1	0	**0**	0	0
FV	**2**	2	0	**3**	2	1	***4**	2	1
GGC	**19**	12	7	**16**	11	5	**5**	2	3
GR	**0**	0	0	**1**	1	0	**0**	0	0
HI	**0**	0	0	**0**	0	0	**0**	0	0
LN	**7**	4	3	**5**	4	1	**6**	4	2
LO	**2**	2	0	**0**	0	0	**2**	2	0
OR	**0**	0	0	**0**	0	0	**0**	0	0
SH	**0**	0	0	**0**	0	0	**0**	0	0
TY	**6**	5	1	**7**	5	2	**19**	12	7
WI	**0**	0	0	**0**	0	0	**0**	0	0
Scotland	**47**	**33**	**14**	**35**	**25**	**10**	**37**	**23**	**13**

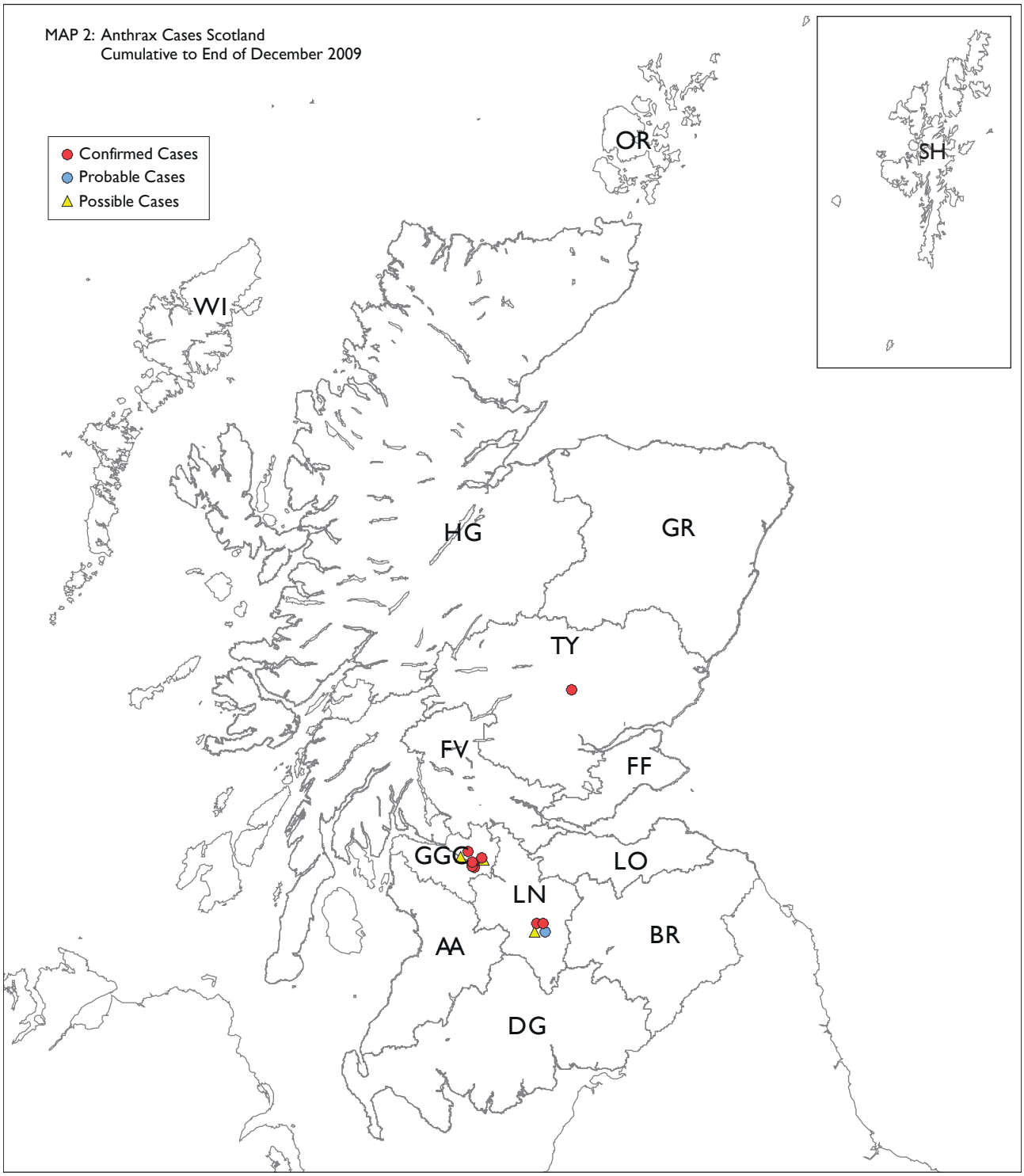
*1 unknown gender

Figures 4 to 8 (maps 1 to 5) show the distribution of cases over time by home location or by NHS board area, where available; postcodes were not available for 4 probable cases and home location data was least complete for possible cases. Figure 4 (Map 1) gives the home location for confirmed and probable cases; Figures 5, 6, 7, 8 (Maps 2 to 5) plot cases from December 2009 to July 2010 cumulatively as they were identified. This illustrates the geographic clustering of cases as the outbreak progressed.

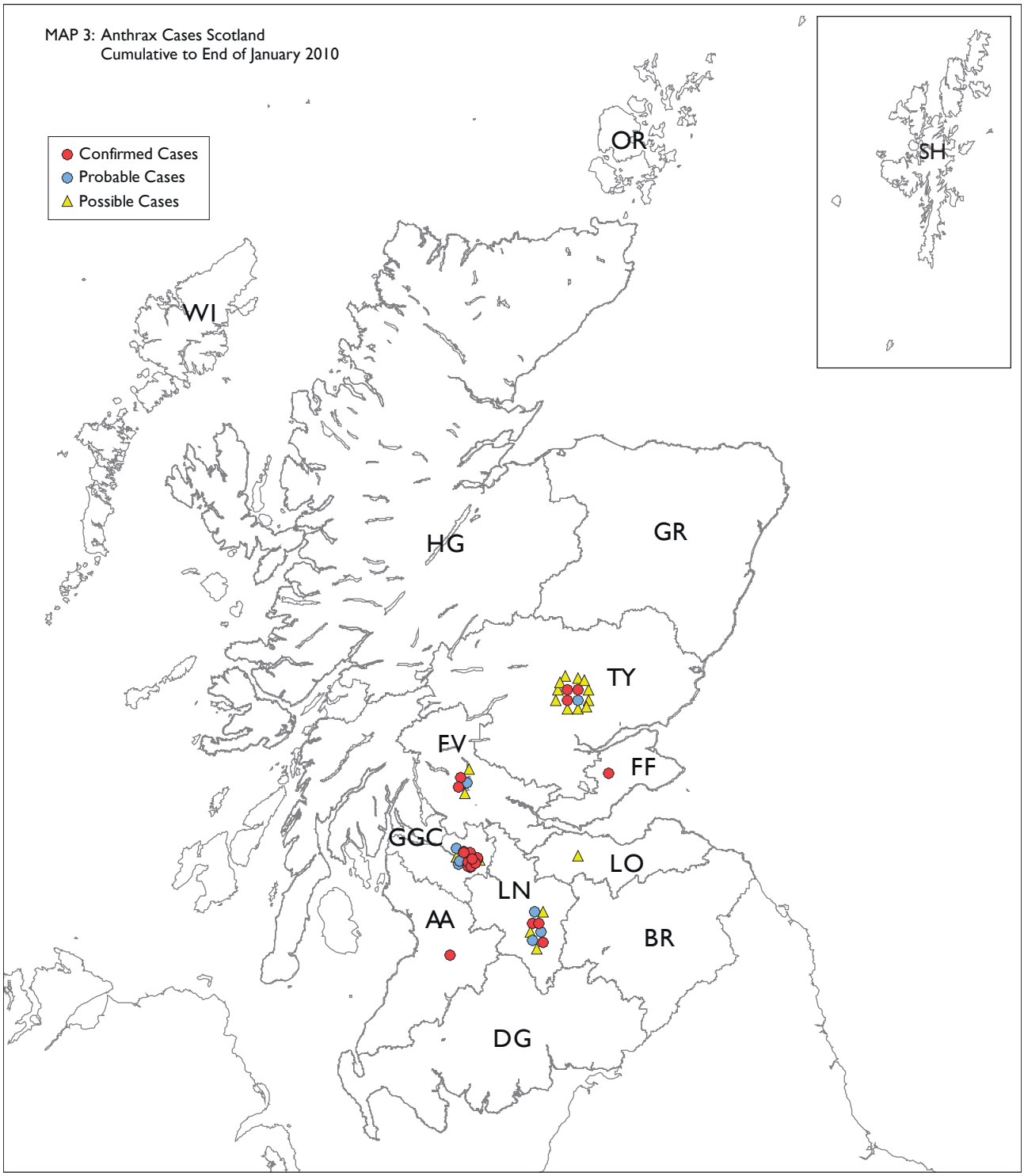
Figure 4: (Map 1) Confirmed and probable anthrax cases by NHS board area



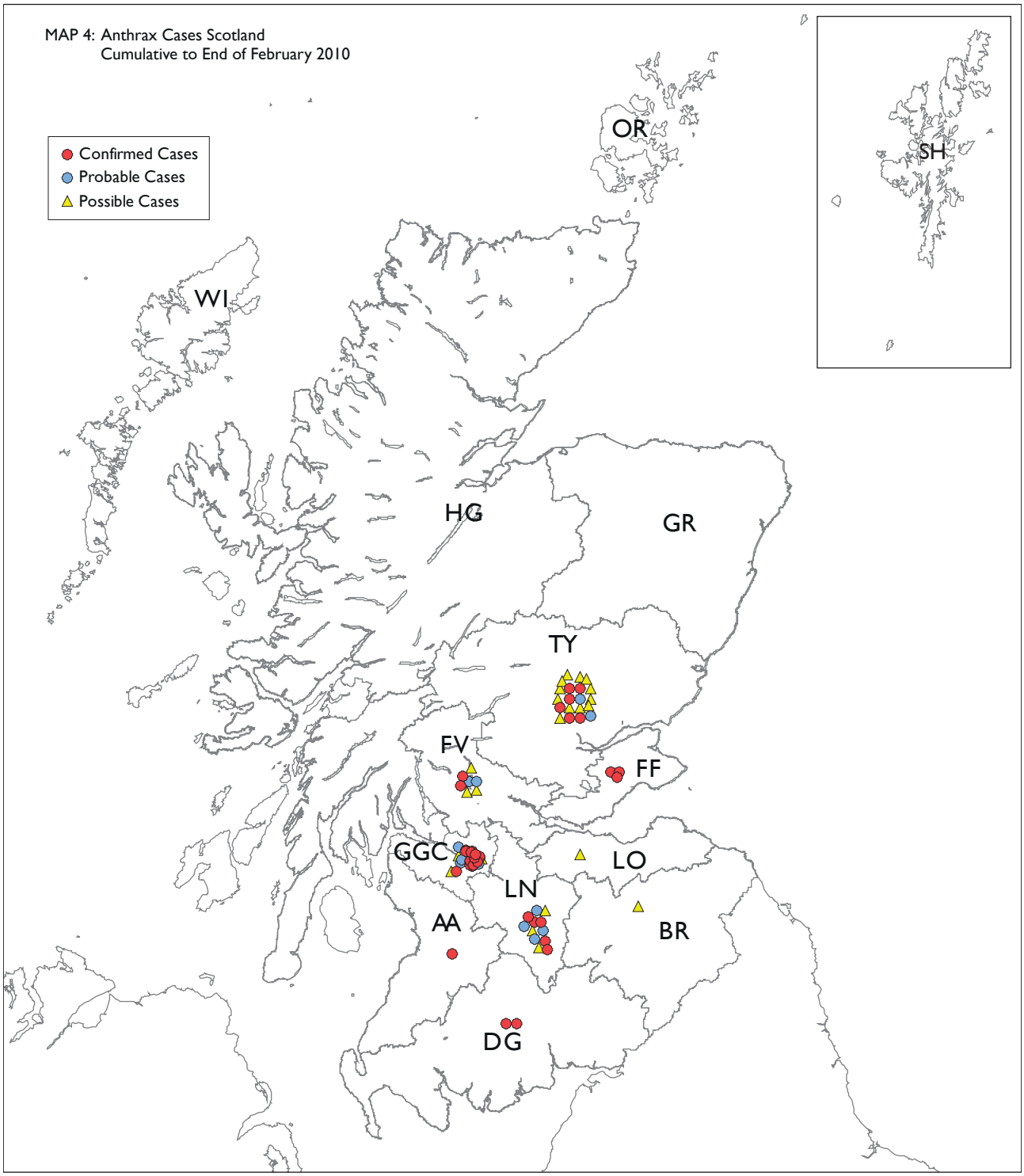
Figures 5: (Map 2) Cumulative distribution of all cases in December 2009 by NHS board



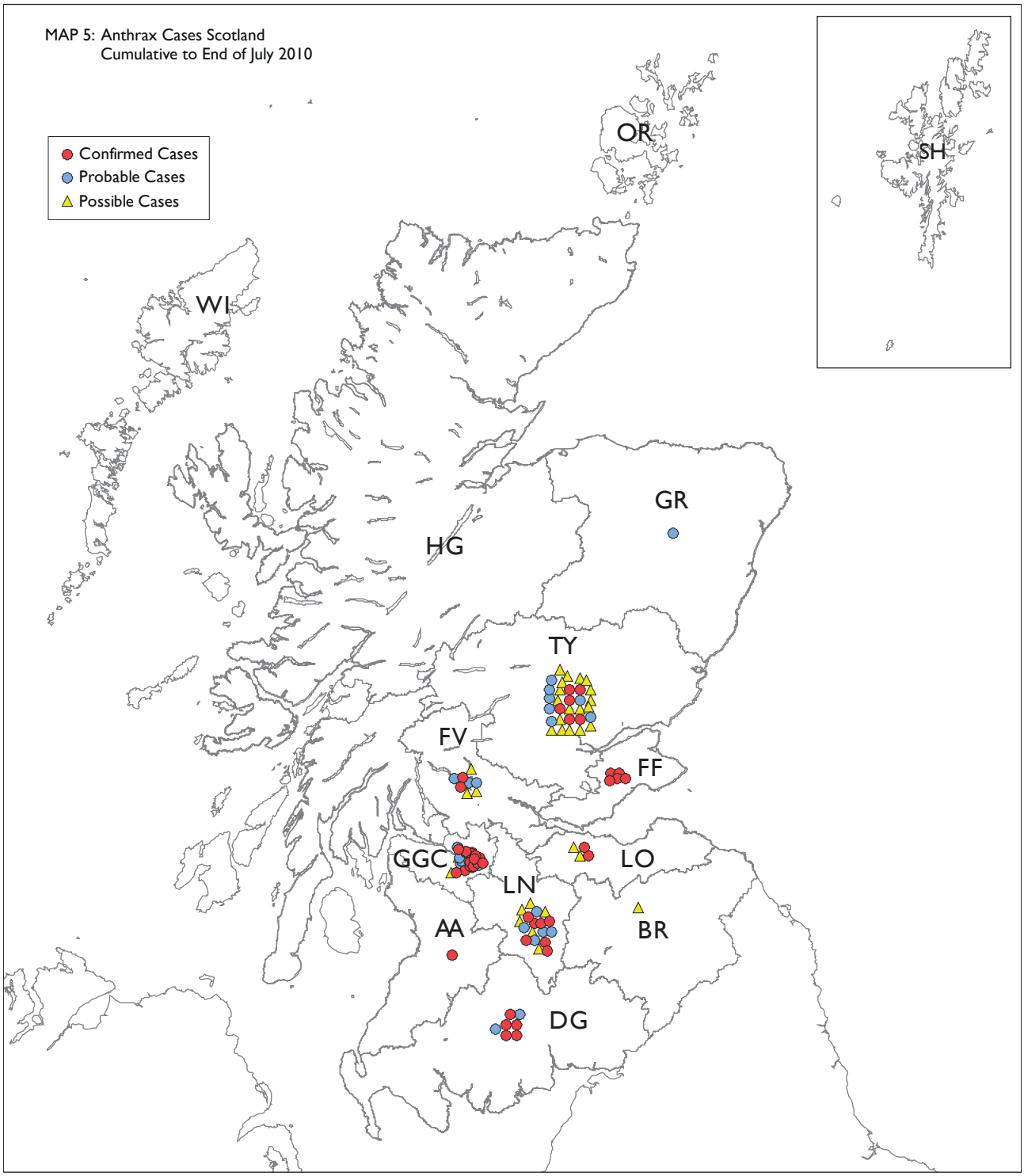
Figures 6: (Map 3) Cumulative distribution of all cases in January 2010 by NHS board



Figures 7: (Map 4) Cumulative distribution of all cases in February 2010 by NHS board



Figures 8: (Map 5) Cumulative distribution of all cases in July 2010 by NHS board



c. Infection attack rate by NHS board of residence

The infection rate (the number of cases per unit population or incidence) was calculated using two denominator populations: (1) cases divided by the total population for each NHS board area (Table 8); (2) cases divided by a denominator derived from the estimated number of active heroin users living within an NHS board area derived from drug user surveys (Table 9). These measures provide the attack rate (incidence) from a whole population perspective and among active drug users as the population at most risk of contracting anthrax from contaminated heroin.

Table 8: Infection rate by NHS board of residence per 100,000 population

NHS board	Population	Confirmed		Probable		Possible		Total	
		Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
AA	**367,160**	1	0.29	0	0	0	0	1	0.29
BR	**112,680**	0	0	0	0	1	0.89	1	0.89
DG	**148,510**	5	3.37	2	1.35	0	0	7	4.71
FF	**363,385**	5	1.38	1	0.28	0	0	6	1.65
FV	**291,383**	2	0.69	3	1.03	4	1.37	9	3.09
GGC	**1,199,026**	19	1.58	16	1.33	5	0.42	35	2.92
GR	**544,980**	0	0	1	0.18	0	0	1	0.18
HI	**310,530**	0	0	0	0	0	0	0	0
LN	**562,215**	7	1.25	5	0.89	6	1.07	18	3.20
LO	**826,231**	2	0.24	0	0	2	0.24	4	0.48
OR	**19,960**	0	0	0	0	0	0	0	0
SH	**22,210**	0	0	0	0	0	0	0	0
TY	**399,550**	6	1.50	7	1.75	19	4.76	37	8.01
WI	**26,180**	0	0	0	0	0	0	0	0
Scotland	**5,194,000**	**47**	**0.90**	**35**	**0.67**	**37**	**0.71**	**119**	**2.29**

The rate of infection per 1000 population was highest in Tayside for total cases, due mainly to the relatively higher number of possible cases. For confirmed and probable cases alone, Dumfries & Galloway had the highest rate. Glasgow & Clyde had the highest numbers of confirmed and probable cases but the population case rate was only second highest for confirmed cases. Total population based case rates are however misleading, since the true denominator for the population at risk is drug users not the whole population. Infection attack rates based on the estimated drug using population in each area gives a truer indication of the variation in case incidence geographically (Table 9). Data on denominators for drug users was derived from studies of drug users in Scotland in 2006 (Hay et al, 2009).

Table 9: Infection rates per 1,000 estimated drug users by NHS board of residence

NHS board	Estimated drug user population	Confirmed		Probable		Possible		Total	
		Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
AA	**2,373**	1	0.42	0	0	0	0	1	0.42
BR	**201**	0	0	0	0	1	4.97	1	4.97
DG	**486**	5	10.29	2	4.11	0	0	7	14.40
FF	**1,270**	5	3.94	1	0.79	0	0	6	4.72
FV	**786**	2	2.54	3	2.54	4	5.09	9	11.45
GGC	**8,862**	19	2.14	16	1.80	5	0.56	35	3.95
GR	**3,056**	0	0	1	0.33	0	0	1	0.33
HI	**734**	0	0	0	0	0	0	0	0
LN	**1,649**	7	4.24	5	3.03	6	3.64	18	10.91
LO	**3,262**	2	0.61	0	0	2	0.61	4	1.23
OR	**-**	0	0	0	0	0	0	0	0
SH	**-**	0	0	0	0	0	0	0	0
TY	**1,254**	6	4.78	7	5.58	19	15.15	37	25.52
WI	**-**	0	0	0	0	0	0	0	0
Scotland	**23,933**	**47**	**1.96**	**35**	**1.46**	**37**	**1.55**	**119**	**4.97**

The overall attack rate of anthrax in heroin users is estimated to have been around 1:200 for all of Scotland. However, rates of infection showed that the geographic distribution of the outbreak across Scotland was very variable. The Highland and Island NHS board areas had no cases. Despite having sizeable heroin using populations, Lothian and Grampian area had lower attack rates for anthrax than the average. This suggests that the distribution of the contaminated heroin itself was very variable. The onset dates of the first cases in Tayside was in December 2009, indicating that contaminated heroin was circulating in the West of Scotland and Tayside around the same time whereas the cases in Dumfries and Galloway occurred later (in 2010), possibly indicating that contaminated heroin took longer to reach that area.

Infection rates per 1000 estimated injecting drug users showed that Tayside had the highest overall infection rate among drug users (partly due to the high rate for possible cases), followed by Dumfries and Galloway, which also had the highest infection rate for confirmed cases. Tayside had the highest rate for probable cases but also second highest for confirmed cases. Hence, although most of the cases occurred in Glasgow and Lanarkshire areas, proportionately they had lower infection rates in their drug user populations than did these other areas. The risk of infection to heroin users in these areas was therefore proportionately much higher than for Glasgow and Lanarkshire.

Rates for the non-anthrax cases (per 1000 drug users) are not tabulated (by NHS board area) but interestingly Tayside had by far the highest ratio of negative (non-anthrax) suspected cases reported (23/1000) compared to Lanarkshire (12.1/1000); Greater Glasgow and Clyde (2.2/1000); Lothian (3.0/1000) indicating probable variation in the thresholds used for reporting suspected cases.

d. Distribution of cases by week and month of onset and presentation

Table 10 gives the distribution of cases by month of symptom onset and separately by month of presentation (presentation date lags behind date of onset by a variable period). Onset dates could not always be determined accurately and in some cases were estimated based on the available evidence from proxies if necessary.

Table 10: Cases (and deaths) by type, by month of onset and month of presentation

	Confirmed		Probable		Possible		All cases		Non-anthrax cases	
Date	**Onset**	**Present**	**Onset**	**Present**	**Onset**	**Present**	**Onset**	**Present**	**Onset**	**Present**
Dec 2009	13 (6)	10 (6)	1	1	6	3	20 (6)	14 (6)	11	10 (1)
Jan 2010	11 (4)	12 (4)	13 (1)	12 (1)	17	19	41 (5)	43 (5)	36 (1)	35
Feb 2010	12 (1)	12 (1)	5	6	4	4	21 (1)	22 (1)	13	15
Mar 2010	5 (1)	7 (1)	4	4	7	8	16 (1)	19 (1)	17 (1)	17 (1)
Apr 2010	3	3	2	2	3	3	8	8	6	6
May 2010	1 (1)	1 (1)	5	5	0	0	6 (1)	6 (1)	4	4
Jun 2010	1	0	4	4	0	0	5	4	0	0
Jul 2010	1	2	1	1	0	0	2	3	0	0
Aug 2010	0	0	0	0	0	0	0	0	0	0
Sept 2010	0	0	0	0	0	0	0	0	1	1
Oct 2010	0	0	0	0	0	0	0	0	1	1
Total	**47 (13)**	**47 (13)**	**35 (1)**	**35 (1)**	**37**	**37**	**119**	**119**	**89**	**89**

The majority of cases had symptom onset between December 2009 and March 2010. Figures 9 and 10 illustrate the epidemic curve of the (total) cases by week and month of symptom onset respectively. The peak of symptom onset occurred at the end of December 2009 and first week of January 2010 (over the Christmas, New Year period) (Figure 9). The peak incidence of total cases by month (Figure 10) was in January 2010. The last cases identified as having anthrax had symptom onset in July, although the last suspected cases had symptom onset in September/October. The majority of suspected cases identified ultimately as non-anthrax cases also had symptom onset over the same period (Table 10).

Figure 9: Total cases (confirmed, probable, possible) by week of symptom onset

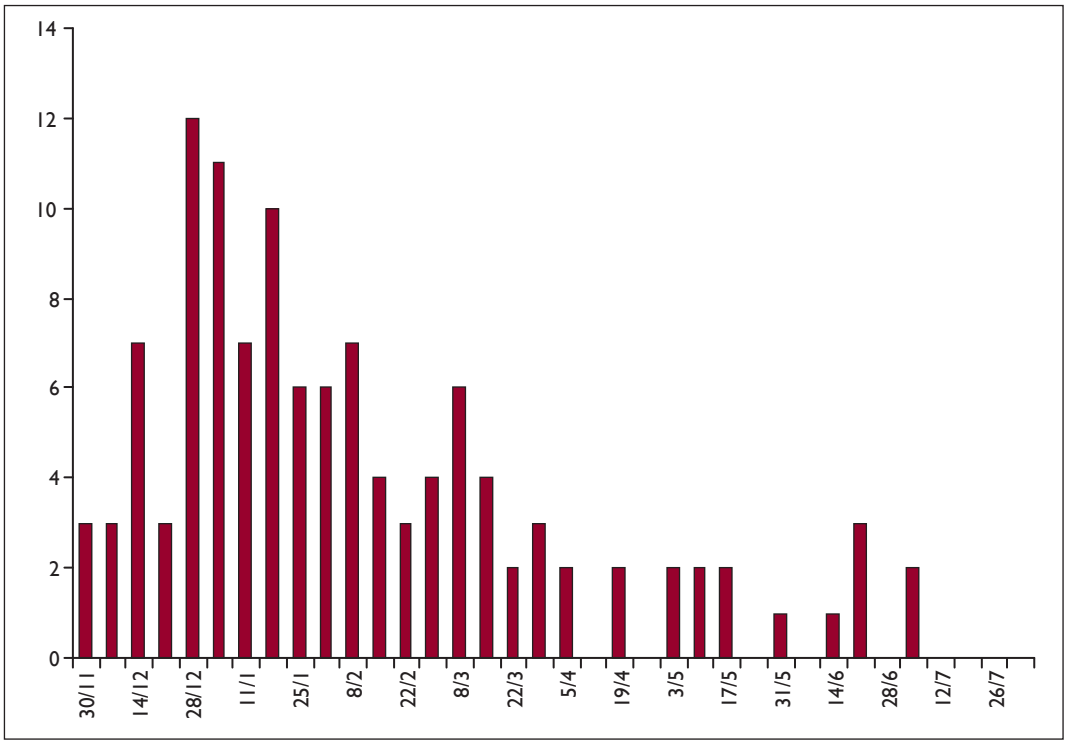


Figure 10: Total cases (confirmed, probable, possible) by month of symptom onset

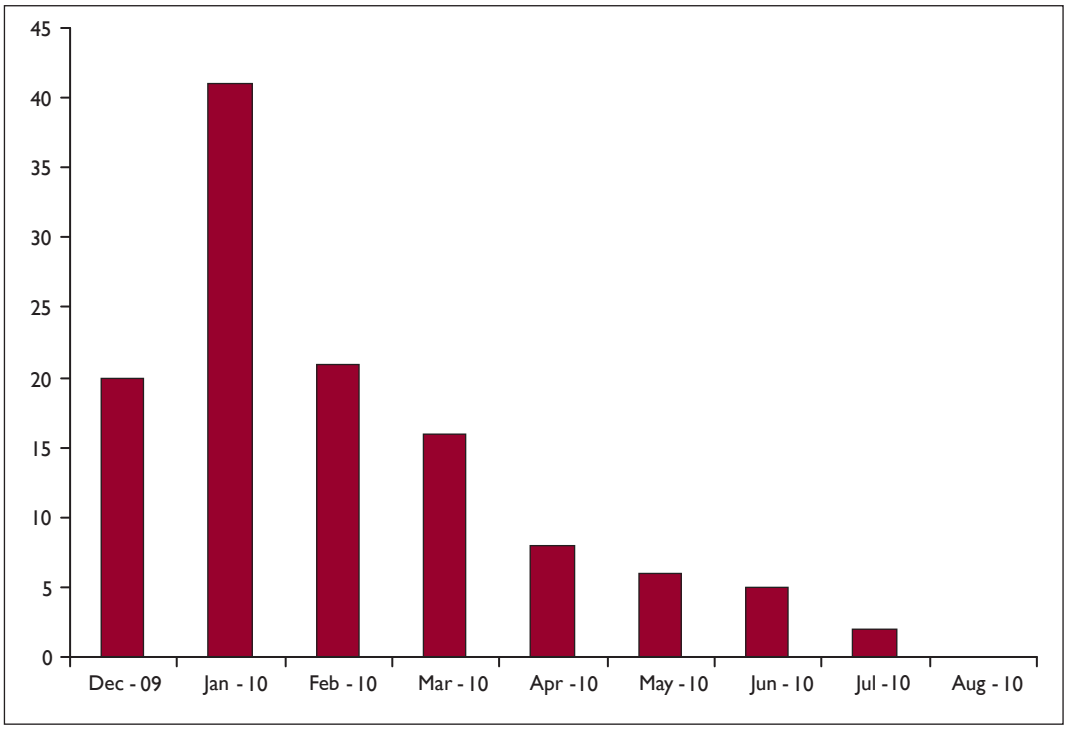
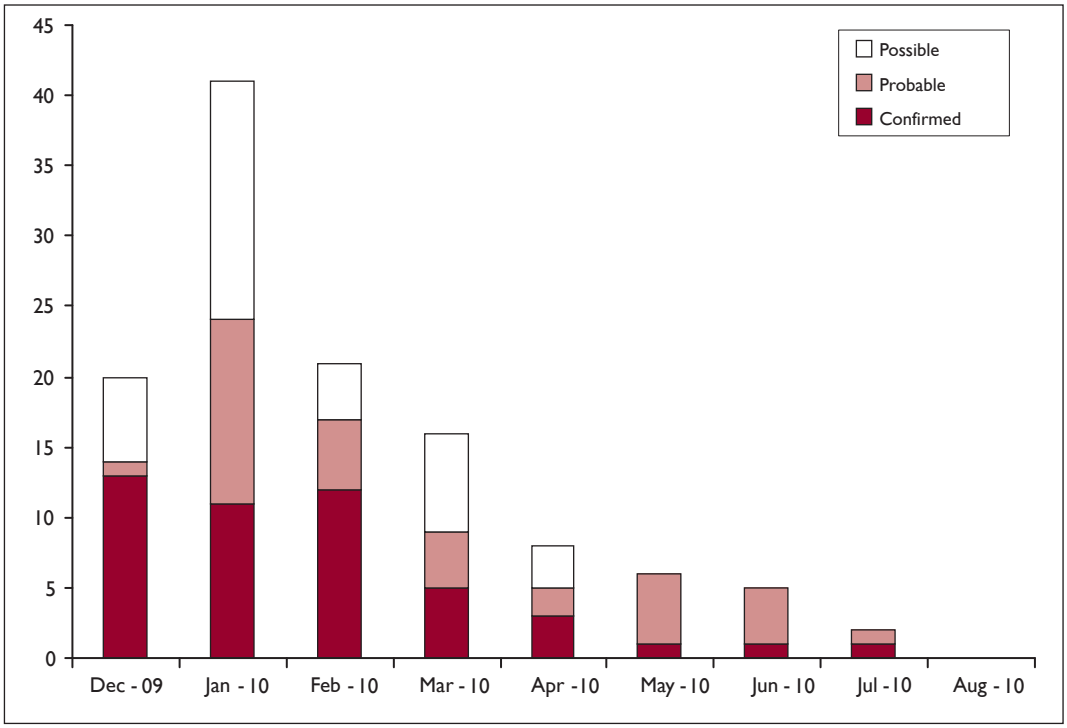


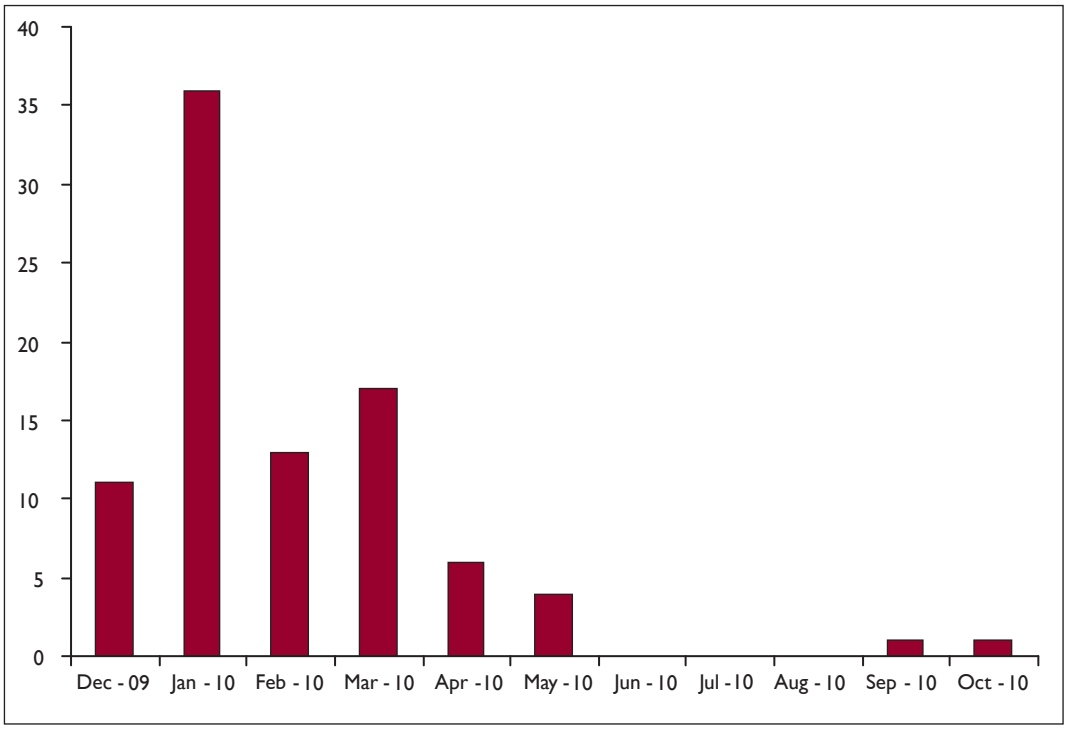
Figure 11 shows the distribution of cases by month of symptom onset by case type; confirmed cases peaked in December 2009 but averaged 12 new cases per month from December to February 2010; probable cases peaked in frequency in January, as did possible cases.

Figure 11: Confirmed, probable and possible cases by month of symptom onset



For comparison, Figure 12 shows onset dates of illness in patients investigated as suspected anthrax but finally classed as (negative) non-anthrax cases; these also peaked in January 2010. Negative suspected cases are an indication of the background level of non-anthrax infections among drug users presenting to hospitals; this suggests there was a general increase in presentations of these around the peak of the outbreak. The last suspected cases investigated and found to be negative had onset dates in September and October 2010.

Figure 12: Non-anthrax (negative) cases by month of symptom onset



e. Incubation periods

Data were analysed by the HPS investigation team to determine the possible incubation period (the time between the suspected exposure to anthrax spores and the time of symptom onset) for confirmed and probable cases (Table 11) (data on possible cases was incomplete). This was problematic due to uncertainly about which dose of heroin was contaminated. In a small number of cases it was possible to narrow the exposure opportunity window and estimate an incubation period with more certainty; e.g. where a case gave a clear history of using one single injection site that subsequently became infected. However, most of cases took heroin three times or more per day and frequently used the same injection site on multiple occasions; an estimated incubation period was then based on the timing of the last injection at an infected site. The incubation periods are therefore only approximations; actual incubation periods could be longer by an unknown margin.

Estimated incubation periods ranged from a day (or less) in 37 of the 92 confirmed and probable cases to ten days or more in three probable cases.

Table 11: Estimated incubation periods for confirmed and probable cases

Estimated incubation period	Confirmed Cases	Probable Cases
≤1 day	23	14
2 days	4	1
3 days	1	1
4 days	2	0
5 days	0	0
6 days	0	0
7 days	1	0
10 days	0	2
>10 days	0	1 (weeks)
Not known	16	16

f. Cases by duration of illness

The length of illness for cases (confirmed and probable only) was calculated as the interval from the initial hospital admission (or GP treatment) to their discharge home (or death) (Table 12). The duration of illness ranged from less than a day to over 28 days; the longest duration of illness occurred in cases who required extensive debridement of damaged tissue and subsequent reconstructive plastic surgery.

Table 12: Duration of illness for confirmed and probable cases by outcome

Duration of illness (days)	Confirmed Cases		Probable Cases	
	Survived	Died	Survived	Died
<1 day	3	1	2	0
1 day	2	4	1	0
2 – 5 days	4	4	8	0
6 – 10 days	6	3	4	0
11 – 20 days	7	0	2	1
21 – 28 days	1	0	0	0
>28 days	9	0	0	0
Not known	2	0	11	0
Not applicable	0	1	6	0
Total	**34**	**13**	**34**	**1**

4.5.2. Epidemiological Exposure Risk Factors

Factors which might have been associated with the risk of infection in individual cases were analysed.

a. Drug history

The level of detail provided in response to this question varied and so data were compared with other sources including the police investigation information or in some cases, post-mortem reports, to verify evidence of specific drugs taken.

A wide variety of drugs were reported as being taken by cases in the week before illness onset (Table 13). Heroin was the only drug that appeared to have been used by all cases before illness developed. Recollections in some cases of events in the week before illness were unclear but all acknowledge the use of heroin in the week before or in the period earlier than one week before symptom onset. Use of illicit (street bought) heroin was therefore a consistent common risk factor. Also 25 confirmed cases and 15 probable cases were taking methadone.

Table 13: Drugs used by cases in the week before symptom onset

Drugs used	Confirmed Cases			Probable Cases		
	Y	N	n/a	Y	N	n/a
Heroin	43	0	4*	22	0	13*
Buprenorphine	0	28	19	1	15	19
Cocaine	2	27	18	4	14	17
Crack	0	29	18	1	16	18
Heroin + cocaine	1	28	18	1	16	18
Heroin + crack	0	29	18	1	16	18
Methadone (prescribed)	24	14	9	13	4	18
Methadone (not prescribed)	1	23	9	2	10	23
Other Drugs Total:	13	1	33	8	0	27
Cannabis	4			2		
Cyclizine	1			0		
Diazepam	0			2		
Ecstasy	1			0		
Suboxone	1			0		
Temazepam	1			0		
Tramadol	1			0		
Tylex	0			1		
Valium	4			4		

(n/a – not answered)

* no information on drug use in week prior to illness but all had a history of heroin use from other data; e.g. police records or hospital case notes.

b. Duration of drug habit

Responses to this question were often incomplete. The confirmed and probable cases who responded, often reported long term use of various drugs, with a mean habit duration of 10 and 12 years respectively (Table 14).

Table 14: Duration of drug habit (years) by case type

Duration (years)	Confirmed Cases	Probable Cases
< 1	0	0
1 – 5	7	2
6 – 10	10	4
11 – 15	7	4
>15	5	3
Not answered	18	22
Mean number of years	10	12
Median number of years	9	12

c. Duration of heroin habit

Cases were questioned specifically on the duration of heroin use (Table 15). Of those confirmed and probable cases who responded, the mean duration of heroin use was of seven and ten years respectively. Three confirmed cases reported starting heroin only recently within the last year. Four cases reported using heroin for more than 15 years.

Table 15: Duration of heroin use (years) by case type

Duration (years)	Confirmed Cases	Probable Cases
< 1	3	0
1 – 5	7	5
6 – 10	9	2
11 – 15	5	3
>15	2	2
Not answered	21	23
Mean number of years	7	10
Median number of years	6.5	6.5

d. Frequency of heroin use

Most cases reported using heroin frequently in the week before symptom onset (Table 16). The mean frequency of use was 9 times per week for confirmed cases and 11 for probable cases. Sixteen confirmed and probable cases reported using heroin more than ten times per week normally.

Table 16: Frequency of heroin use in the week preceding symptom onset by case type

Frequency of Use (per week)	Confirmed Cases	Probable Cases
0	3	0
1	5	3
2 – 5	3	1
6 – 10	10	2
11 – 20	6	4
> 20	4	2
Not answered	16	23
Mean frequency/wk	9	11
Median frequency/wk	7	10

e. Quantity of heroin use by cases

Cases were asked to estimate the quantity of heroin they used per week in terms of a nominal standard amount, colloquially referred to a "tenner" bag (the quantity of heroin bought for £10) generally equating to approximately 0.1g of heroin. The amounts reported in the week prior to symptom onset varied considerably. Three cases denied using heroin in the week immediately preceding symptoms but did report earlier use; 16 confirmed cases and 8 probable cases used in excess of ten bags in the week preceding symptom onset (Table 17).

Table 17: Quantity of heroin use reported in the week prior to symptom onset by case type

Number of bags used in week before symptoms	Confirmed Cases	Probable Cases
None	3	0
≤1 bag	5	3
2 – 5 bags	4	1
6 – 10 bags	7	1
11 – 20 bags	9	3
> 20 bags	7	5
Not answered	12	22

1 bag = £10 = 0.1g

f. Drug purchasing and preparation

Cases were asked if they had done anything unusual or changed their habits in terms of their drug purchasing behaviour in the week before the illness onset. Over a third of cases did not answer. A third of confirmed cases and fewer probable cases changed their dealer in the week preceding symptom onset, hence this does not appear to be a relevant factor (Table 18).

Table 18: Changes in dealer reported in the week prior to symptom onset by case type

Changed Dealer	Confirmed Cases	Probable Cases
Yes	15	4
No	16	15
Don't know	3	0
Not answered	13	16

g. Differences in heroin in the week preceding symptoms

Cases were asked about any differences in the heroin bought prior to becoming ill (Table 19). Of the cases who answered there was no consistent feature reported. Differences in the properties of heroin did not appear to be related with developing illness. The variations in drug appearance and quality were not considered to be sufficiently robust to act as a basis for formulating advice to drug users on the characteristics of heroin that might pose an increased risk of anthrax contamination.

Table 19: Differences in heroin characteristics in the week preceding symptoms by case type

Heroin Characteristic	Confirmed Cases	Probable Cases
Colour (darker/lighter)		
Yes	11	5
No	20	14
Not Known	16	16
Consistency (thicker/grainier)		
Yes	9	6
No	21	13
Not known	17	16
Dissolving (easier/harder)		
Yes	10	5
No	22	14
Not known	15	16
Effect (weaker/stronger)		
Yes	11	5
No	20	14
Not known	16	16

h. Use of substances to dissolve heroin

Cases were asked about their heroin preparation procedures prior to use, especially by injection (Table 20). Most reported using citric acid alone or in combination with other acid materials. All cases who reported dissolving heroin in substances other than citric acid, also reported using citric acid.

Table 20: Substance used to dissolve heroin by case type

Substances Used	Confirmed Cases			Probable Cases		
	Y	N	Not answered	Y	N	Not answered
Citric acid	29	2	16	18	0	17
Vinegar	0	30	17	1	16	18
Lemon juice (Jif)	3	27	17	0	17	18
Lemon juice (fresh)	2	28	17	0	17	18
Descaler crystals	1	29	17	0	17	18
Vitamin C	1	29	17	1	16	18

i. Routes of exposure to heroin

Cases were questioned on their heroin taking habits (Table 21). Cases did not always give clear answers, making it difficult to be certain which routes they had used. It was reported that there was some reluctance to admit to using some routes of heroin use in some cases who were taking prescribed methadone, due to concerns that this might impact on their eligibility for future treatment.

Table 21: Heroin exposure routes used in the week prior to illness by case type

Route of Exposure	Confirmed Cases	Probable Cases
Injection only	15	12
IV exclusively	10	8
IM exclusively	1	1
IV + IM	4	3
Non-injection only (Smoking, snorting)	2	3
Both injection and non-injection routes	16	2
Question not answered or answer incomplete	14	18

Confirmed cases

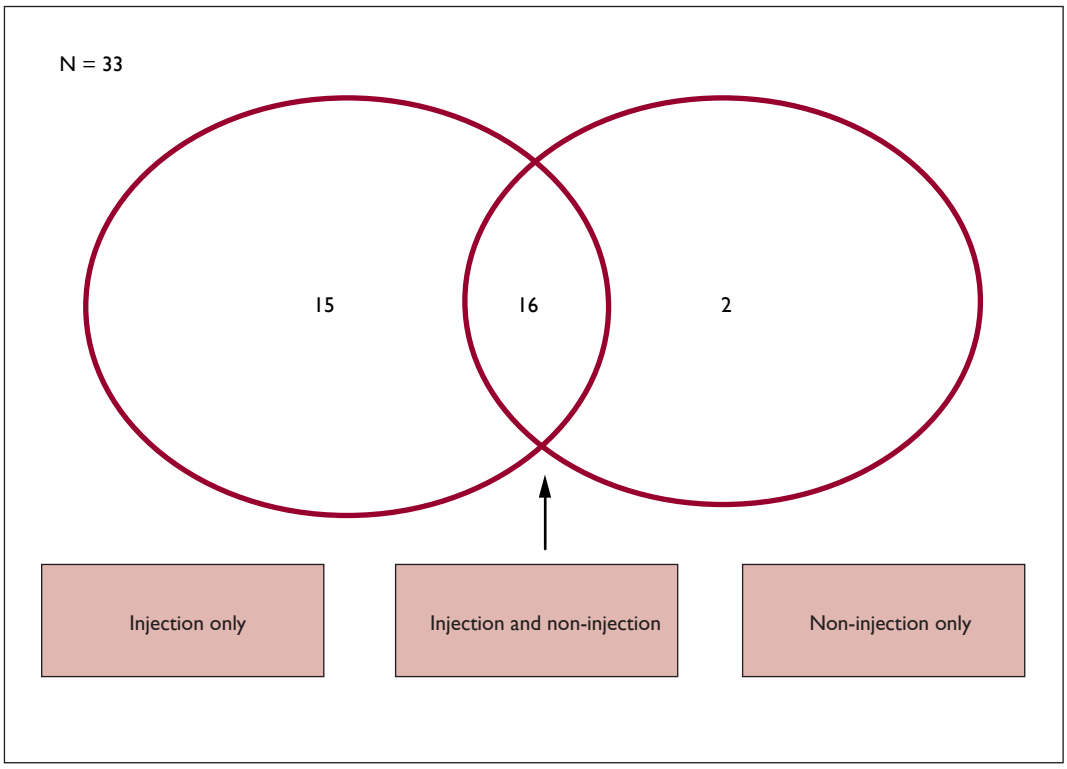
- 8 cases reported injecting but did not answer other questions;
- 1 case smoked but did not answer other questions;
- In 1 case, a proxy believed that the case had smoked but was unable to provide a full history of exposure routes.

Probable cases

- 3 cases reported injection but did not answer other questions.

Of the 33 confirmed cases who answered fully, 15 confirmed cases reported only using heroin by injection but via a variety of injection routes; two reported heroin exposure only via non-injection routes (predominantly smoking); 16 reported using both injection and non-injection routes; 31 injected exclusively or in combination with non-injection methods, whereas 18 of the 33 reported non-injection routes exclusively, or in combination with injection (Fig 13).

Figure 13: Routes of exposure to heroin in confirmed cases



One case reported only taking heroin by smoking and indicated that this was based on advice that smoking might be safer than injecting. Both exposure by injection and by smoking were therefore risk factors. The relative risks of these exposure routes could not however be calculated reliably from these data alone.

4.6. Data on the Clinical Presentation of Cases

The epidemiological investigation questionnaire included data on presenting symptoms of infection reported by the case (or proxy). These questions were not well answered and the data gives only a partial impression. More detailed reviews of hospital case notes and post-mortem records for confirmed cases were therefore carried out separately retrospectively (Appendix H).

The pattern of presenting symptoms was very mixed. Cases did not generally present with the typical features of cutaneous anthrax; few had lesions that resembled the classical black crusted eschar normally associated with cutaneous exposure. Many cases presented with soft tissue infections and/or localised swelling, or features similar to necrotising fasciitis. Swelling was the commonest reported feature across all case types, followed (in confirmed cases) by pain, malaise and fever.

Other cases presented with little or no localised signs of infection but with generalised symptoms suggesting disseminated infection and toxaemia. Some presented with marked abdominal pain, sometimes with other GI symptoms (nausea, vomiting, diarrhoea or rectal bleeding). Others presented with predominantly cerebral/CNS symptoms; severe headache, hallucinations, fitting, collapse, coma. Some died very rapidly after hospital admission or were found dead at home.

Table 22: Symptoms reported at the time of illness onset by case type

Self reported symptoms at time of onset	Confirmed (n=47)		Probable (n=35)		Possible (n=11)		Negative (n=42)	
Headache	12/30	(40%)	4/18	(22%)	3/8	(37%)	14/37	(38%)
Fever	22/34	(65%)	5/18	(28%)	6/9	(67%)	23/38	(61%)
Chills	15/32	(47%)	5/17	(29%)	3/8	(37%)	22/38	(59%)
Anorexia	17/33	(52%)	3/18	(17%)	3/8	(37%)	15/38	(39%)
Malaise	25/34	(74%)	8/20	(40%)	4/8	(50%)	23/37	(62%)
Nausea	17/33	(52%)	4/18	(22%)	3/8	(37%)	16/36	(44%)
Diarrhoea	6/32	(19%)	1/18	(6%)	0/8	(0%)	4/38	(11%)
Vomiting	14/36	(39%)	3/18	(17%)	4/9	(44%)	11/37	(30%)
Abdominal pain	18/39	(46%)	3/18	(17%)	2/8	(25%)	10/37	(27%)
Bloody diarrhoea or vomiting	2/32	(6%)	1/18	(6%)	1/8	(12%)	2/36	(6%)
Leaking infection site	16/31	(52%)	1/19	(5%)	5/11	(45%)	12/37	(32%)
Swelling	32/37	(86%)	18/21	(86%)	10/11	(91%)	34/38	(89%)
Pain	32/38	(84%)	13/21	(62%)	9/10	(90%)	33/38	(87%)
Itching	10/30	(33%)	4/18	(22%)	1/8	(12%)	7/36	(19%)
Breathing difficulties	8/25	(32%)	3/13	(23%)	2/7	(29%)	7/24	(29%)

Confirmed Cases:

39 of 47 reported a specific wound/injection site infection; 7 denied any local site symptoms; of these, 2 denied injecting at all and reported using heroin only by smoking. One case died prior to admission and 5 others died very soon (≤1 day) after admission.

Probable Cases:

24 of the 26 probable cases who answered, reported wound/injection site infection. Of the other 2 cases, 1 was admitted to hospital because they were "generally unwell" and the other case had been "unwell" and was treated (by their GP) for a chest infection for two days before hospital admission.

Deaths and Post-mortem Findings on Fatal Cases:

Of the 13 confirmed cases who died, 1 died before admission, 5 died within 24 hours and 7 died two to seven days after admission to hospital.

11 of the 13 fatal confirmed cases had a Fiscal post-mortem examination carried out; 9 of the 13 had post-mortem evidence of a localised wound infection indicating that the locus of infection was injection related; the remaining 4 had no evidence of injection site infection suggesting non-injection routes of fatal heroin exposure; in 3 of these, death was attributed to haemorrhagic meningitis, a recognised manifestation of systemic/toxaemic illness in fatal respiratory, cutaneous and ingestion anthrax. Some cases did not have full post-mortem examinations; there was no physical examination nor were tissues/fluids retained, only a review of medical notes and an external inspection prior to a death certificate being issued (known as a "view and grant" procedure).

4.7. Analytical Epidemiology: Retrospective Case Control Study Findings

A study was carried out to try to address some of the questions that could not be answered from analysis of the descriptive epidemiological data alone. This retrospective study was designed to compare the characteristics of anthrax cases (confirmed and probable only) with non-anthrax controls; i.e. drug users who were similar in characteristics except for not developing the infection. This study was not completed until after the outbreak had ended. Consequently the results were not available to the NAOCT to influence its decisions.

The anthrax cases were linked to records held on the Scottish Drug Misuse Database (SDMD), the national drug treatment database for Scotland. Confirmed and probable cases of anthrax were probabilistically linked to the SDMD; where a record match was achieved for a case, data from their most recent (or sometimes only) attendance at a drug treatment facility were extracted. Ten controls were then randomly selected from the database for each case. The selection criteria for the controls were: (i) attendance at the same (or a nearby) drug treatment service as the case within a period of +/- 12 months of the case's date of attendance and (ii) reported use of heroin in the month prior to attendance. Controls were deliberately not matched for age or sex to allow comparison with cases. Data variables extracted from the SDMD included: sex; age; drugs

prescribed at the time; illicit drugs taken in the month prior to the clinic attendance (including route of administration, quantity taken and frequency); injecting history; history of sharing needles/syringes or other injecting equipment (where sharing is defined as lending or borrowing); history of blood-borne virus infections (HIV, HBV, HCV); and alcohol consumption in the month prior to attendance (available from 2006 onwards).

Preliminary findings are described. Of the 82 confirmed and probable anthrax cases, 65 (79%) were successfully matched to the SDMD. Conditional (matched) logistic regression was undertaken to analyse the association between variables and case/control status. Cases had a slightly older mean age of 31.9 years vs. a mean of 30.4 years for controls, although this was not statistically significant (p=0.095). Cases and controls had a similar gender distribution (71% male cases vs. 70% male controls). In the adjusted data analyses, being an anthrax case was associated with a longer injecting history; with receiving opioid substitution therapy (at the time of selected attendance) and alcohol consumption (in the month prior to clinic attendance). A history of (only) smoking heroin, in the month prior to clinic attendance, was associated with a lower risk of being a case compared to reporting injecting and/or other routes.

However, these findings must be interpreted with caution due to the design limitations of the study. The retrospective comparison of cases and controls using data generated from a routine data collection system (as opposed to a specifically designed prospective case-control study) meant that the data on drug use behaviour variables was historical, not contemporaneous. The data related to the time of attendance at a drug treatment clinic rather than data collected just before the onset of anthrax; the clinic attendance could have been between one to five years (and sometimes as much as thirteen years) before the case became ill; the data may not therefore have been representative of the cases' behaviour immediately preceding their anthrax illness. The full results of this study will undergo further analysis before submission for peer reviewed publication.

4.8. Police Investigations

Immediately the outbreak was identified, an investigation was launched by Strathclyde Police, who then acted as the lead investigating force for Scotland and then for the whole UK. This was managed by a Detective Superintendent and a dedicated team of officers, who conducted face to face interviews with cases and logged the resulting data on the police major investigations database system (HOLMES).

The police roles and activities included:

- Full investigation of each confirmed and probable case involving, where possible, interview of the victim, often on more than one occasion. Family members and social contacts were interviewed where cases were too ill or had died before they could be interviewed.
- Identification of dealer networks led to the seizure of heroin and the arrest of dealers as necessary. Where the supplier of the contaminated heroin was identified officers carried out house searches under warrant. Any recovered heroin was sent to HPA-NDPL for analysis.
- Gathering intelligence on heroin distribution networks by liaison with other UK police forces and international (European and other) counterparts and drug enforcement agencies.

- Gathering and preparing evidence, acting on behalf of the COPFS, for possible judicial review. There was an unprecedented agreement with the COPFS whereby heroin seized under the Operation Genetic banner would be sent for examination to HPA-NDPL where as part of the examination it would be necessarily destroyed. In some instances this would jeopardise any legal case due to the absence of the original evidence.

- Sending heroin samples for microbiological testing at HPA–NDPL and for toxicological analysis and isotope analysis at specialist laboratories, to determine the composition of the heroin and comparison with standard cutting agent profiles, and to identify any distinguishing characteristics.

- Additional activities including:

  Regular briefings and de-briefings with enquiry team across the country; liaison with German colleagues; dedicated intelligence cell attached to Operations Genetic; the preparation and dissemination of protocols, strategies and guidance to partners; use of analysts to produce meaningful data; use of a geographical profiler; liaison with British armed forces, regional and national airlines; family liaison officers, national de-brief (10000 volt review); information sharing and media relations.

Information on the heroin trade and distribution networks from police intelligence was previously described in the report on the drug use related outbreak of *C. novii* infection in 2000. Many of the features of the heroin trade at that time still applied.

The main source of illicit heroin imported to the UK and Scotland is known to be the heroin producing regions of Afghanistan and Pakistan. The raw product is transported to other countries for conversion into heroin, sometimes via Iran to Turkey, where it is processed in rudimentary laboratories and then packaged for onward trafficking. The rudimentary nature of the processing facilities creates ample opportunity for contamination of heroin, at various locations, by micro-organisms and spores during production and packaging stages.

It is estimated that 80 to 90% of heroin reaching the UK is supplied via criminal networks in Turkey. The final product is sold on via Turkish suppliers and trafficked through the Balkans, Eastern Europe to Western Europe especially the Netherlands/German border areas and then onwards to the UK. The quantities of heroin imported in any year can be significant with fluctuations in demand and apparently increasing supplies imported especially in anticipation of the Christmas and New Year period.

Once in the UK, heroin is distributed in Scotland via distinct networks serving predominately the East or the West separately. In this outbreak, network connections via Bradford were a feature. This compared to importation points such as Liverpool which featured in the previous *C. novii* outbreak, where cases also occurred in Ireland and in England. Strathclyde Police identified reliable intelligence connecting heroin supplies in the West Central Scotland, to dealers in Bradford, linked to suppliers in the Netherlands, the Balkans, Turkey and back to a source in Afghanistan.

The evidence relating to the heroin trade and trafficking routes further supports the plausibility of the main outbreak hypothesis, that contamination is likely to have occurred at an early stage in the transport of a batch of heroin to Scotland, possibly somewhere in Turkey.

4.9. Crown Office and Procurator Fiscal Service (COPFS) Investigation

The role of the local Procurator Fiscal is to investigate sudden suspicious and unexplained deaths. Deaths suspected as being associated with drug taking fall into this category; all of the deaths in which anthrax was suspected were reported to the relevant local Procurator Fiscal.

As the initial deaths occurred in Glasgow, that Area Procurator Fiscal received the police reports and instructed post mortem examinations. Representatives from the Procurator Fiscal's Office attended the meetings of the initial NHS GG&C (local) OCT.

Subsequently, as evidence emerged that the outbreak was considered to be a national incident, the COPFS quickly decided to follow the lead of NHS health protection services, and the police, in co-ordinating its work on these deaths on a national basis. Early involvement of the Glasgow Procurator Fiscal meant that the Senior Fiscal from that office was given the role of National Lead responsible for collating information from, and providing advice to, all COPFS areas which had deaths reported to them.

The illegality of drug possession and use always means that a drug related death will have been preceded by an illegal supply and therefore if evidence emerges of the identity of the supplier, it may be appropriate or necessary to take criminal proceedings. The need to consider the possibility of criminal proceedings was compounded in relation to the anthrax outbreak because there was also the possibility that evidence would emerge of individuals who had contaminated the heroin themselves or had supplied the heroin in the knowledge that it was contaminated (which might have raised the possibility of a charge of culpable homicide). In the event, evidence to support these possibilities did not emerge.

The Procurator Fiscal's duty in suspected drug deaths is to instruct a post-mortem examination with full toxicology. When the anthrax outbreak was declared, there was reluctance on the part of some pathologists in Scotland to conduct post mortem examinations. This meant that three examinations were carried out on a "*view and grant*" basis, meaning that no physical examination was carried out beyond an external inspection of the body and no samples were taken for subsequent analysis. The NAOCT had understandable concerns about this because it was considered that in order to confirm a diagnosis of anthrax adequately and to obtain accurate information on the route of fatal exposure to anthrax spores, a full post-mortem examination with appropriate samples would be necessary to assist its investigations.

Dr. Tim Brooks of HPA-NDPL provided advice to pathologists on the risks associated with post-mortem examinations and on the methodology for safe post-mortem examinations. Despite this, there was still reluctance on the part of some pathologists to conduct an appropriately complete examination. As a result, an arrangement was made for all the remains in cases where anthrax was suspected, to be transported to Glasgow for examination by one of the senior Glasgow pathologists.

Throughout the duration of the outbreak COPFS continued to be represented on the NAOCT and to advise on legal and procedural issues. Another issue which arose was consideration of Article 2 of the European Convention on Human Rights and Fundamental Freedoms. This provides that everyone's right to life shall be protected by law and the jurisprudence of the European Court of Human Rights has imposed responsibilities on States to make appropriate steps to protect the right to life.

Putting that into the context of the work of the NAOCT it is important to analyse the work that was done to educate the general public and drug users in particular, on the enhanced dangers associated with the use of heroin when it was known that heroin contaminated with anthrax had been circulating. Although deaths continued to occur, there was every reason to believe that the message regarding the risk associated with heroin was getting across and that the NAOCT was therefore taking appropriate steps to comply with Article 2.

In Scotland, where it is deemed to be in the public interest, COPFS conduct a Fatal Accident Inquiry (FAI) (a formal legal inquiry) before a Sheriff, where the circumstances of the death justify such a course. Deaths arising as a result of anthrax during the outbreak have been reported to Crown Counsel for a decision on whether there should be any FAI. That decision will be taken once Crown Counsel have had an opportunity to consider the completed report of the NAOCT.

5. Discussion and Lessons Identified

5.1. Introduction

The results of the outbreak investigations are discussed and lessons identified in the course of the investigation relating to the scope for improving future preparedness and outbreak response are considered. These formed the basis for later recommendations (report Section 6).

5.2. Outbreak Hypotheses Investigated

Various explanations for the cause of the outbreak were considered by the NAOCT.

5.2.1. Deliberate Contamination of Heroin

The possibility of deliberate or malicious contamination of heroin was considered. Some evidence might support such an explanation, especially the clonal nature of the organisms isolated from anthrax cases in Scotland and elsewhere (suggesting a single common source). Had deliberate contamination occurred due to the use of an artificially cultured organism, then it is likely that all the cases would have had the same anthrax strain. Police intelligence supported the conclusion that the heroin was from Afghanistan or Pakistan. However, there was no specific intelligence to suggest that deliberate contamination had occurred. Although this possibility cannot be completely eliminated, it seems unlikely; drug users would seem an unlikely target for a deliberate attack.

5.2.2. Inadvertent Contamination of Heroin Via Contaminated Cutting Agents

Heroin is routinely reduced in purity at points in its distribution by successive mixing (cutting) with bulking agents (e.g. materials such as paracetamol etc), which dilutes the active drug. Police intelligence indicated that the cutting agents used within Scotland (and the rest of the UK) at the time of the outbreak were no different to those normally used. Nothing unusual was detected in samples of heroin tested by police. There was no suggestion that the heroin had been mixed with products that might have been more likely to carry anthrax spores (e.g. untreated bone meal or old plaster). Contamination of heroin via cutting agents containing spores therefore seemed implausible.

5.2.3. Contamination at Multiple Points in the Supply Chain

Contamination at multiple points in time and/or location was considered a possibility; either by the drug users, local drug dealers or via storage of heroin in anthrax contaminated surroundings. Had this been the scenario, it is more probable that multiple strains of anthrax would have been detected in the human cases. Investigations in other recent UK anthrax cases (e.g. the 2006 Scottish Borders case) identified multiple anthrax strains in the environment associated with these cases. The single strain found in the drug user cases in Scotland (and elsewhere) was not consistent with multiple spore contamination episodes but was consistent with a single origin and a single contamination episode.

5.2.4. Contamination by Drug Users During Heroin Preparation

Illicit heroin sold in the UK is normally in powder form and is relatively insoluble in water at normal pH. Heroin is therefore normally mixed with water and mildly acidic materials (e.g. citric acid or lemon juice) to improve its solubility. The resulting pH is around 2.5, sufficient to kill non-spore bacteria but not sufficient to destroy spores. The heroin, mixed with water and acidic material, is usually heated over a flame to bubbling point to dissolve the drug prior to injection. The temperatures reached are typically 65 to 75 Celsius, not high enough to destroy spores and indeed might encourage germination (Brett et al, 2005).

Citric acid and other agents used in injecting heroin preparation are usually sourced locally by individual drug users from local chemists or other shops and are therefore very unlikely to have originated from a single common batch. There was no evidence to suggest that materials (such as citric acid) used by drug takers had been contaminated with spores.

Likewise, contamination of drug paraphernalia (needles, syringes etc.) was considered to be an unlikely explanation for the origin of the anthrax spores; finding a single unique strain of anthrax in the cases was unlikely to be consistent with multiple independent paraphernalia contamination events.

It was suggested that inadequate heating (cooking) of heroin, prior to injection might have increased the risk of infection. This hypothesis was based on an assumption that anthrax spores would normally be destroyed by heating as practiced by drug users. However, evidence from the previous *C. novii* outbreak suggests that the temperatures achieved by flame heating of heroin during heroin injection preparation, would be unlikely to destroy all anthrax spores (Brett et al, 2005). Data from work on the temperatures required to destroy anthrax spores indicated that boiling in water at 100 Celsius for 5 to 10 minutes is required (Spotts Whitney et al, 2003; Brazier et al, 2003); heating for this duration is not consistent with preparing heroin for injection use and would probably render the result unusable. On that basis it seems extremely unlikely that anthrax contamination of drug paraphernalia, by the heroin users themselves, or variation in the use of acid solutions or flame heating could explain the distribution of cases and the descriptive epidemiology of the outbreak.

5.2.5. Conclusion on the Most Likely Outbreak Hypothesis

There was a lack of direct evidence to support any specific hypothesis for the cause and distribution of the outbreak. The evidence available consists of the clinical, epidemiological and microbiological data, especially the genotyping data, together with the data from the police investigations.

No cases of anthrax were identified involving anyone other than active users of illegal (street bought) heroin. Contaminated heroin therefore appeared to be the most likely vehicle of spore transmission. Microbiological analysis of heroin samples from a variety of locations failed to find anthrax spores. This was not unexpected, given that the number of spores in any sample was likely to be very small and the heroin used by a case before they became unwell was usually all gone by the time investigations were started. The prospects of finding any contaminated heroin were therefore slim. Nonetheless, the epidemiological evidence in this outbreak suggesting that heroin was the primary vehicle for the transmission of anthrax spores to the cases, was very strong.

How the heroin was actually contaminated will never be known with certainty. However, there was strong evidence to support the view that there had been a single common source for the anthrax spores. The genotyping analysis identified that the anthrax isolated from the outbreak cases all shared a common novel clonal strain, closely related to strains identified previously from anthrax infected goats in Turkey. This was further supported by evidence obtained by Strathclyde and other police forces on the heroin trafficking trade routes. The most likely countries of heroin origin were identified as Afghanistan and Pakistan. Intelligence confirmed that supply networks for heroin involved Turkey, the Balkans, Eastern Europe, Germany/Netherlands then the UK. There were independent reports on the use of goat skins in heroin trafficking. This evidence supports a view that anthrax spores were introduced to illicit heroin at a point sufficiently close to the source country, to enable distribution of a common contaminated batch of drug to dealers and then on to heroin users in Germany, England and Scotland.

5.3. Outbreak Characteristics

5.3.1. Outbreak Chronology

The outbreak started in late December 2009 in the Glasgow and bordering Lanarkshire areas, peaked within a matter of weeks in January to March 2010 but persisted for months into summer 2010. In the UK context the outbreak did not end until November 2010, indicating that contaminated heroin remained in circulation within the UK for a protracted period. This prolonged risk contrasted with the previously held view that heroin turnover would be relatively rapid and that any contaminated heroin was likely to be used up rapidly. However, the prolonged duration was consistent with previous drug use related outbreak experience; e.g. the *C. novii* outbreak in 2000 in Scotland (McGuigan et al, 2002).

Police intelligence indicated that dealers anticipated an increased demand for heroin over the Christmas and New Year period. It might be possible that if the amount of heroin imported into Scotland increased, this could have encouraged importation of poorer quality heroin, carrying a higher risk of environmental microbiological contamination. There is no direct evidence to confirm this theory; however the number of soft tissue infections among drug users during the early outbreak period generally (both anthrax and other infections) was noteworthy. The total number of drug user infections that were anthrax negative (including the additional 153 patients tested for anthrax but not reported) indicates that there was a lot of infection experienced by drug users in the outbreak period and could indicate that the heroin then circulating was more microbiologically contaminated than usual. A variety of co-infections with other organisms were also noted in anthrax cases. The epidemiology of infections in drug users has not been described previously in sufficient detail to enable close comparison.

Anthrax continued to occur in Scotland for (at least) an 8 month period (December 2009 to July 2010) indicating that contaminated heroin remained in circulation for a minimum of that period and in England until November 2010. The apparently prolonged period that contaminated heroin remained in circulation was not consistent with previous expectations regarding the rapid usage of heroin supplies.

5.3.2. Outbreak Distribution

Most anthrax cases occurred among heroin users in the West of Scotland but with notable clusters in Tayside (Dundee) and Dumfries & Galloway (Dumfries). The cluster of cases in Dumfries occurred later than elsewhere suggesting a delay in contaminated material reaching this area. By contrast, some areas of Scotland with sizeable heroin using populations (e.g. Lothian and Grampian NHS areas) had very few cases and others had none at all. Explanations for the distribution of cases across Scotland may include the following:

- Police intelligence indicated that drug supply networks in different parts of Scotland are quite distinctive; networks supplying Edinburgh and the south east of Scotland are normally different to those supplying Glasgow and the west. The distribution of *C. novii* cases in the 2000 outbreak was similar to that for the anthrax outbreak and may also have been related to patterns of heroin distribution at that time. Importation of a single contaminated batch of heroin to a Glasgow distribution node and its subsequent sub-division and dispersal, could explain the subsequent pattern of anthrax cases.
- Police intervention to seize heroin supplies from dealers sequentially in new areas as new cases occurred, might have influenced the subsequent progressive dispersal of suspect heroin supplies from the Glasgow/Lanarkshire locus to elsewhere; e.g. Dumfries, leading to the sequential progress of new outbreak cases in more areas. However, cases occurred at the start of the outbreak in Dundee, in December, indicating that contaminated heroin was already dispersed across Scotland even at an early stage.

5.3.3. Epidemiological Characteristics of Anthrax Cases

Based on comparison with drug users recorded on the Scottish Drugs Misuse Database (SDMD), anthrax cases were slightly but not significantly older than the average in Scotland. Cases were

more likely to have reported taking heroin by injection and for longer compared to non-cases; more cases were recorded as having opioid substitution therapy and were more likely to report alcohol use prior to their last addiction service attendance. Few of the cases gave a history of past infection with hepatitis viruses or with HIV. Other general health status related factors, which might have predisposed individual drug users to developing anthrax infection could not be investigated thoroughly due to lack of data but could not be excluded completely either (e.g. having a high alcohol intake; having generally poorer health or poorer nutrition). All of these factors might have been relevant to determining individual case's susceptibility to infection but would have required a prospective study to investigate further.

5.3.4. Quantity of Heroin Used and Concentration of Spores

Situations occurred wherein two or more heroin users shared a "bag" of heroin; one developed anthrax yet the others did not. This might suggest that the number of anthrax spores in any single heroin dose was very low and that the risk of exposure to anthrax spores may therefore have been relatively random. Alternatively it might suggest that individual medical or other risk factors contributed to the probability of clinical anthrax illness following an exposure to viable spores. As no anthrax spores were identified in any heroin samples, it was not possible to calculate a likely range for the concentration of spores in heroin or to calculate the risk associated with the quantity of heroin used by any individual drug user.

5.3.5. Methods of Heroin Taking (Exposure Routes)

Cases reported a mixed pattern of heroin use; cases often gave a history of injecting heroin either directly into their blood stream (IV injection), or injecting into deep soft-tissues or muscle (IM injection). Some injected into tissues inadvertently by missing a targeted vein, frequently in the groin area. Some deliberately attempted more superficial skin or muscle-popping injections. In many cases, individual drug users used a mixture of injection methods within a short space of time, frequently reporting injecting three or more times per day into the same or different sites. It was therefore very difficult to identify one particular injection episode as being the incriminated (or culprit) injection, responsible for introducing the spores that caused the infection. Calculation of specific risk ratios for exposure associated exclusively with IV, IM, or sub-cutaneous injection was therefore not possible with any confidence from the case data.

In the *C. novii* outbreak, intramuscular injection (muscle-popping) appeared to be a relatively common factor (McGuigan et al, 2002). In the anthrax outbreak muscle-popping did not feature prominently. Most cases (who provided data) reported injection use of some sort, either exclusively or as often in combination with other methods. Some reported exclusively non-injection methods of taking heroin (e.g. smoking).

The retrospective case-control study which compared cases to non-case heroin users (historically) showed that cases had a longer history of injection use of heroin; cases were relatively less likely to have smoked heroin exclusively. The conclusions from this retrospective work are limited to an extent by the study design and the reliance on both cases and controls being drawn only from drug users who had a past history of attending addiction clinics. Attendees at drug clinics may have a longer heroin habit with a longer injection history and may be more likely to have taken heroin by injection and so may be over-represented among heroin users who attend such clinics.

Anthrax spores can cause infection if; inoculated into tissues (via injection); ingested; or inhaled (causing respiratory anthrax). In all these forms of anthrax illness there is an increased likelihood of generalised systemic infection due to blood-borne spread of the organisms and toxins. A number of the early anthrax cases were admitted with advanced systemic infection; some without any history of injecting heroin but a history of taking heroin by other routes, principally smoking.

Smoking or snorting contaminated heroin would allow viable anthrax spores into the upper respiratory tract (mouth, nose and nasopharynx), the lower respiratory tract and/or the gastrointestinal tract. Hence, either ingestion or inhalation of spores could result in illness presenting with haemorrhagic meningitis, circulatory collapse, coma, multi-organ failure, and blood clotting abnormalities. In the early stages of the outbreak, cases presented with such features.

The risk attributable to any one method of taking heroin could not be calculated with confidence and could not therefore be used as a basis for providing advice to drug users at the time. The NAOCT concluded that it could not rule out the risk of anthrax infection via any form of exposure to contaminated heroin, including inhalation. Consequently, no form of heroin use was considered by the NAOCT as safe. The danger of giving falsely reassuring advice on the relative safety of taking heroin by inhalation was highlighted by one drug user, with a history of being a former habitual heroin injector, who changed their habit to smoking heroin on the basis that this might be safer. He subsequently developed systemic anthrax.

5.4. Lessons Identified

5.4.1. Outline of Lessons Identified

Lessons identified during the outbreak and others highlighted as part of the formal NAOCT debriefing relating are described, listed under the major components of the outbreak investigation and response. These form the basis for the recommendations which follow in Section 6 of the report.

5.4.2. Planning and Preparedness for Anthrax Outbreaks

Although this was a highly unusual event, outbreaks of infection with spore forming organisms had occurred previously among injecting heroin users in the West of Scotland drug using population. The risk of anthrax infection specifically, in drug users, was highlighted by the case of anthrax in a drug user in Norway. An outbreak of anthrax somewhere associated with drug use was therefore perhaps almost inevitable.

Planning for anthrax outbreaks in recent years has focussed particularly on the risk of a deliberate organism release (a CBRN attack). Recent experience of anthrax cases (in the UK) has been with non-CBRN, non-drug user cases, associated with exposure to recreational anthrax risks (e.g. contact with contaminated West African Djembe drums). No specific planning had been undertaken for an anthrax outbreak among drug users; the response was therefore modelled on a generic outbreak response.

The anthrax case in the Scottish Borders involving a musician in 2006 raised awareness of the signs and symptoms of anthrax and the potential for unusual anthrax presentations. Microbiologists in Scotland were, at that time, advised on the identification of *Bacillus species* organisms and the need to refer suspicious isolates to the relevant HPA reference laboratories. Information on the signs and symptoms, diagnosis and treatment of infections classed as CBRN threats including anthrax was also distributed by HPS to the NHS in Scotland; Public Health departments, A&E departments and other Clinicians.

The initial clinical presentation of cases in Glasgow (as serious soft tissue infections (SSTIs)) was not unusual for this drug using population; approximately 34% to 37% of injecting drug users seek medical attention for an injection related wound site infection in the UK, in an average year (Hope et al 2008; Hope et al 2010). Features that were thought to be unusual included the degree of limb and other tissue swelling (oedema) associated with localised injection site infection; painless soft tissue infection, even when this resembled severe necrotizing fasciitis; and the absence of a high temperature or other signs of septicaemia, which might normally be expected. Prior to this outbreak clinicians would not have been aware that such features might indicate anthrax infection specifically in drug users.

5.4.3. Microbiological Capacity and Preparedness

Identification of a *Bacillus species* colony in a blood culture from an early case by the microbiology laboratory at the Southern General Hospital was the first indication of a possible anthrax infection. This was subsequently confirmed as *B. anthracis* by the HPA-NDPL. Had specific anthrax confirmation facilities been available within Scotland, this might have reduced by a small margin the time between initial isolation of the suspect organism and positive confirmation. In practical terms, the timing of final confirmation by HPA did not delay commencement of appropriate antibiotic treatment for suspected cases.

The rapid detection of future outbreaks will depend on early recognition of possible cases, appropriate public health investigation, and rapid microbiological confirmation. Periodic refreshing of awareness of anthrax among hospital clinicians, microbiologists and others may be useful in this respect. Monitoring unusual infections and unexplained sudden deaths among drug users could also be important in the early identification of case presentations suggesting anthrax or other unusual infections. Action on such issues could help to enhance planning and preparedness for future anthrax outbreaks, involving drug users or others.

Serological testing for anti-anthrax toxin antibodies formed an important and novel part of the microbiological testing regime in this investigation. Twelve cases were confirmed on the basis of positive paired serology. Serology testing was also used to confirm cases in the 2001 bioterrorism anthrax outbreak in the US and was a critical component in the confirmation of six of those cases. In that outbreak it was noted that due to timing factors and the effect of early antibiotic treatment eradicating live organisms, diagnostic methods such as culture and PCR may fail to yield useful information; hence serology may be the only alternative option to confirm a diagnosis (Quinn et al 2004). Serological data also helped to identify that the earliest US case occurred a week earlier than originally estimated and in a different location (in New York State) to that initially thought. The authors also noted that there is a general lack of data characterising the human immune response to anthrax illness. The serological investigations in this recent outbreak will therefore be an important source of data to add to the body of knowledge on serology in future.

5.4.4. Outbreak Investigation and Management

a. Organisational aspects of the outbreak investigation

Once the outbreak was identified, the formal processes to co-ordinate and manage the outbreak were quickly instituted. The NHS GG&C HPT managed the initial stages of the outbreak including communications with local clinicians, drug users, drug and addiction services and the wider media, including holding a press conference. When it became clear in January 2010 that the outbreak was widespread and had become effectively national, the co-ordination and management transferred to HPS.

The NHS GG&C (local) OCT initiated much of the early work on risk assessment and management activities. This work was continued via the NAOCT. HPS, as national investigation lead, ensured access to national level health protection resources and to UK and international bodies (HPA, ECDC, CDC, WHO etc.). The national nature of the outbreak involved considerable collaboration with non-NHS agencies including the COPFS and Strathclyde Police, taking the lead police force role.

The NAOCT was generally considered (by members and partners) to have worked well, particularly in assisting the efforts of Strathclyde Police and the COPFS to manage the outbreak on a national basis. Other agencies, including HPA, found it helpful to have a single (Scottish) co-ordinating body to liaise with and to harmonise the development of common guidance across the UK. Co-ordination and rapid dissemination of advice and guidance to clinicians and others involved at local level was greatly facilitated by use of the HPS website and dedicated electronic alerting networks.

b. Case identification

Local clinicians were encouraged to report any suspected cases to their local NHS board; details of suspected cases were then passed between NHS boards HPTs and HPS. In general these systems worked well; there was some concern regarding variation between areas in the completeness of reporting of initially suspect cases. It was difficult to maintain an optimal balance between reporting all potentially suspect cases (e.g. every drug user with any soft tissue infection) and a need to use investigation resources efficiently. The submission of specimens to HPA-NDPL from a substantial number of unreported drug users with infections was interesting in this respect; such cases did not (apparently) merit official reporting but local clinicians/ microbiologists clearly valued the reassurance of excluding anthrax by microbiological testing. None of these unreported drug user infections were confirmed as anthrax, suggesting that the anthrax clinical case definition criteria were appropriately discriminatory and were being appropriately used at local level.

c. Case interviews

An epidemiological investigation questionnaire was first developed in late December 2009, for use by the NHS GG&C HPT based on examples from previous drug user infection outbreaks. The completeness and quality of information collected via the questionnaire varied. Cases were sometimes too ill to be interviewed, were often poor historians and sometimes changed their account of events. Forms were sometimes completed by (otherwise busy) clinicians, for whom the public health investigation was not necessarily the priority. To improve data quality, questionnaires

should ideally be completed by HPTs or others familiar with the format and purpose of the questionnaire. Potential improvements to the style and formatting of questions, to facilitate better completion have been noted.

It proved difficult using the available data to carry out a sufficiently robust statistical analysis of heroin taking methods used by cases, to allow a meaningful assessment of the relative risks of different exposure routes. As a consequence, these data were unsuitable as evidence on which to base advice on whether any particular method of taking heroin was associated with a higher or lower risk.

At the NAOCT debrief, the SDF suggested that trained drug workers might provide a useful resource to help conduct case interviews. Such staff have extensive knowledge and understanding of drug-taking practices and might therefore be well placed to help elicit better quality information and so improve the quality of data collected on drug use behaviour.

d. Sharing case information with the police

There was sometimes a reluctance to share information with police at local NHS level. It was agreed that the police would not interview cases unless they were classed as confirmed or probable cases. This inevitably introduced some delay in police questioning. Cases who were only clinically suspected were not usually interviewed by the police. Consequently both public health and police investigation data were lacking detail for cases classed finally as possible cases. Ideally, in any future outbreak, data collection would be more consistent for all suspected cases.

Continual efforts were via the NAOCT to encourage co-operation and information sharing between the NHS and the police. Persistent concerns however, led to the Chief Medical Officer (CMO) for Scotland issuing specific guidance on sharing clinical data during the outbreak. It would be useful to incorporate this advice in future outbreak guidance, to cover scenarios where a joint public health and police/Procurator Fiscal investigation is necessary.

e. Role of drug and addiction services

During the outbreak, drug service co-ordinators played an essential role in relaying advice and warnings to other drug service workers and to drug users directly. The SDF cascaded information and held a number of briefing sessions for drug services staff. SDF acknowledged that this effort relied on a relative small pool of staff and that a wider pool would be useful in any future event, to cascade messages more quickly.

The lessons from the outbreak could be used by the statutory and voluntary drug service agencies to develop plans, including communication protocols and briefings, on dealing with drug contamination outbreaks or incidents in future.

f. Clinical involvement in the outbreak management

Clinical input to the NAOCT was provided via the Anthrax Clinical Network (ACN), operated as a teleconference based forum for clinicians across Scotland (and beyond) who were actively involved in the diagnosis and management of anthrax cases. The ACN was facilitated by HPS and chaired by an Infectious Diseases (ID) Physician, with representation from a wide range of disciplines including: ID physicians; microbiologists; pathologists; intensive care physicians; surgeons and public health consultants.

There was a lack of practical experience within Scotland in managing anthrax infections. This forum acted as a clinical consultation group to help develop guidelines and infection control guidance. The ACN therefore provided a means of establishing a rapid clinical consensus on best practice, especially where published evidence was lacking.

The NAOCT concluded that the ACN mechanism, facilitated by HPS and led by clinicians, enabled a broader range of clinical input to the outbreak investigation and its management than might have been possible via a single clinician as a representative on the OCT. This model could therefore be useful for future outbreaks, especially unusual infections.

The HPA set up a parallel Clinical Network but with a more international focus, involving anthrax experts from the US National Institutes of Health and elsewhere. This parallel network provided useful access to additional international expertise.

g. Risk assessment

Considerable effort was devoted by the NAOCT membership in developing guidance on the potential risks of infection associated with exposure to anthrax spores during social, casual and occupational contact with cases; their homes and belongings and specifically contact with potentially contaminated heroin. Advice was circulated to a wide range of individuals and agencies, both within NHS and beyond including police, prison staff and social work staff. This guidance should remain relevant in any future anthrax incidents.

h. Risk management - control measures and risk communication

Due to the uncertainties in relation to understanding the scenario as it progressed; the options for controlling the outbreak and preventing further cases were limited:

- The total quantity of contaminated heroin in circulation was not known, nor was how long this would remain active within Scotland.
- The source of the heroin was not known and neither was the point at which anthrax spores were introduced; whether at the country of origin (Afghanistan or Pakistan); during transport and re-packaging; whether contamination occurred within Scotland at a very local drug distribution/dealer level, or at multiple different locations and multiple periods.
- It was not known whether there had been a single batch of contaminated heroin imported prior to December 2009, which had been widely distributed or whether multiple batches of contaminated heroin were continuously imported.

As a consequence, it was impossible to predict the scale or duration of the outbreak. The main risk management (control and prevention) interventions therefore relied on action by the police to control drug supplies and action by NHS health protection services, to provide advice on infection risk reduction.

Police Action

Strathclyde and other police forces identified drug dealers and their supply networks; intervened to interrupt these, seized heroin supplies and prevented further heroin distribution. The police interrupted at least one well characterised network that linked Illicit (street bought) heroin supplies in Scotland to a distribution chain leading back from Scotland ultimately to heroin produced in Afghanistan.

There was a clear need to respect legitimate concerns regarding patient confidentiality and to comply with existing legislative and internal NHS requirements for data protection. The concerns of NHS staff regarding patient confidentiality were understandable, as was the wish to have documented guidance.

Intervention on drug supplies however, relied on intelligence gathered by the police, in turn dependent on the ability of the police to interview cases and their contacts. In order to protect public health it was essential for the NHS to work with the police and COPFS, especially given the limited scope for direct NHS intervention to control the hazard (contaminated heroin). The lessons from this experience will be useful in future.

NHS public health action

Public health protection interventions focussed on communicating about the risks of anthrax infection and advising on risk avoidance for heroin users and others.

There was little alternative to the NAOCT but to consider that all heroin supplies within Scotland in circulation from mid December 2009, were potentially contaminated and therefore potentially posed a risk of causing anthrax infection. This conclusion formed the basis of advice that heroin users with symptoms should seek urgent medical attention; should stop using heroin and should seek advice on addiction treatment as a matter of urgency. The NAOCT considered that there was no practical alternative to this advice at the time. The HPA also adopted this advice when cases occurred in England.

Some drug service agencies expressed concern that the advice on heroin avoidance/abstinence would be ignored and would therefore be ineffective. There was pressure to recommend a safe method of heroin use, based on advice issued during the *C. novii* outbreak in 2000. In that outbreak drug users who deliberately injected into muscle tissue (muscle-popped) were at higher risk of infection. Advice was therefore issued that muscle-popping was more dangerous and should be avoided specifically, and that alternatives such as inhalation (smoking) were relatively safer. Providing such advice was not considered to be an option available to the NAOCT.

The risk that heroin (and other recreational drugs) could be contaminated again with anthrax (or other pathogens) remains. Drug users should therefore be reminded of this infection risk and continually advised to avoid high risk exposures, especially any form of injection. Voluntary and statutory drug agencies (SDF etc.) could have a role in communicating such messages.

i. Alternative control measures

(i) Provision of prescribed heroin

Supplying *(*prescribed), spore free heroin to all heroin users in Scotland was suggested as a control strategy. The NAOCT considered that this suggestion was highly controversial and that it would require high level Government consideration from a drug policy perspective. The NAOCT therefore considered this issue to be outside the competence of the group and made no recommendation on the matter. The NAOCT expressed no opinion on the merits or risks of advocating such a control measure. However, the NAOCT recognised that it would be helpful to have definitive guidance on whether or not such an option would be practical as an emergency risk control measure in a future outbreak involving illicit heroin or other drugs. It was therefore considered that relevant Government departments could usefully give this aspect further consideration and provide guidance for future OCTs.

(ii) Vaccination

There was no experience of using the existing UK (human) anthrax vaccine (designed originally for occupational risk protection) to control an active anthrax outbreak. Providing anthrax vaccination to all heroin users in Scotland would have been a major logistical undertaking during the outbreak response and was therefore considered to be impractical in the context of an ongoing outbreak. The multiple dose schedules meant that it would have been very difficult to achieve the levels of uptake necessary for effective immunisation within a reasonable time period. Even when used in the target group for the protection of healthy individuals from occupational risks of exposure, the vaccine has potential adverse effects; the effects of its use in an already unfit population group could not therefore be predicted. For these reasons, vaccination was not considered a practical outbreak control option. Further consideration might be given to the practicability of prospective anthrax vaccination if further evidence justifies the need to consider this further.

(iii) Antibiotic prophylaxis for anthrax

Use of antibiotics to prevent infection in heroin users was considered as a control measure but also dismissed as being impractical, as well as potentially undesirable, by the NAOCT. Prophylaxis would have had to continue for almost a year. Retaining compliance with even three months prophylaxis in well motivated individuals exposed to a risk of anthrax infection can be problematic, as found in the Borders anthrax case in 2006. Compliance in the drug using community was assessed as unlikely to be any better. The logistic and other issues associated with trying to organise delivery of such a strategy were such as to render it completely impractical. This option maybe appropriate in other circumstances (and was used in the US outbreak in 2001). However, prophylaxis is unlikely to be a useful strategy in a future wide-scale drug related anthrax outbreak situation.

5.4.5. International Aspects

The evidence points to the importation of anthrax contaminated heroin from outside Scotland as the vehicle for transmitting anthrax spores to cases.

Detailed investigation of heroin distribution networks across Europe and beyond was carried out by Strathclyde and other police forces. This work helped to develop a plausible explanation linking cases in Scotland, England and Germany (living near the Dutch/German Border), and links to known heroin distribution networks. Intelligence gathered via international links provided strong evidence to support the main hypothesis; that the heroin contamination was more likely to have occurred nearer the heroin source country, than to have occurred locally in Scotland, the UK or elsewhere in Europe. Evidence identified plausible links to heroin distribution chains through Turkey. This was particularly significant in view of intelligence on the use of goat skins in the transport of heroin reported from the Middle East. This was significant especially in terms of the microbiological genotyping evidence that the anthrax strains in Scotland were most closely related to strains previously identified in goats in Turkey.

The health protection investigation also relied on extensive international collaboration with colleagues from the HPA, especially the Novel and Dangerous Pathogens Laboratory (NDPL) at Porton Down, co-ordinated by Dr Tim Brooks, Medical Lead of NDPL. This was pivotal to

the overall outbreak investigation. Colleagues at HPA Colindale Centre for Infections were also particularly helpful in facilitating co-ordination with the HPA OCT, set up to investigate cases in England. There was extensive cross representation between the respective UK constituent country OCTs operated by HPS and HPA. Co-ordinated guidance and advice on the risks of anthrax across the UK was essential to ensure unanimity in the health protection strategy for managing what was in fact a UK outbreak.

HPA provided the link between HPS and the ECDC based in Stockholm, Sweden. One outstanding issue remains the ECDC case definitions for anthrax, which were not ideally suited to the outbreak investigation. It would be helpful to consider the scope for modifications to the ECDC definitions, in collaboration with colleagues in HPA and ECDC.

The investigation was also characterised by the generous and invaluable contributions from international colleagues, especially from the US Centres for Disease Control and Prevention (CDC). CDC staff were involved from a very early stage supporting the outbreak investigation and supervising the use of Anthrax Immune Globulin - Intravenous (AIGIV) (not normally available in the UK), which CDC provided. CDC liaised with the US Department of Health and Human Services (HHS) and other US agencies to maintain supplies of anti-toxin, ensuring rapid access to the treatment for cases from December 2009. The quality of support provided from CDC colleagues cannot be over emphasised and added significantly to the effectiveness of the outbreak response.

Access to international level expertise was also pivotal to the investigation. Professor Paul Keim of Northern University of Arizona played a vital role, working with colleagues at HPA-NDPL, to provide expertise in the typing of anthrax strains and comparison to strains identified globally. This led ultimately to the conclusion that the Scottish strains were most closely related to those from goats infected with anthrax in Turkey.

5.4.6. Drug Policy Aspects

Relevant Government departments may wish to consider the implications of this (and earlier) outbreaks involving infections associated with contaminated illicit drugs. Although potentially controversial, the utility of providing contamination free drug supplies as a strategy to control any future illicit drug related outbreak may deserve further examination. A Government view on this potential control measure could assist the NHS, the police and judicial services within the UK, in planning future outbreak response strategies.

5.4.7. Economic Aspects

The outbreak investigation resulted in the use of considerable resources from the NHS, police, COPFS and other statutory and voluntary sector agencies. The costs to the NHS in Scotland associated with the treatment of outbreak cases alone have been significant. There might be benefit in quantifying the costs of the outbreak in more detail, in order to help inform decision making on the costs and benefits of strategies for controlling or preventing such outbreaks in future.

5.4.8. Future Research

Although the NAOCT were satisfied that a plausible explanation for the outbreak has been identified, linking the epidemiology of the cases to a possible source of anthrax and a plausible vehicle of transmission, many outstanding questions remain.

Further research may be of value to determine why the drug using population, particularly in the West of Scotland, appears to be more prone to such outbreaks of bacterial infection (e.g. *C. novii*, anthrax and other infections).

There is very little data on the sero-epidemiology of anthrax in the UK population. This made the interpretation of serology test results on anthrax anti-toxin levels in cases more challenging. Useful information could be gained from sero-epidemiological work to establish if sub-clinical infection with anthrax occurs in the UK population (especially among drug users). Better data on the background sero-prevalence of antibodies to anthrax in the general population would be useful to better understand the background epidemiology of anthrax exposure and infection within the UK population.

Further work on the interpretation and utility of serological testing for anti-bodies to anthrax toxins would also be useful, to assist in refining the understanding of markers for clinical anthrax infection, and to inform discussions on revision of ECDC anthrax case definitions.

6. Conclusions and Recommendations

6.1. Key Conclusions

6.1.1. Outbreak Genesis

The outbreak was the largest single common source, non-occupational human anthrax outbreak recorded in the UK, since systematic notification of non-occupational cases began in 1960 and was associated with the use of illicit heroin, which probably originated in Afghanistan or Pakistan.

6.1.2. Source of Anthrax Spores

The spores from which the anthrax organisms originated came from a single common source, probably a single infected animal or hide. The anthrax organisms were all identified as being of a single, novel anthrax strain not seen before in the UK or elsewhere but closely related to strains seen previously in goats in Turkey.

6.1.3. Heroin Contamination

The contamination of heroin with anthrax spores probably occurred as a result of contact between heroin and a source of spores, somewhere in the drug distribution network close enough to the country of origin to enable heroin from a single contaminated batch to be imported by drug dealers to all of the countries where anthrax cases occurred (Scotland, England and Germany).

6.1.4. Distribution networks

Heroin users in the West of Scotland especially Glasgow and Lanarkshire, and in Dundee were at increased risk of anthrax infection compared to others living in Lothian (Edinburgh), Grampian (Aberdeen), the Highlands and Islands; probably as a result of the differing distribution networks for illicit heroin in Scotland but possibly also related to unknown underlying factors associated with the general health status of heroin users living in the more heavily affected areas, including their use of alcohol.

6.1.5. Contaminated Heroin Exposure

Infection occurred mainly between December 2009 and March 2010 indicating that the peak exposure to contaminated heroin also occurred just before and during this period then remained in circulation within Scotland (and England) for almost a year. However, the possibility that anthrax contaminated heroin had been imported to Scotland prior to December 2009 cannot be completely excluded only on the basis that no cases were detected earlier.

6.1.6. Drug User History

Drug users with a longer history of heroin use appeared to be more at risk of infection, possibly associated with their increased likelihood of taking heroin by injection methods.

6.1.7. Control Measures

Options for control measures to prevent infection among drug users were limited and relied on police action to reduce the amount of heroin in circulation and curtail heroin dealing, and public health action to advise drug users and others of the risks of continued heroin use. Other control options were considered but were assessed as being impractical.

6.1.8. Advice to drug users

The NAOCT issued advice to drug users not to take any heroin based on the evidence available at the time. Evidence from the subsequent retrospective case-control study suggests that there may have been an increased risk of infection associated with injecting heroin in particular. However, given the limitations of the study method, this evidence has to be interpreted with caution.

6.2. Summary Conclusion

The epidemiological and microbiological evidence supports a conclusion that heroin was the vehicle for transmission of anthrax spores to cases and that exposure was by a variety of routes, particularly by injection but also by smoking (inhalation). The mechanism for and the location of spore contamination are not known, however genotyping evidence strongly suggests that infection was due to a single, novel, anthrax strain related to Trans-Eurasian (TEA) anthrax strains previously identified in goats, in Turkey. This and other intelligence on the heroin trafficking trade supports a conclusion that the contaminated heroin imported to Scotland was from a single batch contaminated with anthrax spores via contact with a single infected animal or contaminated hide, somewhere in transit between Afghanistan/Pakistan and Scotland, probably in Turkey.

6.3. Good Practice Points

Planning and Preparedness for Anthrax Outbreaks

- Local NHS boards Health Protection Teams (HPTs) should encourage early alerting by local clinicians (particularly A&E & ITU) of any unusual patterns of infection among drug users including suspected anthrax. Other sectors involved in drug service provision could also have a role in early alerting (e.g. injection paraphernalia providers). *(Attention of NHS boards).*

- Clinicians (A&E Physicians, ITU Staff and Surgeons etc.) should be reminded periodically about the signs and symptoms of anthrax infection (classical and atypical anthrax presentations) and the need to take blood samples for blood cultures, before antibiotic treatment is commenced for any suspected anthrax infection. *(Attention of Scottish Government, HPS, NHS boards, Scottish Microbiology Forum (SMF)).*

- NHS Scotland microbiologists should be reminded periodically of the microbiological features of anthrax and the protocols for its identification via appropriate professional channels. *(Attention of HPS, SMF).*

- The protocols for sending microbiological and pathology samples for *B. anthracis* testing at HPA-NDPL should be clarified to differentiate clearly between samples that require urgent investigation to exclude anthrax in highly clinically suspicious cases, compared to samples of a less urgent nature. *(Attention of HPS, HPA, SMF).*

- Local NHS board HPTs, statutory and voluntary drug services and local police forces should develop plans for collaborative working and joint public health and police investigations, particularly for future incidents involving the use of contaminated street drugs. *(Attention of NHS boards, police forces and Scottish Drugs Forum (SDF)).*

- HPS should incorporate lessons from the outbreak relating to preparedness, responsibilities and resources into internal plans for managing National outbreaks of drug related infections, including anthrax. *(Attention of HPS).*

- A teleconference based Clinical Forum, as developed in this outbreak, should be considered as a useful mechanism for obtaining broadly based clinical input to any future OCT. *(Attention NHS boards, HPS).*

Outbreak Investigation and Management

- Epidemiological investigation questionnaires for use in the investigation of cases of anthrax should be refined to facilitate improved data collection on a range of potential environmental anthrax exposures, including details of drug use practices associated with possible anthrax exposure. *(Attention of HPS, HPA).*

- In any future drug related outbreaks, NHS boards should consider the potential role of appropriately experienced drug service workers in assisting in the collection of detailed information on drug use behaviours. *(Attention of NHS boards, HPS, SDF).*

Risk Assessment

- The risk assessment and other guidance material on infection control and occupational exposure risks developed during this outbreak should remain available for future use and should be refined further to provide generic guidance for use in future anthrax exposure and infection incidents. *(Attention of HPS, Health Protection Network (HPN))*.

Risk Management (Control Measures)

- Drug addiction and treatment services should take opportunities to advise drug users of the risks of infection from a variety of pathogens including anthrax, associated with using heroin or other uncontrolled street drugs by any method. *(Attention of NHS Scotland, SDF, local drug service providers)*.

Risk Communication

- In any future drug use related incident, NHS board HPTs should seek early involvement of local drug addiction services, to assist with the rapid dissemination of information and advice to drug users. *(Attention of NHS boards, local drug service providers)*.

6.4. Recommendations

The recommendations are derived from the lessons identified and could apply equally well to other parts of the UK and more widely.

Planning and preparedness

1. Further consideration should be given to the practicability of options for enhancing microbiology capability to identify and confirm *B. anthracis* within Scotland. *(Action by HPS, HPA, SMF)*.

Risk management (control measures)

2. Further discussion could usefully be held between Health Protection services and Government Departments with respect to the best ways of engaging drug treatment, care and recovery services during outbreak situations. In addition, the extent, if any, to which emergency outbreak control considerations should influence clinical decisions about the prescribing of a controlled drug such as diamorphine could usefully be clarified, with the aim of providing guidance to future OCTs and addiction services. *(Action by HPS, Scottish Government Health Directorate, HPA, UK Government Department of Health)*.

Risk communication

3. In the event of a future outbreak involving anthrax contaminated heroin, advice to drug users should emphasise that any form of taking heroin (via injection routes or smoking), could result in a fatal anthrax infection and that injecting by any route (IV, IM or SC) is likely to carry a higher risk. Advice should however avoid suggesting that smoking (or snorting) heroin is a risk free alternative to injection. *(Attention of NHS boards, local drug service providers)*.

Knowledge sharing

4. Maximum use should be made of the data collected during this outbreak to ensure effective knowledge management of new learning obtained on anthrax infection, its diagnosis, treatment and prevention, and to identify opportunities for further research. *(Action HPS, Scottish Government).*

Future research

5. Options for research aimed at investigating unresolved questions associated with this event, including the reasons for the preponderance of significant and unusual outbreaks of infection among drug users particularly in West Central Scotland, should be explored. *(Action by HPS, NHS boards, Scottish Government, SDF).*

International aspects

6. In the light of the findings of this outbreak investigation, options for proposing a review of the current ECDC case definitions for anthrax should be explored. *(Action by HPS, HPA).*

Economic aspects

7. The benefits of carrying out a detailed economic appraisal of the costs of the outbreak should be considered further. *(Action by HPS, Scottish Government).*

Acknowledgements

I am indebted to colleagues, both members of the NAOCT and the many others involved, whose work over a prolonged period was essential to the completion of the investigation.

Thanks are owed to the NHS microbiologists and clinicians who reported cases to their local Health Protection Teams (HPTs) and contributed to the work of the Anthrax Clinical Network (ACN); to colleagues in the NHS boards HPTs who conducted the field investigations and who supplied the collated case data for analysis; to Dr Kitty Smith, HPS and Dr Andrew Todd, Monklands General Hospital for facilitating the ACN; Dr John Hood Consultant Microbiologist, Glasgow Royal Infirmary for microbiology support and Dr John Clerk, Consultant Pathologist for his willingness to undertake the majority of the post-mortem examinations of fatal cases in Scotland; colleagues at the HPA Centre for Infections, Colindale, London especially Amanda Walsh, for facilitating liaison with the HPA and its own OCT and Dr Mike Catchpole for providing liaison with the ECDC; Dr Dermot Kennedy (retired) and Dr Erica Peters, Consultants in Infectious Disease, Gartnaval Hospital, Glasgow who undertook the review of clinical data on confirmed cases, assisted by a team of epidemiologists seconded by the US CDC for the purpose.

The significant contribution of other key individuals is gratefully acknowledged, especially the input of Detective Superintendent Derek Robertson and Detective Inspector Gary Thomson of Strathclyde Police, their team of detectives and other police forces across Scotland who assisted; Mr Mike Bell of the COPFS who provided advice on the legal aspects of the enquiry; Dave Liddell of the SDF for assistance in accessing the drug service sector and in targeting information to drug users.

Thanks are also due to colleagues in the SGHD, including the Chief Medical Officers' staff, particularly Dr Andrew Riley and Dr Malcolm McWhirter for providing support on many sensitive issues and for facilitating effective communications with Government colleagues at all levels, including Ministers; also to Mr. Gareth Brown and other Scottish Government staff.

The advice and support from expert colleagues outside Scotland was pivotal, particularly the input from staff of the Health Protection Agency, Novel and Dangerous Pathogens Laboratory (HPA-NDPL), Porton Down, especially Dr Tim Brooks, Medical Lead and his many colleagues such as Dr Jane Osborne, who provided the reference laboratory support essential to the investigation; also staff of the US Government Department of Health and Human Services, and of the US CDC, who provided invaluable support to the investigation and played a major role in providing US Anthrax Immune Globulin-Intravenous (AIGIV) for treating anthrax patients, especially Captain Theresa Smith, Branch Chief, Bacterial Special Pathogens Branch, CDC, Dr Nicki Pesik and Dr Sean Shadomy and the members of the Epidemiology Field Team who assisted in the clinical case record review. Thanks also to Professor Paul Keim of the Northern Arizona University who was instrumental in providing the specialist genotyping expertise that ultimately identified the strain of anthrax and placed it within the anthrax phylogenetic family tree.

I am also indebted to the contributions of staff from within HPS, particularly the members of the HPS Anthrax Investigation Team for managing and analysing the case data and for managing the essential administration aspects and communications via the HPS Website and media liaison

(especially Dr Lynda Browning, Susan Brownlie, David Henderson and Louise Kelly); members of the HPS BBV team for work on the analytical epidemiology studies; and Scottish Government pharmacy colleagues and staff of the Scottish National Blood Transfusion Service (SNBTS) for assistance on the importation and use of AIGIV. Lastly, my thanks are owed to my remaining colleagues in HPS who provided advice and support over a difficult period and especially to Eleanor Webb and Maggie Macdonald for their patience in collating this report.

Dr Colin N. Ramsay

Chair of the National Anthrax Outbreak Control Team

Consultant Epidemiologist
Health Protection Scotland

December 2011

List of Appendices

A. Members of the National Anthrax Outbreak Control Team from January 2010 - December 2010

B. Anthrax Epidemiological Investigation Questionnaire

C. Letter from the CMO for Scotland to the NHS in Scotland

D. Scottish Drug Forum (SDF) Materials

E. ECDC Case Definitions

F. Epidemiological Case Definitions and HPA-NDPL Definitions (01/06/2010)

G. Case Definition Update and Criteria (13/9/2010)

H. Clinical Data Review

I. Bibliography of papers and other publications associated with the 2009/10 Anthrax Outbreak

Appendix A

Members of the National Anthrax Outbreak Control Team from January 2010 - December 2010

Membership changed over the course of the outbreak. The following were involved in at least two meetings, most of which were held as teleconferences.

Agency	Name	Designation
HPS	Dr Colin Ramsay Dr Lynda Browning Dr John Cowden Dr Catherine Smith Susan Brownlie Louise Kelly	Chair of NAOCT, Consultant Epidemiologist Epidemiologist Consultant Epidemiologist Associate Specialist Information Manager Communications Manager
NHS Ayrshire and Arran	Dr Maida Smellie	CPHM
NHS Dumfries and Galloway	Mary Waugh	Nurse Consultant Health Protection
NHS Fife	Dr Margaret Hannah Dr Jackie Hyland Dr Charles Saunders	CPHM CPHM CPHM
NHS Forth Valley	Dr Henry Prempeh	CPHM
NHS Greater Glasgow and Clyde	Dr Syed Ahmed Dr John Hood	CPHM Consultant Microbiologist
NHS Grampian	Dr Emmanuel Okpo Dr Diana Webster Jayne Leith	CPHM CPHM Public Health Infection Control Nurse
NHS Lanarkshire	Dr David Cromie Dr Josephine Pravinkumar	CPHM CPHM
NHS Lothian	Dr Richard Othieno	CPHM
NHS Tayside	Dr Chris McGuigan Dr Julie Cavanagh Dr Finn Romanes	CPHM CPHM CPHM
Strathclyde Police	Derek Robertson Gary Thomson	Superintendent Detective Inspector

Agency	Name	Designation
HPA, NDPL	Dr Tim Brooks Dr Jane Osbourne Dr Gail Thomson	Medical Lead, Consultant Microbiologist Clinical Scientist Consultant ID Physician
HPA, NDPL/BRI	Dr Bob Spencer Amanda Walsh	Consultant Microbiologist Senior Scientist
HPA, CFI	Dr Fortune Ncube	Consultant Epidemiologist
Scottish Government Health Directorate (SGHD)	Dr Andrew Riley Dr Malcolm McWhirter	Senior Medical Officer (Observer) Senior Medical Officer (Observer)
CDC	Dr Theresa Smith Dr Nicki Pesik Dr Sean Shadomy	Captain, Branch Chief Epidemiologist Epidemiologist
Crown Office Procurator Fiscal Service (COPFS)	Mike Bell Katrina Parkes	Prosecutor Fiscal Prosecutor Fiscal
Health Protection Service (Ireland)	Dr Paul McKeown	Observer
Scottish Drugs Death Committee	Dr Roy Robertson	Chair
Scottish Drug Forum	David Liddell	Director

Appendix B

Anthrax Epidemiological Investigation Questionnaire

Case No. _____

HPS Anthrax Questionnaire
Drug related incidents in Scotland

Please return completed questionnaire to:
Susan Brownlie
Health Protection Scotland
Clifton House
Clifton Place
Glasgow
Tel: 0141 300 1180
Fax: 0141 300 1172
sbrownlie@nhs.net

Queries regarding Anthrax outbreak:

colin.ramsay@nhs.net
Tel: 0141 300 1127
lyndabrowning@nhs.net
Tel: 0141 300 1155

Guidance Notes for Completion of Anthrax Questionnaire

- **This questionnaire is for use with all cases - see case definitions**
- **The questionnaire should be completed by a public health specialist or public health nurse**
- **Information on case details, symptoms, drug history and other potential risk factors should be obtained from a case or proxy - in the following preferred order**
  - **The case (if alive) *or***
  - **If the case is deceased or otherwise unable to give a history, a proxy should be used in the following order**
    - **Someone who shared drugs with the case recently**
    - **Partner**
    - **Close friend**
    - **Family member**
- **Information on the clinical history should be obtained from medical notes or attending clinician**
- **Please answer all questions**
- **Please return completed questionnaires within 5 days, preferably as soon as possible.**

Please note that we may require clarification of the answers provided

Case No. _____

Case details

1. Name

Surname	
First name	

2. Gender (circle): Male Female

3. Date of birth ____/____/____ (dd/mm/yyyy) **Age (years)** _____

4.

Address	
Post code	

Is this their? (circle): Permanent address A Hostel

Please indicate where they have been living / sleeping over the last two week (please circle all that apply)

Hostel On Street Own home Prison Other (specify)

_____

5. Case status (*circle*) confirmed probable possible

6. This History is taken from (*circle*) case proxy

If proxy, name, relationship to case and contact number

_____

_____

General history of current illness

7. Were you aware that there was a risk of Anthrax associated with drug use? Y N

If yes, how did you become aware? _____

When did you become aware? _____

8. In relation to your current illness, when did you first develop symptoms

____/____/____ (dd/mm/yyyy)

Case No. _____

9. Briefly describe history and general symptom progression:

What were your first symptoms?
How did things progress?

10. Patient symptoms prior to admission (*circle all that apply*)

Headache	Yes	No	Don't know
Fever	Yes	No	Don't know
Chills	Yes	No	Don't know
Anorexia	Yes	No	Don't know
Malaise	Yes	No	Don't know
Nausea	Yes	No	Don't know
Diarrhoea	Yes	No	Don't know
Vomiting	Yes	No	Don't know
Abdominal pain	Yes	No	Don't know
Bloody diarrhoea or vomiting	Yes	No	Don't know
Leaking wound or infection	Yes	No	Don't know
Swelling	Yes	No	Don't know
Pain	Yes	No	Don't know
Itching	Yes	No	Don't know
Breathing Difficulties	Yes	No	Don't know

Case No. _____

History of drug use

11. Has the patient used or is known to be a drug user? Yes No Don't know

12. In the week prior to the onset of your symptoms which drugs did you use, and how?

Used in week prior to symptom onset			**If yes, how did they use, tick all that apply.**					
			Injecting into a vein: mainlining	Skin or muscle popping **accidental (missed vein)**	Skin or muscle popping **intentional**	Smoking	Snorting or sniffing	Orally
Heroin	No	Yes						
Methadone, prescribed	No	Yes						
Methadone, NOT prescribed	No	Yes						
Cocaine	No	Yes						
Heroin & Cocaine together	No	Yes						
Crack	No	Yes						
Heroin & crack together	No	Yes						
Buprenorphine prescribed	No	Yes						
Other, please specify								

13. Are you currently receiving treatment for your drug use? Yes No.

If yes, when did you start your current treatment? ____/____/____ (dd/mm/yyyy)

and from which agency and what type of treatment are you receiving?

_____

14. For how many years have you been using these drugs? ___ years ____ months

15. For how many years have you been injecting heroin? ___ years____months

- How many times did you inject heroin in the week before your illness? _____
- How *much* heroin did you inject in the week before your illness? Please specify approximate quantity _____
- How many times did you snort or smoke heroin in the week before your illness? _____

- How *much* heroin did you snort or smoke in the week before your illness? Please specify approximate quantity _____

16. Have you changed your dealer or supply of these drugs in the week before you became ill? Yes No Don't know

17. Into which parts of your body do you usually inject? Please list all used

_____

18. In which areas have you bought drugs in the week before you became ill?
Please specify the district or area and the town or city for all purchases in the week before you became ill.

District or area	Town or city

19. Have you noticed anything different about the drugs you used in the week before your illness in terms of:

Colour	Yes	No	Don't know
Consistency	Yes	No	Don't know
Effect	Yes	No	Don't know
Dissolving	Yes	No	Don't know

If yes to any of these please give details:

_____

20. During the week before your illness, have you used any of the following to dissolve your drugs? (*circle all that apply*)

Citric Acid Vinegar Lemon Juice (Jif)

Lemon Juice (fresh) Descaler crystals Vitamin C

Other, please specify _____

21. Have you noticed anything different about what you used to dissolve your drugs?

Yes No Don't know

If yes, please give details _____

Case No. _____

22. In the week before you became ill did you share any of your supply or anything you used to inject with anyone?

Yes No Don't know

If yes, what did you share? (*circle all that apply*)

Your supply (drugs) Citric Acid Needles & syringes

Filter Spoons Water

Other, please specify _____

Did the person that you shared anything with become ill?

Yes No Don't know

23. Do you know if your supply has been cut or mixed with any substance?

Yes No Don't know

If so, do you know what that substance might have been?

Yes, please specify _____ No Don't know

24. Did you mix the drug with anything else before you took it?

Yes No Don't know

If yes, have you noticed anything different about what you mixed with?

Yes No Don't know

If yes, please give details _____

25. Do you know of anyone else with a similar illness?

Yes No Don't know

If yes, please specify _____

26. When you injected in the week before you became ill, what have you used to filter your heroin? (*Circle all that apply*).

Cigarette filter Filter tips Cotton bud

Cotton wool Wool Other clothing fibres

Nothing Other, please specify_____

Did you reuse any filters during that week?

Yes No Don't know

If yes, details_____

Case No. _____

Asking about any specific sites of infection, e.g. abscess

27. Do you have a **specific** infected site?

Yes No Don't know

- If yes, how long has there been **any kind** of infection at this site? _____ days
- Where on the body is this site? _____
- On which days during the last week did you inject **into this**?

  ____/____/____ (dd/mm/yyyy)

  If more than one date please list:

  ____/____/____ ____/____/____ ____/____/____

- Was the heroin you injected **into this site** acquired from your normal source?

  Yes No Don't know

- Did the heroin or the drug solution look the same as usual?

  Yes No Don't know

- If it did not look the same as usual, what was different about its appearance?

  _____

Other potential exposure factors

28. Your occupation

_____

29. Have you been involved in any activities that might expose wounds to soil e.g. gardening, renovation, DIY etc.?

Yes No Don't know

30. Did you have contact with livestock or with the body fluids of livestock in the week before you became ill?

Yes No Don't know

31. Did you have contact with animal products such as untreated animal hair, wool, hides, or animal skin drums in the week before you became ill?

Yes No Don't know

Case No. _____

32. Have you travelled away from home or overseas in the week before becoming ill?

Yes No Don't know

If yes:

Places:	Dates: From	To (dd/mm/yyyy)
_____	____/____/____	____/____/____
_____	____/____/____	____/____/____

Information that follows to be obtained from clinical record/sources

Clinical details

Hospital	
Consultant	
Telephone number	
GP	
Address	
Telephone number	

33. Clinical signs at any time during presentation (*circle all that apply*)

General signs:

Systemically unwell	Yes	No	Don't know
Septic Shock	Yes	No	Don't know
Oropharyngeal lesion	Yes	No	Don't know
Hypotension	Yes	No	Don't know
Sweating	Yes	No	Don't know
Cyanosis	Yes	No	Don't know
Meningeal signs	Yes	No	Don't know
Altered consciousness	Yes	No	Don't know

Case No. _____

34. Please give details of any other general signs and symptoms (please note section for signs associated with localised lesion can be found on the next page)

_____

_____

_____

_____

_____

_____

35. Signs associated with localized lesion:

Pain	Yes	No	Don't know
Tenderness	Yes	No	Don't know
Disproportionate oedema	Yes	No	Don't know
Erythema	Yes	No	Don't know
Eschar	Yes	No	Don't know
Vesicles	Yes	No	Don't know
Cellulitis	Yes	No	Don't know
Lymphadenopathy	Yes	No	Don't know
Lymphangitis	Yes	No	Don't know
Visible injection site	Yes	No	Don't know
Necrotic abscess	Yes	No	Don't know
Necrotising fasciitis	Yes	No	Don't know

36. Please give details of any other signs associated with localised lesion:

_____

_____

_____

_____

Case No. _____

Treatment history

Pre hospital admission treatment

37. Irrespective of whether or not they were admitted to hospital, was the patient seen by a doctor (GP, A&E or both – please circle) on any day prior to admission

Yes No

If yes, were they prescribed any antibiotics?

Yes No

If yes, what date did they start to take antibiotics?

____/____/____ (dd/mm/yyyy)

If yes, what antibiotics (list all)

_____

_____

Hospital admission history

38. Was patient hospitalised? Yes No

If yes, date hospitalised ____/____/____ (dd/mm/yyyy)

Following admission, was the patient prescribed any antibiotics?

Yes No

If yes, what date did they start to take antibiotics?

____/____/____ (dd/mm/yyyy)

If yes, what antibiotics (list all)

_____

_____

Was surgical debridement performed?

Yes No

If yes, dates of surgery ____/____/____ (dd/mm/yyyy)
____/____/____ (dd/mm/yyyy)

Was the patient admitted to intensive care?

Yes No

If yes, date admitted ____/____/____ (dd/mm/yyyy)
date re-admitted ____/____/____ (dd/mm/yyyy)

Case No. _____

Was the patient given anthrax immunoglobulin (AIG)?

Yes No

If yes, on what date was the first dose given?

____/____/____ (dd/mm/yyyy)

How many doses have been given? _____

Samples taken for microbiology

What samples were obtained for microbiological diagnosis?

39. Initial Scottish NHS laboratory results

	Date: dd/mm/yyyy	Positive	Negative	Equivocal
Blood for culture - isolate or gram stain (please circle)	/ /			
Tissue	/ /			
Swab	/ /			
Wound swab	/ /			
Other (specify):	/ /			

40. Reference (Porton Down) laboratory results

	Date: dd/mm/yyyy	Positive	Negative	Equivocal
Blood for culture	/ /			
Blood for PCR (EDTA tube)	/ /			
Serum	/ /			
Serum – toxin levels	/ /			
Acute Serum – anti-toxin AB levels	/ /			
Convalescent Serum – anti-toxin AB levels	/ /			
Wound swab	/ /			
Tissue	/ /			
Other (specify):	/ /			

Case No. _____

Prior Medical issues

41. Does the patient have any chronic health conditions or any underlying conditions that could have led to immunosuppression (including for example HIV, Hepatitis C or any other chronic conditions such as diabetes, rheumatoid arthritis etc) ?

Yes No Don't know

If yes, please give details_____

Is the patient on any prescribed medication (particularly long term)

Yes No Don't know

If yes, please give details_____

Final patient outcome/status

Discharged? Died?

Date died or discharged ____/____/____ (dd/mm/yyyy)

Additional Comments:

Form completed by: _____ Date _____

Designation/role: _____

Appendix C

Letter from the CMO for Scotland to the NHS in Scotland

Please see http://www.sehd.scot.nhs.uk/cmo/CMO(2010)03.pdf

Chief Medical Officer Public Health Directorate

T: 0131-244 6910 F: 0131-244 2157
E: gareth.brown@scotland.gsi.gov.uk

The Scottish Government

Dear Colleague

OUTBREAK OF ANTHRAX IN HEROIN INJECTING DRUG USERS
Confidentiality and Data Sharing Requirements

1. Further to any previous alerts you have received, I am writing to you now to reinforce the need for NHS Boards to share information in relation to anthrax investigations with police and Crown Office colleagues.

2. The anthrax outbreak is continuing. The latest position is that there have been 17 confirmed cases of the disease in drug users, and a total of 8 deaths. Both confirmed cases and deaths have occurred in a number of NHS Boards and it is very possible that we will continue to see cases across Scotland for some time.

3. The Outbreak Control Team, which is being led by Health Protection Scotland on behalf of the Scottish Government, has put in place procedures to gather the relevant information in relation to every case that emerges from NHS Boards. This information is of vital importance in monitoring the public health implications of this outbreak.

4. I would ask all NHS Boards who are engaging with the ongoing investigation to ensure that they comply with the requirements of the Outbreak Control Team in relation to data sharing. This is a necessary public health investigation sanctioned by the Scottish Government.

5. The investigation of this outbreak and the potential to control the risk of future infection and death of this vulnerable population depends on investigation and control measures that span a number of agencies, including Police services.

6. Doctors will find recent GMC guidance "Confidentiality: disclosing information about serious communicable diseases" (September 2009) helpful in the context of this outbreak. This is easily accessed on the GMC website. It is important to read this guidance as a whole but I would highlight the following sections:

From the Chief Medical Officer
Dr Harry Burns MPH FRCS(Glas) FRCP(Ed) FFPH

28 January 2010

CMO(2010)3

Addresses
For action
- Directors of Public Health
- CPHM (CD&EH)
- Medical Directors for circulation to all staff in A&E Depts, Intensive Care units, High Dependency Units and Microbiologists
- All General Practitioners including practice nurses, non-principals and Out of Hours services
- NHS 24
- Scottish Ambulance Service
- Scottish Drugs Forum for cascade to services for drug users
- Crown Office for circulation to Procurators Fiscal

Further Enquiries

Dr Andrew Riley (clinical issues)
Andrew.Riley@scotland.gsi.gov.uk
0131 244 2158

Mr Gareth Brown (policy)
Gareth.Brown@scotland.gsi.gov.uk
0131 244 6910

"Personal information may therefore be disclosed in the public interest without the patients' consent, and in exceptional cases where patients have withheld consent, if the benefits to an individual or to society as a whole outweigh both the public and patient's interest in keeping the information confidential."

"Disclosure of personal information about a patient without consent may be justified in the public interest if failure to disclose may expose others to risk of death or serious harm"

"You should pass information about serious communicable diseases to the relevant authorities for the purpose of communicable disease control and surveillance. You should use anonymised or coded information if practicable and as long as it will serve the purpose"

7. NHS colleagues may also find it helpful to refer to the information sharing protocol NHS Scotland and the Scottish Police Forces which was issued on 13 March 2008 (and which can be accessed at http://www.sehd.scot.nhs.uk/mels/CEL2008_13.pdf). The protocol explicitly address public health issues and patient confidentiality and states:

"Information held in confidence can still be disclosed without the individual's consent, where it can be demonstrated that:

- it needs to be shared by law
- it is needed to prevent, detect or prosecute crime
- there is a public interest
- there is a risk of death or harm
- there is a public health interest
- it is in the interests of the person's health
- it is in the interests of the person concerned"

8. I would also remind Boards that both police colleagues and the Crown Office are fully involved in the national Outbreak Control Team and both organisations have recognised that the public health investigation is paramount. COPFS has agreed that information given by anthrax victims to public health professionals in relation to anthrax cases will not be used against those victims in any criminal prosecutions.

Yours sincerely

Harry Burns

Appendix D

Scottish Drug Forum (SDF) Materials

EARLY TREATMENT CAN SAVE YOUR LIFE.

If you suspect you may have anthrax go to your nearest A&E

If you want advice on local drug treatment services contact:

Know The Score
0800 587 587 9

www.scottishdrugservices.com

ANTHRAX

IS KILLING HEROIN USERS ACROSS SCOTLAND

READ THIS - IT MAY SAVE YOUR LIFE

EARLY TREATMENT WITH ANTIBIOTICS CAN BE LIFE SAVING.

Scottish Drugs Forum

NHS SCOTLAND

ANTHRAX

What is anthrax?
Anthrax is a bug which doctors think got into some batches of heroin sold across Scotland. It can kill if not treated quickly. A number of people in Scotland have died from the anthrax bug.

How can you get anthrax?
All anthrax infections in recent weeks have been among heroin users. You can get anthrax by both injecting and smoking heroin.

How can I tell if my heroin is contaminated with anthrax?
Unfortunately, there is no way of telling if the heroin you have is contaminated with the anthrax bug. It may look the same and it may dissolve or burn the same but it could still contain anthrax.

What are the Symptoms?
If injecting heroin – you may have swelling and redness at the injecting site leading to an abscess or ulcer. You may have other symptoms such as fever and headache.

If smoking heroin – you may have a fever or flu like symptoms, feel sick and find it hard to breathe.

What should I do if I have these symptoms?
If you have any of the symptoms you need to get medical help quickly. Go to A&E as soon as possible.

HOW TO REDUCE THE RISKS

1) **There is no safe way of taking heroin.**

2) **Stop using heroin and if not at least use less.**

3) **Go to your local drug treatment service to discuss alternatives such as methadone.**

4) **If you continue to use heroin, don't share needles, syringes, cookers/spoons or other 'works' with other drug users.**

BE AWARE OF THE EARLY SIGNS AND SYMPTOMS:

- **Redness and swelling at the site of injecting heroin**
- **Fever and flu like symptoms if heroin is smoked**

...AND SEEK HELP AT YOUR NEAREST A&E

Please tell others about this infection.
Early treatment with antibiotics can be life saving.

Appendix E

ECDC Case Definition for Anthrax

ANTHRAX (*Bacillus anthracis*)

Clinical Criteria

Any person with at least one of the following clinical forms:

Cutaneous anthrax

At least one the following two:

- Papular or vesicular lesion
- Depressed black eschar with surrounding oedema

Gastrointestinal anthrax

- Fever or feverishness

  AND at least one of the following two:

- Severe abdominal pain
- Diarrhoea

Inhalational anthrax

- Fever or feverishness

  AND at least one of the following two:

- Acute respiratory distress
- Radiological evidence of mediastinal widening

Meningeal/meningoencephalitic anthrax

- Fever

  AND at least one of the following three:

- Convulsions
- Loss of consciousness
- Meningeal signs

Anthrax septicaemia

Laboratory Criteria

- Isolation of *Bacillus anthracis* from a clinical specimen
- Detection of *Bacillus anthracis* nucleic acid in a clinical specimen

Positive nasal swab without clinical symptoms does not contribute to a confirmed diagnosis of a case.

Epidemiological Criteria

At least one of the following three epidemiological links:

- Animal to human transmission
- Exposure to a common source
- Exposure to contaminated food / drinking water

Case Classification

a. Possible case

NA

b. Probable case

Any person meeting the clinical criteria and with an epidemiological link

c. Confirmed case

Any person meeting the clinical and the laboratory criteria

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:159:0046:01:EN:HTML

Appendix F

Epidemiological Case Definitions and HPA-NDPL Laboratory Definitions (01/06/10)

Anthrax in Drug Users Outbreak

Case Definitions and Laboratory Reporting

For the purposes of the anthrax outbreak investigation, HPS originally defined cases as "*possible, probable, or confirmed*" based on their history, clinical presentation and microbiological findings. These three epidemiological case definitions are detailed in the guidance documents on the HPS website.

http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/case-definition-anthrax-outbreak-v5.pdf

> ***A fourth category (Negative case) has now been added to the HPS case definitions to enable classification of possible or probable cases who have been investigated but found not to have any microbiological evidence of anthrax infection.***

From the outbreak investigation perspective, HPS and local CPHMs will be primarily interested in the HPS case classifications. These are the definitions used to report the outbreak officially on the website, to Scottish Government and to ECDC etc.

In addition to the HPS epidemiological case definitions, the HPA Special Pathogens Reference Unit (SPRU), Porton Down who act as the reference laboratory for all anthrax microbiological testing have also defined a set of case classifications based on the results of tests carried out at SPRU. These use terms which reflect a microbiological opinion on all the accumulated results of all tests carried out on each individual case to date.

SPRU have defined five categories to reflect the range of possible interpretations of the test results, including in particular the results of serological testing. *SPRU use these terms in their reports to local microbiologists, who in turn should pass these on to the Local CPHMs.*

However, these SPRU laboratory result classifications are different from the HPS case definitions which may lead to confusion on a case's status. The following therefore describes in detail the terms used by HPS and SPRU and maps the two sets of definitions to each other. *It would be helpful if all parties could restrict the terms used when describing cases or when communicating results on patients to these agreed terms.*

A. HPS Epidemiological Case Definitions

HPS defines cases as follows for the purposes of the outbreak investigation and management in the detailed guidance.

http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/case-definition-anthrax-outbreak-v5.pdf

1. *Possible* case

"A drug user with a clinical syndrome compatible with Anthrax (see Annex 1, Clinical Presentation) including symptomatic individuals with an epidemiological link to a known confirmed or probable case.

(NB individual drug users who give a history of sharing heroin with a known confirmed or probable case but who are not symptomatic themselves should ***not*** *be classed as "possible" cases but may be investigated as "contacts")"*

Such cases will require epidemiological and microbiological investigation.

2. *Probable* case

A case which fits the epidemiological case definition of a *possible case* but with the addition that *gram positive organisms* have been identified in blood, fluids or tissue samples.

"A drug user with a clinical syndrome compatible with Anthrax (see Annex 1, Clinical Presentation) AND Gram positive bacilli identified or bacterial colony growth (phenotypically resembling Bacillus anthracis) from either a tissue specimen/ swab of lesion or fluid/collection or blood culture."

This is a temporary classification until further investigations allow the case to be either confirmed by SPRU or not. Such cases will therefore require additional microbiological and epidemiological investigation.

3. *Confirmed case*

A case which fits the epidemiological case definition and has microbiological evidence of anthrax infection reported by SPRU.

"A drug user with a clinical syndrome compatible with Anthrax (see Annex 1, Clinical Presentation) AND one or more of:

- *Growth of Bacillus anthracis from a clinical isolate confirmed by the reference laboratory.*
- *Evidence of Bacillus anthracis DNA by PCR on multiple target genes,*
- *Demonstration of Bacillus anthracis in a clinical specimen by immunohistochemistry (IHC)*
- *Serology with seroconversion on paired specimens.*
- *Demonstration of specific anthrax toxin in blood"*

In such cases no further microbiological investigation is necessary to determine the case status but further epidemiological enquiries may be needed.

4. ***A fourth category was not spelt out in the original epidemiological definitions but is now necessary as investigations are completed on individual cases:***

   Negative case

   A case where all the epidemiological and microbiological investigations have been completed and anthrax infection has been effectively ruled out as a diagnosis.

B. HPA SPRU Laboratory Result Classification

The following 5 classifications is used by SPRU, Porton Down, to report the results of tests:

- ***Positive (or confirmed positive)***
- ***Probably positive***
- ***Negative***
- ***Presumed Negative***
- ***Unknown***

1. ***"Positive (or confirmed positive)"* case.**

   A case where the microbiology test results show clear "positive" evidence of anthrax infection.

2. ***"Probable positive"* case**

   A case where there is microbiological evidence of anthrax infection but which is not sufficiently strong to allow classification as a "*confirmed positive*" case. Ideally a further *"convalescent"* serology specimen could help to clarify the status.

   N. B. This category is not the same as a "*probable*" case using the HPS case definitions above.

3. ***"Negative"* case**

   A case where there is clearly no evidence of anthrax infection from microbiological tests.

4. ***"Presumed Negative"* case**

   A case where there is some microbiological evidence indicating possible exposure to anthrax but which is inconclusive and not strong enough to justify a more definitive classification.

5. ***"Unknown"* case**

   A case in which the microbiological evidence (including serology) cannot be categorised clearly in any of the other four defined categories.

C. Mapping of HPS and HPA SPRU case classifications

HPS has mapped these two sets of definitions to each other as follows:

SPRU Laboratory Category	HPS Category	Action
1 "*Positive (or confirmed positive)*" *or* 2 "*Probable positive*"	"*Confirmed case*"	No further investigation considered necessary
3 "*Negative*" *or* 4 "*Presumed Negative*"	"*Negative*" case	No further investigation considered necessary to exclude anthrax
5 "*Unknown*"	"*Possible*" case	The final test results are unable to eliminate the possibility that anthrax infection did occur hence it cannot be reclassified and has to remain a "possible" outbreak case.

When the outbreak is considered to be over from a public health investigation perspective, a final reckoning of all cases will be carried out to provide definitive classifications for each case.

HPS 010610.

Annex 1

Clinical Presentations of Anthrax

Anthrax has only been described once in an injecting drug user (IDU) prior to this present outbreak. Case presentation in this outbreak has varied in terms of the initial signs, symptoms and severity. They have presented, mainly, as injection related soft tissue infections. Not all cases however have presented in this way, a few have presented after having possibly inhaled or snorted heroin. Hence all possible presentations of anthrax need to be considered in anyone with a history of recent heroin use by any route.

Due to the nature of the infection in heroin users clinicians should consider the following as possible presentations of anthrax and discuss the case immediately with their local microbiologist:

1) Injection Anthrax

Where there is a history of recent injection use of heroin the following should be considered as possible presentations: Any IDU who presents with:

- Severe soft tissue infection, including necrotizing fasciitis and cellulitis/abscess particularly if associated with oedema (often marked)
- Signs of severe sepsis even without evidence of soft tissue infection
- Meningitis (especially haemorrhagic meningitis) Also be suspicious of users of heroin who present clinically and/or with CT evidence suggestive of a subarachnoid haemorrhage/ intracranial bleed.

2) Inhalation anthrax

Inhalational anthrax is a rarer form of classical presentation for anthrax associated with direct inhalation of spores into the lungs. There is a potential risk of inhaling anthrax spores from snorting or smoking heroin contaminated with anthrax spores.

Symptoms may begin with a flu-like illness followed by respiratory difficulties and shock after 2-6 days.

The signs and symptoms of inhalational anthrax include:

- Initial flu-like illness, progressing to severe respiratory difficulties and shock
- Chest x-ray signs – mediastinal widening, paratracheal fullness, hilar fullness, pleural effusions, parenchymal infiltrates

(Anthrax in Drug Users: Case Definitions Version 5.0 Final - 13 January 2010 Page 2 of 3)

- Progressively enlarging, haemorrhagic pleural effusions are a consistent feature
- The disease is often biphasic, with a prodrome of general malaise for 2-3 days, followed by a day or two of apparent remission before the full blown picture develops.

- Respiratory symptoms may also be accompanied by signs and symptoms suggesting meningitis or intracranial bleeding in the rapidly advancing stages of the disease process due to haematogenous spread.

3) Cutaneous (skin) anthrax

There have been no reports to date in this outbreak of classical cutaneous anthrax which is normally the most common form. Such typical skin lesions resulting from injection of spores remains a possibility, as does such lesions occurring from simply handling the contaminated heroin itself.

In classical cutaneous anthrax, a lesion normally appears on the skin: on the head, neck, forearms or hands. In injecting users it may be nearer to an injection site on a limb or in the groin area. This lesion starts as a small bump and develops into a characteristic ulcer with a black centre. Marked swelling (oedema) associated with the lesion is a classical finding. It is rarely painful, but if untreated the infection can spread to cause blood poisoning. If untreated, the disease can be fatal in 5% of cases, but recovery is possible with prompt antibiotic treatment.

(Anthrax in Drug Users: Case Definitions Version 5.0 Final - 13 January 2010 Page 3 of 3)

Appendix G

Case Definition Update and Criteria (13/9/2010)

Anthrax in Scottish Drug Users

National Outbreak Control Team – Outbreak Update 13/9/10

The purpose of this communication is to update colleagues on where we stand regarding the outbreak and key developments over recent months.

We have not yet officially declared the "outbreak" to be "over" for reasons set out in more detail. However, we hope to be in a position to do so relatively soon.

Content

- Cases to date (reported on public facing website)
- Revised case definitions
- Criteria for ending the outbreak investigation
- Future work for the OCT

Cases to date

As of Friday 10 September 2010, the number of cases reported on the website remains at 47 "confirmed" cases (13 deaths), based on the original outbreak case definitions.

Work has progressed on defining the significance of serological testing. As a result, the outbreak case definitions have been revised. This will result in the "reassignment" of certain cases from "confirmed" to a new category of "probable" cases and vice versa. The revised case definitions will therefore comprise

1. confirmed
2. probable
3. possible
4. negative

Reconciliation of serological results

HPS, in collaboration with HPA-Special Pathogens Reference Unit (SPRU) Porton Down have reviewed all the data on cases to verify their status in light of the full results of all microbiological tests to date, including serology results.

In parallel with this exercise, HPS and HPA-SPRU have revised the final epidemiological case definitions we will use to describe the outbreak cases, once the outbreak is declared over. This will undoubtedly result in some revision of the correct number of cases which are classified as

"confirmed". However this re-classification exercise does not affect the microbiological results already provided to local microbiologists and clinicians; the terminology used by HPA to describe the results for cases will not change.

NHS Boards will already have been advised of which cases have been reclassified.

Revised case classification

***Possible* case**

"A drug user with a clinical syndrome compatible with Anthrax (annex 1) including symptomatic individuals with an epidemiological link to a known confirmed or probable case".

(NB individual drug users who are not symptomatic but who give a history of sharing heroin or having contact with a known confirmed or probable case should ***not*** *be classed as "possible" cases)*

***Probable* case**

"A drug user with a clinical syndrome compatible with Anthrax (annex 1) including symptomatic individuals with an epidemiological link to a known confirmed or probable case".

AND one or more of the following

- ***Single clearly positive result (raised titre) on a single serology specimen***
- ***Paired serology results with either the same or decreasing titres***
- ***Demonstration of specific anthrax toxin in the blood in the absence of any other toxin or reasonable clinical or microbiological explanation for such toxin being present***

***Confirmed* case**

A case which fits the epidemiological case definition and has microbiological evidence of anthrax infection reported by SPRU.

"A drug user with a clinical syndrome compatible with Anthrax (annex 1) including symptomatic individuals with an epidemiological link to a known confirmed or probable case".

AND one or more of the following

- ***Growth of Bacillus anthracis from a clinical isolate confirmed by the HPA SPRU.***
- ***Evidence of Bacillus anthracis DNA using PCR test methods on multiple target genes,***
- ***Demonstration of Bacillus anthracis in a clinical specimen by immunohistochemistry (IHC)***
- ***Positive serology with a rising titre, on paired specimens, of antibodies to anthrax antigens consistent with seroconversion***

***Negative* case**

A case where all the epidemiological and microbiological investigations have been completed and no evidence was found to substantiate *Bacillus anthracis* as the cause of their illness.

Reclassification of the epidemiological definitions will have no clinical impact in that these changes will all be retrospective involving cases long since deceased or discharged. A change in status, when finally agreed, is therefore academic from the patient and clinical perspective but important for epidemiological consistency.

Criteria for determining the end of the outbreak

Based on the analysis of potential incubation periods and delays in case presentation and confirmation, criteria have been determined to enable a decision on when the outbreak can be considered "over".

Taking an 8 week period after the last possible "exposure" date for the last identified confirmed case; the outbreak will be considered "over" if:

1. there are no new confirmed cases identified with a symptom onset date within the 8 week period or

2. there is only 1 new confirmed case identified with a symptom onset period within the 8 week period

If more than 1 case is identified with a symptom onset within the 8 week period, the outbreak will be considered to be continuing.

If one or more new confirmed case is identified among the drug user community, with a symptom onset outside the 8 week "window" period these cases will be considered to be either:

a. sporadic cases, possibly representing "endemic" contamination of heroin supplies in Scotland or

b. a potential new "cluster" or "outbreak" of cases.

Completion of outbreak investigation

Once the "end of outbreak" criteria have been satisfied the OCT will be reconvened to provide an updated situation report. The final tally of cases, based on the "revised" outbreak case definitions will be provided and placed on the HPS website. A draft plan for completion of the investigation, data analyses and final reporting will be outlined at that point.

A "debriefing" session will be held for OCT members and other relevant parties to allow feedback of comments on the investigation and management of the outbreak by HPS. The results of this debriefing will inform the final outbreak report.

The final output from the OCT will be an outbreak report, drafted by HPS on behalf of the OCT and circulated for comment. This report will include the results of the descriptive epidemiological analysis. This report will be given to the NHS Scotland National Services Scotland (NSS) Board as the relevant "governance" structure. The final report will be a "public" document.

Post-outbreak Investigation Work

Advice and guidance

Once the outbreak is considered to be ended, the advice and guidance during the outbreak will be revised for use in relation to future anthrax cases or outbreaks

Serology testing

Following reclassification of the end of the "outbreak" guidance will be issued on the criteria for requesting serological testing for anthrax.

HPA-SPRU has used their developmental serology test to assist in confirming cases during the outbreak. This test was not intended for use as a "routine diagnostic test" and criteria for requesting serological investigation of "cases" in future will need to be determined. Meantime, serology testing should only be requested as part of the continuing outbreak investigation where a "case" meets the existing clinical case definition for a "possible" case.

Annex 1

Clinical Presentations of Anthrax

Anthrax has only been described once in an injecting drug user (IDU) prior to this present outbreak. Case presentation in this outbreak has varied in terms of the initial signs, symptoms and severity. They have presented, mainly, as injection related soft tissue infections. Not all cases however have presented in this way, a few have presented after having possibly inhaled or snorted heroin. Hence all possible presentations of anthrax need to be considered in anyone with a history of recent heroin use by any route.

Due to the nature of the infection in heroin users clinicians should consider the following as possible presentations of anthrax and discuss the case immediately with their local microbiologist:

1) Injection Anthrax

Where there is a history of recent injection use of heroin the following should be considered as possible presentations: Any IDU who presents with:

- Severe soft tissue infection, including necrotizing fasciitis and cellulitis/abscess particularly if associated with oedema (often marked)
- Signs of severe sepsis even without evidence of soft tissue infection
- Meningitis (especially haemorrhagic meningitis) Also be suspicious of users of heroin who present clinically and/or with CT evidence suggestive of a subarachnoid haemorrhage/ intracranial bleed.

2) Inhalation anthrax

Inhalational anthrax is a rarer form of classical presentation for anthrax associated with direct inhalation of spores into the lungs. There is a potential risk of inhaling anthrax spores from snorting or smoking heroin contaminated with anthrax spores.

Symptoms may begin with a flu-like illness followed by respiratory difficulties and shock after 2-6 days.

The signs and symptoms of inhalational anthrax include:

- Initial flu-like illness, progressing to severe respiratory difficulties and shock
- Chest x-ray signs – mediastinal widening, paratracheal fullness, hilar fullness, pleural effusions, parenchymal infiltrates

(Anthrax in Drug Users: Case Definitions Version 5.0 Final - 13 January 2010 Page 2 of 3)

- Progressively enlarging, haemorrhagic pleural effusions are a consistent feature
- The disease is often biphasic, with a prodrome of general malaise for 2-3 days, followed by a day or two of apparent remission before the full blown picture develops.

- Respiratory symptoms may also be accompanied by signs and symptoms suggesting meningitis or intracranial bleeding in the rapidly advancing stages of the disease process due to haematogenous spread.

3) Cutaneous (skin) anthrax

There have been no reports to date in this outbreak of classical cutaneous anthrax which is normally the most common form. Such typical skin lesions resulting from injection of spores remains a possibility, as does such lesions occurring from simply handling the contaminated heroin itself.

In classical cutaneous anthrax, a lesion normally appears on the skin: on the head, neck, forearms or hands. In injecting users it may be nearer to an injection site on a limb or in the groin area. This lesion starts as a small bump and develops into a characteristic ulcer with a black centre. Marked swelling (oedema) associated with the lesion is a classical finding. It is rarely painful, but if untreated the infection can spread to cause blood poisoning. If untreated, the disease can be fatal in 5% of cases, but recovery is possible with prompt antibiotic treatment.

(Anthrax in Drug Users: Case Definitions Version 5.0 Final - 13 January 2010 Page 3 of 3)

Appendix H

A Review of the Clinical Data from the Confirmed Cases of Anthrax in Scotland

1. Introduction

Data on the confirmed cases was collected in a separate exercise from the main epidemiological outbreak investigation. A separate data collection tool was developed to capture detailed data on all relevant aspects of the clinical diagnosis, investigation and treatment of the confirmed cases, including all those treated with anti-toxin (AIGIV) supplied by the US CDC.

Clinical data on the confirmed cases was analysed to gain an understanding of the patterns of presentation; clinical course; severity of disease; their management and final outcome. It was hoped that this would help to identify: clinical features that might aid in making a more rapid clinical diagnosis; prognostic indicators that could assist decisions on when to transfer a patient for ITU care; and in terms of case management, interventions likely to improve the patient's prognosis and final outcome.

The following describes the key features of the clinical presentations of the confirmed cases (only) as well as aspects of their clinical course and final outcome. This is not an exhaustive account of individual anthrax cases but is a summary of some of the important and novel findings identified during the diagnosis and treatment of the outbreak cases.

2. Methods

This exercise was commissioned specifically by HPS and carried out by two Consultants in Infectious Diseases sequentially, supported in September 2010, by a team of epidemiologists seconded to HPS by the US CDC for two weeks. A specific Excel database was created to hold the data, managed by HPS.

Clinical information on the 47 confirmed anthrax was obtained retrospectively, mainly from hospital case note review of: demographic data; presenting clinical features; laboratory and radiological investigations; and clinical progress. Post-mortem findings were included where relevant; in one case the only information available was from a post-mortem examination.

There was only limited data on 3 of the 47 cases; some cases, especially those who had a rapidly fatal illness had incomplete records. The quality of the data on specific aspects recorded in the case notes was also variable, thus some of the denominators used in the reporting reflect the smaller number of cases considered.

3. Results

Of the 47 confirmed cases, 46 were admitted to hospital. Thirteen cases died; one case was found dead at home. Any case requiring intensive care admission was classified as a "serious" case; 23 cases required ITU admission, 11 died.

The estimated median time from what was thought to be the most likely "culprit" injection, to attending hospital, was 3 days. However, the limited information means that no significant inference can be drawn on whether this time gap was a factor in prognosis between survivors and fatal cases.

The course of the clinical illness was variable; the length of inpatient hospital stay ranged from zero to 69 days. For survivors, the median duration of stay was 12 days, compared to 3 for fatal cases.

The clinical presentation of confirmed anthrax ranged from minor skin conditions to severe and fatal infections. Some cases had a mixed presentation with features affecting multiple body systems. The main presenting features of the illness have been grouped by main body system affected (Table 1).

Table 1: Clinical presentation of confirmed cases.

Clinical Presentation	Number of Cases (total number where symptom was recorded as present/absent)		% of patients where symptom recorded
Skin/soft tissue	39	(42)	93%
Gastro-intestinal	22	(40)	55%
Respiratory	2	(41)	5%
Central Nervous System	14	(42)	33%

Skin/soft tissue infection was the most common reason given for presenting to hospital; 39/42 cases showed skin signs (93%). The sites most commonly recorded are detailed in Table (2).

Table 2: Sites of skin/soft tissue infection recorded for confirmed cases.

Skin/soft tissue Infection Site	Number of Cases	% (N = 42)
Leg	19	44%
Arm	14	33%
Buttock	4	9%
Abdomen	1	2%
Multiple skin sites	1	2%

Symptoms of skin/soft tissue infection was the commonest reason to present; 3 cases were recorded as having no skin involvement at all (in 5 cases neither presence nor absence was recorded). The site of the skin/soft tissue infection appears to reflect the sites of drug-injection used by the cases prior to developing infection. However, the mode of heroin injection was poorly recorded; terms such as "IVDU" and "IDU" were frequently used in case notes but did not necessarily imply accurate descriptions of the injection sites. Such terms are often used to

describe any illegal parenteral drug use and occasionally any form of illegal drug use, regardless of the mode of use. Thus the clinical note data on injection sites used by cases was not considered sufficiently robust for further analysis.

The appearance and description of the skin lesions was variable: descriptors included painless or painful; ulcerated with broken skin; skin intact; with or without erythema. However, the strikingly consistent clinical presenting feature was the appearance of significant oedema surrounding the lesion, often described as in excess of the lesion and extending beyond the limb or area affected. In some cases the appearance was suggestive of necrotising fasciitis. Only rarely was anything noted that was thought to resemble the black eschar described in classical cutaneous anthrax. One patient presented with an urticarial rash; another described itch at the site of the lesion. In a number of patients further sites of skin abnormality, distant from the initial lesion, developed while in hospital.

Surgical debridement was carried out in 25 of the cases, consistent with advice given by the ACN. In some cases this was due to a presumed diagnosis of necrotising fasciitis; in other cases it was mainly to remove necrotic tissue to allay concerns that diseased tissue might be harbouring bacteria still capable of releasing toxins. Surgical decompression was required specifically to relieve significant oedema in a couple of cases. The defect following debridement was so large in some patients that skin grafting was required.

Gastrointestinal signs and symptoms were seen in 22/40 cases, either reported as clinical findings or noted at post-mortem examination. This varied from non-specific symptoms: abdominal pain, nausea and vomiting, to significant gastrointestinal signs: haemorrhage and duodenal ulceration. One patient presented with ascites, described as "gelatinous" when examined. At least 2 patients complained of vomiting in addition to their presentation with skin/soft tissue infection.

Respiratory symptoms and signs were reported rarely. Only two patients presented with respiratory symptoms; one complained of breathlessness but had no pleural effusions or other abnormalities on chest X-ray; this may have been part of a sepsis syndrome. The other presented with pleuritic chest pain but had no abnormality on chest X-ray. A pleural effusion was detected in 10/41 patients.

Central nervous system symptoms or signs were recorded in 14/42 patients. Some presented with agitation and a reduced Glasgow Coma Scale score. Two had seizures but had a past medical history of fits. Two had focal neurology: one had hemiplegia, one had a IIIrd (cranial) nerve palsy. Four patients had a subarachnoid haemorrhage detected by imaging or confirmed post mortem.

All patients admitted to hospital and considered clinically to have anthrax, or already confirmed microbiologically, received antibiotic therapy, usually with a combination of: flucloxacillin, metronidazole, clindamycin, gentamicin and ciprofloxacin. The duration of antibiotic therapy was variable; usually the number of antibiotics was rationalised once confirmatory cultures and antimicrobial sensitivities were known. Some cases had other organisms detected as well as anthrax; 12 cases had such poly-microbial infections. The other organisms may have contributed significantly to the pathology (e.g. *S. aureus*) or they may simply have colonised the site of culture but not influenced the course of the illness.

The clinical course of the 23 patients treated within the ITU setting was also variable; 12 survived but 11 died, reflecting the advanced and serious nature of their infections. Of the 12 survivors treated in ITU the median length of inpatient stay was 33 days. Most of the ITU patients, both survivors and fatal cases, required massive fluid resuscitation and inotropic support. A number had significant bleeding requiring large volume fluid replacement and significant amounts of blood products, including platelets and clotting factors, to try to control the blood loss. This was often seen following debridement in the postoperative setting; there was ongoing oozing and bleeding from the surgical site, despite no obvious bleeding point. A number of patients required frequent surgical reassessment because of these refractory problems. Interestingly in some of the fatal cases, blood pressure was normal although the patient would be described as looking unwell; there would then be a sudden decline with irrecoverable blood pressure despite fluids and maximal inotropic support. Of 10/23 treated in an ITU with cerebral signs, 8/10 died. Only 2 such patients survived, one with focal neurology and one with seizures but without cerebral haemorrhage.

The clinical features of anthrax in this outbreak differed from those of classical disease on a number of levels. Classical cutaneous anthrax is commonly benign with about 5% going on to have systemic symptoms. The typical black eschar of cutaneous anthrax was described in only one case at presentation but oedema, which is also described in classical disease, was very significant and in excess of that seen reported in typical cutaneous presentations. A finding of oedema, out of proportion to the size of a skin lesion or around an injection site, was a significant clinical sign. This feature therefore became a useful diagnostic indicator of the disease. The other classical signs of skin infection; calor (heat), rubor (erythema) and dolour (pain) were variably present but could not be used to distinguish this infection from others commonly seen in this drug user population.

Half of the confirmed cases did not require ITU admission and some patients had only antibiotic therapy without surgical debridement. Their mean inpatient stay was 5 days. The reasons for the variation in clinical course and outcome are not clear but a number of hypotheses have emerged from the clinical review. One hypothesis is that co-infection with other bacteria could have altered the local immune response and affected anthrax pathogenesis. There were a number of cases with poly-microbial infection. In some cases other organisms, even if originally present, would not have been recovered due to the earlier use of antibiotics. Further analytical work may help to clarify the role of multiple infections in relation to the prognosis of the outbreak cases.

Respiratory symptoms and signs were unusual. Unlike cases of typical inhalational anthrax, where pleural effusions occurred they were small and did not cause symptoms or require any treatment. However, of particular note was the finding of anthrax bacilli were recovered from respiratory samples, either from pleural fluid or in 2 cases from bronchial tissues or exudate. This may be evidence that the primary exposure route to anthrax spores was via the inhalational route, potentially from smoking (or snorting) contaminated heroin.

Medical staff commonly employ a variety of clinical and laboratory measures to assess the severity of illness. The *systemic inflammatory response* is a measure of white cell count, respiratory rate, blood pressure and tachycardia; the degree of abnormality in these parameters acting as a predictor of mortality. However, in a number of anthrax cases these parameters were not predictive of mortality, at least not in fatal cases until the last few hours of life. Other biochemical

measures of sepsis such as: lactate; measures of inflammation such as C Reactive Protein (CRP); or measures of perfusion such as renal function, were not significantly abnormal until patients became suddenly extremely sick and then, in many cases, did not respond to maximal aggressive management. This probably reflects the toxaemic pathology rather than the normal bacterial or cytokine driven model of inflammatory response more commonly seen in hospital practice (e.g. in pancreatitis or bacterial sepsis).

4. Conclusion

Early accumulation of the clinical data and the multidisciplinary mix of the clinical team involved in case management, enabled relevant clinical advice to be generated rapidly, then disseminated to those working with heroin users, in the community and in primary and secondary NHS care. Data on the clinical course, prognostic factors and the effect of using anti-toxin (AIGIV) (supplied by US CDC) on the clinical outcome of patients is subject to continuing analysis. The results of further analysis may help to identify significant features that may aid early recognition of the disease, identify prognostic factors and ultimately lead to improvements in the options for clinical management of anthrax infection in future.

Dr Erica Peters
Consultant ID Physician
Gartnaval General Hospital, Glasgow

Dr Catherine Smith
Associate Specialist
Health Protection Scotland/Brownlee Unit, Gartnaval Hospital, Glasgow

Appendix I

Bibliography of papers and other publications associated with the 2009/2010 Anthrax Outbreak

Ramsay CN, Stirling A, Smith J, Hawkins G, Brooks T, Hood J, Penrice G, Browning LM, Ahmed S; NHS GGC; Scottish National Outbreak Control Team.
An outbreak of infection with *Bacillus anthracis* in injecting drug users in Scotland.
Euro Surveill. 2010 Jan 14;15(2). pii: 19465. Erratum in: Euro Surveill. 2010;15(3). pii: 19469.

Christie B.
Heroin contaminated with anthrax has killed 11 people.
BMJ 2010 Feb 15;340:c937.

Booth MG, Hood J, Brooks TJ, Hart A; Health Protection Scotland Anthrax Clinical Network.
Anthrax in Drug Users.
Lancet. 2010 Apr 17;375(9723):1345-6.

Guy Beaumont.
Case report. Anthrax in a Scottish intravenous drug user.
Journal of Forensic and Legal Medicine 17 (2010) 443-445.

Benjamin J Parcell, Andrew D Wilmshurst, Anthony J France, Luisa Motta, Tim Brooks, William J Olver.
Injection anthrax causing compartment syndrome and necrotising fasciitis.
J Clin Pathol 2011;64:95-96.

Arfon GMT Powell, Joseph EM Crozier, Heather Hodgson, David J Galloway.
A case of septicaemic anthrax in an intravenous drug user.
BMC Infectious Diseases 2011 11:21.

Knox D, Murray G, Millar M, Hamilton D, Connor M, Ferdinand RD, Jones GA.
Subcutaneous anthrax in three intravenous drug users: a new clinical diagnosis.
J Bone Joint Surg Br. 2011 Mar;93(3):414-7.

Radun D, Bernard H, Altmann M, Schöneberg I, Bochat V, van Treeck U, Rippe RM, Grunow R, Elschner M, Biederbick W, Krause G.
Preliminary case report of fatal anthrax in an injecting drug user in North-Rhine-Westphalia, Germany, December 2009.
Euro Surveill. 2010 Jan 14;15(2). pii: 19464.

HPA. Anthrax alert for heroin users in London.
http://www.hpa.org.uk/hpr/archives/2010/news0510.htm#nthrx
http://www.hpa.org.uk/hpr/archives/2010/news1010.htm

ECDC. Operational guidance on rapid risk assessment methodology
http://www.ecdc.europa.eu/en/publications/Publications/1108_TED_Risk_Assessment_Methodology_Guidance.pdf

HPS Anthrax Outbreak advice and guidance materials

Resources - Advice and Guidance

General Resources

- Anthrax in drug users: Questions and Answers HPS, Version 1, 18 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/qa-anthrax-drug-users-v1-2010-01-18.pdf)
- Anthrax Alert Poster 13 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/anthrax-drug-user-poster-2010-01-13.pdf)
- Drug Users Information on Anthrax 13 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/anthrax-drug-user-info-2010-01-13.pdf)
- Anthrax and Heroin Users: What Workers Need to Know Scottish Drug Forum (SDF) 1 February 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/anthrax-workers-guide-2010-02-01.pdf)

Guidance for Health Professionals

General

- CMO letter 'Outbreak of Anthrax Infections in Heroin Injecting Drug Users' 28 January 2010 (http://www.sehd.scot.nhs.uk/cmo/CMO(2010)03.pdf)
- CMO letter 'Outbreak of Anthrax Infections in Heroin Injecting Drug Users' 22 January 2010 (http://www.sehd.scot.nhs.uk/cmo/CMO(2010)02.pdf)
- CMO letter 'Outbreak Of Anthrax Infections In Heroin Injecting Drug Users' 11 January 2010 (http://www.sehd.scot.nhs.uk/cmo/CMO(2010)01.pdf)
- Ramsay CN, Stirling A, Smith J, Hawkins G, Brooks T, Hood J, Penrice G, Browning LM, Ahmed S, on behalf of the NHS GGC, on behalf of the Scottish National Outbreak Control Teams. An outbreak of infection with *Bacillus anthracis* in injecting drug users in Scotland. Euro Surveill. 2010;15(2):pii=19465. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19465

Case Investigation

- HPS Anthrax Questionnaire Drug related incidents in Scotland HPS, Version 3, 25 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/anthrax-questionnaire-v3.pdf)

Case Management

- HPS-HPA SPRU Case Definitions Mapping HPS, Version 4, 01 June 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/hps-spru-case-definitions-mapping-v4-010610.doc)
- Interim Clinical Guidance for the Management of Suspected Anthrax in Drug Users HPS, Version 12.1, 19 Mar 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/clinical-guidance-for-use-of-anthrax-immune-globulin-v12-1-2010-03-19.pdf)

- Clinical Algorithm - Clinical Evaluation and Management of Drug Users with Possible Anthrax HPS, Version 12, DRAFT, 17 Mar 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/clinical-algorithm-part-of-clinical-guidance-v12-17032010-asv.pdf)
- Algorithm for the Clinical Evaluation and Management of Persons with Possible Cutaneous Anthrax HPS, Version 1.1, 13 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/algorithm-cutaneous-anthrax-v1-1.pdf)
- Case Definitions for Anthrax in Drug Users HPS, Version 5, 13 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/case-definition-anthrax-outbreak-v5.pdf)

Infection Control

- Infection Control Precautions during the Clinical Management of Drug Users with Probable or Confirmed Anthrax HPS, Version 0.7, 18 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/ic-management-anthrax-v0-7-2010-01-18.pdf)
- Controlling the risks of infection at work from human remains HSE (http://www.hse.gov.uk/pubns/web01.pdf)
- Infection at Work: controlling the risks HSE (http://www.hse.gov.uk/pubns/infection.pdf)
- Safe working and prevention of infection in mortuary and post mortem room HSE (http://books.hse.gov.uk/hse/public/saleproduct.jsf?catalogueCode=9780717622931) [Note access to this resource can also be obtained through Barbour Environment, Health and Safety - http://www.barbour.info/BarbourInfo/hsloginpage.aspx]

Laboratory Investigation

- Laboratory Investigation of Possible Anthrax in Drug Users HPS, Version 1,18 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/lab-guidance-investigation-anthrax-drug-users-v1-2010-01-18.pdf)

Forensic Investigation

- Risk Assessment for forensic investigation of drug-related Anthrax HPA, 15 January 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/risk-assessment-forensic-investigation-anthrax-v1-2010-01-15.pdf)
- Centers for Disease Control and Prevention. Medical examiners, coroners, and biologic terrorism: a guidebook for surveillance and case management. MMWR 2004;53(No. RR-8) (http://www.cdc.gov/mmwr/PDF/rr/rr5308.pdf)
- Guidance on Post Mortem Examination of Possible, Probable and Confirmed Cases of Anthrax, HPS, Version 5.1, 21 Dec 2010 (http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/guidance-post-mortem-procedures-anthrax-v5-1-2011-12-21.pdf)

References

Berdjis CC, Gleiser CA. 1964. Experimental subcutaneous anthrax in chimpanzees. *Exp. Mol. Pathol.* **3**: 63-6.

Brazier JS, Morris TE, Duerden BI. 2003. Heat and acid tolerance of *Clostridium novyi* type A spores and their survival prior to preparation of heroin for injection. *Anaerobe*. **9**: 141-4.

Brett MM, Hood J, Brazier JS, Duerden BI, Hahne SJ. 2005. Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. *Epidemiol Infect*. Aug; **133**(4): 575-82.

CDC. 1974. Cutaneous anthrax acquired from imported Haitian drums, Florida. *MMWR*. **23**: 224.

CDC. 2006. Inhalation anthrax associated with dried animal hides, Pennsylvania and New York City. *MMWR*. **55**(10): 280-282.

DEFRA. 2011. http://www.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/anthrax/

Fee E, Brown TM. 2002. Anthrax and the wool trade. *American J. Public Health.* **92**: 754-7.

Hay G, Gannon M, Casey J, McKeganey N. 2009. Estimating the national and local prevalence of problem drug misuse in Scotland: Executive report. http://www.drugmisuse.isdscotland.org/publications/local/Prevalence_2009.pdf

Hope V, Kimber J, Vickerman P, Hickman M, Ncube F. 2008. Frequency, factors and costs associated with injection site infections: findings from a national multi-site survey of injecting drug users in England. *BMC Infect Dis.* **18**(8): 120.

Hope VD, Marongui A, Parry JV, Ncube F. 2010. The extent of injection site infection in injecting drug users: findings from a national surveillance study. *Epidemiol Infect.* **138**(10): 1510-8.

Hugh-Jones M E, De Vos V. 2002. Anthrax and wildlife. *Rev. Scl. Tech. Off. Int Epiz*. **21**(2): 359-83.

Jackson PJ, Hugh-Jones ME, Adair DM, Green G, Hill KK, Nuske CR, et al. 1998. PCR analysis of tissue samples from the 1979 Sverdlovsk anthrax victims: the presence of multiple *Bacillus* strains in different victims. *Proc. Natl. Acad. Sci. USA*. **95**: 1224-9.

Jernigan DB, Raghunathan PL, Bell BP, Brechner R, Butler JC, et al. 2002. Investigation of Bioterrorism-related anthrax, United States, 2001: epidemiological findings. *Emerging Infectious Diseases* **8**(10). http://www.cdc.gov/ncidod/eid/vol8no10/02-0353.HTM

Keim P, Smith KL. 2002. *Bacillus anthracis* evolution and epidemiology. In: Koeler TM ed. *Anthrax. Current Topics in Microbiology and Immunology.* **271**: 23-32.

Lalitha MK, Anandi V, Walter N, et al. 1988. Primary anthrax presenting as an injection "Abscess". *Indian. J. Pathol. Microbiol.* **31**: 254-56.

McGuigan CC, Penrice G M, Gruer L, Ahmed S, Goldberg D, Black M, Salmon J E, Hood J. 2002. Lethal outbreak of infection with *Clostridium novii* type A and other spore forming organisms in Scottish injecting drug users. *J. Med. Microbiology.* **51**: 971-7.

Meselson M, Guillemin J, Hugh-Jones M, et al. 1994. The Sverdlovsk anthrax outbreak of 1979. *Science*. **266**: 1202-8.

Prince AS. 2003. The host response to anthrax lethal toxin: unexpected observations. *J. Clin. Invest.* **112**: 656-8.

Quinn CP, Dull PM, Semenova V et al. 2004. Immune responses to *Bacillus anthracis* protective antigen in patients with bioterrorism-related cutaneous or inhalation anthrax. *Journal of Infectious Diseases.* **190**: 1228-36.

Riley A. 2007. Report on the management of an anthrax incident in the Scottish Borders, July 2006 to May 2007. NHS Borders.

Ringertz SH, Hoiby EA, Jensenius M, Maehlen J, Caugant DA, Myklebust A, Fossum K. 2000. Injectional anthrax in a heroin skin-popper. *Lancet*. **356**: 1574-5.

Sejvar JJ, Tenover FC, Stephens DS. 2005. Management of anthrax meningitis. *Lancet Infectious Diseases*. **5**: 287-95.

Smith KL et al. 2000. *Bacillus anthracis* diversity in Kruger National Park. *Journal of Clinical Microbiology*. **38**: 3780-4.

Spotts Whitney EA, Beatty ME, Taylor TH Jr, Weyant R, Sobel J, Arduino MJ, Ashford DA. 2003. Inactivation of *Bacillus anthracis* spores. *Emerging Infectious Diseases*. **9**(6): 623-7.

Taylor A, Hutchinson S, Lingappa J, Wadd S, Ahmed S, Gruer l, Taylor TH Jr, Roy K, Gilchrist G, McGuigan C, Penrice G, Goldberg D. 2005. Severe illness and death among injecting drug users in Scotland: a case control study. *Epidemiol. Infect.* **133**(2): 193-204.

United States Department of Justice. Amerithrax Investigative Summary 2010. http://www.justice.gov/amerithrax/docs/amx-investigative-summary2.pdf

WHO. 2008. Anthrax in Humans and Animals. Fourth Edition. World Health Organisation. Ed. Turnbull P. WHO Press. Geneva. http://www.who.int/csr/resources/publications/anthrax_webs.pdf