Prevention of anthrax in people who use heroin (PWUH):

A joint evidence based guidance

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Annual DRD & DRID experts meeting
EMCDDA – European Monitoring Centre for Drugs and Drug Addiction
Freiburg, 3rd June 2013
Case study: Anthrax in PWUH
The agent
The disease
Northern Germany, July 2012
The spores
Manmade anthrax incidents in history

Gruinard Island
This island is government property under experiment. The ground is contaminated with anthrax and dangerous. Landing is prohibited by order 1953.
Sverdlovsk 1979

- Accidental release of weaponised anthrax spores from military production site
- 66 fatal victims, 11 survivors
Aum Shinrikyo Cult, Tokyo 1993
Amerithrax 2001

UNCLASSIFIED

Leahy Letter Powder

Powder in the DC mailings was different in texture and color from the NY mailings.

Higher purity of spores (less cell debris).

UNCLASSIFIED
Anthrax in humans

- Cutaneous anthrax
- Inhalational anthrax
- Gastrointestinal anthrax
- **Injection anthrax**
Cutaneous anthrax
Injection anthrax

- Outbreak among heroin users following to injection of heroin contaminated with *B. anthracis* spores
- New clinical entity since 2009
- Serious soft tissue infection (SSTI), coupled with extensive oedema, developing at from the injection site several days after heroin injection
- Some cases have presented with signs of systemic infection, including signs of fever, raised white cell count, cardiovascular compromise, blood coagulation disorder and multi-organ dysfunction syndrome
- Almost half of all confirmed cases during the 2009/10 Scottish outbreak have required intensive care
Injection anthrax

Grunow, R; Verbeek, L; Jacob, D; Holzmann, T; Birkenfeld, G; Wiens, D; Eichel-Streiber, L v; Grass, G; Reischl, U

Injection Anthrax—a New Outbreak in Heroin Users
Dtsch Arztebl Int 2012; 109(49): 843-8; DOI: 10.3238/arztebl.2012.0843
The recent outbreak

<table>
<thead>
<tr>
<th>Nr</th>
<th>Region, Country</th>
<th>Gend/age</th>
<th>Admiss</th>
<th>Fatal</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Regensburg, Germany</td>
<td>m/51</td>
<td>05. Jun. 12</td>
<td>†</td>
</tr>
<tr>
<td>2</td>
<td>Regensburg, Germany</td>
<td>f</td>
<td>18. Jun. 12</td>
<td></td>
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<tr>
<td>3</td>
<td>Berlin, Germany</td>
<td>f</td>
<td>17. Jun. 12</td>
<td></td>
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<tr>
<td>4</td>
<td>Copenhagen, Denmark</td>
<td>m/55</td>
<td>05. Jul. 12</td>
<td>†</td>
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<tr>
<td>5</td>
<td>Rhône-Alpes, France</td>
<td>m</td>
<td>xx. Jul. 12</td>
<td></td>
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<tr>
<td>6</td>
<td>Lanarkshire, UK (Scotland)</td>
<td>f/33</td>
<td>xx. Jul. 12</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Copenhagen, Denmark</td>
<td>m/39</td>
<td>xx. Jul. 12</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Blackpool, UK (England)</td>
<td>m</td>
<td>xx. Aug. 12</td>
<td>†</td>
</tr>
<tr>
<td>9</td>
<td>Gwynedd, UK (Wales)</td>
<td>m</td>
<td>xx. Aug. 12</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Blackpool, UK (England)</td>
<td>f</td>
<td>xx. Aug. 12</td>
<td>†</td>
</tr>
<tr>
<td>11</td>
<td>Berlin, Germany</td>
<td>m</td>
<td>07. Sep. 12</td>
<td></td>
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<tr>
<td>13</td>
<td>Kent/Medway, UK (England)</td>
<td>f</td>
<td>07. Dec.12</td>
<td>†</td>
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<tr>
<td>14</td>
<td>Suffolk, UK (England)</td>
<td>f</td>
<td>27. Feb.13</td>
<td>†</td>
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<tr>
<td>15</td>
<td>Glasgow, UK (Scotland)</td>
<td>m/49</td>
<td>09. Mar.13</td>
<td>† (7)</td>
</tr>
</tbody>
</table>
2000 Norwegian skin popper
Results from genotyping

- 2012/13: German cases (1,2,3), UK cases (8,10) and Danish cases (4,7) indistinguishable to Ba4599 and from each other
- 2009/10: 71 positive samples from the *B. anthracis* isolates were all of an identical, single strain Ba4599
- Related strains seen in infected goats in the East of Turkey
- 2000, Norwegian case: Isolated strain almost identical with 6 isolates from 5 cases between 2009 and 2012 (R Grunow et al, Eurosurveillance, Vol. 18, Issue 13, 28 March 2013)
Heroin on the go

Map 2: Global heroin flows of Asian origins

Source: UNODC

Flows of heroin (in metric tons)
- 38
- 11
- 6-10
- 1-5

Opium production (in metric tons)
- Afghanistan: 2,700
- Myanmar: 500
- China: 450

Map showing heroin flows from Afghanistan to various regions including South-East Asia, Russia, Europe, and the Middle East.
Contamination hypotheses
Heroin production site I
Heroin production site II
Joint guidance

- Requested by the Commission
- Evidence based approach
- Focus on primary and secondary prevention
- Systematic literature search
- Grading of documents
- Expert’s panel for formulation of recommendations
Formulate recommendations:
- For or against (direction)
- Strong or conditional/weak (strength)

By considering:
- Quality of evidence
- Balance benefits/harms
- Values and preferences

Revise if necessary by considering:
- Resource use (cost)

Grade overall quality of evidence across outcomes based on lowest quality of critical outcomes.

- “We recommend using...”
- “We suggest using...”
- “We recommend against using...”
- “We suggest against using...”
**PIPOH questions**

**Population:** PWUH in the EU/EUA

Does the evidence clarify if any **interventions** targeting:

- Behavioural changes of heroin users
- Non-behavioural prophylactic measures
- Awareness-raising for early recognition and communication

Lead to **outcomes** of:

- Reduction in the incidence of infection with *B. anthracis* in PWUH
- Reduction in the case fatality rate of PWUH with anthrax infection

**Professionals:** Decision makers in prevention programmes at national and regional level, who work in the fields of infectious diseases, general public health, harm reduction and drug-addiction control

**Healthcare settings:** Public health, primary care, harm reduction and drug control, emergency care
Interventions

- Behavioural changes
  - Adherence to opiate substitution therapy (OST)
  - Adherence to heroin assisted treatment (HAT)
  - Adherence to needles & syringe programs (NSP)
  - ...
  - Modifications in the preparation of heroin (heating, filtration, sterile equipment, ...)
  - Alternative administration of heroin (smoking)

- Prophylactic approaches
  - Vaccination
  - Antibiotics
Sources

Guidelines sources:
- GuIdeline.gov, G-I-N database, NHS Evidence

Databases for systematic reviews and primary studies:
- Cochrane Database of Systematic Reviews, MEDLINE, EMBASE, Cochrane Central, CINAHL, AMED, DARE, HTA Database

Other sources:
- Grey literature search, websites hosted by regional or national organisations or institutions that focus on the care, prevention or illness or drug-control/law enforcement
- References identified by citation tracking and personal communication from experts.

All study designs were included if published since 2005 and in English
Study flow

Database records (n=226)

De-duplicated records (n=92)

Filtered (n=31)

Add guidelines and policy documents (n=24)

Add reports and studies from other sources* (n=30)

Referenced documents (n=85)

Guidelines and policy documents (n=24)

Primary studies (n=17)

Background documents (n=44)

* Eg:
  • Grey literature
  • Citation tracking
  • Author lists
  • Personal communication
Findings and grading

- Few primary studies, mostly laboratory studies, case reports, case series, one case-control study
- Guidelines exist, but as this is an emerging area these are mostly consensus-based as there is a lack of empirical evidence
- Applicability and directness of the evidence found for guiding decisions, is an issue. For example:
  - High quality guidelines or systematic reviews for interventions effective in PWUH, but few are directly relevant to anthrax
Developing Recommendations

- The evidence review ends at evidence statements and does not offer advice (what to do)
- Some guidelines use action words to convey the strength of recommendations (should, could, may, don’t)
- Others use grades based on the evidence statements

Crucial role of expert panel
- Consensus finding
- Formulation of recommendations
Systematic literature search & EBM process

1. Systemic reviews of randomised controlled trials
2. Randomised controlled trials
3. Meta-analyses
4. Case control studies
5. Observational studies
6. Case reports
7. Grey literature
Our expert panel

Experts panel "Prevention of anthrax in IDUs": Workshop matrix

<table>
<thead>
<tr>
<th>1. Epidemiology of Anthrax in IDU's in the EU</th>
<th>Comments evidence level</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1. Atypical presentation of anthrax among IDUs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.1. Anthrax among IDUs in the EU has a novel clinical presentation</td>
<td>X X X X X X X</td>
<td>09:50</td>
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<tr>
<td>1.1.2. Typically severe soft tissue infection (SSTI) coupled with extensive oedema</td>
<td>X X X</td>
<td>10:05</td>
</tr>
<tr>
<td>1.2. Case designation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2.1. NAOCt classification: Confirmed / probable / possible / negative</td>
<td>X X</td>
<td></td>
</tr>
<tr>
<td>1.2.2. Outside UK classification (ECDC): Confirmed / probable</td>
<td>X X</td>
<td></td>
</tr>
<tr>
<td>1.3. Descriptive epidemiology of IDUs infected with anthrax</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3.1. 119 confirmed cases in Scotland between 12/2009 and 10/2010 giving infectivity rate round 1 per 200 IDUs in Scotland</td>
<td>X X</td>
<td></td>
</tr>
<tr>
<td>1.3.2. Fatality rate 2009/10 at 1 in 3.61 cases in Scotland</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>1.3.3. Three main foci + sporadic clusters elsewhere in Scotland. During the same period 5 cases in England and 3 in Germany</td>
<td>X X</td>
<td></td>
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<tr>
<td>1.3.4. Mean age of cases 2009/10 was 34; twice as many males as females affected</td>
<td>X X</td>
<td></td>
</tr>
<tr>
<td>1.3.5. In Europe overall mean age for entering treatment for primary opioid use is 34; male to female ratio 3.5:1</td>
<td>X</td>
<td></td>
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<tr>
<td>1.3.6. Since June 2012 additional 12 cases in the EU: 4 in Germany, 2 in Denmark, 1 in France, 3 in England, 1 in Scotland, 1 in Wales; epidemiology is changing, geographical patterns and outbreak dynamics cannot yet be predicted</td>
<td>X X</td>
<td></td>
</tr>
</tbody>
</table>

[Diagram showing a matrix with columns for diagnoses, epidemiology, pathogen characteristics, clinical aspects, prophylaxis, infection control, harm reduction, user preferences, and evidence-based care.]
Recommendations: Public health action & identification

- Appropriately-dosed opiate substitution treatment (OST), including a wide-range of OST options, should be provided to reduce or eliminate illicit heroin use. In countries where heroin-assisted treatment (HAT) is legally possible, it should be seen as an intervention among an extended range of OST options for the prevention of anthrax in PWUH.

- A wide range of professionals in contact with PWUH, but also PWUH themselves and peers should be made familiar with possible symptoms of infection with *B. anthracis*. These include localised soft tissue oedema near to the injection site and generalised symptoms like systemic illness, gastrointestinal, respiratory or CNS-disorders. All symptoms may appear separately or in combination with each other.
Recommendations: Risk communication

- Encourage PWUH to seek early medical attention for any symptoms that arise
- Encourage heroin users to stop heroin use, acknowledging that not all users will be able to avoid use and that these should transition to appropriately-dosed OST.
- Risk communication of anthrax risk messages should be done via locations that heroin users access, involving networks and peer-to-peer systems in addition to traditional media.
Recent insights...

- Outbreak most likely on-going at least since 2000
- Contamination occurs most likely repeatedly in single production site(s) depending on environmental factors
- Importance of early diagnosis and early treatment
- Role of aggressive surgical debridement
- Integration of clinics, public health, harm reduction and drug control for effective management crucial
- Potential of monoclonal antibodies
- Positive heroin sample still missing link to identify and eventually control the source
Thank you!

And, especially to the members of the expert panel: