



JOINT ECDC AND EMCDDA RAPID RISK ASSESSMENT

Anthrax cases among injecting drug users Germany, June-July 2012

Update, 13 July 2012

Main conclusions and recommendations

As of 10 July 2012, five cases of anthrax have been reported among injecting drug users (IDUs) from Germany (n=3), Denmark (n=1) and France (n=1). Reported dates of onset in all five cases range between early June 2012 and 11 July 2012. One German case and the case from Denmark have died. The first two cases from Germany are likely linked through exposure to heroin contaminated by a most likely identical *Bacillus anthracis* strain (based on molecular typing results). For the third German case there is also some laboratory evidence that the strain could be identical with the outbreak strain, but due to the limited amount of DNA, further typing is not possible. The link of the remaining two cases, though probable, needs to be confirmed through molecular typing. The geographical distribution of the potentially contaminated heroin is unknown at this time, but it is possible it has the same source as the contaminated heroin incriminated in the 2009/2010 outbreak in Scotland (with cases also reported from Germany and England).

The risk of exposure for heroin users in European Union (EU) countries is presumably still present and therefore it is not excluded that additional cases among IDUs will be identified in the near future. Information could be disseminated to health care workers, drug treatment and harm reduction centres describing the symptoms of anthrax infection to ensure early treatment, and urging the provision of appropriately-dosed opiate substitution treatment to prevent further anthrax cases.

Link to the previous rapid risk assessment

Rapid risk assessment: Anthrax cases among injecting drug users - Germany, June–July 2012 - Update, 6 July 2012: <http://ecdc.europa.eu/en/publications/Publications/1207-TER-Rapid-risk-assessment-anthrax-IDUs.pdf>

Joint rapid risk assessment: Anthrax cases among injecting drug users, Germany, 22 June 2012:
http://ecdc.europa.eu/en/publications/Publications/120622_TER_Anthrax_IDU_Germany.pdf

Consulted experts

Robert Koch Institute (RKI), Germany: Helen Bernard, Roland Grunow

Staten Serum Institute (SSI), Denmark: Peter Henrik Andersen

Institut Veille Sanitaire (INVS), France: Alexandra Mailles, Marie Jauffret-Roustide

Health Protection Scotland (HPS), Colin Ramsay

Updated event background information

As of 10 July, 2012, five cases of infection with *B. anthracis* among injecting drug users have been reported in Germany, Denmark and France.

The first two cases were reported from the Regensburg region, Bavaria. Both had symptom onset during June and anthrax infection was confirmed by blood culture and PCR [1]. The first case has died. Molecular typing on isolates of *B. anthracis* infecting these first two cases showed that the strains were genetically highly similar to each other and to the strains isolated during the 2009/2010 outbreak [1].

The third case had been reported from the city of Berlin. This patient showed symptom onset in the form of massive oedema and a local necrotic ulcer at the site of injection in the middle of June. Anthrax infection was confirmed by the RKI using PCR from ulcer material several days after initiating antibiotic therapy and serology [2]. The condition of this case has improved following antibiotic therapy. There is no indication that this third case stayed in Bavaria or purchased heroin from Bavaria [2]. Initial molecular typing of *B. anthracis* DNA from this patient suggests that it could be genetically similar to the first two cases in the Regensburg region, as one of the two indicative single nucleotide polymorphism (SNP) markers showed the expected pattern. Due to the limited amount of DNA, further typing was not possible. As the patient started initiated antibiotic treatment prior to sample collection, living bacteria could not be isolated in order to provide a sufficient amount of DNA.

The fourth case has been reported from the city of Copenhagen, Denmark [3]. The person had no recent travel history and reported having purchased heroin in Copenhagen. On July 5 the person was admitted to hospital care with leg pain and a black wound in the groin where the heroin had been injected. The person died on July 8 following septicaemia and organ failure. The diagnosis was made using Maldi-Tof mass spectrometry on samples from blood and ascites fluid. Isolates have been shared with RKI in Germany and genotyping is ongoing. Samples of heroin used by the patient have been cultured and *B. anthracis* has not been detected, nor did culture lead to the identification of any other bacteria.

The fifth case has been reported from Rhône-Alpes region, France [4]. The onset of symptoms occurred on June 11 in the form of moderate fasciitis in the forearm developing to extensive skin necrosis in the arm, shoulder and neck area. The patient was dismissed from the intensive care unit on July 4 and is recovering. Infection with *B. anthracis* was confirmed by PCR on July 9. Genotyping of the strain of *B. anthracis* is ongoing. This patient acquired heroin in the Rhône-Alpes region and did not travel outside of France prior to symptom onset.

Control measures implemented by each of the respective affected countries include:

- alerting emergency departments, intensive care units, on-call services, clinical microbiology departments, infectious disease departments and forensic departments of the existing situation;
- alerting the public (in Germany: www.rki.de/DE/Content/Service/Presse/Pressemitteilungen/2012/09_2012.html);
- coordinated investigations between local and national public health and police authorities with respect to drug distribution routes;
- liaising with support groups, outreach programs and non-governmental organisations that work with and for the IDU community;
- development of information materials for IDUs, clinicians and public health staff in relation to this event (in Germany: www.rki.de/DE/Content/InfAZ/A/Anthrax/aktuell.html).

Actions by European counterparts

The European Union (EU) public health institutes have all been alerted to this event through the Early Warning and Response System. The European early warning network of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), as well as the expert networks on drug-related infectious diseases and drug-related deaths have been alerted to all five cases, and surveillance has been strengthened to report possible additional cases in Europe. On July 11, the European Commission held a teleconference with public health, microbiology and police authorities in affected countries. The European Law Enforcement Agency (EUROPOL), EMCDDA and the European Centre for Disease Prevention and Control (ECDC) also participated.

EUROPOL has been informed and is conducting enquiries in support of the EU Member States' national authorities in an attempt to gather information that may assist in identifying a possible source of contamination. At this time, EUROPOL is not aware of possible deliberate contamination of heroin or cutting agents with *B. anthracis* by either drug traffickers or other criminal or terrorist elements. Consequently, with the information currently available for these five cases, as well as the cases in 2009/2010, accidental contamination seems the most plausible explanation for these incidents.

Evidence for prevention and harm reduction

Currently there is insufficient evidence for the efficacy or feasibility of heat-treatment or filtering of heroin to eliminate anthrax spores in contaminated heroin. Conventional processes for preparing heroin including the use of acidic substrates such as citric acid and flame heating do not destroy anthrax, in particular temperatures achieved by typical flame heating are not high enough to destroy spores [5]. Prophylaxis with ciprofloxacin, and using vaccination (currently only authorised in the United Kingdom) were also considered as preventative measures during the outbreak in Scotland in 2009/2010, but were deemed not to be feasible in the Scottish setting primarily due to practical considerations in terms of defining and accessing the population at risk, and lack of prior evidence of vaccine efficacy as an outbreak control measure [6].

Currently the best way to prevent anthrax infection via contaminated heroin is not to use heroin. Due to the nature of opiate addiction, this recommendation will be difficult for most problem opiate users* to adhere to without opiate substitution treatment. Data from treatment outcome studies and controlled trials demonstrate the effectiveness of methadone and other drug substitution treatments in treating dependence on heroin and other opioids. A large body of evidence from reviews exists regarding the impact of opiate substitution on the incidence of infections as well as of injecting risk behaviour [7–17]. Guidance on drug treatment and the prevention and control of infections among IDUs has recently been issued by ECDC and the EMCDDA:

http://ecdc.europa.eu/en/publications/Publications/111012_Guidance_ECDC-EMCDDA.pdf

As a form of secondary prevention, heroin users and their social networks, as well as health, drug treatment and harm reduction service personnel, can be made aware of the signs and symptoms of anthrax infection and of the importance of seeking medical treatment immediately if infection is suspected. In terms of case finding, evidence from the 2009/10 outbreak identified cases among drug users found dead and classed initially as sudden deaths due to drug overdoses. Increased vigilance for signs of infection among drug users found dead may be a useful additional surveillance mechanism.

* Problematic drug use population — an overview of the methods and definitions used;
<http://www.emcdda.europa.eu/stats11/pdu/methods>

ECDC threat assessment for the EU

The frequent occurrence of skin and soft tissue infections among IDUs is a well known phenomenon [18–20]. However, anthrax infection of injecting drug sites has been reported less frequently. A single case of anthrax was diagnosed in a heroin user in Norway in 2000, but no further cases were detected [21]. The first unusual, large-scale and geographically dispersed outbreak of anthrax infection following injection of heroin, probably from a single batch contaminated with *B. anthracis* was that reported from Scotland, England and Germany between 2009 and 2010 [6, 22–24].

The five cases of anthrax reported from IDUs in Germany (n=3), France (n=1) and Denmark (n=1) between June and July 2012 suggest that *B. anthracis*-contaminated heroin is circulating among the IDU community in at least three countries in the European Union (EU). Similar to the outbreak in Scotland, these recent cases suggest that contaminated heroin or a contaminated cutting agent mixed with the heroin may be a common vehicle of the infectious agent. So far, the only known link between all reported cases is injecting drugs. Strain comparisons of cases from 2009/10 and from German cases in 2012 suggest a common source of contamination, which may still be present, has become present again.

As the precise distribution channels of anthrax-contaminated heroin are not known, the possibility cannot be excluded that additional anthrax-infected IDUs will be identified in the already affected countries and beyond. Investigation of the origin of the drug supply and distribution channels, if possible, may help to identify countries potentially exposed to contaminated heroin.

As anthrax has rarely been associated with severe infection among drug users, clinicians may not consider anthrax in the differential diagnosis of severe infections in this population and this consequently may result in undiagnosed cases or late diagnosis potentially leading to more severe clinical outcome. This highlights the importance of clinical awareness in healthcare settings of the risk of injection-related infection with rare pathogens among the IDU population.

As anthrax cannot normally be transmitted from person to person, the risk to the general population following these five cases is negligible. In healthcare settings where anthrax infected patients are cared for, standard infection control guidelines would be advisable to limit the direct contact with anthrax contaminated materials and infected open wounds. Specific information on the infection risk from infected IDUs to other IDUs through needle sharing is not available, but needle sharing should always be avoided. Infection control guidelines for the clinical management of drug users with possible, probable or confirmed anthrax were developed in Scotland during the 2009/2010 outbreak [25] and guidance for treating clinicians and public health officials has been developed by Germany in 2012 [26]. Additional guidance including documents on case detection, clinical management, post mortem examinations and body disposal are available from the websites of Health Protection Scotland and RKI, Germany:

- <http://www.hps.scot.nhs.uk/giz/anthraxoutbreakdecember2009december2010.aspx>
- <http://www.rki.de/DE/Content/InfAZ/A/Anthrax/aktuell.html>

Conclusions

Based on current information (similar strain and clustered in time and space), it is very likely that the three first cases in Germany are linked through exposure to heroin contaminated by a most likely identical strain of *B. anthracis*. The two cases from Denmark and France are clustered close in time to those in Germany. This suggests that also these cases of anthrax are probably associated with using contaminated heroin from the same source as the cases from Germany. However, this will need to be confirmed by molecular typing of the isolates from the Danish and French case.

The geographical distribution of contaminated heroin is unknown at this time, but it is possible that it has the same source as the contaminated heroin incriminated in the 2009/2010 outbreak. The risk of exposure for heroin users throughout the EU is still present and therefore additional cases among IDUs may occur in the future.

The following measures are relevant for consideration in affected areas and potentially other EU countries:

- increase awareness in hospitals and other healthcare settings, as well as harm reduction and drug treatment services, to support surveillance efforts and to provide information personnel on the distribution of the contaminated products, and on the signs and symptoms of anthrax infection;
- provide information through hospitals and other health care settings, as well as through harm reduction, drug treatment, and outreach services to keep heroin users appropriately informed regarding signs and symptoms of anthrax infection, and regarding the importance of seeking early medical treatment in case of suspected infection;
- encourage heroin users to reduce or eliminate heroin use by promoting access to appropriately-dosed opiate substitution treatment;
- conduct genotyping of isolates of reported cases, if available, to confirm a link among cases as well as with genotypes found in the environment or animals;
- encourage the exchange documents useful for investigation and control, such as case definitions, educational material, investigation questionnaires, protocols for treatment and documents useful to develop a strategy to address communication among vulnerable groups (including materials already developed in Scotland during the 2009/2010 outbreak);
- continue forensic investigations at the national and European levels to identify contaminated batches of heroin, and limit the occurrence of additional anthrax cases.

ECDC and EMCDDA will continue to monitor the evolution of this situation in terms of the epidemiological information available.

References

1. Robert Koch Institute (RKI). Zwei Milzbrandfälle bei Heroinkonsumenten - Ärzte sollten bei Drogengebrauchern frühzeitig an Milzbrand denken. 2012 [05 July 2012]; Available from: http://www.rki.de/DE/Content/Service/Presse/Pressemitteilungen/2012/09_2012.html?nn=2398074.
2. Robert Koch Institute (RKI). Dritter Milzbrandfall bei Heroinkonsument (Berlin); Third case of anthrax in heroin user (Berlin). 2012 [5 July 2012]; Available from: http://www.rki.de/DE/Content/InfAZ/A/Anthrax/Milzbrand-dritter-Todesfall_2012_Berlin.html?nn=2398074.
3. Staten Serum Institute (SSI). Narkoman død af infektion med miltbrand (anthrax). 2012; Available from: http://www.ssi.dk/Aktuelt/Nyheder/2012/2012_07_miltbrand.aspx.
4. Direction Générale de la Santé (DGS). Alerte sanitaire: Maladie du charbon chez des usagers de drogues. 2012 [13 July 2012]; Available from: <http://www.federationaddiction.fr/alerte-sanitaire/#more-5529>.
5. Brett MM, Hood J, Brazier JS, Duerden BI, Hahne SJ. Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. Epidemiol Infect. 2005 Aug;133(4):575–82.
6. Health Protection Scotland (HPS). 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. 2011.
7. Kimber J, Palmateer N, Hutchinson S, Hickman M, Goldberg D, Rhodes T. Harm reduction among injecting drug users- evidence of effectiveness. In: Rhodes T, Hedrich D, editors. Harm reduction: Evidence, impacts, challenges. Lisbon: EMCDDA; 2010.
8. Farrell M, Gowing L, Marsden J, Ling W, Ali R. Effectiveness of drug dependence treatment in HIV prevention. International Journal of Drug Policy. 2005;16(SUPPL. 1):S67–S75.
9. Mattick RP, Kimber J, Breen C, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. [10.1002/14651858.CD002207.pub3 doi]. 2008(2):CD002207.
10. WHO. Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence. Geneva 2009.
11. Tilson H, Aramrattana A, Bozzette SA, Celentano DD, Falco M, Hammett TM, et al. Preventing HIV infection among injecting drug users in high-risk countries: an assessment of the evidence. Washington: Institute of Medicine 2007.
12. Degenhardt L, Mathers B, Vickerman P, Rhodes T, Latkin C, Hickman M. Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed. Lancet. 2010 Jul 24;376(9737):285–301.
13. Kimber J, Copeland L, Hickman M, Macleod J, McKenzie J, De AD, et al. Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. BMJ. 2010;341:c3172.
14. Sorensen JL, Copeland AL. Drug abuse treatment as an HIV prevention strategy: a review. [Review] [70 refs]. Drug & Alcohol Dependence. 2000;59(1):17–31.
15. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, Mattick RP. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. Journal of Substance Abuse Treatment. 2005;28(4):321–9.
16. Wright NMJ, Tompkins CNE. A review of the evidence for the effectiveness of primary prevention interventions for Hepatitis C among injecting drug users. Harm Reduction Journal. 2006;3.
17. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev. 2011(8):CD004145.
18. McGuigan CC, Penrice GM, Gruer L, Ahmed S, Goldberg D, Black M, et al. Lethal outbreak of infection with Clostridium novyi type A and other spore-forming organisms in Scottish injecting drug users. J Med Microbiol. 2002 Nov;51(11):971–7.
19. Murray-Lillibridge K, Barry J, Reagan S, O'Flanagan D, Sayers G, Bergin C, et al. Epidemiological findings and medical, legal, and public health challenges of an investigation of severe soft tissue infections and deaths among injecting drug users -- Ireland, 2000. Epidemiol Infect. 2006 Aug;134(4):894–901.
20. Health Social Services and Public Safety (HSS), Public Health Wales, Health Protection Scotland (HPS). Shooting up: Infections among people who inject drugs in the UK 2010. 2011.
21. Ringertz SH, Hoiby EA, Jensenius M, Maehlen J, Caugant DA, Myklebust A, et al. Injectional anthrax in a heroin skin-popper. Lancet. 2000 Nov 4;356(9241):1574–5.

22. Health Protection Agency (HPA). Anthrax: information on 2010 outbreak. 2010 [21 June 2012]; Available from:
<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Anthrax/AnthraxOutbreakInformation/>.
23. Radun D, Bernard H, Altmann M, Schoneberg I, Bochat V, van Treeck U, et al. 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).
24. Robert Koch Institute (RKI). Ein dritter Fall von Anthrax bei einem i. v. Heroinkonsumenten in Deutschland, 13/12/2010. 2010 [21 June, 2012]; Available from:
http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2010/49/Art_02.html?nn=2386228.
25. Health Protection Scotland (HPS), National Services Scotland (NSS). Infection Control Precautions during the Clinical Management of Drug Users with Possible, Probable or Confirmed Anthrax. 2010; Available from:
<http://www.documents.hps.scot.nhs.uk/giz/anthrax-outbreak/ic-management-anthrax-v0-7-2010-01-18.pdf>.
26. Robert Koch Institute (RKI). RKI-Ratgeber für Ärzte 2012; Available from:
http://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_Anthrax.html;jsessionid=F8FEFABB9C CF64342573C7038E7B929B.2_cid226?nn=2398074.