

## Anthrax—where does the real threat lie?

For more on the **anthrax scare in Jakarta** see <http://www.thejakartapost.com/news/2012/04/25/anthrax-threat-hits-french-embassy.html>

For more on the **scare in Albany** see <http://www.abc.net.au/news/2012-04-26/anthrax-hoax-in-alban/3974764>

For more on **anthrax at Delhi zoo** see [http://zeenews.india.com/news/eco-news/no-anthrax-at-delhi-zoo-officials\\_772961.html](http://zeenews.india.com/news/eco-news/no-anthrax-at-delhi-zoo-officials_772961.html)

For more on the **US Government plan and the FDA's response** see <http://www.businessweek.com/news/2012-04-02/home-stockpiles-of-anthrax-kits-not-the-best-idea-fda-says>

For more on **drug discovery** see <http://www.benthamdirect.org/pages/content.php?CMC/2011/0000018/00000033/0007C.SGM>

For **WHO's report on neglected zoonotic diseases** see [http://whqlibdoc.who.int/publications/2011/9789241502528\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241502528_eng.pdf)

For more on **research into invasion of host tissues** see *Infect Immun* 2012; **80**: 1626–33; DOI:10.1128/IAI.06061-11

For more on the **outbreak of anthrax among Scottish drug users** see <http://www.hps.scot.nhs.uk/ewr/article.aspx>

For more on **research into therapeutic debridement** see *PLoS One* 2012; **7**: e30201; DOI:10.1371/journal.pone.0030201

In late April, the French embassy in Jakarta, Indonesia, and workers in an administration building in the city of Albany (NY, USA) were sent packages accompanied by claims that they contained anthrax spores, while in India, the death of a rhinoceros at Delhi zoo set off an anthrax alert based on scant evidence of infection. Hoaxes such as this have continued on a regular basis since the 9/11 terrorist attacks, prompting the USA to consider some sweeping measures to ensure preparedness. Many experts view these measures as unnecessary and even potentially damaging; the US Food and Drug Administration (FDA) has publicly criticised the US Government's suggestion that every US household should have an anthrax-survival kit containing 10 days' supply of doxycycline. Philip Brachman from Emory University (Atlanta, GA, USA) agrees: "Storing antibiotics in homes is a bad idea. Not only is it initially expensive, antibiotics have a shelf life and would need to be replaced on a regular basis. The risk of increasing antibiotic resistance would also be high as families are likely to become their own health care providers, using the doxycycline inappropriately".

A bioterrorist attack with anthrax is thought imminently unlikely but eventually probable and a prompt

response would be required to save lives. "The most effective strategy for treatment after exposure would need to rely on the well organised deployment of bactericidal drugs that kill the organisms quickly and efficiently. Doxycycline, ciprofloxacin, and penicillin are effective treatments for inhalational anthrax and as such, these have been approved by the FDA", commented Amy Anderson (University of Connecticut, Storrs, CT, USA). Research into anthrax is focusing on the development of new antibiotics that would be even more effective. "Additional members of these classes of antibiotics are now being evaluated in animal models to prove efficacy. Extensive drug discovery is also underway, including development of inhibitors active in several metabolic pathways and against key toxins", Anderson told *TLID*.

Development also includes candidate recombinant vaccines that could replace the present anthrax vaccine originally developed in the 1950s. Two initial doses and a booster dose are used to develop a desired level of immunity and then additional doses are necessary to maintain protective immunity. "We do not yet know the duration of immunity that the vaccines being tested may have, but a one dose vaccine resulting in long-term immunity would be advantageous", Brachman stated. However, even if a new vaccine were approved, Brachmann stresses that he would not recommend large-scale vaccination at present. "I do not feel that an anthrax-based bioterrorist attack is on the horizon. However, people who are at high risk of *Bacillus anthracis* exposure should be vaccinated, as should the armed forces if there is concern that they may be exposed to the organism."

The current human and animal vaccine against anthrax is sometimes used in the less well publicised real outbreaks that occur in anthrax endemic areas in developing countries, such as the upper east region of Ghana.

In late April, anthrax spread from infected cattle to two local people, who subsequently died. "Opportunities for zoonotic transmission of anthrax are likely to be frequent in rural and periurban communities of the developing world due to increased contacts between animal and human populations and local traditions and practices", explains Tiziana Lembo (University of Glasgow, UK). It is ironic that real anthrax outbreaks in these areas of the world, even if they are fatal, generally receive far less news coverage than the many anthrax hoaxes that occur. "It is likely that many cases of anthrax never reach the attention of health authorities as people often die from acute disease at home. In many parts of Africa, contact with infected livestock is very common, with many affected animals butchered by individual families. The cases we see in the hospital records reflect only the less serious, cutaneous form of the disease", noted Lembo.

Although some active anthrax research is in progress, Ian Glomski (University of Virginia, Charlottesville, VA, USA) feels that not enough of it is at the level of basic research into the disease itself. "Unfortunately, in a sense, anthrax is a hypothetical problem; there are very few people dying of anthrax each year in the developed world. Thus, it is hard to maintain the feeling of urgency that is required to attract investment in basic research from governments and private industry", he commented. The issue of low priority for research and control of anthrax is even more noticeable in developing countries. "Despite anthrax being ranked amongst the major poverty-related neglected zoonotic diseases, its study in endemic settings remains neglected, leading to a limited appreciation of the true scale of the human disease problem in these areas", noted Lembo. Under-reporting is a key reason for the scarcity of data



Tiziana Lembo

Zoonotic transmission is far more likely than bioterrorism, but less newsworthy

on disease burden in remote and marginalised communities. “The false perception that morbidity, mortality, and economic impacts of anthrax are low provides little incentive at national and international level to invest in large-scale interventions”, she warned.

Anthrax vaccines in the future might be helpful for high-risk populations in wealthy countries, but are unlikely to be given to the population at large. Glomski believes that, “if we know the molecular mechanisms by which anthrax infection establishes an initial foothold in its victim, and/or we learn to eliminate it from the environment to remove the risk of natural exposure or to keep it out of the hands of those that would weaponise it, then we are one step closer to tossing anthrax on the ash heap of history.” He added that we have too little information about the first two of these points to effectively eradicate the threat of *B anthracis*: only basic research can lead us to this goal.

One major line of research in Glomski’s laboratory suggests that

the Trojan horse model, developed in the 1950s to explain how *B anthracis* spores invade host tissues, needs reassessment. “Our data call into question if it is necessary for a phagocyte to carry spores from luminal spaces into draining lymph nodes. If we are right, prophylactic treatments for high-risk groups that aim to disrupt the mechanism of spore invasion into normally non-phagocytic cells (a process that is potentially very different from phagocytes) could have greater potential than previously thought”, Glomski told *TLID*.

Such treatments could be useful in an unexpected population; in 2010, several cases of anthrax in heroin addicts were reported in Scotland, UK, and in January this year Health Protection Scotland announced that the outbreak had killed 14 people in 2009–10. Injection anthrax has now been added as a fourth major type of the disease, alongside the inhalation, cutaneous, and gastrointestinal forms. Injection anthrax is caused by

contamination of heroin with anthrax spores and leads to a severe infection of the soft tissues around the injection site. Treatment requires extensive surgical debridement and antibiotic therapy, but misdiagnosis is a danger, putting not only patients but also health-care workers at risk.

“Our research in an experimental animal model system has direct implications for injection anthrax; we have assessed the parameters relevant to therapeutic debridement of soft tissues infected with *B anthracis*”, commented Glomski. The group found that, again contrary to the Trojan horse model, the initial site of bacterial entry is vital for progression to systemic disease. “Timely elimination of the initial site of infection via debridement is therefore likely to improve the prognosis, but we can now use this model to establish firm data on which physicians can base their clinical judgements”, he concluded.

Kathryn Senior

## Infectious disease surveillance update

### Measles in the UK

An outbreak of measles on Merseyside in the northwest of England, UK, is the largest in the area since the measles, mumps, and rubella vaccine was introduced in 1988. As of May 1, there had been 210 laboratory-confirmed cases, with a further 92 probable cases under investigation. Around 50% of infections are in children younger than 5 years. The Health Protection Agency has advised children and adults with measles to avoid contact with others, and recommends that teenagers and young adults be vaccinated.

### Disease outbreaks in Chad

Outbreaks of meningococcal meningitis and measles in Chad are adding to the concerns of aid workers, since food shortages—following below average rainfall in 2011—are already causing widespread malnutrition in

parts of the country. The meningitis outbreak began in the second week of January, with 3190 cases and 145 deaths recorded nationwide up to the end of April. Médecins Sans Frontières have also reported that a measles outbreak in the southeast of the country is exacerbating the situation caused by increasing rates of malnutrition.

### Fungal endophthalmitis in USA

At least 33 people across seven states have had fungal endophthalmitis after undergoing ophthalmic procedures, in an outbreak that has been linked to one pharmacy—Franck’s Compounding Lab (Ocala, FL, USA). 20 patients who had undergone vitrectomy were infected with *Fusarium incarnatum-equiseti* species complex originating from a dye used in the procedure, and 13 patients who had received

intravitreal injection of triamcinolone-containing products were infected with *Bipolaris hawaiiensis*. 23 of 30 patients for whom information is available suffered varying degrees of vision loss, and 24 needed repeat surgery.

### Leptospirosis in Fiji

An outbreak of leptospirosis in Fiji has reportedly caused 279 infections and up to 20 deaths in recent months. Health officials have advised that anyone who develops a fever with muscle pain should report to a medical clinic. Many of the infections are likely to have arisen through contact with water during the massive floods in the country in January, with 85% of the reported cases occurring in western region of the island of Viti Levu, which was worst hit by the floods.

Neil Bennet

For more on **measles in the UK** see <http://www.hpa.org.uk/ProductsServices/LocalServices/NorthWest/NorthWestPressReleases/nwest120502Measlesupdate/>

For more on the **situation in Chad** see [http://www.msf.org.uk/disease\\_spreads\\_in\\_Chad\\_as\\_food\\_dwindles\\_20120503.news](http://www.msf.org.uk/disease_spreads_in_Chad_as_food_dwindles_20120503.news)

For more on **fungal endophthalmitis in the USA** see [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6117a5.htm?s\\_cid=mm6117a5\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6117a5.htm?s_cid=mm6117a5_e)

For more on **leptospirosis in Fiji** see <http://www.examiner.com/article/fiji-leptospirosis-outbreak-claims-seven-lives-post-floods>