

Dr Thomas Zink, Biodefense and Healthcare Consultant at Saint Louis University, suggests vaccine should be taken prior to its "Best Before" date

Since the terrorist attacks on the United States in 2001, significant activity has been observed at the federal, state and local levels in the name of homeland security. Undoubtedly, the job of retooling US government agencies, creating new ones, and co-ordinating expertise across the full spectrum of pertinent departments is not easy. And multiple campaigns from various legitimate entities with different perspectives have resulted. To wit, the comprehensive biodefense strategy out of the Bush White House Security Council sought to build a layered approach to prevent (attacks), warn, protect, contain and treat. The Department of Homeland Security has presented its four pillars of biodefense for the 21st Century: threat awareness; prevention/protection; surveillance and detection; response and recovery. And the Assistant Secretary for Preparedness and Response (ASPR) has identified four priorities: building individual and community resilience; emphasising response in the continuum of response to recovery; leveraging the health care system's capabilities; and developing/delivering countermeasures. Common throughout these high-level strategic plans is the emphasis on response.

Now, however, there are considerable signs that US government officials are striking a new balance between post-attack response and pre-event preparedness. The US Centers for Disease Control & Prevention (CDC) has published recommendations on the use of the anthrax vaccine in which voluntary, pre-event vaccination of emergency responders is supported. Recent advice from the US National Biodefense Science Board identifies four key themes: prioritisation; anticipation; synchronisation; and leadership. In so doing, this advisory committee admonishes that more focus is needed on the most important, fruitful work, and greater attention should be given to doing more in advance of incidents. Both actions are extremely pertinent to anthrax, which has long been considered the leading bioterrorism threat.

Thanks to this new shift towards pre-attack preparedness, a new initiative – Project Equal Immunisation Policies &

Anthrax Vaccine – Waste Not, Want Not

Practices (EQUIPP) – has been organised by the Institute for Biosecurity at Saint Louis University to demonstrate how to efficiently distribute anthrax vaccine before attack to civilian responders.

Project EQUIPP is about bringing the same protection provided to Department of Defense and National Guard personnel to the civilian workforce that manages suspicious powder events and those who are responsible for the maintenance of civil order, the dissemination of post-exposure countermeasures and continuity of operations and government.

The idea of protecting against the anthrax weapon is not new. An estimated 150,000 American military personnel received one or two anthrax vaccinations during the Persian Gulf War in 1991. And in March 1998, a much larger vaccination programme began that has now administered more than nine million anthrax vaccinations to 2.3 million personnel. In the current Anthrax Vaccine Immunisation Program, (AVIP), anthrax vaccinations are mandated for military personnel serving in areas judged to be at higher risk (such as Central Command in Iraq, southwest Asia and Korea), as well as for personnel with US homeland biodefense responsibilities.

Routinely vaccinating civilians against anthrax has been a point of consideration dating back to 1999-2000. The CDC Advisory Committee on Immunisation Practices contemplated pre-exposure

emergency responder vaccination well before the 2001 anthrax letter attacks. But because of a limited supply of the anthrax vaccine and what was determined as an "incalculable" risk, the ACIP did not recommend routine pre-exposure immunisation for emergency responders. And even after the covert, multi-wave, multi-site, lethal attacks in 2001, the CDC was silent on emergency responders and left its 2000 recommendation stand in a 2002 Notice to Readers.

Over the last decade, each of the ACIP concerns have been addressed. Relative to anthrax vaccine supply, the manufacturer has worked closely with the FDA and the Department of Defense (DOD) to hardwire cGMP (current and good manufacturing procedures) and to expand production capacity. At the time of the original assessment by the CDC in 2000, the annual production was inconsistent and nearly every dose was allocated to the Department of Defense. In 2010, the manufacturer produces eight to nine million doses each year; 95 per cent of this output is sold to the US government for the Strategic National Stockpile (SNS). And, recently, the company announced it will receive a \$107m award from the US Biological Advanced Research & Development Agency (BARDA) to triple its manufacturing capacity.

Interestingly though, even without this increase in production, ample doses

Anthrax Vaccine – Waste Not, Want Not

are available for vaccinating the critical infrastructure personnel on the front lines of civil defense. While the current status (and total number) of SNS anthrax vaccine doses is difficult to ascertain, the manufacturer reports that 15 million doses were delivered to the SNS before May 2007. And an additional 18.5 million doses were ordered and delivered before January 2010 (ahead of a September 2010 deadline). In a presentation at the JP Morgan 28th Annual Healthcare Conference the manufacturer estimated that, at the end of 2009, approximately 20 million doses of the anthrax vaccine is in the SNS. Almost all of these doses are FDA-licensed for a three-year shelf-life – the manufacturer only began to deliver four-year expiry-dated vaccine in the fourth quarter of 2009. An additional 14.5 million doses have been ordered by US HHS and are to be delivered before September 2011. These doses are approved by the FDA for four years of shelf life.

After a 2007 Presidential Homeland Security Directive and a 2007 General Accounting Office (GAO) report to Congress, the DOD began to develop protocols for sharing countermeasures and medical goods between the SNS and other federal stockpiles. The Department of Defense AVIP requirement fluctuates but is estimated at about 2.5 million doses annually. Even with a DOD SNS allocation (using short-dated vaccine first) the manufacturer estimates that 500,000 doses are currently lost each month to three-year expiry dating. This forces the question, “Now that ample vaccine supplies exists for the DOD, and since a half a million doses of SNS vaccine are being destroyed each month, why not use short-dated anthrax vaccine to protect US civilian emergency responders?”

Regarding the stumbling block of “incalculable” risk, it is proposed that the importance of anthrax bioterrorism is best conceptualised as a (security) threat rather than as a communicable disease. Since anthrax is not contagious, the usual and customary epidemiological calculations to determine the risk of infection and impact of immunisation (force of infection, basic and effective reproductive number, average age at

infection and inter-epidemic period) do not apply. Instead, it is more appropriate to embrace the science of hazard assessment, where threat is calculated as a function of three variables: the probability of danger; the existence of vulnerability; and the degree of impact. In this construct, as any of these variables approaches zero, the overall risk approaches zero.

From all accounts, the probability of an anthrax attack is real and continuing. According to the Department of Homeland Security, the threat of an aerosolised anthrax attack is the most important bioterrorism concern. Declassified information has confirmed that known enemies of the United States, including al-Qaeda, have anthrax weaponisation expertise. In December 2008, the bi-partisan Commission on the Prevention of WMD Proliferation and Terrorism stressed the importance of enhancing the nation’s capabilities for rapid response to prevent a biological attack – particularly with anthrax. On 21 October 2009, the Commission restated these concerns and asserted anthrax is the most likely near-term threat. And those with access to classified intelligence data are routinely administering the anthrax vaccine to US-deployed DOD personnel and National Guard Civil Support Teams. All of this forward thinking is bolstered by the fact that the US has already suffered a covert, multi-site, multi-tier, lethal anthrax attack that killed five people, infected or affected thousands and cost hundreds of millions of dollars.

As it pertains to anthrax, the level of current vulnerability is significant. Most importantly, anthrax can be and has been made resistant to all currently-stockpiled antibiotics. Weaponised anthrax powder is easily re-aerosolised and quickly dissipates into the invisible, odourless, tasteless, gaseous phase. Identifying the safe zone is difficult and not fail-safe. Personal Protective Equipment (PPE) is not fool-proof. In the October 2001 Hart Senate Office building attack, six of nine hazmat responders were infected, despite the use of hazmat suits.

Antibiotics have no effect on anthrax spores or the toxins produced by the organism, and adherence to long-term

antibiotic regimens, as seen in the 2001 anthrax attacks, is poor. Vulnerability is at its greatest in an attack with antibiotic-resistant strains of anthrax. In this scenario, post-exposure antibiotics afford no protection and post-exposure vaccine cannot be expected to confer immunity quickly enough to prevent disease.

In terms of impact, a 1970 World Health Organization (WHO) expert committee estimated that an aircraft release of 50kg of anthrax over an urban, developed population of five million would result in 250,000 deaths (38 per cent would die without treatment) and an additional 125,000 would be severely incapacitated. According to the WHO, the strain on medical resources in such a scenario would be tremendous, ultimately leading to the hospitalisation of approximately 13,000 people, 100 days of antibiotics for 125,000 people, and the disposal of 95,000 dead. In 1993, The US Congressional Office of Technology Assessment confirmed the original WHO data. It is easy to imagine the consequential breakdown in medical resources and civilian infrastructure. More recent modelling puts the destructive capability of weaponised anthrax as equivalent to that of a nuclear bomb. And from an economic perspective, the CDC developed a model suggesting a cost of \$26.2bn per 100,000 persons exposed in an anthrax attack. In the 2001 anthrax attacks, the decontamination of the Hart Senate Office Building in Washington, DC required several months and \$23m dollars. The decontamination of the postal plants in Brentwood, DC, and Hamilton Township, NJ, required more than one year of intense remediation and more than \$100m dollars. Interestingly, the amount of anthrax involved in the contamination of each of these facilities was probably less than one gram.

Enter Project Equal Immunisation Policies & Practices (EQUIPP). Project EQUIPP is based on the observation that an important vaccination disparity exists between local emergency responders and their federally sponsored team mates within the US Department of Defense and National Guard WMD Civil Support Teams. Currently, local civilian emergency responders (such as

Anthrax Vaccine – Waste Not, Want Not

firefighters, police/sheriff/security officers, EMT/Paramedics, Bomb Squads and hazmat members) who respond to every suspicious powder event are not protected with the anthrax vaccine. But their federal counterparts who are summoned to perhaps 1 per cent of the incidents are routinely vaccinated. This disparity has not gone unnoticed by local, civilian emergency responders. To these critical personnel, it seems upside down that, relative to anthrax, the second wave of specialists is vaccinated but those on the bioterrorism frontline are not.

But Project EQUIPP answers a much more dangerous threat than disparity. Project EQUIPP addresses the indisputable fact that antibiotic-resistant anthrax renders post-exposure antibiotics useless, with or without vaccine. Perhaps acknowledging this problem, the CDC Advisory Committee on Immunisation Practices (ACIP) recently released recommendations for pre-exposure immunisation of emergency responders with the anthrax vaccine. As intelligence about weaponised anthrax becomes more sophisticated, and as weaknesses in traditional personal protective equipment (PPE) and post-exposure antibiotic regimens are exposed, there is growing demand within the emergency responder community for the anthrax vaccine.

The undeniable threat of antibiotic-resistant anthrax and the solution of pre-attack vaccination calls for a demonstration project that: measures immunisation status for all pertinent adult vaccines; shares evidence-based data on biologic threats (natural and malicious); and maximises already-established occupational medicine networks to bring the anthrax vaccine to emergency responders in the Missouri Homeland Security Regional Response System (HSRRS). The Missouri HSRRS includes the Midwest Area Response Commission (MARCO), the St Louis Area Regional Response System (STARRS), and rural-based responders with incident management responsibilities. Locally-deployed federal agents (FBI, USPS, USMS, etc) are included too. Through innovatively using the anthrax vaccine pre-exposure, Project EQUIPP will leverage the current health care system to reach the unique emergency responder

population and thereby improve individual and community resilience.

Project EQUIPP is guided by the principles of continuous quality improvement: identify a realistic ideal; measure current status as compared to the ideal; design strategies that address obstacles to achieving the goal; tactically deploy all available resources to improve and reach the target; monitor progress; and adapt as needed. Pre-exposure vaccination against anthrax for emergency responders in the Missouri HSRRS is the realistic ideal. The current status as compared to the ideal was measured. A pilot survey of 264 HSRRS responders stationed throughout Missouri found that 2 per cent (6/264) were already vaccinated against anthrax. Vaccine hesitancy due to concerns about vaccine safety was identified as a potential obstacle. Consequently, a question on willingness to receive the vaccine (at no cost) was included in 20 per cent of the questionnaires. The results from the small sample of respondents (56) revealed that: 66 per cent (37/56) would take the anthrax vaccine; 20 per cent (11/56) were undecided; and 14 per cent (8/56) would decline.

These data are consistent with findings of qualitative research by APCO in 2005 where 1,050 emergency responders in four states (California, New York, Florida, and Michigan) and the District of Columbia were polled by telephone survey to determine a baseline demand for the anthrax vaccine. In that population: 64 per cent (672/1050) were likely or somewhat likely to take the anthrax vaccine; 31 per cent (325/1050) were somewhat unlikely or very unlikely to be vaccinated; and 5 per cent (53/1050) did not know.

This proposal is not the forum to exhaustively discuss all obstacles and resources related to this initiative. Even so, it is important to report that public commentary on the Department of Homeland Security deliberative draft guidance regarding protecting emergency responders after a confirmed wide-area anthrax release was overwhelmingly in support of preventive anthrax vaccination for emergency responders.

A recurring theme that speaks to both

hurdles and solutions is the notion that public education underlies all biodifense policy and that full disclosure of information is essential. Undoubtedly, the national recommendation supporting preventive emergency responder vaccination hinges on the requirement that immunisation is offered on a voluntary basis. The ideal of informed, voluntary decision-making involves awareness of realities and probabilities and therefore requires that anyone offered the vaccine directly receive all that is known about the risks of vaccination and the risks of remaining unvaccinated. In the national smallpox vaccination programme, the paucity of threat and risk information was identified as a key component to the resistance experienced. As a result, dialogue regarding anthrax threat and the safety of the anthrax vaccine is a critical success factor. And so, the last 12 months have been dedicated to introducing the premise and rationale for pre-event vaccination to all stakeholders in the Missouri HSRRS and this will continue for the life of the Project. Key to this effort has been the fact that this is not a mandatory vaccination programme, and that self-assessment of risk to anthrax exposure is the cornerstone.

As a result of this communication campaign, a strong consensus has been built on behalf of Project EQUIPP due in great part to the commitment to dialogue and exchange of data and ideas. Key stakeholders include state and local public health officials, emergency management planners, fire and police leadership and occupational medicine.

Project EQUIPP is poised for implementation and is only awaiting input from the Department of Health and Human Services on funding and access to the short-dated anthrax vaccine doses held within the Strategic National Stockpile. In conclusion, the threat of anthrax bioterrorism is real and continuing. The solution is known and available. Project EQUIPP is one initiative seeking to demonstrate an efficient method of utilising short-dated anthrax vaccine in the SNS to provide needed immunity to local civilian emergency responders in order to maximise community preparedness and resilience.