Assignment 2: Extended Research Proposal

Botulinum toxin has been used as a weapon of bioterrorist during the last 60 years. To the surprise of many Americans, the US established a biowarfare program in the early 1940's at Camp Detrick, Maryland. This program has since been dismantled, largely as a result of the Biological and Toxin Weapons Convention. On April 10, 1972, 108 countries signed a treaty which mandated that they abandon biological weapons research programs designed for offensive attacks. In 2001, however, President Bush declined to ratify the treaty, arguing that it threatened public disclosure of commercial interests in the biotechnology sector. One consequence of this, however, is to create a potential source of bioweapons for terrorists groups.

In recent years, a number of botched terrorists attacks have attempted to release botulinum toxin, but have failed. In April 1990, Aum Shinrikyo, a cult group based in Japan, sent trucks through central Tokyo spraying botulinum toxin. Targets included the U.S. Navy installation at Yokohama and the base at Yokosuka, as well as Narita International Airport. These attacks were unsuccessful, as were two other attempts in subsequent years. In 2001, the attacks on the World Trade Center and the Pentagon, which were followed almost immediately by discovery of letters containing anthrax, spurred U.S. defense programs to tighten security measures. Among the measures taken was the creation of a new Department of Homeland Security.

Instructions

1. Complete the assigned reading and visit websites (suggestions for textbook readings maybe be found in the Teaching Notes to Actvity 5).
2. Consider the scenario sketched below. Play the role of the Director of the Bioterrorism Unit of the Centers for Disease Control and develop a proposal that outlines your strategy for dealing with this situation. Use **Resource Six: Self Assessment of Writing**. The proposal should:
   - Briefly review the options that are currently available.
   - Provide a short-range solution and a long-range solution for combating this attack.
   - Include the economic and public health benefits.
   - Prioritize response activities.
3. Your proposal should also address the questions at the end of this assignment.
4. Exchange your proposal with a peer.
5. Play the role of the Chair of the Senate Appropriations Committee for Bioterrorism and critique your peer's CDC proposal. Use **Resource Five: Peer Assessment of Writing.** This critique should include:
   - A set of questions for the director.
   - Uncover potential pitfalls in the proposal.
   - Suggest alternative strategies.
6. Exchange your peer critiques, revise your proposal and turn in both the critique and your final draft of the proposal to your instructor.

Scenario

1. A shadowy organization which has been suspected of bioterrorist activities has sent a threatening letter to the Secretary of Health and Human Services.

2. This letter contains information suggesting that botulinum attack might occur within one month in one of three U.S. cities: San Francisco, New York City or Chicago.
3. The FBI has determined that the threat should be taken seriously and preparations should be made to minimize the effects of the attack.
4. The Department of Homeland Security has raised the Terrorist Advisory level to Orange, indicating a high risk of terrorist attacks.
5. Botulism, if untreated, will kill 80% of those who become infected.
6. A vaccine for botulism exists and military personnel preparing to engage in combat are required to be vaccinated.

Questions

1. What is botulism? What causes it? How can the causative agent be weaponized?
2. What is a vaccine and how is one made?
3. With respect to vaccination: What are the side effects? What are the benefits? What are the costs?
4. Who, if anyone, should be vaccinated? Should mass civilian vaccination be employed if an outbreak is detected, or should vaccination be restricted to those in closest proximity to the outbreak?
5. Should vaccination be enforced? If so, who will be responsible?
6. What are the likely consequences of a vaccination program, including remote or potentially hidden consequences? What are the alternatives? Is the worst case scenario acceptable?
7. Who benefits? Who is at risk or pays the costs? (Who is upstream, choosing benefits? Who is downstream, experiencing the consequences?) Would you be willing to accept any of the consequences of this policy falling upon yourself?
8. Are there public health alternatives to vaccination? If so, do they provide a more cost effective solution? Are there safer, more effective solutions?
9. How long does it take for a new vaccine or drug to reach the general market—from development through testing?
10. What guidelines and how many testing stages are required for researchers to obtain an NDA (New Drug Application)? Remember that the researchers need to bring an IND (Investigational New Drug) application to the FDA before they can even begin the process.
11. What would the experimental set-up be for the testing of the drug in humans? Describe the target population, sample size, controls.
12. Would this drug be undergoing Phase IV trials or post-marketing surveillance? Explain your answer.
13. How much does it cost to bring a vaccine or drug to market?
14. Since several vaccines are being developed for botulism—why haven't they been licensed? What is the rationale?

Literature (reviews are indicated with **)

1. AAAS. (2002)."Spotlight on Bioterrorism". *Science and Technology in Congress* February: 3, 7.** http://www.aaas.org/spp/cstc/stc/stc02/02-02/bio.htm
2. Arnon, S. S., R. Schechter, et al. (2001). "Botulinum toxin as a biological weapon: medical and public health management." *JAMA* 285(8): 1059-70.** This article is a complete review

of the toxin, its uses and abuses. Read the sections entitled "Therapy," "Prophylaxis," and "Research Needs," and review Figure 1.
http://jama.ama-assn.org/issues/cgi/content/full/285/5/1059
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http://www.sciam.com/article.cfm?articleID=0002F34D-5C49-1C70-84A9809EC588EF21.
4. Byrne, M. P. and L. A. Smith (2000). "Development of vaccines for prevention of botulism." *Biochimie* 82(9-10): 955-66. **
5. Cohen, J. and E. Marshall (2001). "Vaccines for Biodefense: A System in Distress." *Science* 294: 498-501.**
http://microbiology.wustl.edu/training/courses/5391/pdf/498.pdf or
http://www.ph.ucla.edu/epi/bioter/vaccinesfordefense.html
6. Garcia, G. E., D. R. Moorad, et al. (1999). "Buforin I, a natural peptide, inhibits botulinum neurotoxin B activity in vitro." *Journal of Applied Toxicology* 19 Suppl 1: S19-22. This entire supplement is on "Medical Countermeasures to Botulinum Toxins and Topical Skin Protectants Against Nerve and Vesicating Agents"**
http://www3.interscience.wiley.com/cgi-bin/issuetoc?ID=68501553.
7. Mullaney B. et al. (2001). "Epitope mapping of neutralizing botulinum neurotoxin A antibodies by phage display." *Infection and Immunity* 69(10): 6511-4.
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8. Roques, B. P., C. Anne, et al. (2000). "Mechanism of action of clostridial neurotoxins and rational inhibitor design." *Biology of the Cell* 92(6): 445-7.
9. Schmidt, J. J., R. G. Stafford, et al. (2001). "High-throughput assays for botulinum neurotoxin proteolytic activity: serotypes a, b, d, and f." *Analytical Biochemistry* 296(1): 130-7.
10. Sotos, J. G. (2001). "Botulinum toxin in biowarfare." *JAMA* 285(21): 2716.
http://jama.ama-assn.org/cgi/content/full/285/21/2716

Websites

1. Public Broadcasting Service. (2001). "Nova: Bioterror." November 2001. This site contains interviews with bioterror specialists and journalist who cover the field. There are also animations and background information on vaccines and treatments.
http://www.pbs.org/wgbh/nova/bioterror
2. Schindler L, Kerrigan D, Kelly J. Science Behind the News: Understanding the Immune System. This site is a graphic slide show of immune mechanisms and genetic engineering for vaccine development.
http://newscenter.cancer.gov/sciencebehind/immune/immune01.htm
3. FDA. FDA Consumer: From Test Tube To Patient: New Drug Development in the United States. January 1995. This site reviews animal and clinical studies and the regulations that safeguard patients and consumers.
http://www.fda.gov/fdac/special/newdrug/ndd_toc.html
4. The Biological and Toxin Weapons Convention (BTWC) Main Page.(2001). This site reviews the 1972 convention which produced a treaty that prohibits the manufacture,

stockpiling or dissemination of biological weapons for offensive tactics.
http://projects.sipri.se/cbw/docs/bw-btwc-mainpage.html

5. Stockholm International Peace Research Institute (SIPRI), the Vrije Universiteit Brussel (Free University Brussels, VUB) and the International Relations and Security Network (ISN). "Iraq: Biological Weapons Capability" as found in *Educational Module on Chemical & Biological Weapons (non)-Proliferation, Iraq: A case study.* This site reviews the proliferation and subsequent non-proliferation strategies for biological weapons employed by nations at war.
http://cbw.sipri.se/cbw/002060200.html
6. Pearson, G. S., M. R. Dando, et al. (2001). *Review Conference Paper No. 4: 'The US Statement at the Fifth Review Conference: Compounding the Error in Rejecting the Composite Protocol'*. Fifth Review Conference of the Biological Weapons Convention, Palais des Nations, Geneva, Switzerland. This website has a number of papers and audio clips that deconstruct the U.S. position on Biological Weapons and Chemical Weapons Treaty Convention.
http://www.brad.ac.uk/acad/sbtwc/
There are also video clips of policy analysts and their views on the subject. These include Graham S. Pearson, and David Atwood and Jenni Rissanen. The Jenni Rissanen clip is the most informative.
http://www.brad.ac.uk/acad/sbtwc/other/bw-info.htm
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http://www.us-mission.ch/press2001/1911bolton.htm and
http://www.usmission.ch/press2001/1119boltonpress.htm
8. Okonek B, Peters P. *Vaccines—How and Why?*
http://www.accessexcellence.org/AE/AEC/CC/vaccines_how_why.html