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Bioterrorism with Toxins: Laboratory Response Networks

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The continued submission of materials contaminated with powder for select agent testing suggests that acts of terrorism are still on the minds of Americans. First responders submit samples to state public health laboratories where specimens are screened for select agents using validated protocols. First responders and public health laboratorians may suspect these samples do not contain select agents. Regardless, these materials are analyzed and treated as potential bioterrorism materials. The reaction to the terrorist attacks of 2001 was swift and decisive. The Laboratory Response Network (LRN), established by the Centers for Disease Control and Prevention (CDC) in 1999, played a pivotal role in providing "rapid and accurate" analyses of samples (environmental and clinical) suspected of containing select agents. Since anthrax (*Bacillus anthracis*) was the agent of choice in October 2001, materials and methods for its rapid and accurate identification were the first to be distributed to Level B/C laboratories (now called Reference Laboratories), which included most state public health laboratories. The LRN laboratories have shown competency in screening these powdery substances for the presence of *B. anthracis.*

However, other select agents pose an even greater threat due to being: 1. stable, 2. often lethal in a matter of hours, and 3. easy to acquire and/or produce. These include the toxins, ricin and botulinum toxin (botox). Ricin is derived from castor beans and induces its lethal effect by inhibiting protein synthesis; whereas, botox, the most poisonous substance known, causes paralysis by interfering with acetylcholine release at the neuromuscular junction (1, 2). Both of these toxins are or have potential use in medical therapeutics. Botox is used to treat a number of neurological disorders and is very popular in cosmetic treatment (3,4). Ricin is being evaluated as an immunotherapeutic agent for Hodgkin's lymphoma (5). Despite their medical uses, these toxins are

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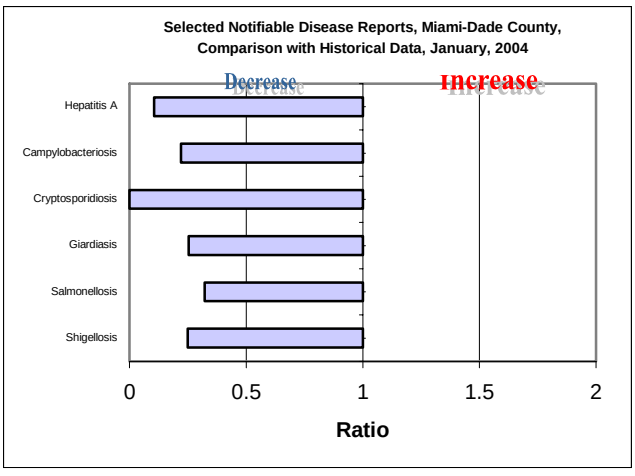
known more for their sinister applications. In January 2003, British law enforcement agencies arrested 6 Algerian men who were charged with producing ricin in their apartment. As a result, in April 2003 the FBI released a warning to law enforcement agencies about these toxins and terrorist activities. Recipes to make ricin have reportedly been found in Al Qaeda hideouts in Kabul and some U.S. supremacist groups have stockpiled the agent (6). The use or threat of use of these agents remains credible.

Clinical diagnostic assays for botox are lacking in most LRN Reference laboratories. If there is a strong suspicion of botox poisoning, hospital laboratorians or infection control practitioners should contact an epidemiologist at their local County Health Department (CHD). The epidemiologist will make the proper arrangements for direct submission of the specimen(s) to the CDC. Hospital laboratorians are encouraged to review the LRN Sentinel laboratory protocols posted on the CDC website: **http://www.bt.cdc.gov/agent/botulism/index.asp**, which outlines specimen collection, important telephone numbers, and proper packaging and shipping of specimens to CDC. There is currently no widely available and reliable clinical diagnostic assay to confirm that a person has been exposed to ricin.

The question remains regarding the hundreds of powdery substances screened at the LRN Reference laboratories. Most of these samples contain unknown substances with no associated adverse effects on human or animal health and well being. Fortunately, an analytical assay for ricin in environmental samples is available to LRN Reference laboratories. This antigen based assay is laborious and time-consuming, but a more rapid, nucleotide based assay will soon be available for use in LRN Reference laboratories.

Many first responders rely on immunochromatographic cards for rapid detection of these toxins despite the lack of scientific evidence for their performance. Manufacturers claim these immunochromatographic cards may detect the toxins and provide results within fifteen minutes. In addition, first responders are using analytical instruments, such as Fourier Transform Infrared Spectroscopy (FTIR), for rapid "detection and identification" of these substances. The role and use of these non-LRN validated assays and analytical methods, based on their specificity and sensitivity, is hotly debated. Consequently, the onus is on public health laboratories to provide rapid and accurate identification of these select agents.

1. Ricin Poisoning. Toxicol Rev 2003; 22 (1): 65-70.
2. Botulinum toxin as a biological weapon. JAMA 2001; 285 (8): 1059-1070.
3. Dystonia: medical therapy and botulinum toxin. Adv Neurol. 2004;94:275-86.
4. BOTOX: a review. Plast Surg Nurs. 2003; 23 (2):64-9.
5. Current strategies of antibody-based treatment in Hodgkin's disease. Ann Oncology 2002; 13 (Supplement1): 57-66.
6. Al Qaeda Recipe. www.foxnews.com



*Ratio of current month total to mean of 15 month totals (from previous, comparable, and subsequent month periods for the past 5 years).

Monthly Report
Selected Reportable Diseases/Conditions in Miami-Dade County, January 2004

Diseases/Conditions	2004 this Month	2004 Year to Date	2003 Year to Date	2002 Year to Date	2001 Year to Date	2000 Year to Date
AIDS *Provisional	134	134	112	96	104	131
Animal Rabies	0	0	0	0	0	0
Campylobacteriosis	3	3	6	2	5	0
Chlamydia trachomatis	210	210	296	472	177	65
Ciguatera Poisoning	0	0	0	0	0	0
Cryptosporidiosis	0	0	2	0	2	0
Cyclosporosis	0	0	0	0	0	0
Diphtheria	0	0	0	0	0	0
E. coli, O157:H7	0	0	0	0	0	0
E. coli, Non-O157	0	0	0	0	0	0
E. coli, Other	0	0	0	0	0	0
Encephalitis (except WNV)	0	0	0	0	0	0
Encephalitis, West Nile Virus	0	0	0	0	0	0
Giardiasis, Acute	5	5	1	3	2	0
Gonorrhea	86	86	143	229	94	46
Granuloma Inguinale	0	0	0	0	0	0
Hepatitis A	1	1	0	0	8	0
Hepatitis B	0	0	0	0	1	0
HIV *Provisional	168	168	131	182	176	175
Lead Poisoning	4	4	3	8	6	3
Legionnaire's Disease	0	0	0	0	0	0
Leptospirosis	0	0	0	0	0	0
Lyme disease	0	0	0	0	0	0
Lymphogranuloma Venereum	0	0	0	0	0	0
Malaria	0	0	0	1	0	0
Measles	0	0	0	0	0	0
Meningitis (except aseptic)	0	0	0	0	0	0
Meningococcal Disease	1	1	1	2	1	1
Mumps	0	0	0	0	0	0
Pertussis	0	0	0	0	0	0
Polio	0	0	0	0	0	0
Rubella	0	0	0	0	0	0
Rubella, Congenital	0	0	0	0	0	0
Salmonellosis	5	5	12	8	10	0
Shigellosis	8	8	13	6	5	0
Streptococcus pneumoniae, Drug Resistant	0	0	4	8	0	0
Syphilis, Infectious	18	18	21	18	10	10
Syphilis, Other	54	54	89	87	29	62
Tetanus	0	0	0	0	0	0
Toxoplasmosis	0	0	0	0	0	0
Tuberculosis *Provisional	12	12	24	13	11	15
Typhoid Fever	0	0	0	0	0	0
Vibrio cholera Type O1	0	0	0	0	0	0
Vibrio cholera Non-O1	0	0	0	0	0	0
Vibrio, Other	0	0	0	0	0	0

* Data on AIDS are provisional at the county level and are subject to edit checks by state and federal agencies.
** Data on tuberculosis are provisional at the county level.