

# ACCF/AHA/CDC Conference Report on Emerging Infectious Diseases and Biological Terrorism Threats

The Clinical and Public Health Implications for the Prevention and Control of Cardiovascular Diseases

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## Introduction

In this report, we summarize the findings from the conference on Emerging Infectious Diseases and Biological Terrorism Threats: The Clinical and Public Health Implications for the Prevention and Control of Cardiovascular Diseases, which was sponsored by the American College of Cardiology Foundation (ACCF), American Heart Association (AHA), and Centers for Disease Control and Prevention (CDC). The conference, held on August 13, 2004, at the Heart House in Bethesda, Maryland, allowed for open discussion, constructive commentary, and the formulation of summary statements resulting in the documents presented in the accompanying reports. The primary objectives of the conference were to review 1) the direct clinical cardiovascular implications of emerging infectious diseases and biological terrorism threats; 2) the indirect or secondary cardiovascular implications of biological terrorist events or preparedness strategies for potential bioterrorist events; 3) the best practices for managing suspected cardiovascular complications associated with emerging infectious diseases and biological terrorism threats; and 4) the basic, clinical, and population science research and training needs in this arena.

Four task forces were formed to address each of the 4 conference objectives. Each task force was charged with producing a report summarizing the relevant conference findings, as well as developing summary statements and future directions for the prevention and control of cardiovascular diseases and complications during an actual bioterrorist attack.

In this executive summary and the accompanying task force reports, the term “emerging infectious diseases” includes both emerging (newly recognized, clinically distinct infectious diseases) and re-emerging infectious diseases (known infectious diseases whose reported incidence is increasing in a given place or among a specific population). The term “biological terrorism threats” includes the poten-

tial intentional release of both infectious and noninfectious (e.g., toxic) agents in terrorist acts. Overall, the primary focus is on the clinical and public health implications of emerging infectious diseases and biological terrorism threats for the cardiovascular system. The cardiovascular implications of other disasters and threats involving radiological or chemical substances are not primary subjects of these reports.

## Background

The threats of emerging infectious diseases and the potential intentional use of biological agents in terrorist acts are important national security concerns (1). They also pose major challenges for clinical medicine and public health in addressing preparedness and response (1,2). The Institute of Medicine alone has held several workshops and published more than a dozen related reports over the last decade on these challenges (3), but none of them specifically addresses the cardiovascular implications of this threat. Both emerging infectious diseases and biological terrorism threats are part of the spectrum of “microbial threats,” including established infectious diseases (4).

Reports on population-based surveillance at several CDC U.S. Emerging Infections Program sites for unexplained death and critical illness of possible infectious causes in the U.S. in 1995 to 1998 identified cardiac signs and symptoms as the third most common clinical presentation (5). Yet, despite the important advances in the scientific understanding of these diseases and the extent of national public health activities in preparedness related to potential intentional releases of biological agents, strategies to address the potential direct and indirect cardiovascular effects of these agents in the evaluation and management of persons with cardiovascular diseases or risk factors remain largely unexplored.

Questions that remain to be answered include: What should the cardiovascular specialist and other health care providers who treat patients with heart disease know about

Please also see the full writing group and task force listing (*Circulation*. 2007;115:1656–1658) and Task Force Reports (*Circulation*. 2007;115:1663–1695). (*Circulation*. 2007;115:1659-1662.)

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emerging infectious diseases? What are the signs, symptoms, and other clinical cardiovascular manifestations of inhalation anthrax or smallpox infection? Would physicians readily recognize the possible cardiovascular symptoms of infection with hantavirus (pulmonary syndrome), avian influenza virus, or endocarditis and other cardiovascular manifestations of brucellosis, tularemia, or Q fever? What are the presenting manifestations of myopericarditis when it complicates smallpox pre-event vaccination? Which people with pre-existing cardiovascular disease should be excluded from preventive interventions, such as pre-event vaccination, against bioterrorist threats? What are the current recommendations for antimicrobial and other preventive interventions? The quest for answers to these questions formed the basis of the conference and the resulting summary and task force reports.

### **TASK FORCE I: Direct Cardiovascular Implications of Emerging Infectious Diseases and Biological Terrorism Threats**

Task Force I reviewed the direct clinical cardiovascular implications of emerging infectious diseases and infection with select agents designated to have potential for intentional release (4,6) as listed and described on the CDC Emergency Preparedness and Response Web site (<http://www.bt.cdc.gov/agent/agentlist.asp>). The report presents the CDC classification of bioterrorism agents and diseases into Categories A, B, and C on the basis of their ease of dissemination or transmission from person to person, potential for causing high mortality or major public health impact, and/or requirement for special procedures or actions during public health preparedness. The Web site presents the routes of infection, associated signs and symptoms, and recommended diagnostic procedures for the evaluation of these agents and diseases, which include anthrax, botulism, plague, smallpox, tularemia, viral hemorrhagic fevers, ricin toxin, brucellosis, Q fever, psittacosis, and salmonellosis.

Although many of these agents are uncommon in the U.S., and most of them do not primarily affect the cardiovascular system, some do have the potential to produce direct cardiovascular effects and have substantial implications for individuals with underlying cardiovascular disease. These possibilities require that health care providers become familiar with the diseases these agents cause and their impact on the cardiovascular system.

In general, the known direct cardiovascular effects of these pathogens and biological toxins fall under 4 predominant syndromes: 1) endocarditis, 2) myocarditis, 3) pericarditis, and 4) endarteritis. The clinical manifestations of these syndromes do not vary by microbiologic etiology. When infection is uncommon and unanticipated in certain populations or geographic settings, or in the event of

intentional release, these signs and symptoms could be indistinguishable from those of naturally occurring infections or the progression of underlying cardiovascular disease. In the case of aggressive pathogens, clinical evidence might develop within hours to days, whereas infection with less virulent microorganisms might produce more subtle, indolent, and initially nonspecific signs and symptoms over weeks or months. Other direct cardiovascular manifestations that pose diagnostic and therapeutic challenges, especially in patients with established cardiovascular disease, include fever, tachycardia, hemodynamic collapse, and other cardiopulmonary effects of systemic toxicity or sepsis.

The report recommends that cardiovascular specialists and other health care providers who treat patients with heart disease develop a general working knowledge of the high-priority potential bioterrorist agents and their possible modes of dissemination, the clinical presentation of infection, and recommended diagnostic evaluations. Health care providers should also become familiar with the federal, state, and local surveillance capabilities and networks of specialized laboratories that are part of national public health preparedness. These resources are invaluable when exposure to a potential bioterrorist agent is suspected. Continuing medical education in these areas should be considered an important aspect of national preparedness.

### **TASK FORCE II: Indirect and Secondary Cardiovascular Effects of Biological Terrorism Agents and Diseases**

Task Force II addressed the indirect or secondary cardiovascular implications of bioterrorism threats and preparedness strategies (e.g., immunization against smallpox using the vaccinia vaccine). Key areas reviewed include the cardiovascular effects of mass pre-event vaccination campaigns; the pathophysiological basis for stress-related triggering of acute cardiovascular events; and the capacity for large-scale terrorist events to overwhelm the emergency medical and health care system, straining a community's ability to provide timely care for patients with more conventional but time-dependent, medical, and surgical emergencies such as acute cardiac events and stroke. The possible use of pharmacologic prophylaxis in vulnerable populations is also addressed.

In addition, the effect of a terrorist attack on the health care system, particularly as it relates to the care of patients with underlying cardiovascular disorders, will depend on how many victims survive and need significant medical care, the nature of the attack, and how long the influx of patients and need for care continues. The report emphasizes that this need for surge capacity for all emergency situations must be addressed. One valuable model discussed is the congressionally funded emergency department renovation plan devel-

oped for the Washington Hospital Center, the Level 1 trauma center serving the nation's capitol (<http://er1.org>).

The report recommends further research on the cardiovascular complications of vaccines to determine whether individuals at higher risk for adverse effects can be identified prospectively and whether alternative preventive and therapeutic interventions should be offered to these individuals. In addition, further study is needed on the links between the psychological stress associated with bioterrorism and acute cardiovascular events, particularly with respect to whether any additional prophylactic measures can be used for individuals at increased risk. The report also recommended further research on the chronic, long-term effects of bioterrorist attacks. Policy considerations addressed include strategies to increase surge capacity of hospitals, establishment of appropriate surveillance systems, and widespread adoption of electronic health records with collection of specific, uniformly defined data elements that could facilitate the use of these data in a real-time national surveillance system.

### **TASK FORCE III: Prevention and Control of Cardiovascular Complications of Emerging Infectious Diseases and Potential Biological Terrorism Agents and Diseases**

Task Force III addressed the current best practices for the prevention and control of cardiovascular complications of emerging infectious diseases and potential bioterrorist threats. The report stresses the importance of early recognition of signs and symptoms suggesting cardiovascular involvement, appropriate management of acute events, and long-term care. It also discusses strategies for preventing the spread of infection or disease in cardiac catheterization laboratories and cardiac care units.

Best practices for patient management are reviewed in the context of the 4 predominant cardiovascular syndromes (endocarditis, myocarditis, pericarditis, and endarteritis) associated with emerging infectious diseases and potential biological threats, as well as their potential metabolic, arrhythmogenic, and hemodynamic impact on the cardiovascular system. Current guidelines for pre-event vaccinations, postexposure prophylaxis where available, protection of health care workers, and the role of cardiovascular specialists and other health care providers in bioterrorism preparedness are also discussed.

The report recommends that all patients with suspected vaccinia-associated heart disease undergo a comprehensive physical examination to identify potential pericardial rub or evidence of heart failure and vaccinia rash, and to collect baseline cardiac diagnostic data including electrocardiogram, chest X-ray, troponin test, and creatinine kinase-MB. The report emphasizes that although the treatment for pericarditis is generally symptomatic, myopericarditis with

severe left ventricular dysfunction may require invasive studies. Most cases of myopericarditis after vaccinia vaccination are mild and resolve with supportive care, but in the unusual case of severe left ventricular dysfunction, endomyocardial biopsy can help define the mechanism of myocarditis (7). The treatment for endocarditis and endarteritis resulting from vaccinia vaccination should follow current clinical guidelines (8).

Current recommendations for delivering pre- and post-event vaccinia vaccination, as well as postexposure antimicrobial prophylaxis, are presented. In general, persons who should not receive pre-event vaccination for smallpox include clinically immunocompromised persons; people with life-threatening allergies to latex or to the smallpox vaccine or any of its ingredients; those with established cardiovascular disorders, including congestive heart failure, ischemic or dilated cardiomyopathy, or a history of myocarditis or pericarditis; and persons with 3 or more risk factors for coronary heart disease (<http://www.bt.cdc.gov/agent/smallpox/vaccination/heartproblems.asp>).

The report highlights the current resources available to clinicians including materials and tools from the CDC and other federal agencies. For example, the CDC has established a free registry to provide clinicians with real-time information to help prepare for (and possibly respond to) terrorism and other emergency events. Participants receive regular e-mail updates on terrorism and other emergency issues and on training opportunities relevant to clinicians (<http://www.bt.cdc.gov/clinregistry/index.asp>; <http://www.bt.cdc.gov/agent/smallpox/clinicians.asp#register>).

Patients suspected to have an emerging infectious disease or be infected with an organism considered a bioterrorism risk—including those with a high likelihood of airborne or blood transmission—may need to undergo special cardiac procedures in a cardiac catheterization laboratory or cardiac care unit. The report discusses the infection control measures needed to avoid nosocomial spread of infection in these settings, including education for hospital personnel, personal protective measures, and environmental safety measures.

### **TASK FORCE IV: Cardiovascular Effects of Emerging Infectious Diseases and Biological Terrorism Threats: Basic, Clinical, and Population Science Research and Training Needs**

Task Force IV addressed gaps in the basic, clinical, and population science research available to guide best practices for the prevention and control of cardiovascular complications resulting from emerging infectious diseases and biological terrorism threats. The report discusses the importance of epidemiologic studies and an appropriate research infrastructure for surveillance and response. Also discussed

are the training needs of health care providers and others (including the lay public) who could be called on to provide care to those experiencing cardiovascular complications from bioterrorist events.

The report notes that translational and interdisciplinary research approaches are required to compile the information from animal, human, and population-based studies needed to achieve a comprehensive understanding of how to identify, prevent, and treat the potential direct and indirect cardiovascular effects of these agents. Needed measures include syndromic surveillance (9,10), studies of the potential cardiovascular complications of immunization, and the use of animal models to study the effect of potential bioterrorist agents on atherosclerotic plaques, the coagulation system, circulatory components, and the conduction system. In particular, the potential role of these agents in triggering acute destabilization of vulnerable plaques, leading to acute coronary syndromes or contributing to atherosclerosis progression (11) deserve further study.

The report urges cardiovascular research scientists, academic institutions, and the cardiovascular professional societies to form strategic partnerships with federal agencies that fund biodefense research. Such partnerships could address these cardiovascular research needs and strengthen the public health infrastructure (12) for future research on the cardiovascular implications of emerging infectious diseases and biological terrorism threats. The report stresses the need to define and implement environmental safety procedures for catheterization laboratories and coronary care or intensive care units that may care for patients infected with highly contagious agents. In addition, the impact of vaccination, anti-toxin and -infective therapy, and post-exposure antimicrobial prophylaxis in patients with pre-existing cardiovascular disease deserve further study.

### Task Force Reports

The reports of each of the 4 task forces follow this executive summary. The authors of each report summarize the relevant conference discussions, as well as the appropriate literature. In addition, the authors offer suggestions for improving our understanding of the cardiovascular effects of potential bioterrorist agents, enhancing our ability to prevent and treat these effects, and better preparing first responders and health care providers to quickly identify and

treat the cardiovascular manifestations that could follow a future bioterrorist attack. These suggestions and the opinions expressed in the reports are those of the authors and should not be construed as necessarily representing the views of their affiliated institutions, the ACCF, AHA, or the CDC.

### REFERENCES

1. Gerberding JL, Hughes JM, Koplan JP. Bioterrorism preparedness and response: clinicians and public health agencies as essential partners. *JAMA* 2002;287:898–900.
2. Hamburg MA. Bioterrorism: a challenge to public health and medicine. *J Public Health Manag Pract* 2000;6:38–44.
3. Institute of Medicine, Board on Global Health, Forum on Microbial Threats. *Biological Threats and Terrorism: Assessing the Science and Response Capabilities*. Available at: <http://www.iom.edu/CMS/3783/3924/4326.aspx>. Accessed on December 21, 2006.
4. Institute of Medicine. *Emerging Infections: Microbial Threats to Health in the United States*. Washington, DC: National Academy of Sciences, 1992.
5. Hajjeh RA, Relman D, Cieslak PR, et al. Surveillance for unexplained deaths and critical illnesses due to possibly infectious causes, United States, 1995–1998. *Emerg Infect Dis* 2002;8:145–53.
6. Rotz LD, Khan AS, Lillibridge SR, Ostroff SM, Hughes JM. Public health assessment of potential biological terrorism agents. *Emerg Infect Dis* 2002;8:225–30.
7. Murphy JG, Wright RS, Bruce GK, et al. Eosinophilic-lymphocytic myocarditis after smallpox vaccination. *Lancet* 2003;362:1378–80.
8. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association—executive summary: endorsed by the Infectious Diseases Society of America. *Circulation* 2005;111:3167–84.
9. Yih WK, Caldwell B, Harmon R, et al. National Bioterrorism Syndromic Surveillance Demonstration Program. *MMWR Morb Mortal Wkly Rep* 2004;53 Suppl:43–9.
10. Loonsk JW. BioSense—a national initiative for early detection and quantification of public health emergencies. *MMWR Morb Mortal Wkly Rep* 2004;53 Suppl:53–5.
11. Libby P, Egan D, Skarlatos S. Roles of infectious agents in atherosclerosis and restenosis: an assessment of the evidence and need for future research. *Circulation* 1997;96:4095–103.
12. Grantmakers in Health. Strengthening the public health system for a healthier future. *Issue Brief* 2003;17:1–41.

### APPENDIX 1. ACCF/AHA/CDC CONSENSUS CONFERENCE REPORT ON EMERGING INFECTIOUS DISEASES AND BIOLOGICAL TERRORISM THREATS: EXECUTIVE SUMMARY—RELATIONSHIPS WITH INDUSTRY

The authors of this report declared that they have no relationships to industry pertinent to this topic.

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