THE CSTE WASHINGTON REPORT

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INSIDE THIS ISSUE

EDITOR'S NOTE: Emerging infectious diseases, which have shaped the course of humanity and caused incalculable suffering and death, will continue to confront society in unpredictable ways as long as humans and microbes co-exist, write authors from the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health in a review article published in the July 8 issue of the journal *Nature*. "The global scientific and public health communities must confront this reality…with vision and sustained commitment to meet a perpetual challenge," write David M. Morens, M.D, Gregory K. Folkers, M.S., M.P.H., and NIAID Director Anthony S. Fauci, M.D. "Broadly based prevention strategies, as well as new and improved countermeasures, including surveillance tools, diagnostics, therapeutics and vaccines, must continually be tested, refined and upgraded," says Dr. Fauci. "This will require a strengthened relationship between public health and basic and clinical science" -- additional details are provided in this Washington Report.

The CSTE Washington Report is provided as an information resource for members of the Council of State and Territorial Epidemiologists on federal legislation and regulation affecting public health and epidemiology in the U.S. Legislation cited in the report can be accessed via http://www.thomas.loc.gov Regulations cited can be accessed via http://www.gpo.gov

APPROPRIATIONS UPDATE – On July 8th, the House Labor-HHS-Education Appropropriations Subcommittee marked up its FY 2005 bill. Although Democrats complained that the bill did not provide enough funding, Members unanimously approved $142.5 billion in discretionary spending, a 2.2 percent increase over FY 2004 and $202 million more than the President's request. The full Appropriations Committee took up the bill on 7/14, but numbers have not changed. Rep. Dave Weldon (R-FL) offered and then withdrew a troublesome amendment that withholds CDC funding for any purchase of 2005-2006 flu vaccine that contains thimerosal and distribution for children under age 6. He may offer the amendment on the Senate floor when the bill is taken up by the full House, possibly as soon as next week. CDC contends in a fact sheet they developed that the Weldon amendment would result in vaccine shortages for the 2005-2006 flu season. Public health groups, with ASTHO in the lead, oppose the amendment.

The Senate Labor-HHS-Education Appropriations Subcommittee currently has no plans to mark up its FY 2005 bill. Democrats want to offer a myriad amendments on the Senate floor to all appropriations bills, and this is causing the Republican leadership to delay taking up any of the measures.

Below are some funding specifics from the House Subcommittee mark up:

State and Local Terrorism Preparedness

FY 2004	$934 million
FY 2005 Pres. Request	$829 million
Subcommittee mark	$934 million (approximate; includes assumption of $27 million to continue Cities Readiness Initiative)
Difference	$0

Health Track Grants

FY 2004	$28 million
FY 2005 Pres. Request	$28 million
Subcommittee mark	$28 million
Difference	$0

HIV/AIDS Surveillance

FY 2004	$58 million
FY 2005 Pres. Request	$58 million
Subcommittee mark	$58 million (estimated)
Difference	$0

Occupational Surveillance

FY 2004	$1.5 million
FY 2005 Pres. Request	$1.5 million (estimated)
Subcommittee mark	$1.5 million (estimated)
Difference	$0

CENTERS FOR DISEASE PREVENTION AND CONTROL

Birth Defects/Developmental Disabilities/Disability and Health

FY 2004	$ 112,743,000
FY 2005 Pres Reqst	$ 112,972,000
Subcommittee Mark	$ 119,214,000
Difference 2004	$+ 6,471,000

Chronic Disease Prevention and Health Promotion

FY 2004	$ 853,378,000
FY 2005 Pres Reqst	$ 915,425,000
Subcommittee Mark	$ 915,711,000
Difference 2004	$+ 62,333,000

Environmental Health

FY 2004	$ 183,212,000
FY 2005 Pres Reqst	$ 183,795,000
Subcommittee Mark	$ 186,113,000
Difference 2004	$+ 2,901,000

Epidemic Services and Response

FY 2004	$ 91,776,000
FY 2005 Pres Reqst	$ 92,485,000
Subcommittee Mark	$ 91,766,000
Difference 2004	$ 0

Health Statistics

FY 2004	$ 127,634,000
FY 2005 Pres Reqst	$ 149,600,000
Subcommittee Mark	$ 149,600,000
Difference 2004	$+ 21,966,000

HIV/AIDS, STD and TB Prevention

FY 2004	$ 1,141,661,000
FY 2005 Pres Reqst	$ 1,143,299,000
Subcommittee Mark	$ 1,149,330,000
Difference 2004	$+ 7,669,000

Immunization

FY 2004	$ 643,344,000
FY 2005 Pres Reqst	$ 644,070,000
Subcommittee Mark	$ 654,070,000
Difference 2004	$+10,726,000

Infectious Disease Control

FY 2004	$ 369,485,000

FY 2005 Pres Reqst $ 400,779,000
Subcommittee Mark $ 398,439,000
Difference 2004 $+ 28,954,000

Injury Prevention and Control
FY 2004 $ 153,591,000
FY 2005 Pres Reqst $ 153,879,000
Subcommittee Mark $ 155,591,000
Difference 2004 $+ 2,000,000

Occupational Safety and Health
FY 2004 $ 276,988,000
FY 2005 Pres Reqst $ 278,587,000
Subcommittee Mark $ 278,587,000
Difference 2004 $+ 1,599,000

Preventive Health and Health Services Block Grant
FY 2004 $ 133,298,000
FY 2005 Pres Reqst $ 133,298,000
Subcommittee Mark $ 110,000,000
Difference 2004 $- 23,298,000

Public Health Improvement
FY 2004 $ 172,562,000
FY 2005 Pres Reqst $ 113,292,000
Subcommittee Mark $ 128,774,000
Difference 2004 $- 43,788,000

TOTAL CDC
FY 2004 $ 4,579,299,000
FY 2005 Pres Reqst $ 4,462,654,000
Subcommittee Mark $ 4,477,878,000
Difference 2004 $- 101,421,000

HEALTH GROUPS REINSTATE RECOMMENDATION FOR THIRD DOSE OF PEDIATRIC PNEUMOCOCCAL CONJUGATE VACCINE (PREVNAR®) --
Public health and physician groups July 8 recommended that healthcare providers increase the number of doses of pneumococcal conjugate vaccine (PCV7, trade name Prevnar®) administered to healthy children from two to three. Production problems earlier this year caused shortages of the vaccine and prompted the Centers for Disease Control and Prevention (CDC) to reduce the recommended four doses to two to most effectively use the limited available doses.

The CDC, the Advisory Committee on Immunization Practices, American Academy of Family Physicians, and the American Academy of Pediatrics also recommended that providers continue to administer the full four-dose series of the vaccine to children up to

15 months of age with health conditions such as sickle cell anemia or immune system disorders, who are at increased risk of severe disease. The groups said providers should defer the fourth dose of the vaccine for healthy children until production and supply data convincingly demonstrate supplies of the vaccine are adequate for routine administration of the four-dose series.

"CDC has worked closely with the manufacturer to assess the situation and manage limited supplies of the vaccine. Supplies are now adequate to reinstate the third dose," said Dr. Steve Cochi, acting director of the CDC National Immunization Program. "We will continue to closely monitor supplies and will make additional recommendations if the supply situation changes."

The vaccine can help prevent serious pneumococcal diseases, such as meningitis and blood infections. Pneumococcal infection can cause serious illness and even death. Invasive pneumococcal disease is the leading cause of bacterial meningitis in the United States. Children under two years of age are at highest risk. Before a vaccine was available, each year pneumococcal infection caused more than 700 cases of meningitis, 13,000 blood infections and about 5 million ear infections.

In February 2004, CDC recommended suspension of the fourth dose of PCV7 when it learned the manufacturer, Wyeth Vaccines (Collegeville, PA), would not be able to produce enough vaccine to meet demand. In March, when it became clear that production would be curtailed for several months, CDC recommended the third dose also be withheld.

The vaccine is normally recommended for young children in a four-dose schedule: one dose each at 2 months, 4 months, and 6 months of age, and one dose between 12 and 15 months of age. This recommendation reinstates the third dose usually administered at 6 months for healthy children. PCV7 is not routinely recommended for children older than two years.

The public health and medical groups today also recommended a catch-up schedule for children who missed the third dose. The highest priority for catch-up vaccination is children at high risk for invasive pneumococcal disease. Second priority is vaccination of healthy children younger than 24 months who have not received any doses of pneumococcal conjugate vaccine. The third priority is vaccination of healthy children younger than 12 months of age who have not yet received 3 doses.

Because of the frequency of health-care provider visits for children during their first 18 months, catch-up vaccination might occur at regularly scheduled visits for most children who receive vaccines from their primary-care provider. Providers who administer vaccinations but do not see children routinely for other reasons should consider a notification process to contact parents of under-vaccinated children.

More information about these recommendations and PCV7 (Prevnar®) is available at: http://www.cdc.gov/nip/news/shortages/.

NEW METHOD ENABLES RESEARCHERS TO MAKE HUMAN SARS ANTIBODIES QUICKLY -- Human antibodies that thwart the SARS virus in mice can be mass-produced quickly using a new laboratory technique developed by an international research team collaborating with the National Institute of Allergy and Infectious Diseases (NIAID), one of the National Institutes of Health. The new technique could become an important tool for developing a cocktail of SARS-specific antibodies that might help protect people recently exposed to the SARS virus or at high risk of exposure. The technique could also make possible the development of a similar approach to prevent or treat other illnesses, such as HIV/AIDS and hepatitis C.

The report describing these findings appears in the July 11, 2004, online issue of *Nature Medicine*."While much has been accomplished in our quest for a vaccine against SARS, a vaccine may provide little benefit to someone already infected," says Anthony S. Fauci, M.D., director of NIAID. "Human SARS antibodies could offer a double benefit: they could be used as a potent frontline defense for health care workers and others at high risk of exposure and as an effective treatment for those individuals newly exposed to the virus." Currently, there is no specific effective treatment for SARS.

SARS is caused by a coronavirus, a family of viruses named for their spiky, crown-like appearance. Highly contagious, SARS typically begins with flu-like symptoms, such as fever, headache and muscle aches, and generally progresses to pneumonia. In the 2003 global outbreak, more than 8,000 people were infected with SARS, 9 percent of whom died. In April 2004, a small outbreak in China is suspected to have begun as a result of negligent laboratory practices.

In the current study, Elisabetta Traggiai, Ph.D., and Antonio Lanzavecchia, M.D., from the Institute for Research in Biomedicine, Bellinzona, Switzerland, together with an international research team, generated human antibodies against SARS far more quickly and efficiently than with current methods. Moreover, collaborators Kanta Subbarao, M.D., and Brian Murphy, M.D., both in NIAID's Laboratory of Infectious Diseases, demonstrated for the first time that these human SARS antibodies, when injected into mice, effectively prevent the virus from multiplying in the respiratory system.

"The antibodies from people who have recovered from SARS may target different parts of the virus than antibodies generated by other animals, such as mice," says Dr. Subbarao. "For this reason, human antibodies — antibodies from recovered patients that may have a proven effectiveness in fighting the disease — are considered most desirable for a possible serotherapy against SARS."

Antibodies are made by special immune system cells called B cells that, to do their job, must first be switched on. In nature, this occurs when the body encounters a new or repeat foreign "invader." In the laboratory, researchers conventionally accomplish this by exposing the B cells to Epstein Barr virus (EBV), a herpes virus that infects B cells, which in turn activates them. Unfortunately, this process is very inefficient, and only one or two B cells out of one hundred are activated this way.

Dr. Lanzavecchia and his research team added a new ingredient to the mix that significantly boosts efficiency. Beginning with B cells from a recovered SARS patient, the researchers added a short stretch of synthetic DNA that mimics DNA found in bacteria and viruses. From 30 to 100 percent of the B cells — in this case called "memory" B cells because they had been exposed to the SARS virus before — were switched back on, enabling them to churn out SARS antibodies at a fast pace. In only a few weeks, the researchers screened hundreds of antibodies and obtained 35 that could neutralize the SARS virus in the laboratory. All the neutralizing antibodies targeted a key SARS protein, the spike protein, found on the virus surface.

Furthermore, when Drs. Subbarao and Murphy injected one of the neutralizing antibodies into mice, they found that these antibodies effectively thwarted the SARS virus from multiplying in the lower respiratory tract, which includes the lungs, and, to a lesser extent, in the upper respiratory tract, which includes the nasal cavity. According to Dr. Subbarao, these results are very promising because replication of SARS in the lungs of humans can result in pneumonia.

A primary benefit of the new activation technique is that it generates a large pool of prospective antibodies from which to choose, so only the most effective SARS fighters can be chosen for use in a possible immune serum. Because viruses can mutate, however, more than one antibody will most likely be needed to achieve the optimal protection or treatment, the researchers contend.

The researchers' next goal is to find additional antibodies against the SARS virus, focusing on those that attach most readily to the virus, are most potent against the virus, and can attach to more than one site on the spike protein. Before the antibodies might be made available for clinical use, researchers need to test them for their effectiveness in other laboratory animals, such as non-human primates, as well as in human clinical trials.

THE CONTINUAL CHALLENGE OF EMERGING INFECTIOUS DISEASES -- Emerging infectious diseases, which have shaped the course of humanity and caused incalculable suffering and death, will continue to confront society in unpredictable ways as long as humans and microbes co-exist, write authors from the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health in a review article published in the July 8 issue of the journal *Nature*.

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"Broadly based prevention strategies, as well as new and improved countermeasures, including surveillance tools, diagnostics, therapeutics and vaccines, must continually be tested, refined and upgraded," says Dr. Fauci. "This will require a strengthened relationship between public health and basic and clinical science."

In their paper, the authors classify three types of emerging infections and consider methods for their control: newly emerging infections (e.g. HIV, SARS); re-emerging/resurging infections (e.g. influenza, West Nile virus); and deliberately emerging infections (e.g. microbes used for bioterror).

The authors note that emerging infectious diseases are superimposed on a constant backdrop of established infections. Approximately 15 million deaths in 2002 were directly attributable to infections, according to the World Health Organization. Tragically, the authors point out, the burden of all infections falls most heavily on those least able to manage them: people living in developing countries, especially infants and children, and indigenous and disadvantaged minorities in developed countries.

Why do infectious diseases emerge and re-emerge? The viruses, bacteria and parasites that cause these diseases continually and sometimes dramatically change over time. The authors note that emergence results from "…dynamic interactions between rapidly evolving infectious agents and changes in the environment and in host behavior that provide such agents with favorable new ecological niches." As a result, new pathogens arise, and familiar ones re-emerge with new properties or in unfamiliar settings. Historically, the authors write, the results have been devastating. For example, importation of smallpox into Central America caused 10-15 million deaths in 1520-1521, effectively ending Aztec civilization. AIDS, first recognized in 1981, now threatens to surpass in global fatality the "Black Death" of the 14th century and the influenza pandemic of 1918-1919, two notable infections that emerged to each kill tens of millions of people.

In the past five years alone, two pathogens well known to countries on other continents were seen in the Unites States for the first time — West Nile virus and monkeypox virus. In addition, a new infectious disease, SARS, emerged in 2003 and has since caused more than 8,000 cases of illness and nearly 800 deaths around the world. In addition, in 2001 the United States was confronted with a third, extremely disquieting category of threat: a disease resulting from the deliberate release of an infectious agent, anthrax, by a terrorist(s).

The authors write that an effective response to any new infectious disease threat, whether it emerges, re-emerges, or is deliberately introduced, involves mobilizing many different types of public health activities. In particular, frontline surveillance and response is critical and depends on rapid detection, clinical diagnosis and containment. Concomitantly, basic and applied research enables the development of medical countermeasures such as surveillance tools, diagnostic tests, vaccines and therapeutics. The authors note that these efforts have been accelerated by advances in fields such as genomics/proteomics, nanotechnology, direct and computational structural determination, immunology, and geographical information systems and satellite imaging.