THE CSTE WASHINGTON REPORT

Marcia S. Mabee, MPH, PhD
Editor
11479 Waterview
Reston, Virginia 20190
mmabee@ix.netcom.com
703-709-3001

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EDITOR'S NOTE: Federal scientists have developed a vaccine that protects mice against the killer 1918 influenza virus. They also have created a technique for identifying antibodies that neutralize this virus, a tool that could help contain future pandemic flu strains. These findings are important, the researchers say, to understanding and preventing the recurrence of the H1N1 influenza virus that caused the 1918 pandemic and to protecting against virulent flu strains in the future, including the H5N1 avian flu virus. Details of the research are available online in *Proceedings of the National Academy of Sciences*-- 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

CSTE WILL OPPOSE HAGEL-TERRY BILL TO CREATE A SYSTEM OF NATIONAL REPORTABLE CONDITIONS TO THE DEPARTMENT OF HOMELAND SECURITY -- On September 14th, Senator Chuck Hagel (R-NE) and Rep. Lee Terry (R-NE) introduced legislation (S. 3898/H.R. 6086) that amends the Homeland Security Act to provide for the health of Americans by implementing a system that detects and identifies, in a timely manner, diseases, conditions, and events that represent a threat to humans, animals, food production and the water supply. The legislation has been referred to the Senate Committee on Homeland Security and Government Affairs and the Subcommittee on Health of the Energy and Commerce Committee. It is very unlikely there will be further action on the bills before the 109th Congress formally adjourns, probably sometime before January 1, 2007, but this will be monitored. CSTE's leadership is committed to opposing the legislation and is developing strategy to defeat it.

CDC AWARDS $5.2 MILLION TO EVALUATE COMMUNITY STRATEGIES TO REDUCE IMPACT OF PANDEMIC INFLUENZA -- The Centers for Disease Control and Prevention October 10 announced $5.2 million in new cooperative agreements designed to evaluate the effectiveness of community-level measures that could be used during an influenza pandemic to reduce the spread of infection.

Because developing a vaccine against a pandemic influenza strain could take several months, community prevention strategies that don't involve vaccines or other drugs (also called "non-pharmaceutical interventions") may serve as a first line of defense to help delay or reduce the spread of disease. However, little scientific research currently exists on the effectiveness and potential impact of such strategies. Therefore, these studies are designed to identify and evaluate quickly what kinds of non-pharmaceutical strategies, alone or in combination, may help reduce or contain the spread of pandemic influenza.

"While we can't predict the severity of an influenza pandemic before it begins, our ability to effectively respond will depend on how well communities and states can take steps to reduce spread of disease," said CDC Director Dr. Julie Gerberding. "Our challenge now is to determine which community-level measures will work best to limit the spread of infection."

Community prevention strategies are public health measures other than drugs, which are aimed at reducing the spread of disease. For pandemic influenza, examples include simple infection control measures such as hand washing, cough etiquette and mask use; social distancing strategies that involve reducing contact with other people including closing schools or workplaces and canceling large public gatherings; voluntary isolation of cases; and voluntary quarantine of household contacts.

The studies and their principal investigators are:

- Effectiveness of Selective Non-Pharmaceutical Interventions in Reducing Influenza-Like Illness Among University Students
  Tomas Aragon, M.D., University of California, Berkeley, CA

- Pittsburgh Influenza Prevention Project
  Donald Burke, M.D. and Sam Stebbins, M.D., University of Pittsburgh, Pittsburgh, PA

- Non-Pharmaceutical Interventions for Pandemic Influenza
  Scott Holmberg, M.D., RTI International, Research Triangle Park, NC

- A Controlled Trial of Masks and Hand Hygiene for Reducing Influenza Transmission
  Gabriel Leung, M.D. University of Hong Kong, Hong Kong, China

- Reducing Transmission of Influenza by Face Masks
  Arnold Monto, M.D. University of Michigan, Ann Arbor, MI

- Stopping Upper Respiratory Infections and Influenza in the Family: The Stuffy Trial
  Elaine Larson, Ph. D. Columbia University, New York, NY

- Pandemic Influenza Control at the Borders of Island Countries and in Households
  Michael Baker, M.D. University of Otago, Otago, New Zealand

- Evaluation of Masks as a Source Control Non-Pharmaceutical Intervention
  Donald Milton, M.D. Ph.D., University of Massachusetts, Lowell, MA

For more information about CDC's efforts to prepare for pandemic influenza, please visit www.pandemicflu.gov.

EXPERIMENTAL VACCINE PROTECTS MICE AGAINST DEADLY 1918 FLU VIRUS -- Federal scientists have developed a vaccine that protects mice against the killer 1918 influenza virus. They also have created a technique for identifying antibodies that neutralize this virus, a tool that could help contain future pandemic flu strains. These findings are important, the researchers say, to understanding and preventing the recurrence of the H1N1 influenza virus that caused the 1918 pandemic and to protecting against virulent flu strains in the future, including the H5N1 avian flu virus. Details of the research are available online in *Proceedings of the National Academy of Sciences*.

Gary J. Nabel, M.D., Ph.D., director of the Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), led the research team in developing the experimental vaccines and conducting the immunological studies in mice. Terrence Tumpey, Ph.D., of the Centers for Disease Control and Prevention (CDC) conducted vaccine studies in mice involving the live, reconstructed 1918 flu virus in a biosafety level 3-enhanced laboratory at the CDC in Atlanta — one of four types of specialized biosafety labs where scientists study contagious and potentially deadly materials under high-level safety and contamination precautions designed to protect the researchers and prevent microorganisms from entering the environment.

ìUnderstanding why this influenza virus was so deadly is an extremely important question,î says NIAID Director Anthony S. Fauci, M.D. ìBy building upon earlier

research where scientists successfully reconstructed the 1918 pandemic flu strain, Dr. Nabel and his colleagues have demonstrated that this virus is vulnerable to intervention. This knowledge will help further our continued efforts to develop treatments and vaccines to protect us against another deadly flu pandemic.î

The 1918-1919 influenza pandemic was the most deadly flu outbreak in modern history, killing 50 million or more people worldwide.

ìA key to containing pandemic flu viruses is to understand their vulnerabilities and determine whether they can evade immune recognition,î says Dr. Nabel. ìWhat we learn about the H1N1 virus that caused the 1918 pandemic is pertinent to other pandemic viruses and to the development of effective and universal vaccines.î

Using the genetic sequence information for the 1918 flu virus, Dr. Nabel and his VRC colleagues created plasmids — small strands of DNA designed to express specific characteristics — carrying genes for the virusí hemagglutinin (HA) protein, the surface protein found in all flu viruses that allows the virus to stick to a cell and cause infection. The researchers created two types of plasmids: one to reflect the HA found in the original 1918 flu virus; the other an altered HA protein designed to attenuate (weaken) the virus.

Mice were then injected with a DNA vaccine containing both types of plasmids to determine whether they would generate immune responses to the 1918 virus. The researchers found significant responses both in terms of production of T-cells, the white blood cells critical in the immune systemís battle against invading viruses, as well as the production of neutralizing antibodies.

To determine the vaccineís protective effects, the CDCís Dr. Tumpey intranasally exposed a group of mice to live, reconstructed 1918 virus 14 days after they were immunized with the experimental DNA vaccine. All 10 vaccinated mice survived the challenge with the deadly virus. To explore how the vaccine protected the animals, the researchers first depleted other mice of T-cells; however, this had no effect on the immunity of the vaccinated mice to the 1918 virus. In contrast, the researchers discovered that transferring antibody-rich immunoglobulin (IgG) from immunized mice to non-immunized mice resulted in antibody levels in the animals at levels only slightly lower than those that were immunized. Further, when the animals were exposed to the reconstructed 1918 flu virus, 8 of 10 mice that received antibodies from the immunized mice survived; none of the 10 mice that received IgG from the unvaccinated control group survived.

ìBy using an existing pandemic flu strain, this research will provide the basis for design of alternative vaccines against influenza viruses with enhanced virulence,î says Dr. Tumpey.

Although the researchers are not discounting the potential role T-cells may have in combating flu viruses, they concluded that in this study, the experimental DNA vaccine protected the mice by stimulating antibodies capable of neutralizing the 1918 flu virus.

ìWho would have imagined five years ago that weíd be able to create a vaccine that protects against one of the deadliest forms of influenza the world has ever seen?î adds Dr. Nabel. ìItís because the 1918 flu virus has been reconstructed that we are now able the further understand it. Hopefully, this virus will help us to develop effective vaccine strategies for current pandemic influenza virus threats.î

To evaluate the vaccineís antibody-inducing capabilities while minimizing exposure of lab personnel to the 1918 flu virus, Dr. Nabel and his VRC colleagues also created artificial viruses, or pseudoviruses, featuring the HA of the 1918 flu virus but stripped of the ability to cause infection. The pseudoviruses were then incubated with antibody-containing blood samples from the mice immunized with the DNA vaccine and those that were not. The researchers found that the antibodies from the immunized mice neutralized the pseudoviruses while the blood samples from the mice that were not immunized had no effect. This method was also effective in identifying neutralizing antibodies to the H5N1 avian flu virus and could be used to screen for monoclonal antibodies that may be used as an antiviral treatment, according to Dr. Nabel.

ìThis technique would be very useful in defining evolving serotypes of flu viruses like H5N1 to develop immune sera and neutralizing monoclonal antibodies that may help to contain pandemic flu,î says Dr. Nabel.

The study authors indicate that further testing will be needed to determine whether DNA vaccination can confer immune protection in people similar to that seen in the study mice. Additionally, the use of DNA-based vaccines are being explored as a potential strategy for creating vaccines to protect against the H5N1 avian flu virus.

This research activity is part of a broader effort by the Department of Health and Human Services to accelerate the development and production of new technologies for influenza vaccines within the U.S., including a $1 billion investment earlier this year to support the advanced development of cell-based production technologies for influenza vaccines and will help to modernize and strengthen the nationís influenza vaccine production by creating an alternative to producing influenza vaccines in eggs.

NIAID grantee Adolfo GarcÌa-Sastre, Ph.D., of the Mount Sinai School of Medicine in New York, also contributed to the study through his work in reconstructing the virus. In addition to Dr. Nabel, other VRC scientists who contributed to the study include: Wing-Pui Kong, Ph.D.; Chantelle Hood; Zhi-yong Yang; Ling Xu; and Chih-Jen Wei.

NIH FUNDS LARGEST LONG-TERM STUDY OF HEALTH AND DISEASE IN HISPANIC/LATINO POPULATIONS -- The National Heart, Lung, and Blood Institute (NHLBI) and six other components of the National Institutes of Health (NIH) today announced contracts totaling $61 million over 6 years to conduct the largest long-term epidemiological study of health and disease in Latin American populations living in the United States.

As many as 16,000 participants of Hispanic/Latino origin — 4,000 at each of four sites — will undergo a series of physical examinations and interviews to help identify the prevalence of and risk factors for a wide variety of diseases, disorders, and conditions.

Participants in the Hispanic Community Health Study will range in age from 18 to 74 years and will be followed over time for occurrence of disease. The study will also determine the role of cultural adaptation and disparities in the prevalence and development of disease. In line with the recommendations of a 2003 NHLBI report on epidemiological research in Hispanic populations, the study will recruit persons who identify themselves as Hispanics or Latinos, but will emphasize Mexican Americans, Puerto Ricans, Cuban Americans, and Central/South Americans.

The Hispanic population is the largest minority population in the United States, and it is expected to triple in growth by 2050. As this population continues to increase — and to experience varying rates of disease — it is vitally important to understand the risk factors and health behaviors that contribute to these diseases. The knowledge gained from this study will benefit not only Hispanic populations but will also enhance understanding of health and disease in other ethnic groups, said NIH Director Elias A. Zerhouni, M.D.

The Hispanic Community Health Study is broad-based, addressing a wide variety of conditions, including heart disease, stroke, asthma, chronic obstructive pulmonary disease, sleep disorders, dental disease, hearing impairment and tinnitus, diabetes, kidney and liver disease, and cognitive impairment.

The study will assess such risk factors as diet, physical activity, obesity, smoking, blood pressure, blood lipids, acculturation, social and economic disparity, psychosocial factors, occupation, health care access, the environment, and medication and supplement use.

Like the landmark Framingham Heart Study which helped us understand the origins of heart disease and its risk factors and the Jackson Heart Study which is looking at heart disease in African Americans, the Hispanic Community Health Study also promises to make a tremendous contribution to the nation’s public health, said NHLBI Director Elizabeth G. Nabel, M.D.

There are many questions to answer, said Nabel. Why are Hispanics experiencing increased rates of obesity and diabetes and yet have fewer deaths from heart disease than non-Hispanics? Why is asthma more common in certain Hispanic groups? Only a long-term epidemiological investigation can answer questions like these and apply what is learned to prevent disease.

In addition to NHLBI, which is the primary funding agency, the following NIH components will provide additional funds: the National Center for Minority Health and Health Disparities; the National Institute on Deafness and Other Communication Disorders; the National Institute of Dental and Craniofacial Research; the National Institute of Diabetes and Digestive and Kidney Diseases; the National Institute of Neurological Disorders and Stroke; and the NIH Office of Dietary Supplements.

Since the risk of disease in a population can be influenced by different cultural and genetic backgrounds, it was important to have the study include population groups from several geographic areas and countries of origin and with residence in the U.S. for varying lengths of time, said project officer Paul Sorlie, Ph.D., chief of NHLBI’s Epidemiology Branch.

The four field study sites awarded contracts are:

- Bronx, NY (Albert Einstein College of Medicine of Yeshiva University, Sylvia Wassertheil-Smoller, Ph.D., Principal Investigator)
- Chicago, IL (Northwestern University, Martha Daviglus, M.D., Ph.D., Principal Investigator)
- Miami, FL (University of Miami, Neil Schneiderman, Ph.D., Principal Investigator)
- San Diego, CA (San Diego State University, Greg Talavera, M.D. M.P.H., Principal Investigator

NHLBI awarded the contract for the study's data coordinating center to the University of North Carolina (UNC), Chapel Hill (Lloyd E. Chambless, Ph.D., Principal Investigator).

According to the study's deputy project officer, Larissa AvilÈs-Santa, M.D. of NHLBI's Epidemiology Branch, there ís a good chance that, like other immigrant groups, as immigrant Hispanic populations adapt to the lifestyle and culture of the U.S., they will increase their risk of developing some chronic diseases. We want to identify the changes in risk associated with immigration and acculturation to living in this country, she said. Then we will identify changes most strongly related to disease risk, and figure out how best to prevent those which are most harmful to health.

NEW CLINICAL RESEARCH FACILITY FOCUSING ON ENVIRONMENTAL HEALTH TO OPEN AT NIEHS IN RESEARCH TRIANGLE PARK, NC -- The first outpatient clinical research facility is being established at the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health, to help bridge the gap between research and patient care and to train future generations of physician-scientists. Initially, clinical studies in the new facility will have a strong focus on pulmonary exposures and diseases such as asthma. The NIEHS expects to begin accepting patients by summer 2007.

"Having a place on the NIEHS campus for physician-scientists to see patients will allow us to focus our research on scientific questions that are clinically relevant," says NIEHS Director, David A. Schwartz, M.D. "Not only is it a great opportunity for our in-house scientists, but it also allows us to give something back to the community."

The 11,500-square-foot facility will be located within a few hundred feet of the main NIEHS building at Alexander Drive in Research Triangle Park, North Carolina. It will operate as an outpatient facility and provide routine evaluations, biological sample collection and processing, pulmonary function testing and bronchial sampling capabilities. Construction of the facility is estimated to cost $4.75 million.

The clinical research facility is part of the Institute's new effort to have a stronger impact on human health and disease as articulated in its 2006 Strategic Plan, "New Frontiers in Environmental Sciences and Human Health". It demonstrates the NIEHS commitment to

translational research by moving research results from the NIEHS portfolio into clinical practice.

“The clinical unit will provide new opportunities for researchers from different disciplines to work together to translate basic laboratory findings to patients,” said Perry J. Blackshear, M.D., D.Phil., Director of Clinical Research at NIEHS “It will also be an excellent resource for training medical students, and postdoctoral and clinical fellows, in clinical aspects of the environmental health sciences.”

In addition to the several clinical investigators already on staff at NIEHS, two more have recently been recruited to staff the new facility. Dr. William Martin, a pulmonary physician, joined the NIEHS leadership team in March 2006 as Associate Director, NIEHS, and Director of Translational Research; and Dr. Michael Fessler, also a physician-researcher who specializes in pulmonary and critical care medicine, recently joined NIEHS to serve as both a Clinical Investigator and head of the New Host Defense Group in the Laboratory of Respiratory Biology. As an example of how the basic and clinical arenas will merge to improve patient outcomes, Dr. Fessler says he will use a disease-oriented translational approach to develop clinical applications out of his group’s work on the pulmonary and immune systems. A staff clinician is also being recruited to oversee day-to-day operations and management of the facility.

“We are very excited about adding this clinical unit to our portfolio. We will be better poised to translate laboratory discoveries into innovative treatments, therapies and interventions to improve the nation's health,” said Dr. Schwartz.