

THE CSTE WASHINGTON REPORT

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

March 31, 2004

Volume 8, Number 7

INSIDE THIS ISSUE

... HOUSE ACTS ON BUDGET

... NEW LEGISLATION NOT EXPECTED

... 2003 TB RATES REMAIN HIGH FOR FOREIGN-BORN, RACIAL AND
ETHNIC MINORITY POPULATIONS IN UNITED STATES DESPITE
OVERALL DECLINE

... FIRST HUMAN STUDY TO SHOW BENEFITS TO NEWBORNS FROM
FEDERAL BAN ON HOME USE OF TWO INSECTICIDES

... MOUSE MODEL MIMICS REAL-WORLD PLAGUE INFECTION

... GENOME SEQUENCE REVEALS LEANER, MEANER INTESTINAL PARASITE

EDITOR'S NOTE: A federal ban on two insecticides has resulted in a significant reduction in their impact on newborns' birth weight and length, according to a new study funded by the National Institute of Environmental Health Sciences of the National Institutes of Health, the U.S. Environmental Protection Agency, and other private foundations. The results of the study — the first one to demonstrate the benefits of the ban during pregnancy in human subjects — will be published in *Environmental Health Perspectives*, the monthly peer-reviewed journal of the NIEHS. It is now available online at <http://ehp.niehs.nih.gov>. The study, released by the Columbia Center for Children's Environmental Health, part of the Mailman School of Public Health at Columbia University, measured the impact on fetal growth of two insecticides — chlorpyrifos and diazinon — whose use in households was banned by the federal government starting in 2000. The insecticides had been among the most commonly-used agents for residential pest control— 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>

HOUSE ACTS ON BUDGET – The House adopted the Budget Committee-passed version of the Budget Resolution last week on a close vote: 215-212. Republican moderates and a number of conservatives agreed to back off their insistence that the measure include PAYGO provisions – enforcement mechanisms requiring that any increases in the budget deficit be paid for, or offset -- in return for a vote on a separate budget process bill that would ostensibly be brought up later. Democrats and some Republican moderates are insisting that the PAYGO rules apply to both spending and tax cuts, but the President and the Republican leadership want PAYGO to apply only to spending. The Senate Budget Resolution, by contrast, applies PAYGO rules to both spending and tax cuts. The differing versions must now be reconciled. All of this maneuvering impacts the overall availability of funding for public health agencies and programs.

Other features of the House-passed Budget Resolution: overall discretionary spending for FY 2005 is held to \$819 billion, \$2 billion below the Senate's level of \$821 billion and \$4 billion below the President's budget request. The House Budget Resolution essentially freezes all non-Homeland Security domestic spending for the five years, including all public health spending, resulting in a nearly 10 percent cut by FY 2009 compared against current services -- what would be required if the current program levels are to be continued out five years factoring in inflation and applicable population growth.

NEW LEGISLATION NOT EXPECTED – Most experienced health advocates do not expect significant legislation to pass this session of Congress because it is an election year, including the Presidential election, and because Congress passed major Medicare legislation last session. However, it is important to note the introduction in the past two months of comprehensive health disparities legislation by Senate Majority Leader Bill Frist (R-TN) (S. 2091/S.2217). Both bills are entitled, Closing the Healthcare Gap of 2004, and address improving federal healthcare quality data collection; standardized health data reporting systems; accurate collection of race, ethnicity, and primary language data for inclusion in the Health Disparities Report; grants for access and awareness to improve the health, and healthcare of health disparity populations; grants to improve outreach for inclusion of eligibles in Medicaid and S-CHIP, and inclusion of minorities in prevention, and disease management activities; strengthening the Office of Minority Health renaming it Office of Minority Health and Health Disparities and workforce diversity programs; strengthening research directed at understanding the causes of health disparities. Additionally, S. 2217 provides tax incentives and other insurance coverage provisions targeted at lower income individuals.

Competing bills introduced last Fall by Senate Minority leader Daschle (D-SD) and Rep. Cummings (D-MD) (S. 1833/H.R. 3459) are supported by Democrats only and are considerably more complex and comprehensive. A broad-based minority advocacy coalition is calling for Senator Frist and Daschle to work together to produce a bill that blends the two efforts so there is some opportunity for real legislative progress.

2003 TB RATES REMAIN HIGH FOR FOREIGN-BORN, RACIAL AND ETHNIC MINORITY POPULATIONS IN UNITED STATES DESPITE OVERALL DECLINE

-- TB rates declined in the United States in 2003, but significant geographic, racial and ethnic disparities remain, and cases have increased in some parts of the country. California, New York, and Texas accounted for more than 40 percent of the 2003 national case total.

TB rates among foreign-born individuals remain disproportionately high, nearly nine times the rate of persons born in the United States. Persons born outside the United States accounted for more than half (53.3 percent) of all new TB cases in 2003.

After more than a decade of falling rates, the rate of decline for persons with active TB in the country is slowing. New surveillance data for 2003 show that 14,871 persons with active TB disease were reported in the United States, comparable to the 15,075 cases reported in 2002.

Overall, the national TB rate was 5.1 cases per 100,000 persons in 2003, a slight decline of 1.9 percent in case rate since 2002. This is the smallest one-year decline since 1992. Blacks remain at heightened risk for TB. National rates for non-Hispanic blacks are nearly eight times higher than rates for non-Hispanic whites and two times higher than rates for Hispanics.

CDC continues to work with partners to identify contributing factors and to develop strategies to eliminate existing disparities among racial and ethnic minorities, including demonstration projects to eliminate TB in African-American communities in the United States. CDC collaborates with domestic and international partners to assist countries with a high burden of TB. In addition, CDC is working to improve TB screening among applicants for immigrant and refugee visas.

FIRST HUMAN STUDY TO SHOW BENEFITS TO NEWBORNS FROM FEDERAL BAN ON HOME USE OF TWO INSECTICIDES

-- A federal ban on two insecticides has resulted in a significant reduction in their impact on newborns' birth weight and length, according to a new study funded by the National Institute of Environmental Health Sciences of the National Institutes of Health, the U.S. Environmental Protection Agency, and other private foundations.

The results of the study — the first one to demonstrate the benefits of the ban during pregnancy in human subjects — will be published in *Environmental Health Perspectives*, the monthly peer-reviewed journal of the NIEHS. It is now available online at <http://ehp.niehs.nih.gov>.

The study, released by the Columbia Center for Children's Environmental Health, part of the Mailman School of Public Health at Columbia University, measured the impact on fetal growth of two insecticides — chlorpyrifos and diazinon — whose use in households was banned by the federal government starting in 2000. The insecticides had been among the most commonly-used agents for residential pest control.

In the study, researchers measured the levels of the two insecticides in blood drawn from the umbilical cords after delivery, both before and after the ban, and correlated those levels with the babies' birth weight and length. All blood samples were frozen and stored at -70 degrees Centigrade in order to ensure the stability of the pesticides. Subsequent analyses were performed on frozen samples at three different times — spring 2001, summer 2002 and fall 2002.

They found that prior to January 2001, newborns with combined insecticide exposures in the highest 26th percentile had birth weights averaging almost 200 grams (almost half a pound) less than infants with no detectable pesticide levels. The researchers also noted a highly significant inverse association between the combined exposures and newborn birth length. However, when they looked at the relationship between insecticide exposures and fetal growth after January 2001, the exposure levels had been reduced substantially, and the impact on weight and length was no longer apparent.

"This human study confirms the developmental impact, shown previously in animal studies, of these insecticides," said Dr. Robin M. Whyatt, an Assistant Professor at the Mailman School and principal author of the study. "It also demonstrates the positive effect of the federal ban, which has substantially reduced exposures and benefitted human health."

"The differences in fetal growth seen here are comparable to the differences between babies whose mothers smoke during pregnancy and babies whose mothers don't," said Whyatt. "The fact that the ban was associated with such an immediate change in birth weight and length provides considerable evidence of cause and effect."

According to the study investigators, the widespread use of the two pesticides makes them good candidates for a residential study of this kind. Chlorpyrifos, for instance, was the most frequently used residential insecticide in New York City prior to the ban. Both compounds are still widely used in agriculture and continue to be found in the food supply.

"This study is good news for our nation's children," said Dr. Frederica P. Perera, Director of the Center and the study team leader. "The evidence that birth weight increased following the Environmental Protection Agency's regulatory action implies important benefits for the children's future health and development. At the same time, the results highlight the need to address continuing prenatal exposures to these and other toxic pesticides."

The study is part of a broader, multi-year research project, "The Mothers & Children Study In New York City," started in 1998, which examines the health effects of exposure

of pregnant women and babies to air pollutants from vehicle exhaust, the commercial burning of fuels, and tobacco smoking, as well as from residential use of pesticides and allergens. The present study included a sample of 314 infants of African American and Dominican women in Washington Heights, Central Harlem and the South Bronx. Other co-authors of this study include Dr. Virginia Rauh from the Columbia Center, Dr. Dana Barr from the Centers for Disease Control and Prevention, and David Camann from Southwest Research Institute.

MOUSE MODEL MIMICS REAL-WORLD PLAGUE INFECTION -- An experimental plague vaccine proved 100 percent effective when tested in a new mouse model for plague infection developed by scientists at Rocky Mountain Laboratories (RML), part of the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health. The scientists developed their model to mimic the natural transmission route of bubonic plague through the bites of infected fleas. The flea-to-mouse model provides a more realistic test setting than previously used methods, enabling a better assessment of a vaccine's ability to protect against a real-world challenge.

The new report, authored by lead researcher and RML plague expert B. Joseph Hinnebusch, Ph.D., appears in the April edition of *Infection and Immunity*, now available online. Collaborators included Clayton O. Jarrett, M.S., and Florent Sebbane, Ph.D., of RML in Hamilton, MT; and Jeffrey J. Adamovicz, Ph.D., and Gerard P. Andrews, Ph.D., of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), where the recombinant plague vaccine tested in the model was made.

"Replicating the natural transmission of plague from flea to host in this model is tedious and unusual work," notes NIAID Director Anthony S. Fauci, M.D. "This creative approach, however, brings researchers much closer to answers to real-life questions."

In their study, the RML scientists first infected fleas by letting them feed on blood containing a virulent strain of *Yersinia pestis*, the bacterial agent of plague. The infected fleas then fed on 15 mice that had been inoculated with the experimental vaccine containing an adjuvant (an immune booster). For comparison, the researchers let infected fleas also feed on a second group of 15 mice that had received only the adjuvant.

Although all 15 vaccinated mice remained symptom-free even after multiple feedings by the fleas, plague occurred in 14 of the 15 mice that had received the adjuvant alone.

"This research shows that the vaccine worked in a real-world context," Dr. Hinnebusch says. "The vaccine had prior successes in rodents and non-human primates, but in those experiments, the animals received laboratory-grown plague bacteria and were artificially exposed to it by needle and syringe."

Despite these earlier successes, says Dr. Hinnebusch, "It wasn't a given that this vaccine would work in a natural setting." With natural flea transmission, he explains, the bacteria exist in a special form and are deposited along with flea saliva into the skin of the animal in a way that cannot be duplicated artificially. During a natural infection, the digestive system of some fleas becomes blocked with a highly infectious bacterial mass. When these "blocked" fleas continue to feed, the host blood hits the mass, becomes tainted with concentrated plague bacteria, and is regurgitated back into the host.

In their experiment, the RML scientists made certain that numerous blocked fleas — in some cases as many as 13 — fed repeatedly on the vaccinated mice to ensure that the rodents could withstand multiple bites by infected fleas.

"It's difficult to do a natural challenge for an arthropod-transmitted disease, particularly with plague," Dr. Hinnebusch says, explaining why this method is uncommon. "You have to have flea colonies. You have to be able to infect them safely. You need medical entomology, microbiology and biosafety expertise. It's much easier to infect a host artificially with a needle and syringe."

Dr. Hinnebusch and his colleagues will use the natural challenge model to test other plague vaccines in development. They also will try to learn how plague bacteria spreads through a host after being transmitted by a flea, with hopes of developing new treatments to counteract the spread of plague in an infected person.

A plague vaccine available until the mid-1990s is no longer being made, Dr. Hinnebusch says, because of its short-term effectiveness and many side effects.

The experimental plague vaccine invented at USAMRIID is a fusion of protective proteins referred to as F1-V. The F1-V vaccine has been shown to protect mice, black-footed ferrets and monkeys against injected plague. Furthermore, USAMRIID has shown the vaccine protects both mice and monkeys against the highly lethal form of inhaled plague.

"Two factors — the threat of antibiotic — resistant plague and the possible use of plague by bioterrorists-have the public health system scrambling to come up with an effective vaccine and alternative treatments," Dr. Hinnebusch says. "Plague has been used as a bioweapon before and it could be again."

Bubonic plague killed millions of people in Europe in the Middle Ages. The World Health Organization now reports some 2,500 new cases of plague annually, including about 180 annual deaths; 75 percent of the new cases and deaths are in Africa. The United States experiences 10 to 15 cases annually, according to the Centers for Disease Control and Prevention. The most common source of infection is bites from infected fleas carried by wild rodents.

Bubonic plague is characterized by painful, swollen lymph nodes called buboes that are often hot to the touch. Symptoms usually include fever, extreme exhaustion and headaches. Onset of bubonic plague generally occurs 2 to 6 days after exposure. If untreated in humans, the disease spreads rapidly, and the bacteria can invade the bloodstream (leading to plague septicemia) and the lungs (leading to pneumonic plague).

GENOME SEQUENCE REVEALS LEANER, MEANER INTESTINAL PARASITE --

Cryptosporidium parvum — an insidious, one-celled, waterborne parasite that lodges in the intestines of infected people and animals and for which there is currently no effective treatment — is missing key structures normally found in similar parasites, say researchers supported by the National Institute of Allergy and Infectious Diseases (NIAID), one of the National Institutes of Health. The results of their genome sequencing

project, now available in the online issue of *Science*, could help scientists home in on new drug targets that may lead to therapies for the disease.

C. parvum is an extremely hardy parasite found in water supplies throughout the world, including the United States. In persons with healthy immune systems, symptoms of infection include diarrhea, stomach cramps, upset stomach and fever. For persons with weakened immune systems, however, such as individuals with HIV/AIDS, symptoms may be more severe and can lead to serious or life-threatening illness. Because *C. parvum* could potentially be used as a bioterrorist agent, the NIAID has classified it as a Category B priority pathogen.

After reconstructing the predicted genes and resulting proteins of one form of *C. parvum*, researcher Mitchell S. Abrahamsen, Ph.D., University of Minnesota, St. Paul, MN, and his team discovered that *Cryptosporidium* is missing two organelles commonly found in related protozoan parasites. Gone is the apicoplast, a cellular component that provides essential metabolic functions in related parasites, including those that cause malaria and toxoplasmosis, respectively. Also absent is the mitochondrion, the so-called "energy factory" found in the cells of most plants, animals, fungi and one-celled organisms. In addition, the researchers found that *Cryptosporidium* has significantly fewer genes than related parasites, and, as a result, can carry out fewer metabolic functions on its own. Because *Cryptosporidium* has been so difficult to study up until now — presumably because its demands for energy and nutrients have made it virtually impossible to grow in the laboratory — the decoding of the genome sequence provides valuable opportunities to inform and study the organism's biology. And with an understanding of its biology, researchers are better positioned to find treatments that zero in on unique biological processes essential for the organism's survival.

NIAID is a component of the National Institutes of Health, an agency of the U.S. Department of Health and Human Services. NIAID supports basic and applied research to prevent, diagnose and treat infectious diseases such as HIV/AIDS and other sexually transmitted infections, influenza, tuberculosis, malaria and illness from potential agents of bioterrorism. NIAID also supports research on transplantation and immune-related illnesses, including autoimmune disorders, asthma and allergies.