THE CSTE WASHINGTON REPORT

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EDITOR'S NOTE. A new diabetes prevention resource designed to encourage and help faith–based and community organizations get actively involved in deterring preventable diabetes among African–Americans was released by the National Diabetes Education Program (NDEP), a joint venture of the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health. The new interactive educational kit, *Power to Prevent: A Family Lifestyle Approach to Diabetes Prevention*, provides hands–on instruction and guidance in making behavior changes that can help prevent diabetes… 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.

CSTE INTEGRATED SURVEILLANCE BILL SECURES DEMOCRATIC SPONSOR AND SUPPORT FROM SISTER PUBLIC HEALTH ORGANIZATIONS – The "National Integrated Public Health Surveillance Systems and Reportable Conditions Act," developed by CSTE with strong input from the Association of Public Health Laboratories and the National Association of State Public Health Veterinarians, is winning support among other sister public health agencies. The bill, still in draft form as CSTE carefully vets it with Democratic Congressional sponsors and other public health organizations, is sponsored by Rep. Lee Terry (R-NE) in the House and Sen. Chuck Hagel (R-NE) in the Senate. The lead House Democratic sponsor is Rep. Tammy Baldwin (D-WI) and CSTE is reaching out to possible lead Senate Democratic sponsors. Organizations that have expressed support for the bill include the American Public Health Association, the American Society of Microbiology. CSTE also expects support will be forthcoming soon from the Association of State and Territorial Health Officials and the National Association of County and City Health Officials.

CSTE WINS STRENGTHENED REPORT LANGUAGE FOR OVERSEAS SCREENING AND TREATMENT FOR TB – CSTE has long been interested in strengthening overseas health screening and treatment for both U.S. bound refugees and immigrants and developed a position paper regarding the concerns involved in 2005. Bills addressing reauthorization of the domestic TB program have been introduced in the current Congress (S. 1551; H.R. 1532) and the Senate bill recently passed the Health, Education, Labor and Pensions Committee. CSTE, working with a coalition of advocacy groups, succeeded in strengthening developing report language accompanying the Senate bill to address the problem of overseas screening and treatment of latent and active TB as noted in blue below:

> "This act recommends the expansion of programs to identify immigrants with latent TB infection and active TB disease and offer treatment, when indicated. The committee intends to encourage increased screening and treatment, when appropriate, of persons from countries with a high incidence of TB. Effective implementation of expanded screening and treatment will require additional resources for both overseas screening activities and domestic programs that provide follow-up and treatment. These activities may benefit from collaboration with the ICE whose expertise in immigration policy and the feasibility of altering current practices will be useful in determining the best approach to the high incidence of TB among immigrants. It should be noted that the committee does not necessarily endorse mandated latent TB testing for immigrant visa and permanent residency applicants. The committee encourages the CDC to work with the ICE to develop targeted screening programs that are effective in screening and treating latent TB without endangering the rights of all immigrants and refugees in the United States."

NIAID SCIENTISTS IDENTIFY NEW CELLULAR RECEPTOR FOR HIV -- A cellular protein that helps guide immune cells to the gut has been newly identified as a target of HIV when the virus begins its assault on the body's immune system, according to researchers from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH).

"The identification of this new receptor opens up new avenues of investigation that may help further elucidate the complex mechanisms of the pathogenesis of HIV infection" says NIAID Director Anthony S. Fauci, M.D., chief of the Institute's Laboratory of Immunoregulation (LIR) and senior author of the new study.

Several other immune cell receptors bind to HIV. Most important among these, the CD4 molecule, identified as an HIV receptor in 1984, functions as the principal receptor for HIV. The CCR5 and CXCR4 molecules, discovered in 1996, serve as co-receptors that HIV uses to enter its target cells. In the new study, which appears online Feb. 10, 2008 in *Nature Immunology*, NIAID scientists identify a cell adhesion molecule known as integrin alpha 4 beta 7 as another potentially important receptor for HIV.

Early in the course of HIV infection, the virus rapidly invades and replicates in gut-associated lymphoid tissue (GALT), the immune cells of the gut. Once seeded with HIV, the gut is rapidly depleted of CD4+ T cells, the main target of HIV, triggering the process that ultimately leads to AIDS.

"In the very early days of infection, it is in the GALT where most of the damage caused by HIV occurs," says Elena Martinelli, Ph.D., a lead author of the paper and a fellow in Dr. Fauci's laboratory. "The gut is where the virus really takes hold. We found that integrin alpha 4 beta 7, whose natural function is to direct T cells to the GALT, is also a receptor for HIV. It is very unlikely that this is a coincidence."
Dr. Martinelli, along with Claudia Cicala, Ph.D., James Arthos, Ph.D., and their colleagues found that the gp120 protein, part of the HIV envelope, binds to integrin alpha 4 beta 7 on CD4+ T cells, which promotes the formation of a stable junction, or synapse, between neighboring cells.

"A synapse is a junction that allows two cells to adhere in a stable way," says Dr. Arthos. "Many viruses have found a way to trick cells into forming these stable junctions. Now it appears that HIV can also trigger synapse formation."

Specifically, a short piece of the HIV gp120 protein in a region known as the V2 loop recognizes the alpha 4 chain of the integrin molecule on host cells. This stretch of the V2 loop is similar to part of the naturally occurring molecules that bind integrin alpha 4 beta 7. Thus, it appears that HIV is mimicking the natural molecular partners, or ligands, that normally bind to the receptor. The authors note, however, that some HIV isolates react more strongly to integrin alpha 4 beta 7 than others.

"The ability of a particular virus to bind to integrin alpha 4 beta 7 may determine whether it will have a major impact in targeting the gut lymphoid tissue," says Dr. Fauci. "This finding could be a significant determinant in the pathogenic mechanisms that lead to AIDS."

As part of the natural homing process, integrin alpha 4 beta 7 binds to its natural ligands and activates a protein known as LFA-1. According to Dr. Arthos, HIV can co-opt this process by mimicking the cells' alpha 4 beta 7 receptor natural ligands. When HIV gp120

protein binds to the alpha 4 beta 7 receptor it facilitates the formation of a synapse. Thus, HIV tricks an infected cell into binding to an uninfected cell, enabling HIV to readily gain access to the uninfected cell.

"While this study provides important new information concerning the various mechanisms by which HIV debilitates the human immune system, it also raises new questions and challenges that our laboratory and others will pursue," notes Dr. Cicala. For more information on HIV/AIDS, see http://www3.niaid.nih.gov/healthscience/healthtopics/HIVAIDS/overview.htm.

NEW RESOURCE FOR PREVENTING DIABETES IN AFRICAN-AMERICANS -- A new diabetes prevention resource designed to encourage and help faith–based and community organizations get actively involved in deterring preventable diabetes among African–Americans was released by the National Diabetes Education Program (NDEP), a joint venture of the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health.

The new interactive educational kit, *Power to Prevent: A Family Lifestyle Approach to Diabetes Prevention*, provides hands–on instruction and guidance in making behavior changes that can help prevent diabetes.

“Too many African–Americans have, or will get, diabetes,” said Ann Albright, PhD., director of CDC’s Division of Diabetes Translation. “Fortunately, many people and families can take steps to prevent that from happening. It′s often difficult to change or adopt new behaviors, but this new resource gives many examples of things that most people can do that will help them avoid a very serious life–long disease. This program also helps faith–based and community organizations which are very important to many African–American families provide the support that can make a difference in helping people take on new nutrition and exercise habits.”

The Power to Prevent program includes 12 interactive group sessions that provide hands–on instruction in ways to prevent diabetes, and shows how families and individuals can change their daily habits so that they get more physical activity, make healthy food choices and better control their food serving sizes. The sessions are designed to be led by various members of the faith–based or community organization, such as a recreation director.

“We know that churches, faith–based organizations and community groups can be very effective in helping people learn about diabetes, and in helping take steps that can prevent diabetes for most people,” said Albright. “That’s why we created this new tool. We need faith and community–based organizations to be actively involved in diabetes prevention among their members, and with this easy–to–use program, they can do that effectively.”

Diabetes is the sixth leading cause of death in the United States; and the prevalence rate more than doubled among African–Americans from 1980 to 2005, from 3.3 to 6.8.

Diabetes is a disease associated with high levels of blood glucose resulting from defects in insulin production that causes sugar to build up in the body. It can cause serious health complications including heart disease, blindness, kidney failure, and lower–extremity amputations; and can also lead to premature death. It is estimated that, among Americans aged 20 and older, more than 20 million have diabetes, of which more than 3 million are African–Americans. After taking into consideration the age differences in the various populations, non–Hispanics blacks are 1.8 times as likely to have diabetes as non–Hispanics whites.

The CDC Division of Diabetes Translation, through the NDEP (co–sponsored by the NIH), provides diabetes education to improve the treatment and outcomes for people with diabetes, promote early diagnosis, and prevent or delay the onset of diabetes. While the design and appearance of *Power to Prevent* is specifically directed toward African–Americans because of the increasing prevalence in this group, the basic content can be useful and relevant to all populations.

To download or order a free single printed copy of *Power to Prevent* go to www.cdc.gov/diabetes/ndep/power_to_prevent.htm. For general information about diabetes, please visit www.cdc.gov/diabetes.

NIH SCIENTISTS DETECT FATAL COPPER DISORDER AT BIRTH -- A test developed by NIH scientists could greatly extend the survival of infants with Menkes disease, a rare, otherwise fatal disorder of copper metabolism. The scientists devised a test to diagnose the condition early, when the chances for successful treatment are greatest. A study appearing in the February 7 *New England Journal of Medicine* describes how the scientists devised the test to diagnose the condition early, when the chances for successful treatment are greatest.

Untreated, Menkes disease results in irreparable harm to the brain and nervous system. Treatment consists of injections with a copper-containing drug. Children with Menkes disease typically die during the first decade of life. Previously, there was no blood test for early detection of Menkes disease.

"The study represents an important advance in the diagnosis and treatment of a rare but devastating genetic disorder," said Duane Alexander, M.D., Director of NIH's National Institute of Child Health and Human Development (NICHD), the lead NIH institute that conducted the study. "The laboratory techniques the researchers used to detect Menkes disease eventually may provide the basis for a newborn screening test to identify children with Menkes at birth, so they have the greatest chance to benefit from treatment."

The study was a collaboration between researchers in the NICHD, the National Institute of Neurological Disorders and Stroke (NINDS), and the NIH Clinical Center. The NINDS researchers contributed expertise in testing for nervous system chemicals known as catecholamines. Catecholamine levels are determined by a copper-dependent enzyme and for this reason are abnormal in Menkes disease infants.

Menkes disease occurs in about one in 100,000 newborns and is caused by a defect in a gene that regulates copper levels in the body, explained Stephen G. Kaler, M.D., Clinical Director of the NICHD and lead author of the study. This defect, in the gene designated ATP7A, causes abnormally low levels of copper in the brain and liver as well as excessive amounts of copper in the kidneys and intestines. Copper, although only needed in trace amounts, is an essential nutrient that plays a critical role in brain development, he said.

Infants with Menkes disease usually appear normal at birth but start to show developmental delays at 6 to 8 weeks. Affected children may experience seizures and below normal body temperature. Children with Menkes disease also develop distinctive kinky hair, which is steel-colored or colorless and is easily rubbed off the skull.
Dr. Kaler explained that copper is needed for the production of myelin, an insulating material that surrounds certain types of brain and nerve cells. The deposition of myelin around brain and nerve cells is nearly completed by age 2, so the disorder can potentially be treated if copper replacement therapy is started soon after birth. Symptoms of Menkes disease do not usually develop until 2 to 3 months of age, but by that time, the copper deficiency has already caused significant brain damage which treatment seems unable to reverse, Dr. Kaler said.

The defective gene in Menkes disease is located on the X chromosome. Because males have only one X chromosome, they have only one copy of the ATP7A gene and so are severely affected by the disorder. Females have two X chromosomes. If they have a defective ATP7A gene, they are not severely affected, because their remaining X chromosome usually has a functioning ATP7A gene.

In their research, Dr. Kaler and his co-workers evaluated male infants who were considered to be at risk for Menkes disease.

Based on catecholamine levels, the researchers predicted 12 male newborns would develop Menkes disease and administered the copper-containing drug, beginning at a very early age. DNA studies of the ATP7A gene confirmed the diagnosis in each case. The infants were given the copper injections for three years, receiving two shots daily for the first year and one shot a day during the second and third years. Because long-term exposure to copper can damage the kidneys, the copper injections were stopped after 3 years. The researchers followed the infants throughout childhood to track their survival rates and mental development. Those who received injections soon after birth had a much greater survival rate when compared with a previously documented group of Menkes disease infants who had not received early copper injections.

Of the 12 males in the study, 92 percent were still alive an average of 4.6 years later. Only 13 percent of the males in the earlier group of late-diagnosed patients were alive an average of 1.8 years after diagnosis.

Dr. Kaler said that the study participants did not show any decline in health after stopping the copper replacement.

The boys varied in their response to the copper treatment. Two developed relatively normally, whereas the remainder had varying degrees of developmental impairment. When Dr. Kaler and his coworkers examined the nature of the defect in the boys' ATP7A gene, they found that boys with particular alterations in the gene responded better to the copper injections than did boys with other defects in the gene. They demonstrated that the ATP7A genes of the boys who had the best clinical responses to the copper injections retained some rudimentary capacity to regulate copper.

Dr. Kaler and his colleagues are now working to develop from their research a test that health care providers could use to routinely screen newborn males for Menkes disease. "I think our findings may be especially meaningful to parents who have suffered due to this condition and lost children to it," Dr. Kaler said. "Menkes disease and other rare disorders of childhood convey a burden to families that is unfair and underappreciated. That a disorder occurs rarely is meaningless if one's child, grandchild, or sibling is affected."