



physician, Katon said. “Our data suggest primary care physicians should seriously consider screening kids with asthma for anxiety and depression because they are a very high risk group.”

PTSD LINK EXPLORED

The other study offers the first evidence that asthma also may be linked to PTSD. Renee D. Goodwin, MPH, PhD, of the Mailman School of Public Health at Columbia University in New York City, and colleagues found that Vietnam veterans who report the most symptoms of PTSD are 2.3 times more likely to have asthma than those who report the least PTSD symptoms, based

on an analysis of 3065 male twin pairs from the Vietnam Era Twin Registry (Goodwin RD et al. *Am J Respir Crit Care Med.* 2007;176[10]:983-987). The work also confirmed other studies’ findings of an association between asthma and depression in adults.

Further analysis involving a comparison of the results within identical and fraternal twin pairs did not find a substantial difference between the two groups, suggesting that genes do not play a large role in the association between asthma and PTSD. The scientists also probed the relative contributions of some environmental or behavioral factors, including body mass index, smoking, exposure to

combat trauma, and the sociodemographic characteristics of the individuals, and found none that fully explained the link between asthma and PTSD.

Goodwin and her team are planning longitudinal studies of children to examine whether prenatal factors, such as having a mother who smoked during pregnancy, may explain the association between asthma and psychiatric problems.

In the meantime, Goodwin said, physicians should be aware that patients with asthma who are exposed to trauma or other difficult life events might have an elevated risk of developing PTSD or other psychiatric disorders, and consider screening them for such comorbidities. □

Exercise May Boost Aging Immune System

M. J. Friedrich

BOSTON—Aging brings with it a progressive decline in immune function that can lead to a variety of health issues. Among the various strategies being studied to offset abnormal immune function in the elderly is moderate exercise training.

“Exercise clearly has effects on immune functioning,” said Jeffrey Woods, PhD, associate professor of kinesiology, nutritional science, and pathology at the University of Illinois at Urbana/Champaign. “However, we still know very little about the details of how exercise affects the immune system of older adults.”

Woods’ research team has been examining whether exercise at “doable” levels can potentiate immune function to speed wound healing and reduce the risk for infectious diseases. He discussed animal and human studies at Tufts University’s 2007 Friedman School Symposium on nutrition, held here in October.

Woods (Emery CF et al. *J Gerontol A Biol Sci Med Sci.* 2005;60[11]:1432-1436). In a recent animal study, Woods and his colleagues found that this effect results



Some evidence suggests that exercise might improve immune function in older adults.

HEALING WOUNDS

Delayed wound healing is not uncommon in the elderly, so finding ways to speed the process along is an important challenge in geriatric care.

Research in human subjects has suggested that exercise may accelerate-wound healing in older adults, said

at least in part from exercise’s ability to reduce the inflammatory response in the wounds (Keylock KT et al. *Am J Physiol Regul Integr Comp Physiol.* doi:10.1152/ajpregu.00177.2007 [published online ahead of print November 14, 2007]). Ear-

lier data had suggested that exaggerated inflammation in the wounds of aging animals may slow healing (Dovi JV et al. *J Leukoc Biol.* 2003;73[4]:448-455).

Woods’ team studied young mice (3 months old) and old mice (18 months old) and divided them into two groups. The mice in one group exercised moderately (at 70% of their maximum oxygen consumption) by running for 30 minutes on a motorized treadmill for 3 days before receiving a cutaneous wound and then for 5 days afterward. The other mice were sedentary.

No exercise-related differences in wound size were found among the younger animals, which healed faster than the older ones. In the older mice, however, the wounds in the exercising animals healed more quickly than those in the control animals. Woods’ team theorized that exercise encouraged healing by decreasing local inflammation, as the wounds in the exercising mice had lower levels of inflammatory cytokines compared with the wounds in the sedentary mice.

BOOSTING IMMUNITY

Woods and his colleagues also are investigating whether exercise can strengthen the aging immune response to infectious diseases.



In a study comparing animals engaging in different doses of exercise (moderate or prolonged) with sedentary animals, Woods' group showed that 4 days of moderate exercise started early after infection with the influenza virus—before symptoms set in—could significantly increase the survival rate in older mice (Lowder et al. *Brain Behav Immun.* 2005;19[5]:377-380). Prolonged exercise, however, increased morbidity and tended to reduce survival.

In a subsequent study, Woods' group found that moderate exercise shifted the immune response from a Th1 inflammatory response to a Th2 anti-inflammatory response, decreasing lung pathology (Lowder T et al. *Exerc Immunol Rev.* 2006;12:97-111). "We think what leads to mortality is not the virus per se, but the host's response to the virus, and what exercise does is actually decrease the immunopathology within the lungs," said Woods.

In a cross-sectional study of highly fit vs sedentary older adults, Woods' group examined whether cardiovascular fitness could improve immune responsiveness

to influenza vaccination (Keylock KT et al. *J Appl Physiol.* 2007;102[3]:1090-1098). The fit elderly had higher antibody responses than the low-fit group to vaccination, but there were no differences between the groups in cell-mediated immune responses.

To look prospectively at whether cardiovascular exercise can improve immune response in previously sedentary older adults, Woods and colleagues performed a longitudinal study called the Immune Function Intervention Trial (ImFIT). The researchers randomly assigned 150 men and women between the ages of 63 and 82 years into 2 groups. Over 10 months, a cardiovascular training intervention group met 3 times a week for 60-minute sessions of walking, cycling, and the like, while a control group met 2 times a week for 60 minutes of flexibility and balance training. Preliminary data, still under study, suggest that cardiovascular exercise delays the reduction in antibody response to the influenza vaccine, which may provide exercisers with

longer-lasting protection from influenza, said Woods.

However, Woods added, using influenza vaccine to look at intervention-induced changes in antibodies has limitations: many people have already encountered influenza, so their immune response to vaccination is not a primary response. To examine how exercise influences primary immune response in older adults, the researchers inoculated some of the ImFIT participants with a novel antigen called keyhole limpet hemocyanin, a protein derived from a sea mollusk that stimulates a primary immune T-cell-dependent antibody response. The researchers found that cardiovascular exercise induced a significant increase in antibody response to the novel antigen.

Woods noted that much more work needs to be done to understand the mechanisms involved. Still, he said, "the take-home message is that regular exercise appears to reduce inappropriate inflammation—a common thread in many pathologies." □

Scientists Build Map of Imprinted Genes

Tracy Hampton, PhD

WHILE IMPRINTED GENES HAVE been linked to a variety of diseases, until now only several dozen have been identified. But a new report reveals a map of 156 new likely imprinted genes scattered throughout the human genome (Luedi PP et al. *Genome Res.* 2007;17[12]:1723-1730).

Unlike the majority of genes—in which both the maternally and paternally inherited copies are active—in imprinted genes, one of these copies is silenced.

"We're hoping this new roadmap will help us and others find more information about how these genes affect our health and well-being," said Randy Jirtle, PhD, a genetics researcher in the departments of radiation oncology and pathology at Duke University in Durham, NC, and a senior author of the study.

Jirtle and colleagues used DNA sequence information from known imprinted genes to uncover other genes likely to be imprinted. Two of the identified genes were studied in depth and validated as imprinted genes. The *KCNK9* (potassium channel, subfamily K, member 9) gene is expressed predominantly in the brain and is a known cancer-causing oncogene. It also may play a role in bipolar disorder and epilepsy because it encodes a potassium ion channel that mediates neuronal excitability. The other validated gene, *DLGAP2* (disks large-associated protein 2), is a candidate bladder cancer tumor suppressor. Both of these genes lie on chromosome 8, which had not previously been suspected to contain imprinted genes.

Many of the other newly identified imprinted genes lie within chromosomal regions that have been linked to

the development of such diseases as cancer, diabetes, and autism. But more work is needed to determine if the genes play an active role in these disorders and whether they might be used in strategies for disease prevention and management.

Scientists suggest that manipulating imprinted genes to improve health may be feasible because imprinting is an epigenetic phenomenon that can change a gene's function without altering the sequence of its DNA, and it can be influenced by external factors. "Imprinted genes are unusually vulnerable to pressures in our environment," said Jirtle.

More research is needed to determine whether all of the new genes found in this study are truly imprinted—and if other imprinted genes remain to be identified. □