THE LATEST FINDINGS ON THE COMPARISON OF MEDICATION VERSUS PERCUTANEOUS CORONARY INTERVENTION (PCI), THE TERM CURRENTLY USED FOR ANGIOPLASTY AND STENTING, FOR STABLE CORONARY ARTERY DISEASE—THIS TIME ASSESSING QUALITY OF LIFE—HAS SHOWN THAT WHILE BOTH GROUPS’ HEALTH STATUS AND QUALITY OF LIFE IMPROVED, PCI HAD A SLIGHT ADVANTAGE OVER MEDICAL TREATMENT ALONE DURING THE FIRST TWO YEARS.

Patients suffering from more severe angina received greater benefit from PCI and medication than those suffering from milder angina, the study showed, but even these improvements were not sustained long term.

Significantly, patients’ health improved with either treatment. These quality-of-life findings from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial conducted by the National Heart, Lung, and Blood Institute (NHLBI) were published in the August 14, 2008 issue of the New England Journal of Medicine (NEJM). "What these important results mean to everyday patients with stable angina is that they can expect substantial symptomatic improvement, regardless of whether they receive PCI or intensive medical therapy," says William E. Boden, MD, clinical chief of the Division of Cardiac Surgery, University of California, Irvine; and chairman of the Cardiovascular Medical Group, University of California, Irvine.

Boden notes that the results should not be interpreted to mean that expressing one’s thoughts and feelings is harmful or that if someone wants to express his or her emotions they should not do so. "It’s important to remember that not everyone copes with a tragedy but who do not experience a direct loss of a friend or family member. It focused on people’s responses to the terrorist attacks of September 11, 2001, but the results may generalize to include responses to other collective traumas. The findings have important implications for expectations of how people should respond in the face of a collective trauma affecting a whole community or even an entire nation, says Seery, an assistant professor of psychology. Seery notes that the results should not be interpreted to mean that expressing one’s thoughts and feelings, and testing the length of their responses, they found a similar pattern. People who expressed more were better off than those who did not express their feelings."

The study investigated the mental and physical effects of collective traumas on people who are exposed to a tragedy who do not want to express their thoughts and feelings after experiencing a collective trauma. In fact, they can cope quite successfully and, according to our results, are likely to be better off than someone who does want to express his or her feelings. "This perfectly exemplifies the assumption in popular culture, and even in clinical practice, that people need to talk in order to overcome a collective trauma," he says. "Instead, we should be telling people there is likely nothing wrong if they do not want to express their thoughts and feelings after experiencing a collective trauma. In fact, they can cope quite successfully and, according to our results, are likely to be better off than someone who does want to express his or her feelings."

Using a large national sample, Seery and co-researchers tested people’s responses to the terrorist attacks of 9/11, beginning immediately after the event and continuing for the following two years. In an online survey, respondents were given the chance to express their thoughts and feelings on the day of 9/11 and a few days afterward. The researchers then compared people who chose to express their thoughts and feelings versus those who chose not to express. "We assessed various alternative explanations in secondary analyses, but nothing else accounts for this effect," Seery says.

Seery’s co-researchers were Roxane Cohen Silver, PhD, professor of psychology and social behavior, and E. Alison Holman, PhD, assistant professor of nursing science, University of California, Irvine; and Whitney A. Ence and Thai Q. Chu, doctoral students, University of California, Santa Barbara.
**Potential Boost for Vaccines**

**UB researcher examines new methods of immunization**

**BY LOIS BAKER**

Two novel proteins studied by a UB professor of microbiology and immunology appear to have the potential to enhance the production of antibodies against a multitude of infectious agents.

**ERREY D. CONNELL, PHD, professor of microbiology and immunology in the Witslokay Center for Microbial Pathogenesis in the UB School of Medicine and Biomedical Sciences, developed and patented the LT-IIa and LT-IIb enterotoxins and their respective mutant proteins as new mucosal adjuvants, or “boosters,” that can enhance the potency of existing and future vaccines.

Connell and his colleagues—the only researchers in the scientific community investigating the immunology of these adjuvants—published five papers in 2007 describing their advances. The researchers are currently working to develop a safe and effective method to deliver the immune-enhancing molecules to the body’s mucous membranes (the first line of defense against most pathogens) in order to elicit protective immune responses on those membranes.

“Almost every bacterium and virus that attacks us doesn’t bore through the skin,” says Connell. “These infectious agents enter by colonizing the mucosal surfaces on the eye, sinus, mouth, gut lining, lungs and genital tract.” To date Connell and colleagues have determined, using a mouse model, that the nasal passage is the best mucosal surface on which to apply LT-IIa and LT-IIb as mucosal adjuvants. Mixing a very small amount of LT-IIa or LT-IIb with an existing antigen and dripping the mixture into a mouse’s nose subsequently produces a strong antigen-specific immune response in the nasal passages, as well as in saliva, the urethra, the olfactory tract and the bloodstream, their research shows.

In contrast, immunizing the mouse with only the antigen generates a much lower level antigen-specific immune response at those sites. This method of application is particularly suitable for immunizing populations in underserved areas, says Connell. “If I want to immunize somebody in Uganda with a vaccine that must be injected, for instance, I have to bring needles, everything must be sterile and everything must be kept cold, which means we need refrigeration.

“But if I can vaccinate through the nose, all I have to do is dry the antigen and my adjuvant. When I get to the middle of Uganda, I boil some water, pour it in the antigen and adjuvant. Stir it up, put it in an atomizer and ‘sniff.’ The mixture doesn’t even have to be sterile because the nose isn’t sterile.”

Connell began studying the two adjuvants as a postdoctoral researcher at the Uniformed Services University of the Health Sciences (USUHS) in Washington, DC, in 1989. The enterotoxins had been isolated five years earlier by Randall K. Holmes, MD, PhD, his postdoctoral advisor, in studies to characterize their role in diarrheal disease. Connell began his investigations into the activities of LT-IIa and LT-IIb at the USUHS by mapping the regions of the two enterotoxins that were important for receptor binding, toxicity and assembly of the multisubunit proteins. John Hu, a UB undergraduate who recently spent a semester in the Connell laboratory, identified and cloned LT-IIc, a new type II heat-labile enterotoxin. Experiments are ongoing to determine if this third LT-II enterotoxin exhibits mucosal adjuvant activities similar to or different from those of LT-IIa and LT-IIb.

LT-IIa, LT-IIb and LT-IIc are similar to cholera toxin in three-dimensional structure and toxic activity. Yet, the amino-acid sequences of the binding subunits of LT-IIa, LT-IIb and LT-IIc are significantly different from the amino-acid sequence of the binding subunit of cholera toxin. These amino acid differences underlie the specificity of LT-IIa, LT-IIb and LT-IIc for ganglioside receptors, which are different from the ganglioside bound by cholera toxin. (A ganglioside is a complex molecule that contains both lipids and carbohydrates, and is found in the outer membrane of many kinds of cells.)

Connell hypothesizes that it is these different ganglioside-binding activities that contribute to the unique immunological activities of LT-IIa and LT-IIb and to the expected immunological activities of LT-IIc, the newest member of this novel family of adjuvants.

“Basically, LT-IIa and LT-IIb are molecules you can add to any vaccine candidate to augment the immune response to that vaccine, whatever it may be,” Connell explains. The one problem researchers may encounter and on which they are currently working is to ensure that their vaccine booster doesn’t travel to the brain via the olfactory nerve, or, if the booster does traffic to the brain, that it doesn’t have harmful properties. Connell says some of the current LT-IIa, LT-IIb and LT-IIc adjuvants they have recombinantly engineered appear to exhibit no toxicity in cells, and thus have the potential to exert no harmful effects on neuronal cells. His molecules may be ready for human trials in a year, he says.

**Safer Surgery for Children**

**Antimicrobial sutures reduce infections in hydrocephalus cases**

Children born with hydrocephalus must have shunts implanted to drain the fluid away from the brain to reduce harmful pressure.

While shunts do their job well, the rate of shunt infection in children is very high for a variety of reasons, which requires putting the child through another surgery to replace the shunt, bringing with it more hospital time, potential additional neurological complications and an increased risk of death.

A NEW TRIAL CONDUCTED by faculty in the School of Medicine and Biomedical Sciences has shown that using antimicrobial sutures to secure the shunt and close the wound significantly reduces the number of shunt infections arising during the first six months after surgery.

“Many techniques and devices have been investigated to reduce shunt infections,” says Curtis J. Rozzelle, MD, assistant professor of neurosurgery and first author on a paper about this study that was published in the August 2008 issue of the Journal of Neurosurgery: Pediatrics.

“Some studies, but not all, found that antibiotic-impregnated shunt systems, in particular, appear to reduce infection risk; unfortunately, none of these studies was prospective, randomized and double-blind,” notes Rozzelle, who also is surgical director of the Comprehensive Epilepsy Program at the Women and Children’s Hospital of Buffalo.

“In animal trials sutures coated with the antimicrobial triclosan have been shown to reduce the number of bacteria adhering to sutures, but only one study has been published to date on their effect in preventing surgical site infection, so we decided to conduct our own trial,” he says.

“Our results showed that using antimicrobial sutures reduced infection risk by 16 percent.”

Antibiotic-impregnated shunts, which are used in some surgeries, have several limitations, adds Rozzelle. “They don’t provide complete protection, they can’t be used in patients who are allergic to the antibiotics and they are a lot more expensive than nonimpregnated shunts.

“Closing wounds with antimicrobial sutures may reduce infections in procedures implanting other devices, such as pacemakers and neurostimulators, pumps that deliver pharmaceuticals and shunts elsewhere in the body,” he suggests.

Rozzelle and colleagues are planning to conduct a larger randomized controlled trial to confirm their initial findings.

Jody Leonardo, MD, clinical assistant instructor, and Vertaa Li, MD, associate professor, both from the UB Department of Neurosurgery and Kaleida Health, contributed significantly to the study.

—LOIS BAKER