



In a study of 1,500 patients, DMS gastroenterologist Douglas Robertson, M.D., found that those with diets high in processed meats had a higher risk of developing precancerous colon polyps.

Diabetes: Progress against complications

Is diabetes a complicated disease? Or a disease of complications? Dartmouth diabetes researcher Paul Beisswenger, M.D., clearly favors the latter view. For unknown reasons, the developed world is in the midst of a diabetes epidemic. Although diabetics who control their blood sugar clearly have better outcomes, years of research and experience have shown that even the most scrupulous regulation of blood glucose does not always prevent progression of the disease.

In 2002, the U.S. spent \$132 billion on diabetes care, yet it remains the leading cause of blindness, amputations, and atherosclerosis. It also causes nearly half of all cases of end-stage renal disease. In all these complications of the disease, there is a very long “silent” phase in which tissue damage smolders at undetectable levels. It has been a source of immense frustration to caregivers that there have been no good ways to evaluate disease progression or to identify the patients most likely to suffer complications so they can be targeted for more aggressive treatment.

Beisswenger’s team has been exploring the chemical causes of this tissue damage. The researchers have focused on the most prevalent theory—that glycation, a non-enzymatic reaction of highly reactive sug-

ars, results in the formation of adducts, or compounds, that interfere with normal structure or function. For many years, doctors have evaluated diabetics by measuring a glycated adduct called hemoglobin A1c; it does not itself cause complications but offers a way, along with blood sugar levels, to track the disease’s progression.

Sugars: Fifteen years ago, Beisswenger’s team became interested in sugars called dicarbonyls. Glycation of dicarbonyls can result in a process called oxidative stress. The most common dicarbonyl, methylglyoxal (MG), is thousands of times more reactive than glucose. MG is elevated in diabetics, and its concentration seems to correlate with the severity of complications. Beisswenger has shown that people produce varying amounts of MG, perhaps accounting for why only some diabetics progress to serious complications.

He’s also found that diabetics have less of a peptide called glutathione (GSH). The body has protective mechanisms to inactivate MG that may be affected by GSH. But do diabetics who progress make more dicarbonyls such as MG, or lack mechanisms to inactivate them?

Beisswenger recently published, in the journal *Diabetes*, results of studies on three groups of patients: 1) a pilot population at DHMC, 2) a larger group at the University of Minnesota, and 3) a group of Pima Indians in Arizona. The researchers measured their levels of GSH, MG and a related dicarbonyl, and other indicators of oxidative stress.

When those whose disease progressed were compared to nonprogressors, the results clearly indicated that progressors had higher levels of both dicarbonyls and oxidative stress. These findings, if confirmed by a larger study Beisswenger is running, will provide superior tools for identifying progressors as well as targets for new treatments. ROGER P. SMITH, PH.D.

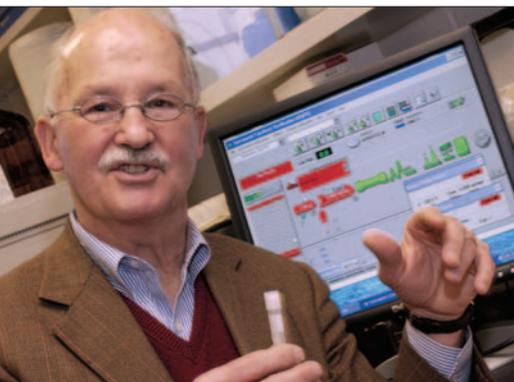
A no-brainer

Heart bypass surgery, in rare cases, can lead to brain injury, but a recent study from DMS and Maine Medical Center suggests a way to reduce the risk. In a small study, the researchers found that papaverine—a drug commonly used during bypass surgery to improve blood flow—was more effective when applied topically to a vessel than when injected into a vessel. Signals indicating reduced blood flow to the brain were observed in seven of 12 patients who were injected with papaverine versus none of 28 who received the drug topically.



Real-world result

A common treatment for post-traumatic stress disorder (PTSD) doesn’t produce the same result in the real world as it does in randomized controlled trials. DMS researcher Claudia Zayfert, Ph.D., and colleagues observed that only 28% of patients undergoing cognitive behavioral therapy for PTSD finished their treatment, whereas 73% of patients in randomized controlled trials did. The completion rate, they observed in the *Journal of Traumatic Stress*, “although disturbingly low, was better than expected.” And since research definitions of completion differ from clinical definitions, they say, the gap between the studies may not be quite so large.



ION GILBERT FOX

A team of researchers led by Paul Beisswenger is teasing out subtle differences among diabetics.