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Written by Ann Gerhardt, MD

DOES 'NORMAL' BLOOD SUGAR INCREASE HEART DISEASE RISK IN DIABETICS??? *by Ann Gerhardt, MD* (02/2008)

Bottom Line at the Top: Two recent studies of diabetes control, taken together, suggest that trying to normalize blood sugar alone does not prevent heart disease. We are still missing the exact formula to do so.

The National Heart, Lung, and Blood Institute (NHLBI) is sponsoring the ACCORD study (**A**ction to **C**ontrol **C**ardiovascular **R**isk in **D**iabetes) to see if very low blood sugar prevents heart disease in diabetics. Heart disease is the number one killer of diabetics. The study follows two groups of patients taking medication to lower hemoglobin A1c (HgbA1c), a measure that reflects sugar control for the preceding 3 months. The 'tight-control' group has aimed for HgbA1c less than 6%, and the 'usual-care' group has settled for 7 – 7.9%, the level of success most commonly achieved by diabetics. The American Diabetes Association has long recommended a goal of HgbA1c < 7%.

The study's **Data and Safety Monitoring Board stopped the 'tight control' goal, because after 4 years those patients were dying at the rate of 3 more deaths per 1000 participants each year**. They don't yet know why more of the people with good sugar (glucose) control died more often. One obvious possibility is use of Avandia (see related article in this issue), but there was no difference in the numbers of people taking it in the two groups. The NHLBI reports that the tight control group had more trouble with extremely low blood sugars. This makes sense, since HgbA1c is just an average of the highs, lows and middles: A lower average frequently means more lows. It is not clear if low blood sugar played a role in the deaths. The data has not yet been published, pending further analysis.

I have a theory: Diabetes experts have long contended that diabetics have more heart disease because of high blood sugar. A perfectly normal HgbA1c in a non-diabetic is < 5%. In the ACCORD study, more people died with HgbA1c levels that were approaching perfectly normal. So what is the difference between diabetics and non-diabetics with normal blood sugar?

The diabetics in this study achieved their normal levels with medication. Non-diabetics don't take those medications, maintaining normal glucose levels with normal metabolism and possibly even a healthy lifestyle.

Many diabetes medications make it very difficult to lose weight, and in fact may drive up hunger and body weight from fat. More fat, particularly in the spare-tire area common in diabetics, perpetuates metabolic abnormalities common to 'apple' shaped people. Those include worse inflammation, oxidation, blood vessel spasm, cholesterol, triglycerides and clotting, all of which contribute significantly to heart disease.

I posit that driving diabetics' blood sugar to normal levels with medication increases abdominal fat mass, which leads to heart-disease-causing metabolism, independent of blood sugar.

It will be very interesting to see what happened to the weight and waistlines of ACCORD's tight-control group. If the investigators also measured parameters of inflammation, oxidation and clotting, it would add invaluable information and possibly the explanation for ACCORDS's findings.

A Danish study recently published in the New England Journal of Medicine tried to address many factors as well as lowering glucose. They added aspirin, cholesterol-lowering medication and a specific type of blood pressure drug that prevents kidney disease to the 'tight-control' group.

In its initial phase there were equal numbers of heart disease deaths in the 'tight-control' and usual care groups. Though the goal for 'tight' control was HgbA1c<6.5%, people only achieved an average of 7.9%, and the 'usual-care' group wasn't too far off.

During the follow-up phase, the 'usual-care' group's average HgbA1c *improved* and most added the same extra medications to help metabolism, but they had many more heart disease deaths. Both groups increased weight and waistline.

The official conclusions of the study were that tight control helps over the long-haul, but the 'tight-control' groups glucose control wasn't so tight – It ended up the same as the other group's.

The only real difference between the two groups at the end of follow-up was the higher rate of aspirin use by the group with less heart disease. So either aspirin is the answer, or we are missing something completely. While we look for it, diabetics do much better if they rid themselves of diabetes with lifestyle changes.