ABSTRACT

Bruce B. Duncan

Central obesity and the insulin resistance syndrome — new elements in the etiology of non-communicable diseases

Departamento de Medicina Social, UFRGS

Major advances in our understanding of cardiovascular and other chronic diseases are important for the health of Brazilians. Brazilian adult populations, in age standerdized international comparisons, have some of the highest cardiovascular disease rate reported. These high rates are due in large part, I believe, to our lack of attention to the problem. In infant health, identified as a national priority, the results of the last 15 years are dramatically favorable. The same can and must be done for adult health, for studies of developing countries in general, and Brazil in particular, have shown that the changing demographic pattern will greatly increase the country's health burden, producing an increasing predominance of chronic adult diseases.

In this regard, what have we learned recently that may help us prevent these diseases? One thing is that past appraoches are inadequate. Studies show that previous recommendations for agressive therapy of hypertension and hypercholesterolemia are inefficient ways of preventing coronary deaths. Probably less than half of hypertensives treated by previous criteria should receive pharmacologic treatment by today's standards, and recent meta-analyses suggest that the treatment of asymptomatic hypercholesterolemia, besides costing a fortune, may do more harm than good. A recent MONICA Study showed that only 25% of variability in ischemic heart disease could be explained by differences in the distribution across countries of the traditional risk factors smoking, blood pressure and cholesterol.

Identification and treatment of hypertension and hypercholesterolemia have been, for the last decade, the cornerstones of clinicial preventive therapy aimed at those with hemodynamic and metabolic risk for heart disease. Hypertension can be effectively managed, but we can't expect too much in return. Further, given the difficulty of centering a clinical strategy to reduce metabolic risk on cholesterol, we need new approaches which can identify patients metabolically at risk early on in their lives so that we may target them for non-pharmacologic therapies. One potential approach may be related to obesity, central obesity and the insulin resistance syndrome.

A national public health disaster is ocurring with respect to obesity. It's prevalence increased 100% in Brazilian men and 70% in Brazilian women over a period of 15 years ending in 1989. Currently 48% of Brazilian women, by World Health Organzation criteria, are above normal weight. One quarter of these women are frankly obese.

Obesity has been shown to increase the risk of hypertension, dyslipidemia and diabetes. However, its real importance in causing death is unclear. Recent studies suggest that the bodily localization of adipose tissue, specifically central, of visceral excess, is much important to overral obesity. In a study of over 40,000 U.S. women, when the waist-to-hip ratio (WHR) — a measure of central obesity — was greater than 0.90, the risk of the death was doubled, compared to when ratio was less than 0.76. Similar findings, though not as strong, have been found for men. Data from Porto Alegre shows the importance of the association between central obesity and diabetes. In analyses controlling for age, family history of diabetes and overall obesity, women with a high WHR had almost five times the prevalence of diabetes of those with low WHR, men more than two times the prevalence. U.S. studies show women with high WHR to be at greater risk breas for it cancer; men, for colon cancer.

Where does insulin resistance fit in? *Insulin sensitivity* can be thought of conceptually as the facility with which the body matabolizes a glucose load. *Insulin resistance* is the opposite of insulin sensitivity. Metabolic studies, using so-called glucose clamp techniques, have confirmed that such resistance is a major predictor of diabetes, and have so also donstrated a high frequency of insulin resistance in adults with lesser degrees of glucose intolerance, as well as in many glucose tolerant individuals. Insulin resistance is intimately related to central obesity, and may be more directly involved in the etiology of chronic disease. Epidemiologic studies, using various markers of resistance, have demonstrated an important clustering of cardiovascular risk factors with this resistance. To mention one, in the ARIC study of over 12000 U.S. middle aged adults, the distribution of six abnormalities — hypertension, diabetes mellitus, high LDL-C, high triglyce-

rides, low HDL-C and high uric acid — factors associated with ischemic heart disease — was studied. Althoug overall obesity, central obesity and fasting insulin all contributed in an independent manner to this clustering, the association with insulin was most notable. In white women, where the associations are strongest, the risk of having three or more of these abnormalities was 6 times higher in those with high fasting insulin, of having 4 or more, 12 times higher. Serum insulin levels, a surrogate measure of insuline resistance, have been shown to predict the development of hypertesion as well as of diabetes.

How might central obesity and the insulin resistance syndrome be used in a prevention program for those at metabolic risk for chronic disease?

Through identifying central obesity, and perhaps screening biochemically for insulin resistance, individuals metabolically at high risk could be identified. Interventions in these individuals would then be aimed at helping them stay healthy, using standard approaches such as increased physical activity and weigth maintenance or loss - which current evidence shows are not impossible tasks for many patients - and newer interventions, such as stimulating moderate alcohol consumption, and diets with anti-oxidant, anti-atherogenic and anti-thrombogenic properties. Dietary therapies have been shown in randomized trials to be successful in prevention of coronary disease, at least in trials of secondary prevention. All of the above factors have strong inverse associations with ischemic heart disease in cohort studies. All can be administered as health promotion activities, without labeling these high risk individuals as diseased. These interventions, which are merely intensified variants of what, to one degree or another, can be general health promotion strategies for adults, can be implemented presumably at a fraction of the cost of later pharmacologic interventions.

Before launching such a program much further research is needed. But this approach appears to hold much promise. The current mix of prevention and therapy for chronic diseases within the SUS is weighted too much toward therapy. We need to be constantly looking for ways to change this picture.