Glucose tolerance abnormalities and type 2 diabetes in youth: New developments

Until only 10 years ago, diabetes in children and adolescents was in almost all cases related to autoimmune type 1 diabetes, and in rarer instances, to monogenic subtypes of the disease such as maturity onset diabetes of the young (MODY –2). However, this face of diabetes in youth is changing. Today, the rising incidence of both obesity and reduced levels of physical activity are associated all around the world with abnormalities in glucose tolerance and non–insulin-dependent diabetes—close to the classic form of type 2 diabetes (T2DM) observed later in life. While recent epidemiological data from the US emphasize the epidemic progression in all communities, longitudinal studies indicate that the mechanisms involved in the development of this new form of diabetes in youth compare well with those demonstrated in T2DM in adults.

The Search for Diabetes in Youth Study was initiated in 2000 by the National Institutes of Health to assess and describe childhood diabetes in the major ethnic groups in the US.[1] The aims of the study were to estimate the prevalence and incidence of physician-diagnosed diabetes in patients under the age of 20 years, by age, sex, ethnicity, and diabetes type, and to characterize risk factors for complications. Results observed in the 5 major ethnic groups in the US were recently reported this year in a supplement of Diabetes Care. Focus is given to T2DM in the age range of 10 to 19 years, as T2DM remains rare before the age of 10 years.

In non-Hispanic white youths,[2] the prevalence of T2DM was 0.18/1000, higher in females than in males (0.22/1000 versus 0.15/1000), with an incidence rate of 3.7/100 000. These rates are several-fold higher than those observed in European countries. Cardiovascular risk factors were frequent, including increased low-density lipoprotein (LDL) cholesterol in 40% of those assessed, and smoking in 26%. Results were worse in the other ethnic groups. In Hispanic American youths,[3] the incidence was 6.9/100 000 in females and 4.8/100 000 in males. In Asian and Pacific Islander US youths,[4] the incidence was 12.1/100 000. In African American youths,[5] the prevalence of T2DM was 1.06/1000, and the incidence was 19/100 000, while the highest rate was observed in Navajo youths, reaching 39.4/100 000 in adolescents aged 15 to 19 years.[6]

As in adults, T2DM in youth results from the failure of the β-cell to compensate for decreased insulin sensitivity.[7] Cali et al[8] demonstrated a similar course of metabolic events in 60 obese adolescents with normal glucose tolerance at inclusion who were followed over a period of 30 months. Dynamic, static, and total b -cell responsivity, as well as insulin sensitivity and disposition index (insulin secretion adjusted for insulin sensitivity), were studied on 3 occasions. While 46 subjects remained with normal glucose tolerance during the follow-up (nonprogressors), 14 (23%) progressed to impaired glucose tolerance (progressors). At baseline, insulin sensitivity was similar in

nonprogressors and progressors, but insulin defects were present only in progressors. Over time, insulin sensitivity remained stable in nonprogressors, and decreased by 45% in progressors. In nonprogressors, b -cell responsiveness was unchanged, while it decreased by 20% in progressors. The disposition index progressively decreased in progressors, and modestly improved in nonprogressors.

In young subjects progressing to impaired glucose tolerance, glucose intolerance results from both a primary defect in insulin secretion, and progressive decline in insulin secretion with time. This sequence of events is close to that observed in T2DM
in adults.

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