CHAPTER 11

RISK FACTORS FOR TYPE 1 DIABETES

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SUMMARY

The incidence of type 1 diabetes is increasing at an annual rate of 3%–5%, which suggests a major environmental exposure has changed, by either the gradual introduction of a susceptibility factor or the removal of a protective factor, during the past 60 or more years. Outbreaks and seasonality of type 1 diabetes may suggest an infectious cause, perhaps related to increasing sanitation and loss of herd immunity. Early childhood diet and environmental toxins are also of interest.

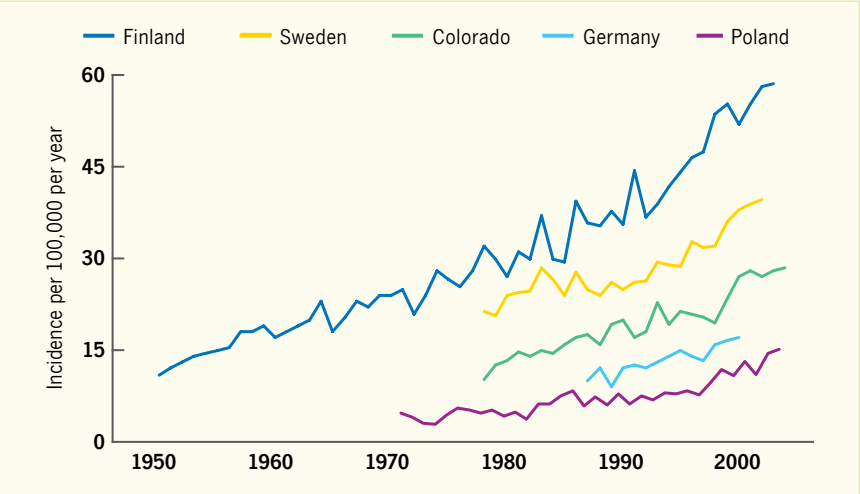
Prospective studies following high-risk children from birth to development of the subclinical phase of the disease (islet autoimmunity) and diabetes have been the most reliable source of information regarding risk factors for type 1 diabetes. Prenatal and early postnatal exposures appear to be critical, as the incidence of islet autoimmunity peaks in the second year of life. Among the infectious agents, enteroviral infections (particularly if they are persistent and acquired in early childhood) have gained most interest. Early leads suggesting the role of cow's milk exposure in the initiation of islet autoimmunity have not been confirmed by large prospective studies and a large randomized clinical trial. While numerous studies have reported 1.5–2-fold increases in the risk of islet autoimmunity or type 1 diabetes with various components of early childhood diet and infectious exposures, none of the associations appears particularly strong or universal across different populations.

In the United States, 1 in 300 children and adolescents develop type 1 diabetes by age 20 years, but 1 in 40 offspring of mothers with type 1 diabetes and 1 in 15 offspring of fathers with type 1 diabetes develop type 1 diabetes. The disease is likely caused by the interplay of genetic and environmental factors. Systematic investigation of gene-environment interactions in large, prospectively followed cohorts of young children may help to identify and fully characterize modifiable risk factors and design trials to fully evaluate the strongest candidate triggers of autoimmunity.

INTRODUCTION

The incidence of type 1 diabetes is increasing worldwide, by 3%–5% annually (1), with rates doubling every 20 years (2,3). The rising incidence, outbreaks (4), and a seasonal pattern (5) may suggest that infectious agents play a role in the pathogenesis. However, the incidence has been increasing since at least the 1950s (Figure 11.1) (2,3,6,7,8,9,10,11). Such a secular trend is unlikely to result from a new infectious agent; however, similar to the polio model (12), an "old" microbe could express its diabetogenic effect due to increasing hygiene and decreasing herd immunity. Changes in early childhood diet have also been implicated, as type 1 diabetes has increased the most in the youngest children. Prospective studies (13,14,15) following high-risk children from birth have made important inroads into the understanding of the role of infectious

FIGURE 11.1. Incidence of Type 1 Diabetes Per 100,000 Per Year in Children Age 0–14 Years, 1950–2003



Type 1 diabetes incidence is increasing 3%–5% per year and has doubled every 20 years.

SOURCE: Reference 11. Data for Finland are from the Finnish National Public Health Institute (3); data for Sweden are from the Swedish Childhood Diabetes Registry (6); data for Colorado are from the Colorado IDDM Registry, the Barbara Davis Center for Childhood Diabetes, and SEARCH for Diabetes in Youth (2,7); data for Germany are a compilation of two reports (8,9); data for Poland are from seven regional registries (10).

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