

An inexplicable upsurge: the rise in type 1 diabetes

Elizabeth B. Snouffer

When I was diagnosed with type 1 diabetes, I wasn't told what specifically triggered the destruction of my insulin-producing pancreatic β -cells but I was told genetics played a role, that diabetes was a serious condition and I would be dependent upon exogenous insulin and a strict dietary regime for life. As I navigated through school and community (Baltimore, Maryland (USA)), I carried juice boxes, syringes, and a vial of insulin in my backpack. I was open about my condition in part because I wanted to meet another student with type 1 diabetes, just like me. For many years, I never met another young person living with type 1 diabetes until I was introduced to another high school senior at a different school. We commiserated about our longing for ice-cream and the delight in managing hypoglycaemic episodes with all our favorite but forbidden foods. Sadly, he did not live to see his 20th birthday due to complications of diabetes, but I thought about him this October as I celebrate 40 years with type 1 diabetes. I've come a long way and yet, we still do not know what triggers β -cell autoimmunity and further, why so many more children and young adults are developing autoimmune diabetes.

Dr. Marian Rewers, Head of the Colorado Center of "The Environmental Determinants of Diabetes in the Young" (TEDDY) study does admit there was little awareness for the rise in type 1 diabetes at first, but says documents providing evidence were from the early 1980s: "The first registry-based observation of the epidemic in 1982-84 was published in Diabetes in 1987, followed by an international study confirming the epidemic in most of the 10 countries that had a registry in 1990. Looking back, the incidence probably started to rise already in the 1950's but there was no reliable data until the late 1960's."

The fact is that the incidence of type 1 diabetes has risen considerably in the past 30 years¹, and while many experts might argue different cases for possible identifiable triggers – one thing is certain, the jury is still out and a great deal of research is still needed.

An inexplicable upsurge

According to the 8th Edition of the IDF Diabetes Atlas, the number of young people <20 years living with type 1 diabetes worldwide is estimated to be 1,106,500 million² which is double the number cited in the previous Diabetes

Atlas³ due to the expansion of the age group by five years. This may raise other questions but one thing is clear, the incidence and prevalence of type 1 diabetes are both growing with great variation worldwide.⁴

IDF's Europe and North America and Caribbean regions, have the largest number of children with type 1 diabetes (Table).² The US has the largest incidence and prevalence of children with type 1 diabetes in age groups under 15 and 20 years.² However, type 1 diabetes is most common in Finland (>60 cases per 100,000) and Sardinia (around 40 cases per 100, 000).⁵ Additionally, Europe has seen increases in children younger than 5 years of age,⁶ and annual increase rates have been reported in Norway, Germany, and in Finland.⁷

In the US, the SEARCH for Diabetes in Youth Study reported the prevalence of type 1 diabetes in children and young adults ages <20 years rose by 21 percent between 2001 and 2009 and showed a significant impact on minority populations—unusual as these populations had previously low rates of the disease.⁸ More recent data from a new US study (in collaboration with the SEARCH for Diabetes in Youth study) strengthens this position: non-Hispanic white youths had the smallest annual increase in type 1 diabetes diagnoses while Hispanic youths had the highest annual increase in incidence (4.2%).⁹ Overall the US study reported the annual increase for the 10-year period was nearly two percent for type 1 diabetes diagnoses and nearly five percent for type 2 diabetes.⁹ While it's no surprise that type 2 diabetes in youth, particularly in the US, has developed in tandem with rising rates of obesity, type 1 diabetes has a much less identifiable explanation.

Professor Elizabeth Mayer-Davis, PhD, Professor of Nutrition and Medicine, and Chair of the Department of Nutrition, at the University of North Carolina at Chapel Hill, primarily focuses on type 1 diabetes in youth and young adults, and has concerns about the rate seen in Hispanic children in the US. "It could be that Hispanic population genetics are different in such a way that environmental triggers for autoimmunity and disease progression are affecting them. What we do know is that here is a subgroup in the US with a higher rate of change and we need to figure out what the exposures are for these children."

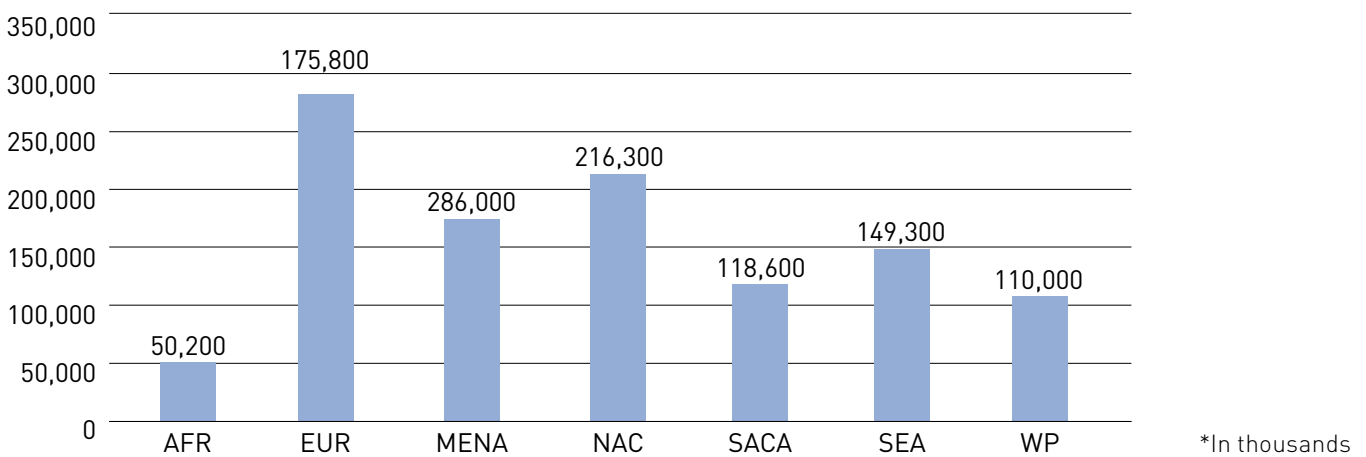
Moving away from the high rates of type 1 diabetes in North America and Europe, it is of particular interest to assess countries where type 1 diabetes was nearly unheard of or rare in the past, but where there now exists a range of global variation in incidence that reflects a somewhat random pattern.

- In a 30-year study in a Brazilian municipality (Bauro, Brasil) the annual incidence of type 1 diabetes increased 4% in children ages ≤14 years.¹⁰ Brasil has the third largest incidence and prevalence of children with type 1 diabetes worldwide.²
- While incidence of type 1 diabetes in China has to a large degree been unclear, a 2016 systematic review and meta-analysis confirmed increasing incidence of type 1 diabetes over time in mainland China: from 0.57 (0.43–0.75) in 1990 to 1.04 (0.64–1.68) in 2000 and 3.36 (1.66–6.82) in 2010. (p<0.0001).¹¹
- Researchers studied the incidence of type 1 diabetes in Kuwaiti children 0-14 years during 2011 to 2013 and compared results with data collected during 1992 to 1997. The incidence of type 1 diabetes in Kuwaiti children 0-14

years has doubled in the last 2 decades.¹²

- Type 1 diabetes is the second most common chronic disease in children in India,¹³ and the IDF Atlas estimates that India has the second largest incidence and prevalence of children with type 1 diabetes worldwide.²
- In Saudi Arabia, studies indicate a significant increase in incidence rates of type 1 diabetes in groups older than 12 years.¹⁴ Saudi Arabia is eighth on a list of top 10 countries for number of children diagnosed per year, just after the United Kingdom.²

Experts believe if the current rates continue to increase, the global incidence of the number of children and youths developing type 1 diabetes could double in a matter of years.



Estimated number of children and adolescents (<20 years) with type 1 diabetes by IDF region, 2017. Source: IDF Diabetes Atlas 8th Edition 2017

Factors for progression

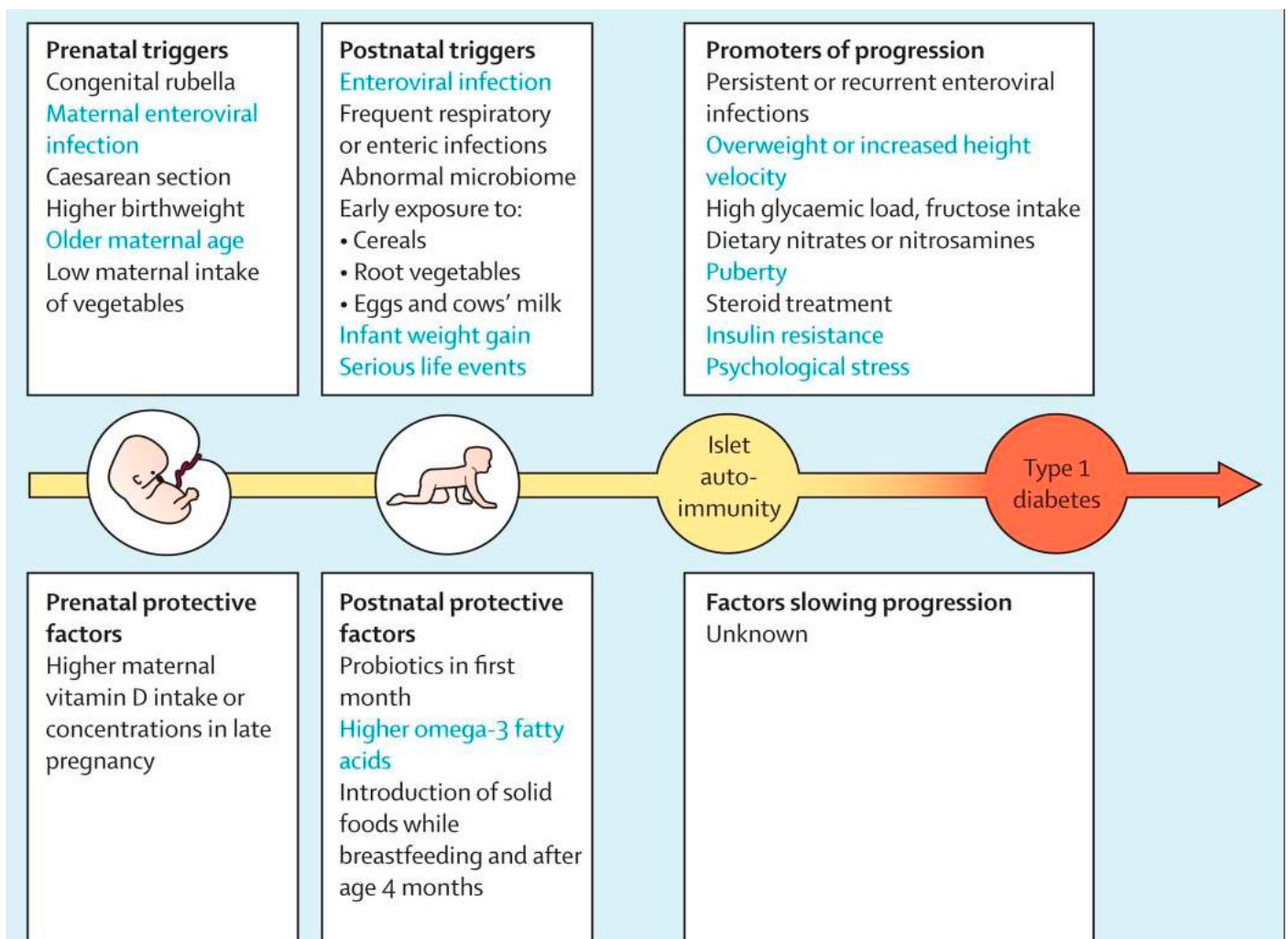
For many decades, there has been a long list of possible factors that may drive progression from autoimmunity to overt type 1 diabetes in genetically predisposed individuals. Though genetic markers identify risk, islet autoimmunity can only begin once multiple islet autoantibodies are present. Individuals who express two or more positive autoantibodies are likely to develop type 1 diabetes.

However, the time to diabetes diagnosis varies tremendously, and the factors influencing progression are not understood. Most experts agree that a trigger from the environment is needed for the development of a type 1 diabetes diagnosis.¹ Environmental triggers include infections, diet, and toxins that could have an effect on children in all phases of early development (Figure).

Some of the most promising candidate environmental factors for type 1 diabetes include¹:

- Respiratory infections;¹⁵
- Infant formulas;¹⁶
- Intestinal microbiota (associated with C-section deliveries, use of antibiotics; early childhood nutrition);¹
- The hygiene hypothesis variant (decreased herd immunity to enteroviruses)¹

Additionally, the accelerator and β -cell stress hypotheses proposes how several environmental factors could be at play in a child's risk development including: overweight,



Environmental triggers and protective factors for islet autoimmunity and promoters of progression to type 1 diabetes for which an association has been suggested. Triggers and factors with the strongest evidence base are shown in blue. (Rewers M, Ludvigsson J. Environmental risk factors for type 1 diabetes *Lancet* 2016;387: 2263-2350.)

fast growth, a range of dietary deficiencies, trauma, psychological stress—alone or combined could drive pancreatic β -cell exhaustion, resulting in islet failure and type 1 diabetes.¹ Many factors thought once to be strong triggers for type 1 diabetes are no longer seen as candidates: vaccines and cow's milk.¹

Professor Johnny Ludvigsson and Dr. Marian Rewers authors of the 2016 publication *Environmental risk factors for type 1 diabetes (Lancet)* both believe that research currently has not established what trigger could be identified as the most likely, “we just don't know.” However, key for further study (Figure) would be “infant diet, patterns of infections and environmental pollutants.” says Professor Ludvigsson, while Dr. Rewers adds that “studying infections in mothers during pregnancy” may be very significant. As for why type 1 diabetes is appearing in places like Asia, where it was once rarely seen, Dr. Rewers believes “high incidence in parts of Asia, especially the Middle East, suggests changes not only in diagnosis (versus those undiagnosed and early death) but also an increase of incidence due to changes in lifestyle,” he says.

The current type 1 diabetes population is characterized by diversity: stark differences in age, race, genetic identity and phenotype. If anything, environmental exposures leading to type 1 diabetes vary greatly which explains the current inconsistencies worldwide. More tests are needed to study genetic background and environmental exposures. Research must continue to define the environmental causes of type 1 diabetes—in part by studying different populations—to broaden our understanding and prevent or delay the current and continued rise in type 1 diabetes.

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