

Chapter 3

Type 1 Diabetes

Type 1 diabetes is one of the most common chronic disorders of childhood. Unfortunately, it is increasing in incidence, particularly in young children. The reason for this is unknown, although it is most likely related to the environment (see below). It is also the most common form of diabetes to occur in people under age 40. Type 2 is the most common form after age 40. The list of famous people: sport stars, politicians, movie stars and artists, who have type 1 or type 2 diabetes is long. Following diagnosis, children frequently discover classmates who also have diabetes. Their looks, personalities and activities are no different from those of anyone else.

The rate of development of type 2 diabetes in children has increased in recent years. There is also a worldwide increase in type 2 diabetes in adults. This is due primarily to eating high calorie and high fat foods as well as a lack of exercise resulting in excess weight gain. Type 2 diabetes will be discussed in Chapter 4.

CAUSES

We know that diabetes is not catching, like a cold. We also know that type 1 diabetes isn't caused from eating too much sugar.

Three risk factors seem to be important in determining why a person develops type 1 diabetes:

1. inherited (or genetic) factors
2. self-allergy (autoimmunity)
3. environmental damage (e.g., from a virus or chemical)

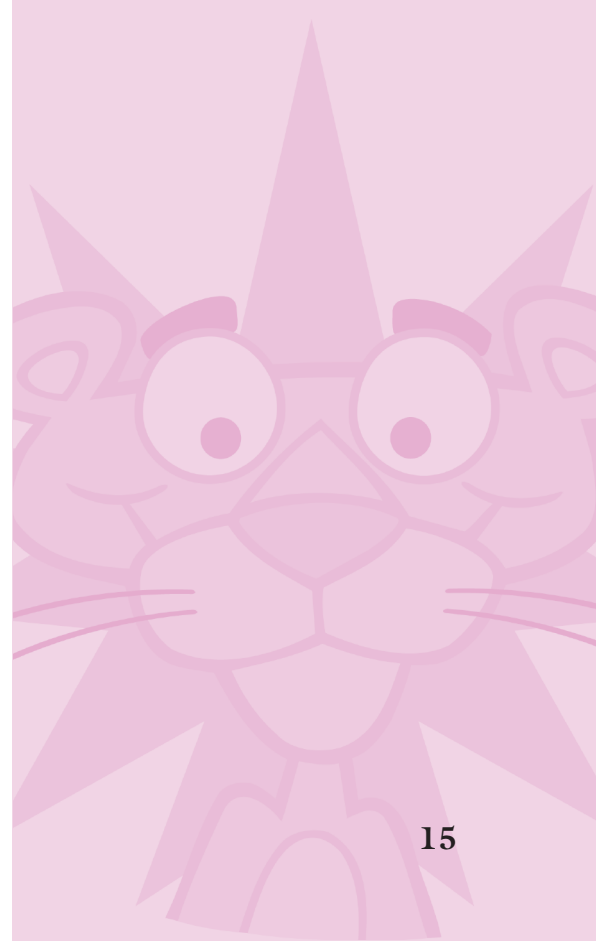
TEACHING OBJECTIVES:

Design an educational plan with the family that will ensure an adequate diabetes knowledge foundation on which to build.

LEARNING OBJECTIVES:

Learners (parents, child, relative or self) will be able to:

1. List two causes each for type 1 and type 2 diabetes.
2. State one major difference in the treatment of type 1 and 2 diabetes.



1. Inheritance (genetic)

The first important reason seems to be an inherited or genetic factor, such as the way a person inherits the color of the eyes from a mother, father or other relative.

Facts about inheritance:

🐾 People with type 1 diabetes are more likely to have inherited certain cell types (called **HLA types**). Those who don't have diabetes are less likely to have these HLA types.

🐾 The HLA types are determined by using *white blood cells* (WBCs) for typing. Blood types (A, B, AB and O) are determined using red blood cells.

🐾 Nearly all people with type 1 diabetes have an HLA type **DR3** or **DR4**.

Fifty-three percent of people with type 1 diabetes have one DR3 and one DR4, **with one of these coming from each parent**.

🐾 Only three percent of people without diabetes have this DR3/DR4 combination. This combination makes a person more likely to develop diabetes. This is especially true when they have a relative with diabetes.

🐾 Over half of the families (up to 90 percent in one study) have no close relative with type 1 diabetes. Perhaps a family has a DR3 or a DR4 gene, but no family member has ever married into a family with the other DR gene. If a family member with a DR3 gene then marries into another family carrying the DR4 gene, the child may end up with the DR3/DR4 combination. They may then be at high risk for diabetes.

🐾 It is now known that there are also different genes that help to protect a person from developing diabetes.

🐾 Children from a family who have a child with diabetes have a greater chance of developing it than without a family history. A brother or sister of a child with diabetes has about a 1 in 20 (five percent) chance of developing diabetes.

🐾 The cause is not completely due to heredity. We know this from studies of identical twins. When one identical twin gets diabetes, only in half of the cases does the other twin also develop the disease. If it were entirely due to heredity, both twins would always develop it. We don't completely understand the inheritance factors. We do believe that **both** mother and father transmit the tendency to develop diabetes to their child.

2. Self-allergy (autoimmunity)

The second cause that seems to be important in type 1 diabetes is self-allergy (or autoimmunity). Normally, our immune systems protect our bodies from disease.

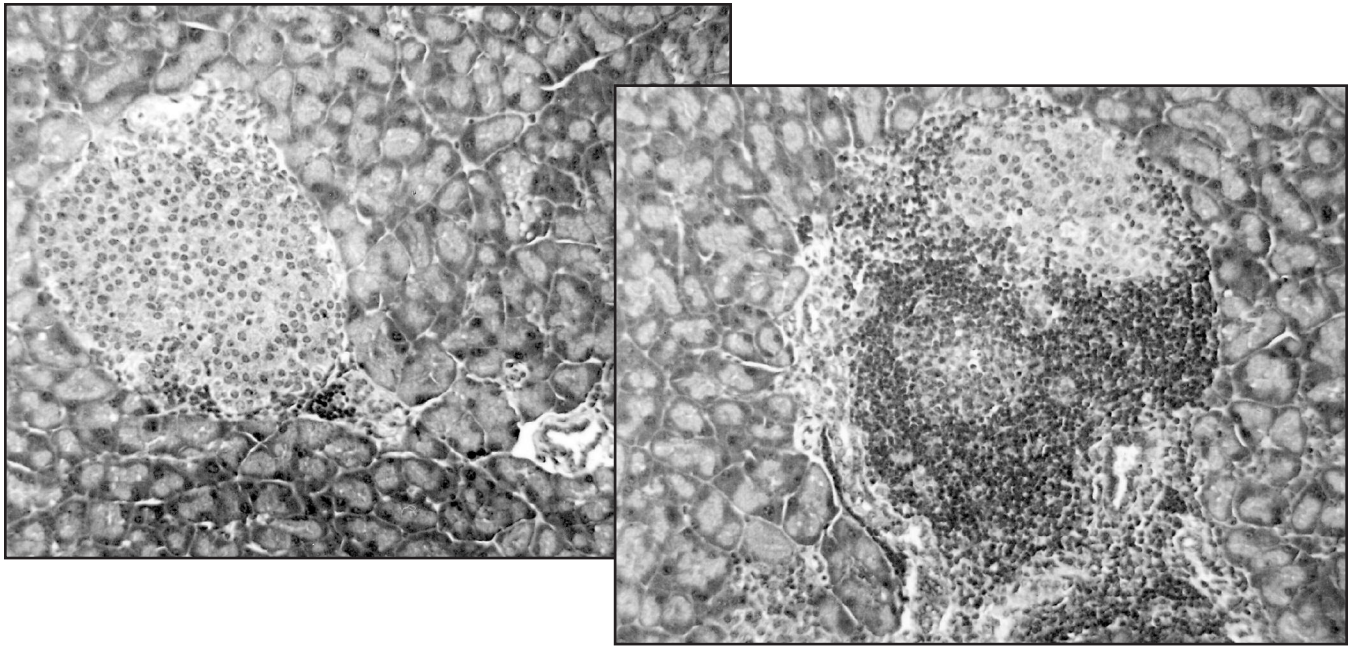
Facts about self-allergy (autoimmunity):

🐾 In the case of type 1 diabetes and other autoimmune diseases such as lupus, arthritis and multiple sclerosis, the immune system turns against a body part.

🐾 There can be evidence of this allergic reaction found in the blood. The allergic reaction is against the cells in the pancreas (islet cells) that make insulin. Most Anglo and about half of Hispanic and African-American children show this allergy when they develop diabetes. The evidence in the blood is called an antibody or, more specifically, an **“islet cell antibody” (ICA)**. We now know that some people can have this antibody present in their blood for many years before they need insulin.

🐾 Other diabetes antibodies called biochemical antibodies (“GAD” antibodies, insulin autoantibodies [IAA] and ICA 512 antibodies) can now be measured. They are easier to measure and have also been found in the blood of people who are developing diabetes.

🐾 Identifying these antibodies in the blood has made it possible to screen people who are at risk to develop diabetes. This screening has led to research trials (see Chapter 28) which will try to prevent diabetes. We



MICROSCOPIC PHOTOGRAPH OF PANCREATIC ISLET:

The photo on the left shows a normal islet (center) surrounded by other pancreatic tissue. This other tissue is responsible for making digestive enzymes. The photo on the right is from a diabetic animal. The white blood cells (WBCs) have invaded and destroyed the islet.

believe it is important for brothers, sisters and other relatives to have this screening.

- 🐾 The antibodies gradually disappear from the blood after the onset of type 1 diabetes. Within one year, many people will no longer have them.
- 🐾 People who develop type 2 diabetes (previously called adult-onset) do not have these antibodies, even if they are under age 21 at onset.

3. Environmental (virus or chemical)

A third factor is also believed important. This environmental factor may either be a virus or something in the food we eat or something we do not yet know about. This factor may be the bridge between the genetic (inherited) part and the allergic reaction.

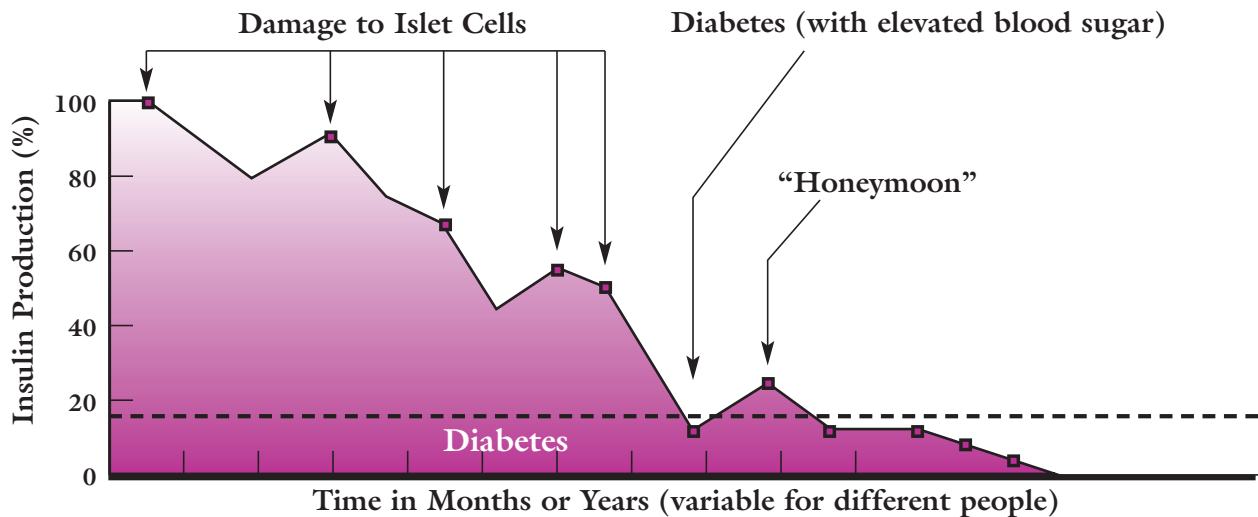
An example of the sequence of events might be:

- 🐾 A person *inherits* the tendency for diabetes.
- 🐾 This tendency might allow a virus to injure the islet cells.

- 🐾 Part of the damaged islet cell may then be released into the blood.
- 🐾 The body would then make islet cell antibodies (an allergic or autoimmune reaction).
- 🐾 The damage can attract white blood cells (WBCs) to the area of the islet. These now active WBCs produce chemicals, which further injure the other islet cells.
- 🐾 Anything that activates the WBCs in the future (viral infections, certain foods, stress, etc.) may result in more of the islet cells being destroyed.

We now know that most people who get diabetes don't just suddenly develop it. They have been in the process of developing it for many years, sometimes even from birth. Most likely many viral infections and other factors result in damage and destroy a few more islet cells. As more and more islet cells are destroyed the person moves closer to having diabetes (see Figure below where diabetes is represented by the broken line).

The Gradual Onset of Type 1 Diabetes



It is now believed that diabetes develops gradually, over many months or many years. It does not just come on suddenly in the week or two before the elevated blood sugars. Many insults (represented by the arrows in this Figure) likely result in further damage until the diagnosis of diabetes is made. The insults may include viral infections, stress, chemicals in the diet or other agents. These agents may work by “activating” white blood cells in the islets to make toxic chemicals that cause injury to the insulin-producing cells (beta cells). However, a “genetic-predisposition” (inherited factors) must be present for the process to start.

TYPE 2 (ADULT-ONSET) DIABETES:

Chapter 4 explains type 2 diabetes in more depth.

The three main risk factors for type 2 diabetes are:

1. **Overweight**
 2. **Insulin insensitivity**
 3. **Inheritance (genetics)**
1. **Overweight (obesity):** is an important risk factor for type 2 (adult-onset) diabetes. In contrast, it is not a risk factor for type 1 diabetes.
 2. **Insulin insensitivity:** Insulin does not seem

to work normally in the person with type 2 diabetes. Initially it can still be made in normal or above-normal amounts. This is different from type 1 diabetes, where insulin cannot be made at all or is made in small amounts. Later, people with type 2 diabetes may also have reduced insulin production. They will then need insulin shots.

3. **Inheritance (genetics):** Type 2 diabetes also has a strong inherited (genetic) cause. People with type 2 diabetes do not have the same association with the HLA genes as do people with type 1 diabetes. They also do not make islet cell antibodies. The causes of the two types of diabetes seem to be completely different.

DEFINITIONS

Allergy: A special reaction of the body to some material. This is similar to what happens if you are allergic to something that makes you sneeze.

Antibody: The material we measure in the blood if someone has an allergy (example: milk antibodies might be present if someone has a milk allergy).

Autoimmunity (self-allergy): The process of forming an allergic reaction against one's own tissues. This happens in diseases such as lupus and arthritis. People with type 1 diabetes make an antibody against their islet cells (where the insulin is made).

Genetic (inherited): Features, such as eye color, that are passed from both parents to children.

HLA type: The way to group cell types just as red blood cells are grouped into A, B, AB and O blood types. HLA stands for Human Leukocyte Antigen. A leukocyte is another name for a white blood cell. The white blood cell is the type of cell used in HLA typing.

Identical twins: Twins that come from the same egg. All their features (genetics) are exactly alike.

Islet cell (pronounced eye-let): The groups of cells within the pancreas that make insulin.

Islet cell antibody: The material we measure in the person's blood to show that they have had an allergy against the cells in the pancreas (the islet cells) that make insulin.

QUESTIONS AND ANSWERS FROM NEWSNOTES

Q My daughter was in a car accident the week before the onset of her diabetes. Could that have caused the diabetes?

A It is now accepted that diabetes comes on gradually over many months or many years. It is not just brought about by one event. After initial damage occurs to the islets in the pancreas (where insulin is made), islet cell antibodies may be positive, indicating that some damage has occurred. We have followed many people with positive islet cell antibodies. Some have not needed to start insulin treatment for as long as ten years.

After the initial damage, many factors may cause activation of white blood cells (WBCs) in the islets. These factors may include some viral infections, content of the diet or even stress. When the WBCs in the islets are activated by these factors, they produce toxic chemicals that destroy a few more islets each time. Gradually, a person gets closer to having full-blown diabetes. Thus, the stress of the automobile accident may have been the final precipitating event, but it was most likely only one of several insults over many years.

Q What is the role of inflammation in causing diabetes?

A Inflammatory markers have been shown to be developed prior to the onset of type 2 diabetes, gestational (pregnancy) diabetes and in some, not all, young infants prior to the onset of type 1 diabetes. In the young infants (*"Diabetes"* 53,2569, 2004) the inflammatory markers correlated with who was most apt to progress to diabetes. They were not a marker for the development of antibodies.

"Think
Pink!"

