Diabetes

What is diabetes?

Diabetes is the condition in which the body does not properly process food for use as energy. Most of the food we eat is turned into glucose, or sugar, for our bodies to use for energy. The pancreas, an organ that lies near the stomach, makes a hormone called insulin to help glucose get into the cells of our bodies. When you have diabetes, your body either doesn't make enough insulin or can't use its own insulin as well as it should. This causes sugars to build up in your blood. This is why many people refer to diabetes as “sugar.” Diabetes can cause serious health complications including heart disease, blindness, kidney failure, and lower-extremity amputations. Diabetes is the seventh leading cause of death in the United States.

What are the symptoms of diabetes?

People who think they might have diabetes must visit a physician for diagnosis. They might have SOME or NONE of the following symptoms:

- Frequent urination
- Excessive thirst
- Unexplained weight loss
- Extreme hunger
- Sudden vision changes
- Tingling or numbness in hands or feet

• Feeling very tired much of the time

• Very dry skin • Sores that are slow to heal

• More infections than usual Nausea, vomiting, or stomach pains may accompany some of these symptoms in the abrupt onset of insulin-dependent diabetes, now called Type 1 diabetes.

What are the types of diabetes?

Type 1 Type 1 diabetes, previously called insulin-dependent diabetes mellitus (IDDM) or juvenile onset diabetes, may account for 5 percent to 10 percent of all diagnosed cases of diabetes. Risk factors are less well defined for Type 1 diabetes than for Type 2 diabetes, but autoimmune, genetic, and environmental factors are involved in the development of this type of diabetes.

Type 2 diabetes was previously called non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. Type 2 diabetes may account for about 90 percent to 95 percent of all diagnosed cases of diabetes. Risk factors for Type 2 diabetes include older age, obesity, family history of diabetes, prior history of gestational diabetes, impaired glucose tolerance, physical inactivity, and race/ethnicity. African Americans, Hispanic/Latino Americans, American Indians, and some Asian Americans and Pacific Islanders are at particularly high risk for type 2 diabetes.

Gestational diabetes develops in 2 percent to 5 percent of all pregnancies but usually disappears when a pregnancy is over. Gestational diabetes occurs more frequently in African Americans, Hispanic/Latino Americans, American Indians, and people with a family history of diabetes than in other groups. Obesity is also associated with higher risk. Women who have had gestational diabetes are at

increased risk for later developing Type 2 diabetes. In some studies, nearly 40 percent of women with a history of gestational diabetes developed diabetes in the future. 2 3 Other specific types of diabetes result from specific genetic syndromes, surgery, drugs, malnutrition, infections, and other illnesses. Such types of diabetes may account for 1 percent to 2 percent of all diagnosed cases of diabetes.

Treatment for Type 2 diabetes

Treatment typically includes diet control, exercise, home blood glucose testing, and in some cases, oral medication and/or insulin. Approximately 40 percent of people with type 2 diabetes require insulin injections.

Can diabetes be prevented?

A number of studies have shown that regular physical activity can significantly reduce the risk of developing type 2 diabetes. Type 2 diabetes is also associated with obesity.

Is there a cure for diabetes?

In response to the growing health burden of diabetes mellitus (diabetes), the diabetes community has three choices: prevent diabetes; cure diabetes; and take better care of people with diabetes to prevent devastating complications. All three approaches are actively being pursued by the US Department of Health and Human Services.

AMINOACIDOPATHIES

Rare inherited disorders of amino acid metabolism•Abnormality in either activity of specific enzyme, in metabolic pathwayor in the membrane specific transport systemfor amino acid.•These defects lead to accumulation of amino acid itself, its precursor or a by-product.•Excessive accumulation in blood leads to physical symptoms of the disease.

PHENYL KETONURIA (PKU)

•Deficiency of phenylalanine hydroxylase (PAH), that catalyses the conversion of phenyl-alanine into tyrosine.

•Phenylalanine is metabolized via alternative pathway leading to the accumulation of Phenyl pyruvic acid (product of phenylalanine de-amination). It's circulation is found in bothblood and urine giving urine a characteristic mustyodors.

TYROSINEMIA

•Excretion of tyrosine and tyrosine catabolytes in urine.
•Deficiency of fumaryl-acetoacetate hydrolase results in type I (more common) or defect in amino transferase results in type II tyrosinemia.
•Elevated levels of tyrosine lead to liver damage which may be fatal during infancy or to liver cirrohsis and liver carcinoma later on in life.
•Rate of incidence is 1 in 100,000

ALKAPTONURIA

•Lack of homogenisate oxidasein the tyrosine catabolic pathway
•Incidence rate is 1 in 250,000
•Very important physical symptom includes darkening of urine upon exposure to atmosphere which is due to homogentstic acid (HGA) oxidising to produce dark polymer.
•Initially patients have no significant symptoms but high level of HGA gradually starts depositing in connective tissues causing arthritis-like degeneration

MAPLE SYRUP URINE DISEASE (MSUD):

•Hereditary disease with characteristic maple syrup or burnt sugar type odour of urine, breath and skin.
•Complete absenceor reductionin activity of branched-chain keto acid decarboxylaseenzyme hence blocking the normal metabolism of three essential amino acids i.e leucine, isoleucineand valine.

•Results in the accumulation of branched-chain amino acids and their corresponding keto-acids in blood, urineand CSF.

Physical symptoms of MSUD include:
•Mental retardation and convulsions due to presence in CSF. In blood however: keto-acidosis and hypoglycaemia takes place.

•Death occurs in 1st year after birth if untreated however the rate of incidence is very low i.e. 1 in 216,000

•Diet supplements low in protein should be strictly administered and therefore early diagnosis through routine screening is highly recommended. However due to rarity of disease many centers don't have the screening facility for MSUD

HOMOCYSTINURIA

•Rate of incidence 1 in 200,000MethionineHomocysteineCystathionineCysteineCystathionine β-synthase•It's a hereditary disorder with impaired activity of Cystathionine-βSynthase•There is accumulation of precursors i.e. homocysteine & methionine

CYSTINURIA

•Defect in amino acid transport system rather than metabolic pathway affecting renal system and other vital organs.
•20 to 30 fold increase in urinary excretion of cysteine due to genetic defect in renal re-absorption mechanisms.
•Cysteine is insoluble therefore precipitates in kidney tubules.
•Laboratory analysis is the same as that of homocysteinuria where a reddish-purple colour is produced in cyanide-nitroprisside test.

Dyslipidemia – unbalanced or unhealthy cholesterol levels

Dyslipidemia is the name for an unhealthy balance of blood fats. Dyslipidemia is the term for unbalanced or unhealthy cholesterol levels. Whilst the term 'cholesterol levels' is used; a more accurate term is 'lipid levels'.

There are different forms of dyslipidemia which includes too high cholesterol but can also refer to too low cholesterol or when the balance of total and HDL cholesterol is unhealthy.

Cholesterol and lipoproteins

Cholesterol serves an important role in the body and is used in the membranes of all our body's cells.

When we have our cholesterol levels measured, what are actually being measured are tiny proteins in the blood which carry the cholesterol.

These lipoproteins include:

- LDL – sometimes known as 'bad' cholesterol
- HDL – sometimes known as 'good' cholesterol

High cholesterol

Having too high cholesterol (hypercholesterolemia) can signify a higher risk of heart problems.

Too high cholesterol can include one or more of the following:

- Too high total cholesterol
- Too high LDL cholesterol
- Too high triglyceride levels

Many people with type 2 diabetes will often find they have high cholesterol either when diagnosed or before finding out they have type 2 diabetes.

Some people may have high cholesterol because they have a condition called familial hypercholesterolaemia. This is a genetic condition that affects about one in 250 people.

People with this condition will have had higher cholesterol levels than normal from birth. However, as high cholesterol rarely presents symptoms, the condition may not be diagnosed until adulthood.

Other factors can also cause higher cholesterol levels include certain medications such as:

- Steroids
- Beta blockers
- Diuretics

Unbalanced cholesterol

High cholesterol can indicate poor health but it is possible to high total cholesterol and still have healthy cholesterol levels, as long as your HDL cholesterol levels are sufficiently high.

Anemia

Anemia happens when there is a decreased number of circulating red blood cells in the body. It is the most common blood disorder in the general population. Symptoms can include headaches, chest pains, and pale skin.

It currently affects more than 3 million Americans and an estimated 1.62 billion people, globally.

It often results when other diseases interfere with the body's ability to produce healthy red blood cells or abnormally increase red blood cell breakdown or loss.

Symptoms

There are many potential causes of anemia.

The most common symptom of all types of anemia is a feeling of fatigue and a lack of energy.

Other common symptoms may include:

- paleness of skin
- fast or irregular heartbeat
- shortness of breath
- chest pain
- headache
- light-headedness

In mild cases, there may be few or no symptoms.

Some forms of anemia can have specific symptoms:

- **Aplastic anemia**: fever, frequent infections, and skin rashes
- **Folic acid deficiency anemia**: irritability, diarrhea, and a smooth tongue
- **Hemolytic anemia**: jaundice, dark colored urine, fever, and abdominal pains
- **Sickle cell anemia**: painful swelling of the feet and hands, fatigue, and jaundice

Causes

The body needs red blood cells to survive. They carry hemoglobin, a complex protein that contains iron molecules. These molecules carry oxygen from the lungs to the rest of the body.

Some diseases and conditions can result in a low level of red blood cells.

There are many types of anemia, and there is no single cause. It can sometimes be difficult to pinpoint the exact cause.

Below is a general overview of the common causes of the three main groups of anemia:

1) Anemia caused by blood loss

The most common type of anemia—iron deficiency anemia—often falls into this category. It is caused by a shortage of iron, most often through blood loss.

When the body loses blood, it reacts by pulling in water from tissues outside the bloodstream in an attempt to keep the blood vessels filled. This additional water dilutes the blood. As a result, the red blood cells are diluted.

Blood loss can be acute and rapid or chronic.

Rapid blood loss can include surgery, childbirth, trauma, or a ruptured blood vessel.

Chronic blood loss is more common in cases of anemia. It can result from a stomach ulcer, cancer, or tumor.

Causes of anemia due to blood loss include:

- gastrointestinal conditions, such as ulcers, hemorrhoids, cancer, or gastritis
- use of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen
- menstrual bleeding

2) Anemia caused by decreased or faulty red blood cell production

Bone marrow is a soft, spongy tissue found in the center of bones. It is essential for the creation of red blood cells. Bone marrow produces stem cells, which develop into red blood cells, white blood cells, and platelets.

A number of diseases can affect bone marrow, including leukemia, where too many abnormal white blood cells are produced. This disrupts normal production of red blood cells.

Other anemias caused by decreased or faulty red blood cells include:

- **Sickle cell anemia**: Red blood cells are misshapen and break down abnormally quickly. The crescent-shaped blood cells can also get stuck in smaller blood vessels, causing pain.
- **Iron-deficiency anemia**: Too few red blood cells are produced because not enough iron is present in the body. This can be because of a poor diet, menstruation, frequent blood donation, endurance training, certain digestive conditions, such as Crohn's disease, surgical removal of part of the gut, and some foods.
- **Bone marrow and stem cell problems**: Aplastic anemia, for example, occurs when few or no stem cells are present. Thalassemia occurs when red blood cells cannot grow and mature properly.
- **Vitamin deficiency anemia**: Vitamin B-12 and folate are both essential for the production of red blood cells. If either is deficient, red blood cell production will be too low. Examples include megaloblastic anemia and pernicious anemia.

3) Anemia caused by the destruction of red blood cells

Red blood cells typically have a life span of 120 days in the bloodstream, but they can be destroyed or removed beforehand.

One type of anemia that falls into this category is autoimmune hemolytic anemia, where the body's immune system mistakenly identifies its own red blood cells as a foreign substance and attacks them.

Excessive hemolysis (red blood cell breakdown) can occur for many reasons, including:

- infections
- certain drugs, for example, some antibiotics
- snake or spider venom
- toxins produced through advanced kidney or liver disease
- an autoimmune attack, for instance, because of hemolytic disease
- severe hypertension
- vascular grafts and prosthetic heart valves
- clotting disorders
- enlargement of the spleen

Treatment

There is a range of treatments for anemia. They all aim to increase the red blood cell count. This, in turn, increases the amount of oxygen the blood carries.

Treatment will depend on the type and cause of anemia.

- **Iron deficiency anemia**: Iron supplements or dietary changes. If the condition is due to loss of blood, the bleeding must be found and stopped.
- **Vitamin deficiency anemias**: Treatments include dietary supplements and B-12 shots.

- **Thalassemia**: Treatment includes folic acid supplementation, removal of the spleen, and, sometimes, blood transfusions and bone marrow transplants.
- **Anemia of chronic disease**: This is anemia associated with a serious, chronic underlying condition. There are no specific treatments, and the focus is on the underlying condition.
- **Aplastic anemia**: The patient will receive blood transfusions or bone marrow transplants.
- **Sickle cell anemia**: Treatment includes oxygen therapy, pain relief, and intravenous fluids. There may also be antibiotics, folic acid supplements, and blood transfusions. A cancer drug known as Droxia or Hydrea is also used.
- **Hemolytic anemias**: Patients should avoid medication that may make it worse and they may receive immunosuppressant drugs and treatment for infections. Plasmapheresis, or blood-filtering, might be necessary in some cases.

Types

There are more than 400 types of Anemia currently known, and these are divided into three main groups according to their cause:

- Anemia caused by blood loss
- Anemia caused by decreased production or production of faulty red blood cells
- Anemia caused by the destruction of red blood cells

Types of anemia within these categories include:

- sickle cell anemia

- vitamin deficiency anemia
- iron deficiency anemia
- blood-loss anemia
- Cooley's anemia
- pernicious anemia

Diagnosis

A complete blood count can help diagnose anemia.

There are different ways to diagnose anemia, but the most common is a blood test known as a complete blood count (CBC).

This measures a number of blood components, including hemoglobin and hematocrit levels, or the ratio of the volume of red blood cells to the total volume of blood.

A CBC can give an indication of the person's overall health and whether they have any conditions, such as leukemia or kidney disease.

If the red blood cell, hemoglobin, and hematocrit levels are all below "normal," then anemia is likely.

However, it does not provide a definitive diagnosis. It is possible to be outside the normal range but still healthy.

Liver diseases

Liver Overview

The liver is the largest solid organ in the body. People may not know that the liver is also the largest gland in the body. The liver is actually two different types of gland. It is a secretory gland because it has a specialized structure that is designed to allow it to make and secrete bile into the bile ducts. It also is an endocrine gland since it makes and secretes chemicals directly into the blood that have effects on other organs in the body. Bile is a fluid that both aids in digestion and absorption of fats as well as carries waste products into the intestine.

What Is the Size of the Liver?

The liver weighs about three and a half pounds (1.6 kilograms). It measures on average, about 8 inches (20 cm) horizontally (across), and 6.5 inches (17 cm) vertically (down), and is 4.5 inches (12 cm) thick.

Liver Location and Anatomy

The liver is located just below the diaphragm (the muscular membrane separating the chest from the abdomen), primarily in the upper right part of the abdomen, mostly under the ribs. However, it also extends across the middle of the upper

abdomen and part way into the left upper abdomen. An irregularly shaped, dome-like solid structure, the liver consists of two main parts (a larger right lobe and a smaller left lobe) and two minor lobes. As you can see in the diagram below, the upper border of the right lobe is at the level of the top of the 5th rib (a little less than 1/2 inch below the nipple), and the upper border of the left lobe is just below the 5th rib (about 3/4 inch below the nipple). During inspiration (breathing in), the liver is pushed down by the diaphragm and the lower edge of the liver descends below the margin of the lowest rib (costal margin).

What Is Liver Function?

- The liver is the largest solid organ in the body, weighing on average about 3.5 pounds.
- The liver carries out a large number of critical functions, including manufacture of essential proteins, and metabolism of fats and carbohydrates.
- The liver also serves to eliminate harmful biochemical waste products and detoxify alcohol, certain drugs, and environmental toxins.
- The liver forms and secretes bile that contains bile acids to aid in the digestion and intestinal absorption of fats and the fat-soluble vitamins A, D, E, and K.
- Diseases that may affect the liver include hepatitis (inflammation of the liver), cirrhosis(scarring), fatty liver, and liver cancer (hepatocellular carcinoma).
- Symptoms of liver disease may include:
    - bleeding or easy bruising,
    - swelling,

- fatigue, and
- jaundice (yellow coloring to the skin and whites of the eyes).

What Are Common Liver Diseases?

The most common liver diseases are various types of:

- acute (sudden) hepatitis (inflammation),
- chronic (long duration) hepatitis,
- fatty liver disease,
- cirrhosis (scarring), and
- cancer.

Cancers that affect the liver are most commonly metastatic cancers that have spread via the bloodstream to the liver from other sites in the body. However, primary cancers (cancers that arise in the liver) can also occur. The most common type of primary liver cancers are known as hepatocellular carcinomas.

Common causes of liver disease include:

- viruses,
- drugs - prescription, over-the-counter (OTC), herbal supplements, vitamins, and dietary supplements (for example, acetaminophen [Tylenol and others],
- alcohol,
- metabolic problems,

- immune (defense) system, and
- genetic (hereditary) abnormalities.

But note that, contrary to a popular misconception, alcohol is only one of the many causes of liver disease. Moreover, sometimes the cause of the liver disease is not known.

What Are Liver Disease Symptoms and Signs?

Acute and chronic liver diseases can interfere with the functions of the liver and thereby cause symptoms. However, the liver has a hefty reserve capacity. In other words, it usually takes substantial damage to the liver before a disease interferes with the functions of the liver and causes symptoms. Examples of such symptoms are:

- Jaundice (yellow skin) that can occur when the liver is unable to properly metabolize or secrete the yellow pigment bilirubin in bile
- Bleeding or easy bruising that can occur when the liver is unable to make enough of the normal blood clotting proteins
- Swelling of the legs with fluid (edema) that can occur when the liver is unable to make enough albumin and the serum albumin gets too low
- Fatigue that is of unknown cause, but may be related to some impaired metabolic function of the liver

What Are Liver Function Tests?

Damage to the liver often gives rise to telltale abnormalities in certain blood tests (suggesting liver disease), the so-called liver blood tests (for example, ALT, AST, and alkaline phosphatase enzymes). The liver blood tests often are collectively

referred to as liver function tests. But, abnormalities in only some of them (i.e., elevated bilirubin, low albumin, and prolonged prothrombin time) actually reflect, at least in part, abnormal function of the liver. And, it turns out that abnormalities of the other liver blood tests may reflect the actual injury to the liver. For example, viral hepatitis can cause the ALT or AST enzymes in injured liver cells to spill into the blood stream and increase their level in the blood.

Sometimes, the pattern of liver blood test abnormalities provides a clue as to the type of liver disease. For example, an AST to ALT ratio greater than two (as long as both are less than nine times normal) suggests alcoholic hepatitis or cirrhosis of any type.

Other blood tests are more specific for the diagnosis of particular liver diseases. For example, there are antibody tests for most of the different types of viral hepatitis and immunological tests for primary biliary cirrhosis (antimitochondrial antibodies) or chronic autoimmune hepatitis (smooth muscle antibody). Additionally, there are special tests for hemochromatosis (iron-related tests), Wilson's disease (copper-related tests), and liver cancer (tumor markers).

Why does the doctor examine the liver?

The doctor examines the liver as part of the abdominal physical examination to try to gain helpful diagnostic information about a patient's liver condition. For example, the liver can be tender (painful to touch) with acute hepatitis or feel hard and irregular (bumpy) with cancer of the liver. Also, some conditions can cause the liver to enlarge (fatty liver or certain types of chronic hepatitis or cirrhosis), while others can make the liver smaller (advanced cirrhosis).

What Is a Liver Biopsy?

The most accurate way to diagnose the type of liver disease is by doing a liver biopsy, although a biopsy is not necessary in most cases. This procedure involves removing, with a thin hollow needle, a small piece of liver tissue for microscopic study. The tiny tissue sample is usually representative of the disease (pathology) in the rest of this large organ. Put another way, most liver disease involves the entire liver. When the disease is localized to only a small part of the liver, as for example, cancer usually is, the biopsy can be done with ultrasonic visual guidance to be certain that the small, involved area is biopsied.

What Is Liver Regeneration?

The liver has an extraordinary capacity to regenerate (reproduce itself). For example, when the liver is damaged, it will soon regenerate in an attempt to restore its functions. Cut out a part of the liver, and it likewise will grow back (regenerate) rapidly. In fact, when a person donates a part of her or his liver for transplantation, much of the part that is removed will soon grow back.

There's a famous story in Greek and Roman mythology that testifies to the liver's great capacity to regenerate. Witness Prometheus chained to a rock on a mountain. This confinement was his punishment because he had displeased the ruler Zeus (Jupiter, if you prefer Latin to Greek) by providing fire (and other benefits) to humankind. Picture a vulture pecking away at the liver of the helpless Prometheus. He survived, however, according to the legend, because his liver renewed itself as fast as the vulture devoured it.

Fatty Liver Disease

What Causes Fatty Liver Disease?

Fatty liver can be classified as alcohol and nonalcohol related. Alcohol is a direct toxin to the liver and can cause inflammation. Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic related steatohepatitis (NASH) are markedly different illnesses and there are many potential causes that are linked to fat accumulation in the liver.

Some of the causes of fatty liver include:

- Diet: Consumption of excess calories in the diet (the excess caloric intake overwhelms the liver's ability to metabolize fat in a normal fashion, which results in fat accumulation in the liver).
- Diseases: Fatty liver is also associated with type II diabetes, obesity, and high triglyceride levels in the blood, celiac disease, and Wilson's disease (abnormality of copper metabolism).
- Medical conditions: Rapid weight loss and malnutrition.
- Medications: Medications such as tamoxifen (Soltamox), amiodarone injection (Nestorone), amiodarone oral (Cordarone, Pacerone), and methotrexate (Rheumatrex Dose Pack, Trexall) are associated with NAFLD.

Kidney diseases

- Kidneys are as important to your health as your heart or your lungs. Kidneys remove waste products from your body, regulate water and produce

hormones. In this chapter we will briefly look at how the kidneys work. If you know what the kidneys do when they work properly, it will be easier to understand what can happen if your kidneys begin to fail.

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- How do kidneys work?
- Normally, people have two kidneys, one on each side of the spine under the lower ribs. They are reddish brown in colour and shaped like kidney beans. Each kidney is about the size of your clenched fist.
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- One of the main jobs of the kidneys is to remove wastes from the blood and return the cleaned blood back to the rest of the body. Every minute, about one litre of blood (one fifth of all the blood pumped by the heart) enters the kidneys through the renal arteries. After the blood is cleaned, it flows back toward the heart through the renal veins.
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- Inside each kidney there are more than one million tiny units called nephrons. Each nephron is made up of a very small filter called a glomerulus, which is attached to a tubule. Water and waste products are separated from the blood by the filters and then flow into the tubules. Much of this water is reabsorbed by the tubules and the wastes are concentrated into urine.
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- The urine is collected from the tubules in the funnel-like renal pelvis and then flows through tubes called the ureters into the bladder. Urine passes out of the body through a tube called the urethra. Together, the kidneys normally make one to two litres of urine every day depending on how much you drink.

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- Usually, the kidneys are able to provide more than twice as much kidney function as your body needs to work well. A normal kidney can greatly increase its workload: if you were born with one kidney or if one kidney is injured or donated, the remaining kidney can work harder to keep your body healthy.
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- Why are kidneys so important?
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- Your kidneys are important because they do three essential things:
- 1. Kidneys regulate water
- For your body to work properly, it must contain just the right amount of water. One of the important jobs of the kidneys is to remove excess water from the body or to keep water when the body needs more.
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- 2. Kidneys remove waste products and help to balance the body's minerals
- Many of the substances in the blood and other body fluids must be kept at the correct level for the body to function properly. For example, sodium (salt) and potassium are minerals that come from food. The body needs these minerals for good health, but they must be kept at certain levels. When the kidneys are working properly, extra minerals, such as sodium and potassium, leave your body in the urine. The kidneys also help to adjust the levels of other minerals, such as calcium and phosphate (which are important for bone strength, growth and other functions).
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- Your kidneys help remove waste products, such as urea and creatinine, from your body. Urea and other wastes are made when the body breaks down protein, such as meat. Creatinine is a waste product of the muscles. As kidney function decreases, the levels of urea and creatinine in the blood increase. The creatinine level in the blood is a very useful measure of kidney function. It is measured by a simple blood test.
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- 3. Kidneys produce hormones
- Normal kidneys also make important chemicals in your body called hormones. These hormones circulate in the bloodstream like “messengers” and regulate blood pressure, red blood cell production and the calcium balance in your body.
- What is chronic kidney disease (CKD)?
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- Chronic kidney disease (CKD) is the presence of kidney damage, or a decreased level of kidney function, for a period of three months or more. There are two key tests which are used to detect kidney damage and to assess how well your kidneys are functioning at removing toxins and waste products from your blood.
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- Blood test
- A blood test is used to measure your serum creatinine level which helps to indicate how well the kidneys are filtering the blood. Creatinine is a waste product made from muscle use and the breakdown of the protein you eat. As the blood creatinine rises, kidney function decreases. Decreased kidney function means that your kidneys are not able to remove the toxins and

waste products from your blood as well as someone with normal kidney function.

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- The estimate (or percentage) of kidney function is called the glomerular filtration rate (GFR). Sometimes the GFR is also referred to as the estimated glomerular filtration rate (eGFR). Glomeruli are tiny blood vessels in the kidney that help to filter waste. The GFR is a way of measuring how well the kidneys are working by determining the rate at which the glomeruli are filtering waste products from your blood. The eGFR is the most common way to measure kidney function at kidney clinics.
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- Urinalysis
- Simple laboratory tests such as urinalysis (a urine dipstick), which looks for blood and a protein called albumin in the urine, are also useful in detecting kidney damage at an early stage and determining your risk of losing more kidney function. The filters of the kidney do not normally allow protein in the urine so if protein (albumin) is detected, it is a sign that the filters of the kidney are being damaged. The more albumin that you have in your urine, the greater the risk of losing kidney function over time.
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- Other blood tests, X-rays, kidney ultrasound or a kidney biopsy may also be needed to diagnose the specific type of kidney disease and to determine the appropriate treatment.
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- Understanding CKD
- Kidney disease can range from mild to severe and in some cases, lead to kidney failure. Kidney failure is sometimes referred to as end-stage kidney

disease (ESKD). Kidney disease often starts slowly and develops without symptoms over a number of years, so CKD may not be detected until it has progressed to the point where your kidney function is quite low. Fortunately, most people do not progress to end-stage kidney disease, especially if they are diagnosed early and are able to take steps to preserve their remaining kidney function.

- What causes chronic kidney disease?
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- There are many different kidney diseases and disorders. Some kidney diseases are present at birth and others develop as we grow older. Often, kidney disease is associated with other medical conditions such as diabetes, high blood pressure and heart disease.
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- Most diseases of the kidney attack the filtering units in the kidney, damaging their ability to remove wastes and excess fluids. There is no cure, but it may be possible to prevent CKD or slow it down. This is especially true in people with diabetes and/or high blood pressure, the leading causes of kidney failure.
- Diabetes
- Diabetes is a disease that is caused by a lack of insulin in the body or the body's inability to properly use normal amounts of insulin. Insulin is a hormone that is a very important chemical messenger that regulates the level of glucose (sugar) in the blood. The body must have insulin to function. Therefore, people with diabetes may take medications that can either make

the pancreas produce more insulin, or help the body properly use the insulin that is being produced, or they may take insulin by injection or pump.

- Even with the use of insulin or other medications, people who have had diabetes for some time often suffer from damage to the small blood vessels such as the ones in the filters of the kidney.
- High blood pressure
- High blood pressure (also called hypertension) may cause chronic kidney disease. The reverse is also true: chronic kidney disease frequently causes high blood pressure.
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- High blood pressure damages the small blood vessels that deliver blood to the kidneys' filters. Long-standing, untreated high blood pressure, or very severe high blood pressure, will reduce the flow of blood into the filters and may lead to CKD.
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- The kidneys also produce a hormone that helps in the control of blood pressure. When the kidneys are damaged or fail, this hormone may increase and cause high blood pressure. In turn, this may lead to further kidney damage. It is important to control high blood pressure to try to prevent long-term kidney damage.
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- Chronic kidney inflammation (Glomerulonephritis)
- Chronic kidney inflammation (glomerulonephritis or nephritis) is a condition in which the glomeruli are damaged. Glomeruli are the tiny filters that help clean the blood. There are many types of glomerulonephritis: some types recover without medical treatment, while others can be treated with

medications. Sometimes, some types of glomerulonephritis cannot be successfully treated despite using many different medications. If this happens, dialysis may be needed if the kidney filters become more scarred and are not able to do their job properly.

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- There are many types of glomerulonephritis associated with different conditions such as systemic lupus erythematosus (lupus), vasculitis (inflammation of blood vessels), Hepatitis B or Hepatitis C just to name a few.
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- Polycystic kidney disease
- Polycystic kidney disease (PKD) is the most common inherited disease of the kidneys. It will be passed to 50% of the children of an affected parent. Polycystic means “many cysts”. Polycystic kidneys become very large and have a bumpy surface because of fluid-filled cysts. Pressure from the cysts as they expand can slowly damage the kidneys, which may lead to kidney failure. People who are found to have the disease very early will be monitored and have their blood pressure and general health watched closely.
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- Urinary tract obstruction
- The kidneys may be damaged if there is an obstruction (or blockage) of urine from the kidneys. Obstructions may occur in the ureters or at the outlet of the bladder. When the blockage occurs in the fetus during pregnancy, the kidneys may not develop properly and this could lead to CKD in children. In adults, causes of urinary tract obstruction can be an enlarged prostate gland, kidney stones or tumours.
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- Kidney stones
- A kidney stone can develop when certain chemicals in the urine form crystals that stick together. The crystals may grow into a stone ranging in size from that of a grain of sand to a golf ball. While small stones may pass through the urinary system without problems, larger stones may block the flow of urine or irritate the lining of the urinary tract. Multiple kidney stones can cause scarring of the kidneys and result in reduced kidney function.
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- Drug- and medication-induced kidney problems
- Illegal drugs
- The use of illegal drugs, such as heroin and cocaine, can cause kidney damage.
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- Over-the-counter medications (non-prescription)
- These medications, including anti-inflammatory medications like ibuprofen, may damage the kidneys if used in large doses over a long period of time.
-
- Prescription medications
- At times, even prescription medications may cause kidney dysfunction. Sometimes the damage can be repaired but sometimes it cannot. However, many prescription medications can be safe for people with kidney disease as long as your doctor makes changes to the dosage (amount). You should always ask your doctor or pharmacist about the possible side effects of prescription medications for people with kidney disease.

Vitamins

Vitamins: What are they and what do they do?

Vitamins are organic compounds that are needed in small quantities to sustain life. Most vitamins need to come from food.

This is because the human body either does not produce enough of them, or it does not produce any at all.

Each organism has different vitamin requirements. For example, humans need to consume vitamin C, or ascorbic acid, but dogs do not. Dogs can produce, or synthesize, enough vitamin C for their own needs, but humans cannot.

People need to get most of their vitamin D from exposure to sunlight, because it is not available in large enough quantities in food. However, the human body can synthesize it when exposed to sunlight.

Different vitamins have different roles, and they are needed in different quantities.

This article explains what vitamins are, what they do, and which foods provide each type. Follow the links for more information about each type of vitamin.

Fast facts on vitamins

Here are some key points about vitamins. More detail and supporting information is in the main article.

- There are 13 known vitamins.
- Vitamins are either water-soluble or fat-soluble.
- Fat-soluble vitamins are easier for the body to store than water-soluble.
- Vitamins always contain carbon, so they are described as "organic."

- Food is the best source of vitamins, but some people may be advised by a physician to use supplements.

What are vitamins?

Fruits and vegetables are good sources of a range of vitamins.

A vitamin is one of a group of organic substances that is present in minute amounts in natural foodstuffs. Vitamins are essential to normal metabolism. If we do not take enough of any kind of vitamin, certain medical conditions can result.

A vitamin is both:

- an organic compound, which means it contains carbon
- an essential nutrient that body cannot produce enough of and which it needs to get from food

There are currently 13 recognized vitamins.

Fat-soluble and water-soluble vitamins

Vitamins are either fat-soluble or water-soluble.

Fat-soluble vitamins

Fat-soluble vitamins are stored in the fatty tissues of the body and the liver. Vitamins A, D, E, and K are fat-soluble. These are easier to store than water-soluble vitamins, and they can stay in the body as reserves for days, and sometimes months.

Fat-soluble vitamins are absorbed through the intestinal tract with the help of fats, or lipids.

Water-soluble vitamins

Water-soluble vitamins do not stay in the body for long. The body cannot store them, and they are soon excreted in urine. Because of this, water-soluble vitamins need to be replaced more often than fat-soluble ones.

Vitamin C and all the B vitamins are water soluble.

Types

Here are the different types of vitamins.

Vitamin A

Chemical names: Retinol, retinal, and four carotenoids, including beta carotene.

- It is fat soluble.
- **Deficiency** may cause night-blindness and keratomalacia, an eye disorder that results in a dry cornea.
- **Good sources** include: Liver, cod liver oil, carrots, broccoli, sweet potato, butter, kale, spinach, pumpkin, collard greens, some cheeses, egg, apricot, cantaloupe melon, and milk.

Vitamin B

Chemical name: thiamine.

- It is water soluble.
- **Deficiency** may cause beriberi and Wernicke-Korsakoff syndrome.
- **Good sources** include: yeast, pork, cereal grains, sunflower seeds, brown rice, whole-grain rye, asparagus, kale, cauliflower, potatoes, oranges, liver, and eggs.

Vitamin B2

Chemical name: Riboflavin

- It is water soluble
- **Deficiency** may cause ariboflavinosis
- **Good sources** include: asparagus, bananas, persimmons, okra, chard, cottage cheese, milk, yogurt, meat, eggs, fish, and green beans

Vitamin B3

Chemical names: Niacin, niacinamide

- It is water soluble.
- **Deficiency** may cause pellagra, with symptoms of diarrhea, dermatitis, and mental disturbance.
- **Good sources** include: liver, heart, kidney, chicken, beef, fish (tuna, salmon), milk, eggs, avocados, dates, tomatoes, leafy vegetables, broccoli, carrots, sweet potatoes, asparagus, nuts, whole-grains, legumes, mushrooms, and brewer's yeast.

Vitamin B5

Chemical name: Pantothenic acid

- It is water soluble.
- **Deficiency** may cause paresthesia, or "pins and needles."
- **Good sources** include: meats, whole-grains (milling may remove it), broccoli, avocados, royal jelly, and fish ovaries.

Vitamin B6

Chemical names: Pyridoxine, pyridoxamine, pyridoxal

- It is water soluble.
- **Deficiency** may cause anemia, peripheral neuropathy, or damage to parts of the nervous system other than the brain and spinal cord.
- **Good sources** include: meats, bananas, whole-grains, vegetables, and nuts. When milk is dried, it loses about half of its B6. Freezing and canning can also reduce content.

Vitamin B7

Chemical name: Biotin

- it is water soluble.

- **Deficiency** may cause dermatitis or enteritis, or inflammation of the intestine.
- **Good sources** include: egg yolk, liver, some vegetables.

Vitamin B9

Chemical names: Folic acid, folinic acid

- It is water soluble.
- **Deficiency** during pregnancy is linked to birth defects. Pregnant women are encouraged to supplement folic acid for the entire year before becoming pregnant.
- **Good sources** include: leafy vegetables, legumes, liver, baker's yeast, some fortified grain products, and sunflower seeds. Several fruits have moderate amounts, as does beer.

Vitamin B12

Chemical names: Cyanocobalamin, hydroxocobalamin, methylcobalamin

- It is water soluble.
- **Deficiency** may cause megaloblastic anemia, a condition where bone marrow produces unusually large, abnormal, immature red blood cells.
- **Good sources** include: fish, shellfish, meat, poultry, eggs, milk and dairy products, some fortified cereals and soy products, as well as fortified nutritional yeast.

  Vegans are advised to take B12 supplements.

Vitamin C

Chemical name: Ascorbic acid

- It is water soluble.
- **Deficiency** may cause megaloblastic anemia.
- **Good sources** include: fruit and vegetables. The Kakadu plum and the camu camu fruit have the highest vitamin C contents of all foods. Liver also has high levels. Cooking destroys vitamin C.

Vitamin D

Chemical names: Ergocalciferol, cholecalciferol.

- It is fat soluble.
- **Deficiency** may cause rickets and osteomalacia, or softening of the bones.
- **Good sources**: Exposure to ultraviolet B (UVB) through sunlight or other sources causes vitamin D to be produced in the skin. Also found in fatty fish, eggs, beef liver, and mushrooms.

Vitamin E

Chemical names: Tocopherols, tocotrienols

- It is fat soluble.

- **Deficiency** is uncommon, but it may cause hemolytic anemia in newborns. This is a condition where blood cells are destroyed and removed from the blood too early.
- **Good sources** include: Kiwi fruit, almonds, avocado, eggs, milk, nuts, leafy green vegetables, unheated vegetable oils, wheat germ, and whole-grains.

Vitamin K

Chemical names: Phylloquinone, menaquinones

- It is fat soluble.
- **Deficiency** may cause bleeding diathesis, an unusual susceptibility to bleeding.
- **Good sources** include: leafy green vegetables, avocado, kiwi fruit. Parsley contains a lot of vitamin K.

Thyroid hormones

Through the hormones it produces, the thyroid gland influences almost all of the metabolic processes in your body. Thyroid disorders can range from a small, harmless goiter (enlarged gland) that needs no treatment to life-threatening cancer. The most common thyroid problems involve abnormal production of thyroid hormones. Too much thyroid hormone results in a condition known as hyperthyroidism. Insufficient hormone production leads to hypothyroidism.

Although the effects can be unpleasant or uncomfortable, most thyroid problems can be managed well if properly diagnosed and treated.

The thyroid gland is a small, butterfly-shaped organ in your throat, and it is very important to your health and well-being. The thyroid is part of the endocrine system, which is essentially a collection of glands. Glands produce hormones that regulate mood and various functions in the body.

"Thyroid hormones impact a host of vital body functions, including heart rate, skin maintenance, growth, temperature regulation, fertility and digestion," said Dr. Jerome M. Hershman, a professor of medicine at the David Geffen School of Medicine at UCLA and author of the thyroid sections of the Merck Manual.

Size

The thyroid gland is 2 inches (5 centimeters) wide and it weighs between 20 and 60 grams (0.7 to 2.1 ounces), according to the U.S. National Library of Medicine. The gland stretches across the front of the neck, below the voice box. Like a

butterfly, it has two wings called lobes that stretch around the windpipe. The wings are connected by a small piece called the isthmus.

Function

The thyroid gland, in particular, controls just about every cell in the human body. It secretes hormones calcitonin, T4 (thyroxine, or tetraiodothyronine) and T3 (triiodothyronine) into the bloodstream. The hormones control the rate at which cells and organs turn nutrients into energy and the amount of oxygen cells use.

"In this way, the thyroid gland is the body's master metabolic control center," said Cindy Samet, a chemistry professor at Dickinson College in Carlisle, Pennsylvania. "Brain, heart and kidney function, as well as body temperature, growth and muscle strength — and much more — are at the mercy of thyroid function."

The thyroid also regulates the brain and nerve function and development, plus the function of the skin, hair, eyes, heart and intestines.

The thyroid works in conjunction with the pituitary gland. The pituitary gland regulates how much hormones the thyroid releases.

The thyroid gland produces a large amount of T4, but that hormone is not very active. T4 is converted to T3 via an enzyme that removes one of its iodine atoms. "Although T3 is much more potent than T4, there is much evidence to support that people with hypothyroidism feel much better when they receive a combination treatment that includes a small amount of T3 with the commonly prescribed T4," Samet said.

Diseases & conditions

Thyroid conditions affect an estimated 20 million Americans, and as many as 60 percent of people with a thyroid disease don't know they have a problem, according to the American Thyroid Association.

"Women are particularly at risk for a thyroid issue," Hershman said. "One in eight women will develop a thyroid disorder during the course of their lives — that's five to eight times the rate in men."

One of these conditions is called Graves' disease, which was discovered by the Irish doctor Robert James Graves in 1835. Graves' disease is an autoimmune disorder. The immune system attacks the thyroid gland and makes it become overactive. An overactive thyroid is a condition called hyperthyroidism. A bulge on the neck, called a goiter is a common symptom. The patient may also experience an increased heart rate, according to the National Library of Medicine (NLM).

Hypothyroidism is the opposite of Graves' disease. It occurs when the thyroid gland does not produce enough hormones. This can cause body functions to slow down or stop completely. Screening newborns for hypothyroidism is mandatory in the United States, Hershman said.

Cancer is another disease that can affect the thyroid. A 2017 study published in in the Journal of the American Medical Association (JAMA) has found that between 1975 and 2013 the number of thyroid cancer cases diagnosed each year has more than tripled. Cases of advanced forms of the disease rose by about 3 percent each year while deaths rose by about 1 percent each year. A lump or swelling on your thyroid gland is called a nodule. Nodules can be harmless, but some can cause a production of too much hormone or be cancerous, according to the Endocrine Society.

"Up to 70 percent of middle-age females and 40 to 50 percent of middle-age males have thyroid nodules, said Dr. Melanie Goldfarb, an endocrine surgeon and director of the Endocrine Tumor Program at Providence Saint John's Health Center in Santa Monica, California, and an assistant professor of surgery at the John Wayne Cancer Institute in Santa Monica. "You can also be born with an extra piece anywhere as high up as the base of your tongue."

In some medical cases, such as cancer, the thyroid is removed. Humans can live without their thyroid if a hormone pill is taken daily.

What Causes Thyroid Problems?

All types of hyperthyroidism are due to an overproduction of thyroid hormones, but the condition can occur in several ways:

- Graves' disease: The production of too much thyroid hormone.
- Toxic adenomas: Nodules develop in the thyroid gland and begin to secrete thyroid hormones, upsetting the body's chemical balance; some goiters may contain several of these nodules.
- Subacute thyroiditis: Inflammation of the thyroid that causes the gland to "leak" excess hormones, resulting in temporary hyperthyroidism that generally lasts a few weeks but may persist for months.
- Pituitary gland malfunctions or cancerous growths in the thyroid gland: Although rare, hyperthyroidism can also develop from these causes.

Hypothyroidism , by contrast, stems from an underproduction of thyroid hormones. Since your body's energy production requires certain amounts of thyroid hormones,

a drop in hormone production leads to lower energy levels. Causes of hypothyroidism include:

- Hashimoto's thyroiditis : In this autoimmune disorder, the body attacks thyroid tissue. The tissue eventually dies and stops producing hormones.
- Removal of the thyroid gland: The thyroid may have been surgically removed or chemically destroyed.
- Exposure to excessive amounts of iodide: Cold and sinus medicines, the heart medicine amiodarone, or certain contrast dyes given before some X-rays may expose you to too much iodine.You may be at greater risk for developing hypothyroidism if you have had thyroid problems in the past.
- : This drug has also been implicated as a cause of hypothyroidism.

Untreated for long periods of time, hypothyroidism can bring on a myxedema coma, a rare but potentially fatal condition that requires immediate hormone treatment.

Growth Hormone Deficiency

NORD gratefully acknowledges Joe Head, NORD Intern and Richard A. Levy, MD, Director of Pediatric Endocrinology Section, Rush University, for their assistance in the preparation of this report.

Subdivisions of Growth Hormone Deficiency

- acquired GHD
- congenital GHD
- idiopathic GHD
- TEST

General Discussion

Growth hormone deficiency (GHD) is a rare disorder characterized by the inadequate secretion of growth hormone (GH) from the anterior pituitary gland, a small gland located at the base of the brain that is responsible for the production of several hormones. GHD can be present from birth (congenital), resulting from genetic mutations or from structural defects in the brain. It can also be acquired later in life as a result of trauma, infection, radiation therapy, or tumor growth within the brain. A third category has no known or diagnosable cause (idiopathic). Childhood-onset GHD may be all three: congenital, acquired, or idiopathic. It results in growth retardation, short stature, and maturation delays reflected by the delay of lengthening of the bones of the extremities that is inappropriate to the chronological age of the child. Adult-onset GHD is most often is acquired from a pituitary tumor or trauma to the brain but may also be idiopathic. It is characterized by a number of variable symptoms including reduced energy levels, altered body composition, osteoporosis (reduced bone mineral density), reduced muscle strength, lipid abnormalities such as increased LDL cholesterol, insulin resistance, and impaired cardiac function. Treatment for GHD requires daily injections of recombinant human growth hormone (rHGH). Patients with GHD that have no known cause are diagnosed as having idiopathic GHD. Genetic tests may reveal a congenital anomaly, but are often considered unnecessary after confirmation of

GHD since they will have no effect on treatment. However, it is recommended that children be retested for GHD when they transition from pediatric to adult care since GH levels may normalize upon reaching adulthood. The level of GH considered normal for an adult is much lower than that for a child, especially one undergoing the pubertal growth spurt.

Signs & Symptoms

A child with GHD is usually of normal size at birth. A few children may become hypoglycemic (low blood sugar) during the newborn period. Males may have a small penis (micropenis). Later, children with GHD may present with delayed rates of development of facial bones, slow tooth eruption, delayed lengthening of long bones, fine hair, and poor nail growth. They may also demonstrate truncal obesity, a high pitched voice, and delayed closure of the sutures of the skull, causing delayed closure of the fontanelles.

Growth increments are the most important criteria in the diagnosis of GHD in children. Normal levels of growth usually follow a pattern, and if growth during a recorded six to twelve month period is within those levels it is unlikely that a growth disorder exists.

Growth in the first six months of life is usually 16 to 17 cm and in the second six months approximately 8 cm. During the second year 10 cm or more is normal. Growth in the third year should equal 8 cm or more and 7 cm in the fourth year. In the years between four and ten, an average of 5 or 6 cm is normal. A 10% decrease in these growth rates can result in an insufficient growth velocity, and thus a noticeable decline on the growth chart. When that is recognized, even before the child has fallen to a significantly low percentile (1.2% = -2 SD), he/she should then be tested for abnormally low levels of growth hormone.

An individual who acquires GHD later in life presents more generalized symptoms. They may notice a relative increase in fat mass, especially abdominal and visceral, along with a decrease in muscle mass. Decreased energy levels, anxiety, and/or depression are also common. Lipid levels are also affected, resulting in an increase in LDL-cholesterol and triglyceride levels.

Causes

Congenital GHD results from genetic error, and may be associated with brain structure defects or with midline facial defects such as a cleft palate or single central incisor.

Several genetic defects have been identified:

Growth hormone deficiency IA is autosomal recessive and is characterized by growth retardation in utero. Affected children are small in relation to their siblings. The infant usually has a normal response to administration of human growth hormone (hGH) at first, but then develops antibodies to the hormone and grows into a very short adult.

Growth Hormone Deficiency IB is also autosomal recessive and is similar to IA. However, there is some growth hormone (GH) present in the child at birth and usually the child continues to respond to hGH treatments.

Growth Hormone Deficiency IIB and III are similar to IB, but IIB is autosomal dominant and III is X-linked.

Classic genetic diseases are the product of the interaction of two genes, one received from the father and one from the mother.

Dominant genetic disorders occur when only a single copy of an abnormal gene is necessary to cause a particular disease. The abnormal gene can be inherited from

either parent or can be the result of a new mutation (gene change) in the affected individual. The risk of passing the abnormal gene from affected parent to offspring is 50% for each pregnancy. The risk is the same for males and females.

Recessive genetic disorders occur when an individual inherits two copies of an abnormal gene for the same trait, one from each parent. If an individual receives one normal gene and one gene for the disease, the person will be a carrier for the disease but usually will not show symptoms. The risk for two carrier parents to both pass the defective gene and have an affected child is 25% with each pregnancy. The risk to have a child who is a carrier like the parents is 50% with each pregnancy.

The chance for a child to receive normal genes from both parents and be genetically normal for that particular trait is 25%. The risk is the same for males and females.

Parents who are close relatives (consanguineous) have a higher chance than unrelated parents to both carry the same abnormal gene, which increases the risk of having children with a recessive genetic disorder.

X-linked genetic disorders are conditions caused by an abnormal gene on the X chromosome and manifest mostly in males. Females that have a defective gene present on one of their X chromosomes are carriers for that disorder. Carrier females usually do not display symptoms because females have two X chromosomes and only one carries the defective gene. Males have one X chromosome that is inherited from their mother and if a male inherits an X chromosome that contains a defective gene he will develop the disease.

Female carriers of an X-linked disorder have a 25% chance with each pregnancy to have a carrier daughter like themselves, a 25% chance to have a non-carrier

daughter, a 25% chance to have a son affected with the disease and a 25% chance to have an unaffected son.

If a male with X-linked disorders is able to reproduce, he will pass the defective gene to all of his daughters who will be carriers. A male cannot pass an X-linked gene to his sons because males always pass their Y chromosome instead of their X chromosome to male offspring.

Acquired GHD can occur as a result of many different causes including brain trauma (perinatal or postnatal), central nervous system infection, tumors of the hypothalamus or pituitary (pituitary adenoma, craniopharyngioma, Rathke's cleft cyst, glioma, germinoma, metastases), radiation therapy, infiltrative diseases (Langerhans cell histiocytosis, sarcoidosis, tuberculosis), or, if without another diagnosis, it is considered idiopathic.

Affected Populations

Prevalence and incidence data vary widely due to the lack of standard diagnostic criteria. While congenital GHD and most cases of idiopathic GHD are thought to be present from birth, diagnosis is often delayed until the patient's short stature is noticed in relation to their peers. Diagnosis most often occurs during two age ranges. The first is around 5 years of age when children begin school. The second is around 10-13 years old in girls and 12-16 years in boys associated with the delay in the pubertal growth spurt.

There is no apparent racial difference in the incidence of GHD. However, the National Cooperative Growth Study (NCGS), Genentech's now closed large North American database, revealed that 85% of patients receiving GH treatment for idiopathic GHD were white, 6% were black, and 2% were Asian. Similar distributions were seen with patients with other forms of short stature. Patients

from other racial groups tend to be shorter than their white counterparts at the time of diagnosis.

Growth hormone deficiency affects males and females equally except for GHD III which affects only males. However, given the greater concern for boys with short stature in most societies, diagnosis tends to favor males over females. 73% of patients with idiopathic GHD in the NCGS were male. Additionally, patients with GHD from organic causes such as tumors and radiation, in which no gender bias should be present, were still 62% male.

Related Disorders

Symptoms of the following disorders can be similar to those of Growth Hormone Deficiency. Comparisons may be useful for a differential diagnosis:

Small for gestational age (SGA) generally describes any infant whose birth weight and/or length was less than the 3rd percentile (adjusted for prematurity). Children with SGA are shorter and thinner than his or her peers. Typical characteristics for these children include low birth weight, short birth length, inadequate catch-up growth in first two years, persistently low weight-for-height proportion, and lack of muscle mass and/or poor muscle tone. The FDA has approved growth hormone therapy as long-term treatment of children who were born SGA and who have not achieved catch-up growth by two years of age.

Short stature homeobox-containing gene (*SHOX*) deficiency refers to short stature caused by a mutation in one copy of the *SHOX* gene and is associated with some cases of Turner syndrome, Leri-Weil syndrome and dyschondrosteosis. Turner syndrome is only seen in females, whereas Leri-Weil syndrome and dychondrosteosis is seen in males and females. Growth hormone therapy is FDA-approved for SHOX deficiency.

Idiopathic short stature (ISS) is defined as having a height significantly shorter than the normal population (-2.25 SD, that is shorter than 1.2% of the population of the same age and gender), a poor adult height prediction (generally defined by having less than the calculated mid-parental height or, as a rough guide, less than 5'4″ for males and less than 4'11" for females), and no detectable cause for short stature. Growth hormone therapy is FDA-approved to treat ISS.

Turner syndrome is a chromosomal disorder affecting 1 of 2,500 females and is characterized by short stature and the lack of sexual development at puberty. Other physical features may include webbing of the neck, heart defects, kidney abnormalities, and various other anomalies. Among affected females, there is also a heightened incidence of autoimmune disease such as Hashimotos's hypothyroidism and celiac syndrome. There appears to be great variability in the degree to which girls with Turner syndrome are affected by any of its manifestations since classical Turner, completely lacking one X chromosome, comprises only 60% of the total. The other 40% have a wide variety of genetic abnormalities including deletion of segments of the long or short arm of the X (or Y) and mosaicism with different populations of cells. (For more information on this disorder, choose "Turner" as your search term in the Rare Disease Database.)

Noonan syndrome is a genetic disorder that is typically evident at birth (congenital) and is thought to affect approximately one in 1,000 to one in 2,500 people. The disorder is characterized by a wide spectrum of symptoms and physical features that vary greatly in range and severity. In many affected individuals, associated abnormalities include a distinctive facial appearance; a broad or webbed neck; a low posterior hairline; a typical chest deformity and short stature. Characteristic abnormalities of the head and facial (craniofacial) area may include widely set eyes (ocular hypertelorism); skin folds that may cover the eyes'

inner corners (epicanthal folds); drooping of the upper eyelids (ptosis); a small jaw (micrognathia); a depressed nasal root; a short nose with broad base; and low-set, posteriorly rotated ears (pinnae). Distinctive skeletal malformations are also typically present, such as abnormalities of the breastbone (sternum), curvature of the spine (kyphosis and/or scoliosis), and outward deviation of the elbows (cubitus valgus). Many infants with Noonan syndrome also have heart (cardiac) defects, such as obstruction of proper blood flow from the lower right chamber of the heart to the lungs (pulmonary valvular stenosis). Additional abnormalities may include malformations of certain blood and lymph vessels, blood clotting and platelet deficiencies, mild intellectual disability, failure of the testes to descend into the scrotum (cryptorchidism) by the first year of life in affected males, and/or other symptoms and findings. Noonan syndrome is an autosomal dominant genetic disorder which may be caused by abnormalities (mutations) in a number of genes, four of which are *PTPN11*, *KRAS*, *SOS1* and *RAF1*. (For more information on this disorder, choose "Noonan" as your search term in the Rare Disease Database.)

Prader-Willi syndrome (PWS) is a genetic disorder characterized by low muscle tone, short stature, incomplete sexual development, and a chronic feeling of hunger that, coupled with a metabolism that utilizes fewer calories than normal, can lead to excessive eating and life-threatening obesity. The food compulsion makes constant supervision and food restriction necessary. Average IQ is 70, but even children with normal IQs almost all have learning issues. Social and motor deficits also exist. At birth the infant typically has low birth weight for gestation, hypotonia (weak muscles) with difficulty sucking which can lead to a diagnosis of failure to thrive. The second stage ("thriving too well"), has a typical onset between the ages of two and five, but can be later. The hyperphagia (extreme unsatisfied drive to consume food) lasts throughout the lifetime. Younger children with PWS have

sweet and loving personalities, but this phase is also characterized by increased appetite, weight control issues, and motor development delays. As the child becomes older, there are more behavioral problems and medical issues. (For more information on this disorder, choose “Prader-Willi” as your search term in the Rare Disease Database.)

Primary growth hormone insensitivity (GHI), also known as Laron syndrome, is a group of extremely rare genetic disorders in which the body is unable to use the growth hormone that it produces. GHI can be caused by mutations in the growth hormone receptor gene or mutations in genes involved in the signaling pathway within the cell after growth hormone binds to its receptor, preventing production of insulin-like growth factor (IGF-1), the intermediary hormone responsible for the growth effects of growth hormone. Children with GHI who are treated with IGF-1 before puberty have improved growth, but, unlike children with growth hormone deficiency given growth hormone treatment, they do not have normal growth restored.

GHI is characterized by normal or high levels of circulating growth hormone, delayed bone age and onset of puberty, prominent forehead, low blood sugar and obesity in adulthood. Except for an extremely rare form of GHI, where the gene for IGF-I is defective, brain development is normal but some may have mild intellectual impairment. (For more information on this disorder, choose “primary growth hormone insensitivity” as your search term in the Rare Disease Database.)

Diagnosis

Testing is very important in determining whether the child with growth retardation does indeed have growth hormone deficiency. Various agents may be used including insulin, arginine, clonidine and l-dopa. These tests are meant to stimulate

the pituitary to secrete GH allowing for the testing of blood samples for the levels of GH at timed intervals.

Physicians often test for other hormone deficiencies that may be the underlying cause of short stature. FreeT4, TSH, cortisol, celiac antibodies, etc. are measured to rule out underlying organic causes of short stature.

IGF-1, a protein produced primarily by the liver but present in all tissues in response to GH stimulation, can be measured to screen for GHD and later to titrate GH therapy.