CONDITION

Primary immunodeficiency

Primary immunodeficiency is a group of genetic conditions in which part of the immune system does not work properly.

WHAT IT IS
Group of genetic conditions causing part of immunity to malfunction

BODY SYSTEM
Immune system and organs affected by infection

MAIN SYMPTOMS
Repeated infections, severe infections, poor growth, chronic inflammation

WHAT CAUSES IT
Inherited or new gene changes affecting immunity

HOW IT IS DIAGNOSED
Blood immune tests and sometimes genetic testing

MAIN TREATMENT
Infection control, immunoglobulin, targeted medicines, or stem cell transplant

CAN IT BE CURED?
Sometimes - transplant or gene therapy

IS IT AN EMERGENCY?
Sometimes - severe infection or breathing difficulty

LONG-TERM OUTLOOK
Often manageable, though severe types can shorten life

Overview

Primary immunodeficiency is the older, widely used name for a large group of conditions now also called inborn errors of immunity . In these conditions, one or more parts of the immune system are missing or do not work as expected.

The immune system normally fights infections and helps control inflammation. Depending on which part is affected, primary immunodeficiency may cause repeated infections, unusually severe infections, autoimmune problems, allergies, or ongoing inflammation. Autoimmune problems happen when the immune system mistakenly attacks the body's own tissues.

Some forms are mild and are not recognized until adulthood. Others cause serious illness in infancy or childhood. Primary immunodeficiency is different from secondary immunodeficiency , which develops because of another issue such as certain medicines,

cancer treatments, HIV, or severe malnutrition.

Recognizing the condition matters because treatment can reduce infections and help prevent lasting damage to the lungs, digestive system, and other organs.

Symptoms

Symptoms differ greatly between types. Having frequent common infections does not by itself mean that you have primary immunodeficiency. Clinicians look at the type, severity, duration, and pattern of illness.

Possible signs include:

The pattern can offer clues. For example, some antibody problems mainly cause bacterial sinus and chest infections. Conditions affecting T cells, which coordinate immune responses, may cause severe viral, fungal, and other unusual infections.

Symptoms may be present from birth, but they do not always appear early. A person with a milder immune defect may remain well until later childhood or adulthood.

- Repeated ear, sinus, chest, skin, or digestive infections
- Infections that are severe, last longer than expected, or return quickly
- Infection with an organism that rarely causes illness in healthy people
- Poor growth or difficulty gaining weight in a child
- Persistent mouth thrush or fungal skin infections
- Deep skin or organ abscesses, which are pockets of infection
- Long-lasting diarrhoea
- Enlarged lymph nodes or spleen
- Unexplained fevers, joint swelling, rashes, or bowel inflammation
- Autoimmune conditions, low blood cell counts, or severe allergies

Causes and risk factors

Primary immunodeficiencies usually result from a gene change that affects how the immune system develops or works. A change may be inherited from one or both parents. It may also arise for the first time in the affected person.

The way a condition is inherited differs by type. Some affect people of any sex equally. Certain

X-linked conditions are more likely to cause symptoms in boys and men because the altered gene is on the X chromosome.

A family history of immune problems, unexplained early deaths, or repeated severe infections can increase the chance of an inherited condition. However, many affected people have no known family history. A new gene change, a milder condition in a relative, or an unrecognized diagnosis can explain this.

Primary immunodeficiency is not caused by poor hygiene, stress, or something you did. It is not contagious.

Diagnosis

Diagnosis usually starts with a detailed history. A clinician may ask about the number and type of infections, how they responded to treatment, autoimmune symptoms, growth, medicines, and family history. Medical records and laboratory results from earlier infections can be useful.

Initial blood tests may include:

More specialized tests can count different types of lymphocytes, including B cells and T cells. Laboratory testing may also examine how immune cells respond to germs or chemical signals.

Genetic testing can confirm many types and may help guide treatment or family testing. A negative genetic test does not always rule out primary immunodeficiency because not every responsible gene change is currently known.

Results can be affected by age, a recent infection, medicines, or previous treatment. Diagnosis may therefore require repeat testing and assessment by a clinical immunology team. Clinicians also check for secondary causes of reduced immunity.

In some countries, newborn screening uses a heel-prick blood sample to look for severe combined immunodeficiency, or SCID. This is a serious condition in which key immune cells are absent or do not function properly.

- A complete blood count to measure different immune cells
- Immunoglobulin levels, which measure infection-fighting antibodies
- Tests of antibodies produced after vaccination
- Complement tests, which assess a group of proteins that help destroy microbes

Treatment and management

Treatment is based on the exact immune problem, its severity, and the infections or inflammation it causes. Not everyone needs every treatment.

Infections may require prompt testing and antimicrobial medicines. These include antibiotics like amoxicillin or doxycycline for bacteria, antivirals like acyclovir or oseltamivir for viruses, and antifungals like fluconazole or terbinafine for fungal infections. Some people take preventive antimicrobial treatment when their risk of repeated or serious infection is high.

Immunoglobulin replacement provides antibodies collected from screened donated plasma. It can be given through a vein or under the skin. It is used for certain antibody deficiencies, but it does not correct every type of immune problem. Treatment is often long term when the body cannot make enough effective antibodies.

Ongoing lung care may include breathing tests, chest imaging, physiotherapy to clear mucus, and treatment for asthma-like symptoms. Digestive, skin, autoimmune, and inflammatory problems may need care from other specialists.

Medicines that reduce or redirect immune activity can control harmful inflammation or autoimmunity. Their use requires careful monitoring because suppressing immunity may also increase infection risk.

A stem cell transplant replaces the cells that produce the immune system. It may cure some severe conditions, including certain forms of SCID, but it has important risks and is only suitable in selected cases. Gene therapy can treat a small number of specific genetic conditions at specialist centres. Access and long-term experience differ by therapy.

Vaccination plans need to match the type of immune deficiency. Some live vaccines may cause infection in people with particular T-cell or combined immune defects. Other vaccines may be safe but produce a weaker response. Do not stop routine vaccines without advice from the immunology team familiar with your condition.

Complications

Repeated chest infections can damage and widen the airways, causing bronchiectasis . This can lead to ongoing cough, mucus, breathlessness, and further infections.

Other possible complications include chronic sinus disease, hearing problems, poor growth, malnutrition, liver disease, and damage from long-lasting inflammation. Some types raise the risk of autoimmune conditions or particular cancers, especially cancers of immune cells.

Complications are not inevitable. Early diagnosis, infection treatment, appropriate preventive care, and regular monitoring can reduce some risks.

Prevention

The genetic change behind primary immunodeficiency usually cannot be prevented. If a specific change is known, genetic counselling can explain how it may be inherited and discuss testing options for relatives or future pregnancies.

You can still take practical steps to reduce infections:

Most people do not need to avoid school, work, friends, or public places. Precautions should reflect the specific immune condition rather than infection fear alone.

- Keep recommended vaccines up to date using an individualized vaccine plan
- Wash hands regularly without trying to create a germ-free home
- Look after dental health and have routine dental care
- Avoid smoking and second-hand smoke, which can worsen lung damage
- Follow food and water safety advice, especially during travel
- Seek early advice when an infection is not improving as expected

Living with it and what to expect

Most primary immunodeficiencies are lifelong unless a treatment such as stem cell transplant or gene therapy successfully corrects the immune problem. The course can remain mild, change over time, or become clearer after particular infections. It cannot be predicted from the diagnosis alone.

Regular follow-up may include blood tests, lung function testing, review of infections, and checks for autoimmune or inflammatory complications. Keeping a record of infections, test results, vaccines, and treatments can make care easier across different services.

Treatment may involve regular home or clinic appointments. Some people receiving immunoglobulin learn to give it under the skin at home. Others need only monitoring and prompt treatment when infections occur.

Children can often attend school and join normal activities with an agreed plan for illness and missed treatment. Many adults work, travel, exercise, and raise families. Fatigue, appointments, and uncertainty about infections can still affect daily life, even when the condition is medically stable.

Research and genetic testing continue to identify new immune conditions and more targeted treatments. Your management plan may change if new information becomes available or if

your symptoms change.

When to get medical help

Routine follow-up is important even when you feel well. Arrange a non-urgent review if infections are becoming more frequent, your usual treatment is less effective, or new symptoms such as weight loss, persistent diarrhoea, swollen joints, or ongoing cough appear.

Contact your usual medical team promptly if:

Follow any condition-specific emergency plan you have been given. People with severe immune deficiencies may need assessment earlier than someone with a healthy immune system.

Call emergency services for severe breathing difficulty, blue or grey lips, confusion, collapse, a seizure, extreme difficulty waking, or signs of a rapidly worsening infection. A stiff neck with fever, a non-fading rash, or severe dehydration also needs emergency assessment.

- A fever or infection is worsening rather than improving
- You cannot keep down fluids or medicines
- A wound becomes increasingly red, painful, or swollen
- You develop a new persistent cough, breathlessness, or chest pain
- You have been exposed to a significant infection covered by your care plan

Common questions

Is primary immunodeficiency the same as an autoimmune condition?

No. Immunodeficiency means that part of the immune response is missing or ineffective. Autoimmunity means the immune system attacks the body's own tissues. However, the same immune regulation problem can cause both infection risk and autoimmunity.

Can primary immunodeficiency first appear in adults?

Yes. The underlying immune difference is usually genetic, but milder forms may not cause obvious problems until adulthood. Symptoms may become noticeable after repeated infections or the development of autoimmune or inflammatory illness.

Is primary immunodeficiency contagious?

No. You cannot catch the immune condition from another person. An infection affecting someone with immunodeficiency may still be contagious, depending on the germ involved.

Can I have vaccines?

Often, but the safest and most useful vaccine plan depends on the specific immune defect and treatment. Some live vaccines may be unsafe in certain conditions. Immunoglobulin treatment can also affect the timing or effectiveness of particular vaccines.

Can I pass primary immunodeficiency to my children?

Some forms can be inherited, but inheritance patterns differ. A person may pass on the condition, carry a gene change without symptoms, or have a new change not found in either parent. Genetic counselling can provide information based on your test results and family history.

Will I need immunoglobulin for life?

Only some types require immunoglobulin. When the body cannot make effective antibodies, treatment is commonly ongoing. The need may change after a successful stem cell transplant or other immune-restoring treatment, but it should not be stopped without specialist reassessment.

Sources

- Tangye SG, Al-Herz W, Bousfiha A, and colleagues. "Human Inborn Errors of Immunity: 2022 Update on the Classification from the International Union of Immunological Societies Expert Committee." Journal of Clinical Immunology . 2022;42:1473-1507.
- Bonilla FA, Khan DA, Ballas ZK, and colleagues. "Practice Parameter for the Diagnosis and Management of Primary Immunodeficiency." Journal of Allergy and Clinical Immunology . 2015;136(5):1186-1205.e78.
- McCusker C, Upton J, Warrington R. "Primary Immunodeficiency." Allergy, Asthma & Clinical Immunology . 2018;14(Suppl 2):61.
- National Institute of Allergy and Infectious Diseases. "Primary Immune Deficiency Diseases." Patient and public health information.
- Centers for Disease Control and Prevention. "Altered Immunocompetence." General Best Practice Guidelines for Immunization .
- Immune Deficiency Foundation. Patient & Family Handbook for Primary Immunodeficiency Diseases . Sixth edition.