CONDITION

Hyperimmunoglobulin E syndrome

Hyperimmunoglobulin E syndrome is a group of inherited immune conditions that cause recurrent infections, eczema, and often very high IgE levels.

WHAT IT IS
Inherited conditions affecting immune defence and other body tissues

BODY SYSTEM
Immune system, skin, lungs, bones, and teeth

MAIN SYMPTOMS
Eczema, recurrent infections, skin abscesses, severe allergies

WHAT CAUSES IT
Inherited immune-system gene changes

HOW IT IS DIAGNOSED
Clinical assessment, immune blood tests, and genetic testing

MAIN TREATMENT
Infection control, skin care, immune therapy, sometimes stem cell transplant

CAN IT BE CURED?
Sometimes - stem cell transplant can correct some forms

IS IT AN EMERGENCY?
Sometimes - breathing trouble or signs of severe infection

LONG-TERM OUTLOOK
Lifelong care, with outcomes shaped by genetic subtype

Overview

Hyperimmunoglobulin E syndrome, often shortened to HIES, is a group of inherited conditions that affect the immune system. It is sometimes called a primary immunodeficiency or an inborn error of immunity. This means part of the immune system does not work as expected because of a genetic change present from birth.

"Immunoglobulin E," or IgE, is an antibody involved in allergic reactions and defence against certain parasites. People with HIES often have much higher IgE levels than usual. However, a high IgE result by itself does not mean someone has HIES. Eczema, allergies, parasitic infections, and other conditions can also raise IgE.

There are several genetic forms of HIES. Two of the best understood involve changes in the STAT3 and DOCK8 genes.

STAT3-related HIES often causes eczema, repeated bacterial infections, lung damage, retained baby teeth, and changes affecting bones or connective tissue. DOCK8 deficiency often causes severe allergies, repeated skin or lung infections, and persistent viral skin infections. Other, less common genetic changes can produce overlapping features.

Finding the exact subtype matters because the likely complications and treatment options are not the same for every form.

Symptoms

Symptoms often begin in infancy or childhood, but their timing and severity differ. Some features may not become clear until later childhood or adulthood.

Common symptoms include:

Skin abscesses are often caused by Staphylococcus aureus bacteria. In STAT3-related HIES, an abscess may have less warmth, redness, or tenderness than expected. This is sometimes called a "cold" abscess, although it still requires medical assessment and treatment.

Repeated pneumonia can damage lung tissue. Air-filled spaces called pneumatoceles may remain after an infection, particularly with STAT3-related HIES. These spaces can later become infected by bacteria or fungi.

People with DOCK8 deficiency may have widespread or difficult-to-clear viral skin infections. These can include warts, molluscum contagiosum, cold sores, or shingles. Significant food allergies and asthma are also more common with this subtype.

STAT3-related HIES can affect tissues outside the immune system. Possible features include delayed loss of baby teeth, scoliosis, bones that fracture easily, unusually flexible joints, and differences in facial features. Not everyone develops all of these signs.

- Eczema or an itchy, inflamed skin rash
- Repeated skin infections or deep abscesses
- Recurrent sinus, ear, or lung infections
- Persistent fungal or viral infections
- Food allergy, asthma, or severe allergic reactions in some subtypes

Causes and risk factors

HIES is caused by a harmful change in a gene involved in immunity. The genetic change can

also affect bones, teeth, blood vessels, or connective tissue, depending on the gene.

STAT3-related HIES usually follows an autosomal dominant inheritance pattern. This means one altered copy of the gene can cause the condition. A person may inherit the change from an affected parent, or it may arise for the first time in that person.

DOCK8 deficiency usually follows an autosomal recessive pattern. A person must inherit an altered copy of the gene from both parents. The parents are usually healthy carriers.

Having a family history can increase the chance of HIES, but an affected person may have no known family history. The condition is not caused by diet, hygiene, parenting, or something done during pregnancy.

Diagnosis

HIES cannot be diagnosed from an IgE level alone. Diagnosis usually involves an immunology specialist reviewing the pattern of infections, eczema, allergies, dental development, fractures, and family history.

Blood tests may measure:

Cultures from infected skin, sputum, or other samples can identify the organism causing an infection. Chest imaging may look for pneumonia, widened airways called bronchiectasis, or pneumatoceles.

Genetic testing can confirm a specific subtype when it finds a disease-causing change. Sometimes testing does not identify a known genetic cause even though the clinical and immune findings strongly suggest HIES. Testing and interpretation may need to be updated as knowledge of immune-system genes develops.

Close relatives may be offered targeted genetic testing if a specific change is found. Genetic counselling can explain what a result means for the individual and their family.

- IgE and other antibody levels
- Numbers and types of white blood cells
- Eosinophils, which are immune cells often raised in allergic conditions
- Antibody responses to previous vaccines
- Other measures of immune function

Treatment and management

Treatment is tailored to the genetic subtype, infection history, immune test results, and organs affected. Care is often coordinated by a clinical immunology team.

Bacterial, fungal, and viral infections need prompt treatment with medicines chosen for the organism and infection site. Cultures can help guide treatment. Some people take preventive antimicrobial medicines over a longer period, but the choice is individual and requires specialist oversight.

Skin care aims to reduce eczema, breaks in the skin, and bacterial growth. It may include regular moisturising, prescribed anti-inflammatory treatment, and an antiseptic skin-care plan. Abscesses may need drainage as well as antibiotics like amoxicillin or doxycycline .

Immunoglobulin replacement therapy may help people who do not make effective protective antibodies, even if their total antibody levels appear normal. It is given by infusion into a vein or under the skin.

Lung care may include airway-clearance techniques, treatment of asthma, and regular imaging or breathing tests when needed. Existing pneumatoceles or bronchiectasis may require input from a respiratory specialist. Surgery is considered cautiously because abnormal lung spaces can be difficult to manage.

A hematopoietic stem cell transplant replaces the blood-forming cells that produce immune cells. It is an established potentially curative treatment for DOCK8 deficiency and some other severe forms of HIES. It has significant risks and requires assessment by an experienced transplant team.

The role of transplant in STAT3-related HIES is less straightforward. It may improve immune function in selected people, but it does not necessarily correct established lung, bone, dental, or blood-vessel changes.

Dental care can address retained baby teeth and help permanent teeth come through correctly. Bone health, scoliosis, and fractures may need monitoring and treatment from relevant specialists.

Complications

Repeated pneumonia can cause permanent widening and scarring of the airways, known as bronchiectasis. Damaged areas can collect mucus and become a focus for further bacterial or fungal infection.

Other possible complications include:

The complications are not identical across all subtypes. Regular monitoring is intended to find

changes before they cause major symptoms.

- Long-lasting or deep skin infections
- Fungal infection within damaged lung spaces
- Reduced lung function
- Dental crowding from retained baby teeth
- Scoliosis, low bone strength, or fractures
- Blood-vessel abnormalities in STAT3-related HIES
- Severe allergy or anaphylaxis, especially with DOCK8 deficiency
- Increased risk of certain cancers, particularly in DOCK8 deficiency

Prevention

The inherited genetic change that causes HIES cannot currently be prevented through lifestyle choices.

Genetic counselling can help families understand inheritance and discuss reproductive options. This is a personal choice rather than a requirement.

Not every infection can be prevented, but an agreed infection plan, skin care, dental care, and regular lung monitoring can reduce some risks. Avoiding tobacco smoke and vaping is especially important when the lungs are vulnerable.

Vaccination plans need individual review. Many routine vaccines may be useful, but some live vaccines may be unsafe in particular immune deficiencies. Household members may also need specific advice. An immunology team can provide a plan based on the exact subtype and immune test results.

Living with it and what to expect

HIES is usually lifelong. Its course is strongly influenced by the gene involved, the frequency of infections, and whether lasting lung or other organ damage has developed.

Symptoms can change with age. Eczema and infections may begin early, while dental, skeletal, or lung features become clearer later. IgE levels can also change and do not reliably show whether the condition is stable.

Many people need long-term appointments with immunology and other services, such as

respiratory medicine, dermatology, dentistry, allergy, or bone specialists. Follow-up may include blood tests, lung-function tests, dental checks, and imaging.

With an effective plan, many people attend school, work, exercise, travel, and take part in family life. Daily treatment and frequent appointments can still be demanding. Written plans for infections, allergies, school, and travel can make care more manageable.

DOCK8 deficiency can become progressively more serious without immune-restoring treatment because of severe infections, allergy, and cancer risk. Stem cell transplantation can substantially change this course, although recovery and long-term follow-up take time.

For STAT3-related HIES, good infection control may limit further lung damage, but established bronchiectasis, dental changes, or skeletal features may remain. No single outcome can be predicted from an IgE result alone.

When to get medical help

Seek emergency care for:

Contact the person's medical team urgently for a new fever, worsening cough, shortness of breath, chest pain, a rapidly spreading skin infection, or a painful swelling that may be an abscess. People with HIES do not always develop strong redness, pus, or fever, so a change from their usual health still matters.

Persistent viral skin sores, unexplained weight loss, swollen lymph nodes, or repeated night sweats also need prompt assessment.

Routine follow-up is appropriate for stable eczema, planned monitoring, medication reviews, dental concerns, and discussion of test results. Do not wait for the next routine appointment if symptoms suggest a significant infection.

- Severe trouble breathing, blue or grey lips, or inability to speak normally
- Signs of anaphylaxis, such as throat swelling, wheezing, faintness, or breathing difficulty
- Confusion, extreme drowsiness, collapse, or other signs of severe infection
- Coughing up a large amount of blood

Common questions

Is a high IgE level the same as hyperimmunoglobulin E syndrome?

No. High IgE is common in eczema and allergy and can occur for several other reasons. HIES is

identified from the overall pattern of symptoms, immune testing, and, when possible, genetic testing.

Is hyperimmunoglobulin E syndrome contagious?

No. It is caused by an inherited or newly arising genetic change. The infections that occur in someone with HIES may sometimes be contagious, but HIES itself cannot spread between people.

Can hyperimmunoglobulin E syndrome be cured?

Some forms can be treated with a stem cell transplant that replaces the affected immune system. This is particularly important in DOCK8 deficiency. Transplant is not suitable or equally effective for every subtype, and it has significant risks.

Does treatment make the IgE level normal?

Not necessarily. IgE may stay high even when infections and eczema are better controlled. Treatment decisions are based more on symptoms, infections, organ health, and immune function than on one IgE result.

Can someone with HIES have vaccines?

Often, but the plan must match the specific immune problem. Some live vaccines may be unsuitable. An immunology team should review the vaccine schedule rather than vaccines being stopped or delayed without advice.

Can a person with HIES go to school, work, or travel?

Many can. Plans may be needed for medicines, allergy emergencies, infection symptoms, and access to medical care. Travel planning is especially important when preventive medicines or immunoglobulin treatment must continue.

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