CONDITION

Human cyclic neutropenia

Human cyclic neutropenia is a condition in which infection-fighting neutrophil levels fall at regular intervals.

WHAT IT IS
Repeated episodes of very low infection-fighting white blood cells

BODY SYSTEM
Blood and immune system

MAIN SYMPTOMS
Fever, mouth ulcers, sore throat, skin infections

WHAT CAUSES IT
Usually inherited ELANE gene changes

HOW IT IS DIAGNOSED
Repeated blood counts, sometimes genetic testing

MAIN TREATMENT
White blood cell growth factor and prompt infection treatment

CAN IT BE CURED?
Sometimes - stem cell transplant can cure selected severe cases

IS IT AN EMERGENCY?
Sometimes - fever during neutropenia needs urgent assessment

LONG-TERM OUTLOOK
Usually manageable with monitoring and treatment

Overview

Human cyclic neutropenia is a condition that causes regular drops in the number of neutrophils in your blood. Neutrophils are white blood cells that help protect you from bacterial and fungal infections.

The low point in each cycle is called the nadir . It often occurs about every three weeks, although the timing differs between people. Neutrophil levels may remain very low for several days before recovering. Between episodes, the count may return to a normal or nearly normal level.

When neutrophils are very low, your body may have difficulty controlling infections. Fever, mouth ulcers, sore throat, and skin infections are common during this part of the cycle. Some people have few symptoms between low-count periods.

Cyclic neutropenia often begins in infancy or childhood, but it may not be recognised until later. It is different from severe congenital neutropenia, in which neutrophil counts remain low rather than following a repeating pattern.[1]

Symptoms

Symptoms usually appear when the neutrophil count is at its lowest. They may improve as the count rises again.

Common symptoms include:

Repeated gum inflammation can lead to periodontitis , an infection and inflammation of the tissues supporting the teeth. Without dental care and control of the neutropenia, this can loosen or damage teeth.

Symptoms often follow a recognisable schedule, but the cycle is not always exact. An illness or treatment may also affect the pattern. Some people do not notice clear symptoms even when their neutrophil count is low.

Because neutrophils help create pus and inflammation, an infection may look less obvious during severe neutropenia. Fever or increasing pain may be more important than the amount of redness or discharge.

- Fever or chills
- Painful mouth ulcers
- Sore throat or inflamed gums
- Swollen lymph nodes, sometimes called glands
- Skin redness, swelling, boils, or other infections
- Tiredness or feeling generally unwell
- Abdominal pain or digestive symptoms

Causes and risk factors

Most cases are caused by a change in a gene called ELANE . This gene provides instructions for making an enzyme used by neutrophils. Certain ELANE changes disrupt neutrophil production in the bone marrow, causing the cell count to rise and fall in cycles.[1]

Cyclic neutropenia is usually inherited in an autosomal dominant pattern. This means one altered copy of the gene can cause the condition. A parent with an ELANE-related condition

has a 1 in 2 chance of passing the altered gene to each child.

Sometimes the gene change begins in the affected person and neither parent has it. This is called a de novo , or new, gene change. For that reason, having no family history does not rule out cyclic neutropenia.

The condition is not caused by diet, stress, poor hygiene, or something a parent did during pregnancy. It is not contagious.

Diagnosis

Diagnosis depends on showing that neutrophil levels fall and recover in a repeating pattern. A single normal or low blood count cannot confirm the condition.

You may have a complete blood count with differential , often shortened to CBC with differential. This test measures blood cells and reports the absolute neutrophil count , or ANC.

Blood samples are usually taken several times a week for about six weeks. This allows the healthcare team to look for repeated low points and recovery periods. Other blood cells, including monocytes, may also change during the cycle.[1,2]

Genetic testing can look for an ELANE change. A positive result may support the diagnosis and help with family testing. A negative result does not always explain why the neutrophil count is cycling, so the pattern of blood counts remains important.

Other tests may be used to rule out medicines, infections, immune conditions, nutritional deficiencies, or other causes of neutropenia. A bone marrow test is not required for every person, but it may be considered if the diagnosis is uncertain or the blood results are unusual. Bone marrow is the soft tissue inside bones where blood cells are made.

Treatment and management

Treatment aims to reduce the time spent with very low neutrophil levels and prevent serious infections. Care is usually coordinated by a haematology team, which specialises in blood conditions.

The main treatment is granulocyte colony-stimulating factor , or G-CSF. Filgrastim is one form of G-CSF. It encourages the bone marrow to produce and release neutrophils.

G-CSF can shorten the low-count period and reduce fever, mouth ulcers, and infections.[3,4] It is given by injection. The amount and schedule are adjusted to the person's blood counts, symptoms, and response rather than being the same for everyone.

Bone or muscle pain can occur with G-CSF. Other possible effects and the need for blood-count monitoring should be discussed with the prescribing team. Do not change or stop treatment without medical guidance.

Infections may need prompt antibiotic or antifungal treatment. The choice depends on the infection, its severity, test results, and whether the neutrophil count is low. Antibiotics like amoxicillin or doxycycline are not a substitute for urgent assessment when fever occurs during severe neutropenia.

Regular dental care is especially important. A dentist can help manage gum inflammation, mouth ulcers, and plaque that may increase infection risk. Gentle brushing with a soft toothbrush is often more comfortable when the mouth is sore.

A haematopoietic stem cell transplant , also called a bone marrow transplant, replaces the cells that produce blood cells. It can cure neutropenia, but it carries major short-term and long-term risks. Because G-CSF usually works well in cyclic neutropenia, transplant is generally reserved for unusual, severe cases that cannot be managed in other ways.[1,2]

Complications

The main complication is infection during a low-neutrophil period. Infections can involve the mouth, throat, skin, lungs, or bloodstream.

A bloodstream infection can lead to sepsis , a serious body-wide response to infection. This is not inevitable, but the risk makes fever during known or suspected severe neutropenia an urgent concern.

Repeated inflammation and infection in the mouth can cause gum recession, damage around the teeth, and tooth loss. Consistent dental care and control of neutropenia can lower this risk.

Some people develop severe abdominal pain from inflammation or infection in the digestive tract. Sudden or worsening abdominal pain during neutropenia needs urgent assessment.

Cyclic neutropenia is not cancer. Unlike severe congenital neutropenia, it has not been clearly associated with an increased risk of myelodysplastic syndrome or acute myeloid leukaemia.[1] Your team may still monitor blood counts over time to assess the condition and treatment response.

Prevention

The inherited gene change that usually causes cyclic neutropenia cannot currently be

prevented. It is not caused by lifestyle choices.

Treatment can help prevent many low-count symptoms and infections. Practical measures include careful handwashing, good dental hygiene, safe food handling, and prompt care for cuts or skin infections. You generally do not need to avoid normal school, work, or social contact, although extra care may be useful around people with a known contagious illness.

Routine vaccinations are usually important, but the appropriate schedule should be confirmed with your healthcare team, especially if you have another immune condition or are being considered for a transplant.

If an ELANE change has been identified, genetic counselling can explain inheritance, testing for relatives, and reproductive options. Genetic counselling provides information and support; it does not tell you what decision to make.

Living with it and what to expect

Cyclic neutropenia usually continues over many years. The timing and severity of episodes may become familiar, but cycles are not always perfectly predictable. Treatment can change their length and intensity.

Many people remain well between low-count periods and take part in school, work, exercise, and family life. During a nadir, you may need extra rest or time away because of mouth pain, fever, or infection. Effective G-CSF treatment often reduces this disruption.

Your care may include regular blood counts, review of infections and mouth symptoms, dental checks, and monitoring for treatment effects. Keeping a record of fever, mouth ulcers, infections, and blood results can help show whether symptoms follow a cycle. A diary cannot replace a blood test because a low neutrophil count does not always cause symptoms.

Children may need an age-appropriate plan for school or childcare. It can explain who to contact if fever develops and whether medicine needs to be stored or given during the day. Most children can still join ordinary activities when they feel well.

Pregnancy is possible, but planning is useful because the condition can be inherited and treatment decisions may need review. A haematology team, pregnancy care team, and genetic counsellor can work together before and during pregnancy.

Long-term outlook is often good when infections are recognised quickly and neutrophil levels respond to treatment. Individual experiences differ, so follow-up focuses on your infection history, dental health, blood counts, and response to G-CSF rather than the diagnosis alone.

When to get medical help

Seek urgent medical assessment if you have known or suspected neutropenia and develop a temperature of 38°C or higher. Follow any lower threshold or specific emergency plan provided by your haematology team. Do not wait for the next clinic appointment to see whether the fever settles.

Go to emergency care promptly for:

Tell the emergency team that you have cyclic neutropenia and, if known, when your last low count occurred. Fever may be the only clear sign of infection.

Arrange routine follow-up if mouth ulcers, gum bleeding, dental pain, skin infections, or low-count symptoms are becoming more frequent. Also seek a review if treatment side effects are troublesome, injections are being missed, or your usual cycle appears to have changed.

- Shaking chills, confusion, faintness, or severe weakness
- Difficulty breathing or chest pain
- Severe or rapidly worsening abdominal pain
- Repeated vomiting or inability to drink
- Rapidly spreading skin redness, swelling, or severe pain
- Fever with a central line or after a recent transplant

Common questions

How often does the neutrophil count fall?

The classic pattern is about every 21 days, with a low period lasting several days. Some cycles are shorter or longer, and the timing may shift. Repeated blood tests are more reliable than calendar estimates.

Is cyclic neutropenia cancer?

No. It is a condition affecting neutrophil production. It is also different from leukaemia and from severe congenital neutropenia, which has a different pattern and long-term risk profile.

Is cyclic neutropenia contagious?

No. You cannot catch it from another person or pass it through everyday contact. Most cases are linked to an inherited or newly occurring ELANE gene change.

Can I tell when my neutrophil count is low?

Mouth ulcers, sore throat, fever, or tiredness may suggest a low period, but some people have no symptoms. A blood test is the only reliable way to measure the neutrophil count.

Can my children inherit it?

If you have an ELANE change that follows autosomal dominant inheritance, each pregnancy has a 1 in 2 chance of inheriting that change. A genetic counsellor can explain testing and what a result may mean for your family.

Can people with cyclic neutropenia live a normal life?

Many people have active lives, especially when G-CSF controls the low-count periods and infections are treated promptly. Ongoing blood and dental follow-up remains important.

Sources

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