CONDITION

Culture-negative endocarditis

Culture-negative endocarditis is an infection of the heart lining or valves that does not grow in standard blood cultures.

WHAT IT IS
Heart infection with negative standard blood cultures

BODY SYSTEM
Heart and circulation

MAIN SYMPTOMS
Fever, fatigue, breathlessness, night sweats

WHAT CAUSES IT
Infection hidden by antibiotics or hard-to-grow organisms

HOW IT IS DIAGNOSED
Blood tests, heart imaging, serology, and molecular tests

MAIN TREATMENT
Targeted antimicrobials, with heart valve surgery when needed

CAN IT BE CURED?
Yes - prompt treatment can clear infection

IS IT AN EMERGENCY?
Yes - suspected infection needs urgent hospital assessment

LONG-TERM OUTLOOK
Often good, but lasting valve damage may occur

Overview

Culture-negative endocarditis is a form of infective endocarditis. This is an infection of the inner lining of the heart, usually involving one or more heart valves.

"Culture-negative" means that standard blood cultures do not grow the germ causing the infection. Blood cultures are tests in which blood samples are placed in special containers to see whether bacteria or fungi grow.

A negative culture does not always mean there is no infection. Antibiotics like amoxicillin or doxycycline taken before the samples were collected may stop germs from growing. Some organisms are also difficult or impossible to detect with routine culture methods.

Endocarditis can damage a valve, interfere with blood flow, or cause infected material to travel

to another part of the body. For this reason, suspected culture-negative endocarditis usually needs urgent specialist assessment in hospital.

The condition can be challenging to identify. Doctors often combine symptoms, examination findings, heart scans, blood tests, and specialised laboratory tests rather than relying on one result.

Symptoms

Symptoms may begin suddenly over several days or develop more gradually over weeks. They can be mild at first and may resemble another infection or an inflammatory condition.

Possible symptoms include:

A clinician may hear a new or changed heart murmur. A murmur is an extra sound caused by blood moving through the heart. Small spots under the nails or on the skin can occur, but they are not present in everyone.

Symptoms caused by an embolus may appear suddenly. An embolus is material that breaks away from the infected heart valve and blocks blood flow elsewhere. Depending on where it travels, it can cause a stroke, limb pain, abdominal pain, or problems in the lungs.

- Fever, chills, or feeling unusually cold
- Marked tiredness or weakness
- Night sweats
- Shortness of breath
- Reduced appetite or unplanned weight loss
- Muscle, joint, back, or chest discomfort
- Headache or confusion
- Swelling of the feet, ankles, or abdomen

Causes and risk factors

The most common reason for negative blood cultures is antibiotic treatment before the cultures were collected. Even a short course can make some bacteria harder to grow.

Other cases are caused by organisms that need special laboratory methods. These include Coxiella burnetii , which causes Q fever, and species of Bartonella . Less common causes

include Brucella , Tropheryma whipplei , certain fungi, and other difficult-to-grow organisms.

Travel, contact with farm animals, cat exposure, homelessness, body lice, unpasteurised dairy products, and immune problems can provide useful diagnostic clues. These exposures do not prove that a particular organism is present.

Factors that can increase the chance of endocarditis include:

Rarely, a non-infectious condition can produce growths on heart valves that resemble endocarditis. This is called nonbacterial thrombotic endocarditis. It may be linked to cancer, lupus, or another condition that increases inflammation or blood clotting. Recognising this difference matters because antibiotics do not treat a non-infectious cause.

- An artificial heart valve or material used to repair a valve
- Previous infective endocarditis
- Certain congenital heart conditions present from birth
- Damaged or abnormal heart valves
- A cardiac device, such as a pacemaker
- Long-term intravenous lines
- Injecting drugs
- A weakened immune system

Diagnosis

No single negative blood culture confirms culture-negative endocarditis. Diagnosis begins with several blood culture samples, ideally collected before antibiotics when it is safe to do so. Treatment should not be delayed in someone who is seriously unwell.

Tell the hospital team about recent antibiotics, even if they were taken for an unrelated problem. Exposure to animals, recent travel, dental treatment, implanted heart material, and injecting drug use can also guide testing.

An echocardiogram uses sound waves to create pictures of the heart. A transthoracic echocardiogram is performed through the chest. A transoesophageal echocardiogram uses a probe passed into the food pipe after sedation. Because the food pipe lies close to the heart, this test can give clearer pictures of valves and artificial heart material.

Doctors look for infected growths, called vegetations, as well as valve leakage, abscesses, or other damage. An early scan may be normal, so repeat imaging may be needed when suspicion remains high.

Other tests can include:

Specialists interpret these findings using recognised diagnostic criteria. A diagnosis may remain "possible" until repeat imaging, specialised tests, or tissue analysis provides stronger evidence.

- Antibody tests, called serology, for organisms such as Coxiella and Bartonella
- PCR or other molecular tests that search for genetic material from a germ
- Blood counts and tests of kidney, liver, and inflammatory activity
- CT, MRI, or PET imaging to look for valve infection or complications elsewhere
- Laboratory examination of valve tissue if surgery is performed

Treatment and management

Treatment usually takes place under a team that may include heart, infection, microbiology, imaging, and cardiac surgery specialists.

If endocarditis is strongly suspected, blood samples are collected and broad antimicrobial treatment may be started before the exact cause is known. "Antimicrobial" includes medicines that treat bacteria, fungi, or other infectious organisms.

The treatment is adjusted when serology, molecular testing, or tissue analysis identifies a likely cause. The choice and length of treatment are influenced by the organism, whether the valve is natural or artificial, previous antibiotics, kidney and liver function, and any complications. Treatment commonly lasts several weeks.

Many people initially receive medication through a vein. Blood tests are used to check whether treatment is working and to watch for effects on the kidneys, liver, or blood cells. Some medicines also require measurement of drug levels.

Heart valve surgery may be recommended when:

Surgery may involve repairing or replacing the affected valve and removing infected tissue. Not everyone with culture-negative endocarditis needs an operation.

If testing points to a non-infectious valve condition, treatment changes completely. Management then focuses on the underlying condition and, when appropriate, preventing blood clots.

- Valve damage causes heart failure
- Infection cannot be controlled with medication

- An abscess or another deep infection develops around the valve
- An artificial valve becomes unstable
- Large infected growths create a serious risk of further emboli

Complications

Endocarditis can make a valve leak severely. This may lead to heart failure, meaning the heart cannot pump blood effectively enough to meet the body's needs.

Infection can spread into nearby heart tissue and form an abscess. It can also affect the heart's electrical pathways, causing a new abnormal rhythm or unusually slow heartbeat.

Fragments from a vegetation can travel through the bloodstream. This may cause a stroke or damage the spleen, kidneys, bowel, limbs, or other organs. Infection on the right side of the heart can send material to the lungs.

Kidney problems may result from the infection, the immune system's response, reduced circulation, or treatment side effects. Some people continue to have valve leakage after the infection has cleared and need long-term heart monitoring.

Prompt diagnosis and treatment reduce these risks, but complications can sometimes develop even after therapy has begun.

Prevention

Not every case can be prevented. Some germs are acquired through exposures that are difficult to recognise, and some people have underlying valve problems they cannot change.

Good dental care can reduce the number of bacteria entering the bloodstream from unhealthy gums. Brush regularly, attend routine dental care, and seek treatment for ongoing dental infection.

Preventive antibiotics before certain dental procedures are recommended only for selected people at highest risk of a poor outcome from endocarditis. This may include some people with artificial valves, previous endocarditis, or particular congenital heart conditions. They are not routinely used for everyone with a heart murmur or valve problem.

Do not take leftover antibiotics or stop prescribed antibiotics to improve the chance of a positive culture. If endocarditis is suspected, tell the medical team exactly what you have taken and when.

Avoid injecting non-prescribed drugs. If you do inject, using sterile equipment and never sharing needles can reduce infection risk. Skin infections and problems around intravenous lines or implanted devices should receive timely medical attention.

Living with it and what to expect

Treatment and recovery often extend over weeks or months. Some people remain in hospital for much of their intravenous treatment. Others may complete part of it through a closely supervised outpatient service when clinically stable.

Tiredness, weakness, and reduced stamina can continue after the infection is controlled. Recovery may be slower after surgery, a stroke, heart failure, or a long period of illness. Activity is usually increased gradually according to the advice of the hospital team.

Follow-up may include blood tests, repeat blood cultures, heart scans, and appointments with heart and infection specialists. These checks look for returning infection, medication effects, and lasting valve damage.

Some people recover without major long-term limitations. Others have continuing valve leakage, reduced heart function, or effects from an embolus. A damaged valve may need monitoring for years and can sometimes require later repair or replacement.

Endocarditis can return, especially if an infected device remains in place or the original source cannot be removed. A new fever does not necessarily mean the infection has returned, but it should not be ignored after recent endocarditis.

Culture-negative endocarditis is not normally passed from person to person. Everyday contact with family, friends, or coworkers does not spread the heart infection.

When to get medical help

Seek emergency help now if you have symptoms that could indicate a stroke or a severe heart complication, including:

Arrange urgent same-day medical assessment for an unexplained persistent fever, especially if you have an artificial valve, previous endocarditis, congenital heart condition, implanted heart device, or recent bloodstream infection.

If you are being treated for endocarditis, contact your treatment team promptly about a returning fever, worsening breathlessness, new swelling, a new rash, reduced urine, severe diarrhoea, or problems with an intravenous line.

Gradually improving tiredness can be discussed at routine follow-up. Keep scheduled blood tests and heart scans even if you feel better, because valve damage or medication effects may not cause obvious early symptoms.

- Sudden weakness or numbness on one side
- New trouble speaking, seeing, or walking
- Severe breathlessness, blue or grey lips, or chest pressure
- Fainting, collapse, or new severe confusion
- A cold, pale, very painful arm or leg

Common questions

How can I have endocarditis if my blood cultures are negative?

Blood cultures only detect organisms that grow under the laboratory conditions used. Previous antibiotics can stop growth, while some bacteria and fungi need antibody tests, molecular testing, or examination of valve tissue. Doctors also consider non-infectious conditions that can resemble endocarditis.

Can antibiotics cause culture-negative endocarditis?

Antibiotics do not usually cause endocarditis. However, antibiotics taken before blood cultures can suppress the germ and make the cultures negative without fully clearing an established heart valve infection.

How long does treatment take?

Treatment usually lasts several weeks. The exact course is based on the suspected or identified organism, the affected valve, complications, surgery, and how you respond. Culture-negative results can make careful specialist review especially important.

Will I need heart surgery?

Not necessarily. Surgery is more likely if there is severe valve leakage, heart failure, infection around the valve, an unstable artificial valve, uncontrolled infection, or a high risk of further emboli.

Is culture-negative endocarditis contagious?

The heart infection itself is not generally contagious. Some organisms associated with it may come from animals, food, insects, or the environment, but ordinary contact with someone receiving treatment does not usually spread endocarditis.

Can culture-negative endocarditis come back?

It can recur or a new episode can develop. The risk is higher when damaged or artificial valves, infected devices, ongoing bloodstream exposure, or an untreated source remain. New fever or similar symptoms after treatment need prompt assessment.

Sources

- Delgado V, Ajmone Marsan N, de Waha S, et al. 2023 ESC Guidelines for the management of endocarditis . European Heart Journal . 2023;44:3948-4042.
- Fowler VG Jr, Durack DT, Selton-Suty C, et al. The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis . Clinical Infectious Diseases . 2023;77:518-526.
- DeSimone DC, Beisiegel M, Dayer MJ, et al. Blood Culture-Negative Endocarditis: A Scientific Statement From the American Heart Association. Journal of the American Heart Association . 2025.
- Liesman RM, Pritt BS, Maleszewski JJ, Patel R. Laboratory Diagnosis of Infective Endocarditis . Journal of Clinical Microbiology . 2017;55:2599-2608.
- McHugh J, Abu Saleh O. Updates in Culture-Negative Endocarditis . Pathogens . 2023;12:1027.