CONDITION

Methemoglobinemia

Methemoglobinemia is a blood condition in which altered hemoglobin cannot deliver oxygen normally.

WHAT IT IS
Abnormally altered hemoglobin that cannot carry oxygen effectively

BODY SYSTEM
Blood and oxygen circulation

MAIN SYMPTOMS
Blue-gray skin, headache, breathlessness, fatigue

WHAT CAUSES IT
Oxidant exposures or inherited hemoglobin changes

HOW IT IS DIAGNOSED
Blood co-oximetry; genetic testing for inherited forms

MAIN TREATMENT
Remove the cause, oxygen, and antidote treatment

CAN IT BE CURED?
Sometimes - acquired forms often resolve

IS IT AN EMERGENCY?
Sometimes - breathing difficulty, confusion, or collapse

LONG-TERM OUTLOOK
Usually good when acquired cases are treated promptly

Overview

Methemoglobinemia is a condition in which some of the hemoglobin in your blood changes into an abnormal form called methemoglobin.

Hemoglobin is the protein inside red blood cells that carries oxygen from your lungs to the rest of your body. In methemoglobin, the iron within that protein has been chemically altered. It can no longer carry oxygen normally. It can also make the remaining hemoglobin hold on to oxygen more tightly instead of releasing it to tissues.

Everyone has a very small amount of methemoglobin. The body normally changes it back into working hemoglobin using natural enzymes. Methemoglobinemia develops when methemoglobin forms faster than the body can remove it, or when one of those protective enzyme systems does not work properly.

The condition may be acquired after exposure to certain medicines or chemicals. Less often, it is inherited because of a gene change present from birth.

A characteristic sign is blue, gray, or slate-colored skin or lips, called cyanosis. The blood may look unusually dark or chocolate brown. Symptoms range from none to severe oxygen shortage, depending on the amount of methemoglobin and your general health.

Symptoms

Mild methemoglobinemia may cause no symptoms other than a blue-gray color around the lips, skin, or nail beds. This color may not improve as expected when oxygen is given.

As the amount of methemoglobin rises, symptoms may include:

Skin color changes can be harder to recognize in darker skin. They may be more noticeable on the lips, tongue, gums, inside the eyelids, palms, or soles.

Symptoms do not always match a single methemoglobin measurement. Someone with anemia, which means too few healthy red blood cells, may become unwell at a lower level. Heart or lung conditions can also reduce the body's ability to cope with impaired oxygen delivery.

An inherited form may cause long-standing blue-gray skin from birth or childhood without major breathing problems. Other rare inherited forms can cause serious neurological problems, including developmental delay, movement problems, and seizures.

- Headache, dizziness, tiredness, or weakness
- Shortness of breath or rapid breathing
- A fast heartbeat
- Nausea
- Difficulty concentrating, confusion, or unusual sleepiness
- Fainting, seizures, an abnormal heart rhythm, or loss of consciousness in severe cases

Causes and risk factors

Most cases are acquired. They happen after a medicine or chemical oxidizes, or chemically alters, hemoglobin.

Possible triggers include:

This list is not complete. A medicine can sometimes cause methemoglobinemia even when used as directed, although risk may increase with excessive exposure or repeated doses. Do

not stop a prescribed medicine without medical advice unless you are having a suspected emergency.

Babies younger than about 6 months are more vulnerable to nitrate-related methemoglobinemia. Their protective enzyme systems are less mature, and their stomach conditions make conversion of nitrate to nitrite easier. Water from private wells can be a source of excess nitrate.

Inherited methemoglobinemia is uncommon. One form results from changes affecting cytochrome b5 reductase, an enzyme that converts methemoglobin back into normal hemoglobin. A red-blood-cell-limited form mainly causes lifelong cyanosis. A generalized form affects other tissues and can cause severe neurological disability.

Hemoglobin M is another inherited cause. In this form, the structure of hemoglobin itself makes it unusually easy to oxidize and difficult to restore.

- Local anesthetics such as benzocaine or prilocaine
- Dapsone, a medicine used for certain skin conditions and infections
- Nitrates and nitrites, including contaminated well water
- Some antibiotics and antimalarial medicines
- Aniline dyes and certain industrial chemicals
- Recreational inhalants containing nitrites

Diagnosis

Diagnosis starts with your symptoms, recent exposures, medicines, work environment, and personal or family history. A clinician may suspect the condition when blue-gray coloring does not improve normally with oxygen or when oxygen readings do not fit the overall clinical picture.

A standard fingertip pulse oximeter can be misleading. It may remain near the mid-80% range even when the true oxygen level is different. A blood gas test may calculate a normal oxygen saturation despite an abnormal pulse oximeter result. This mismatch is sometimes called a "saturation gap."

The confirming test is co-oximetry. This blood test uses several wavelengths of light to measure methemoglobin directly and distinguish it from other forms of hemoglobin.

Other tests may look for anemia, red blood cell breakdown, kidney or liver problems, or another explanation for the symptoms. If an inherited form is suspected, testing may include enzyme

activity measurements, analysis of hemoglobin, or genetic testing.

Because methemoglobin can fall after an exposure ends, testing is most useful while symptoms are present or soon afterward.

Treatment and management

Treatment depends on your symptoms, the measured methemoglobin level, the cause, and conditions such as anemia or heart and lung disease.

The first step in acquired methemoglobinemia is to stop further exposure to the suspected trigger. Supportive care may include oxygen and monitoring of breathing, heart rhythm, blood pressure, and repeat methemoglobin levels.

Methylene blue is the main antidote for clinically significant methemoglobinemia. It helps the body convert methemoglobin back into working hemoglobin. It is usually given into a vein in a monitored medical setting.

Methylene blue requires special care in people with glucose-6-phosphate dehydrogenase deficiency, often shortened to G6PD deficiency. In this inherited enzyme condition, it may work poorly and can contribute to red blood cell breakdown. It can also interact with medicines that increase serotonin, including some antidepressants like sertraline or fluoxetine , and may cause serotonin toxicity. The treating team should review current medicines and known enzyme conditions before using it.

Vitamin C, also called ascorbic acid, can reduce methemoglobin more slowly. It may be considered in selected inherited cases or when methylene blue is unsuitable. It is not a rapid substitute for emergency treatment.

Rarely, severe cases that do not respond to usual treatment may require a blood transfusion, exchange transfusion, or hyperbaric oxygen. Hyperbaric treatment delivers oxygen under increased pressure in a special chamber.

People with an inherited form may not need treatment if cyanosis is their only symptom. Treatment decisions focus on symptoms, daily impact, and the specific underlying form.

Complications

Severe methemoglobinemia can prevent enough oxygen from reaching the brain, heart, and other organs. Possible complications include seizures, abnormal heart rhythms, coma, organ injury, or death. These outcomes are more likely with a large or continuing exposure and

delayed treatment.

Some medicines remain in the body for a long time or are absorbed slowly. Methemoglobinemia may therefore return after initially improving. Dapsone is one example. Continued observation and repeat blood tests may be needed.

Treatment can also have complications. Methylene blue may contribute to red blood cell breakdown in susceptible people and can interfere with some oxygen measurements. High or repeated exposure can itself worsen methemoglobinemia.

The generalized inherited enzyme deficiency can cause lifelong neurological disability. By contrast, the form limited to red blood cells and hemoglobin M usually cause persistent cyanosis without the same neurological damage.

Prevention

Inherited methemoglobinemia cannot currently be prevented. Genetic counseling may help people with an inherited form understand how it could be passed through a family.

Many acquired cases can be prevented by reducing avoidable exposure:

Boiling nitrate-contaminated water does not make it safe. Boiling can concentrate nitrate as water evaporates. Use a safe alternative water source until the well has been assessed.

Do not avoid necessary prescribed treatment solely because a medicine has been associated with this condition. The risk and alternatives should be discussed with the prescriber.

- Use medicines and numbing products only as directed
- Keep medicines and chemicals away from children
- Tell healthcare and dental teams about previous methemoglobinemia
- Use protective measures around aniline dyes, nitrates, and industrial oxidants
- Test private well water for nitrate when recommended locally, especially before using it for infant formula

Living with it and what to expect

Acquired methemoglobinemia often improves after the trigger is removed and appropriate treatment is given. Recovery may occur over hours or days. The time needed depends on the substance involved, how long it stays in the body, and whether methemoglobin rises again.

Follow-up may include repeat blood tests and a review of medicines or chemical exposures.

Keep a record of the suspected trigger. This can help prevent accidental re-exposure during future medical or dental care.

People with the inherited form limited to red blood cells may have blue-gray skin throughout life but otherwise remain well. Cyanosis can become more noticeable during illness or after exposure to an oxidizing medicine. Some people choose treatment for symptoms or the effect of skin color on daily life.

Hemoglobin M also tends to cause lifelong cyanosis. Standard antidote treatment may not work because the problem lies within the hemoglobin structure.

The generalized inherited enzyme deficiency has a different course. Neurological problems usually begin early in life and can be severe. Ongoing care may involve neurology, rehabilitation, nutrition support, and help with communication or mobility.

When to get medical help

Call emergency services now if blue-gray lips or skin appear with:

Move away from a chemical exposure if you can do so safely, but do not enter a contaminated area without proper protection. Do not make yourself vomit unless a poison service specifically instructs you to.

Seek urgent medical assessment for new blue-gray coloring, unexplained shortness of breath, or symptoms beginning after a medicine, numbing product, recreational inhalant, contaminated water, or workplace chemical. Bring the product container or medicine list if it is safe to do so.

Routine follow-up is appropriate after recovery to review the cause and reduce the chance of another episode. Long-standing cyanosis without acute symptoms also deserves a medical assessment, particularly if it has never been explained.

- Severe or worsening breathing difficulty
- Confusion, extreme sleepiness, or loss of consciousness
- A seizure
- Chest pain, collapse, or a very abnormal heartbeat
- A significant chemical or medication exposure

Common questions

Can a pulse oximeter detect methemoglobinemia?

It may suggest a problem, but it cannot confirm the condition. Readings often remain around the mid-80% range and may not improve normally with oxygen. Co-oximetry on a blood sample is needed for confirmation.

Why does the blood look chocolate brown?

Methemoglobin absorbs light differently from normal oxygen-carrying hemoglobin. This can make a blood sample look dark brown rather than bright red. The color may remain brown even after the sample is exposed to oxygen.

Can benzocaine cause methemoglobinemia?

Yes. Benzocaine, including some mouth and throat numbing products, has been linked to acquired methemoglobinemia. The reaction can occur after a single use. New cyanosis, breathlessness, dizziness, or confusion after benzocaine needs urgent assessment.

Is methemoglobinemia inherited?

Sometimes. Most cases are caused by a medicine or chemical exposure, but rare forms result from inherited enzyme deficiencies or abnormal hemoglobin. Lifelong cyanosis or a family history may lead to enzyme or genetic testing.

Does oxygen cure methemoglobinemia?

Oxygen supports the tissues but does not directly convert methemoglobin back into normal hemoglobin. Significant cases may need an antidote or other treatment aimed at the altered hemoglobin.

Will the blue-gray skin color go away?

In acquired cases, it usually fades as methemoglobin returns to normal. In inherited forms, cyanosis may be lifelong even when the person otherwise feels well. The expected course depends on the exact inherited change.

Sources

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