CONDITION

Fulminating hyperpyrexia

Fulminating hyperpyrexia is a life-threatening reaction to certain general anaesthetic drugs in susceptible people.

WHAT IT IS
Severe anaesthetic-triggered overheating and muscle reaction

BODY SYSTEM
Muscles, heart and circulation, kidneys, and nervous system

MAIN SYMPTOMS
Rising carbon dioxide, muscle rigidity, fast heartbeat, very high temperature

WHAT CAUSES IT
Inherited muscle sensitivity to certain anaesthetic drugs

HOW IT IS DIAGNOSED
Contracture testing or a disease-causing genetic variant

MAIN TREATMENT
Dantrolene and intensive supportive care

CAN IT BE CURED?
No - inherited susceptibility usually remains lifelong

IS IT AN EMERGENCY?
Yes - any suspected reaction during or after anaesthesia

LONG-TERM OUTLOOK
Usually good after prompt treatment; severe complications can be fatal

Overview

Fulminating hyperpyrexia is an older term usually referring to a severe malignant hyperthermia reaction. It is a rare but life-threatening response to certain medicines used during general anaesthesia. "Fulminating" means developing rapidly, while "hyperpyrexia" means an extremely high body temperature.

A high temperature may not be the first sign. The earliest clue is often an unexpected rise in carbon dioxide produced by the body. Muscles may become rigid, the heart may beat very quickly, and the blood can become dangerously acidic. Temperature may then rise rapidly.

The reaction occurs when susceptible skeletal muscle cells release too much stored calcium after exposure to a triggering anaesthetic. The muscles contract and use energy uncontrollably, producing heat, carbon dioxide and harmful chemical changes.

This condition is an emergency. Anaesthesia teams monitor for early signs and keep the specific treatment, dantrolene, available where triggering anaesthetics are used. Rapid recognition and treatment allow many people to recover.

Susceptibility does not usually cause day-to-day symptoms. It may only be discovered after an anaesthetic reaction, a relative's reaction or specialist testing.

Symptoms

Most reactions begin during general anaesthesia. Some become apparent soon after the triggering medicine is stopped, usually while the person is still being monitored.

Early findings can include:

As the reaction progresses, body temperature may rise quickly. Sweating, mottled skin, abnormal heart rhythms and unstable blood pressure can occur.

Muscle cells may break down, causing rhabdomyolysis . This releases potassium and a muscle protein called myoglobin. High potassium can disturb heart rhythm. Myoglobin may make urine dark brown or cola-coloured and can damage the kidneys.

A high temperature alone does not mean someone has malignant hyperthermia. Fever after surgery can have other causes, including infection, inflammation, medication reactions and overheating. Clinicians consider the anaesthetic medicines used, carbon dioxide levels, muscle findings and test results.

- An unexplained, continuing rise in exhaled carbon dioxide
- A fast heartbeat
- Rapid breathing if the person is breathing independently
- Tight or rigid muscles, sometimes first noticed in the jaw
- Acid building up in the blood

Causes and risk factors

The main triggers are volatile anaesthetic gases and the muscle relaxant succinylcholine, also called suxamethonium. They can start a reaction in someone who is susceptible.

Susceptibility is often inherited. Changes in the RYR1 gene are the most common known cause. Less often, genes such as CACNA1S are involved. These genes help control calcium movement within muscle cells.

Inheritance is usually autosomal dominant, meaning a person with a relevant variant can pass it to a child. However, not everyone with the variant will have a reaction, and some affected families have no identifiable genetic change.

Risk is higher if you have:

Previous general anaesthetics without problems do not rule out susceptibility. Earlier procedures may not have used a trigger, or exposure may not have caused a reaction.

Most susceptible people do not develop malignant hyperthermia from ordinary fever, exercise or hot weather. Some people with particular RYR1 variants can experience muscle breakdown after extreme heat or intense exercise, but this is not the usual anaesthetic-triggered reaction.

- A confirmed malignant hyperthermia susceptibility test
- A close relative with confirmed susceptibility or a previous reaction
- A previous unexplained reaction during general anaesthesia
- Certain muscle conditions linked to relevant genetic variants

Diagnosis

During an acute reaction, treatment starts as soon as malignant hyperthermia is suspected. The team does not wait for confirmation.

Clinicians look for rising exhaled carbon dioxide despite increased ventilation, muscle rigidity, a fast heartbeat, increasing temperature and muscle breakdown. Blood tests assess acidity, blood gases, potassium, kidney function, clotting and creatine kinase. Urine may be tested for myoglobin.

Other emergencies can resemble malignant hyperthermia, including inadequate ventilation, severe infection, heatstroke, thyroid crisis, serotonin syndrome and neuroleptic malignant syndrome. Anaesthetic exposure and timing help distinguish them.

After recovery, specialist testing may clarify ongoing susceptibility. The most sensitive established test uses a fresh muscle biopsy to measure contraction after exposure to caffeine and halothane. It is called the caffeine-halothane contracture test in North America and the in-vitro contracture test in Europe. Only specialist centres perform it.

A blood or saliva genetic test may identify a disease-causing variant and confirm susceptibility. A negative result does not always rule it out because not every responsible variant is known or detectable.

Relatives may be offered targeted testing if a familial variant is found. Otherwise, a specialist centre can advise whether muscle contracture testing is appropriate.

Treatment and management

A suspected reaction requires immediate treatment in the operating room or recovery area. The team stops triggering medicines and uses non-triggering anaesthesia if surgery must continue. The person receives high-flow oxygen and increased ventilation to remove excess carbon dioxide.

Dantrolene controls the abnormal calcium release in muscle. Further doses may be needed according to the person's response and emergency protocols.

Treatment may also include active cooling, intravenous fluids, correction of dangerous potassium levels and management of abnormal heart rhythms. Blood and urine tests are repeated to monitor muscle breakdown, kidney injury and clotting problems.

Cooling is stopped before body temperature becomes too low. Some medicines used for heart rhythm problems can interact dangerously with dantrolene, so the emergency team selects treatments carefully.

After the initial reaction is controlled, monitoring continues in critical care or another closely supervised unit because the reaction can return.

People known or suspected to be susceptible can usually still have surgery. The anaesthesia plan avoids triggers and uses prepared equipment. Regional and local anaesthesia and many intravenous anaesthetic medicines are not malignant hyperthermia triggers.

Complications

Complications are more likely when treatment is delayed. They can include:

Severe reactions can be fatal. Prompt dantrolene, cooling when needed and careful monitoring greatly improve the chance of recovery.

Dantrolene can cause temporary muscle weakness, nausea or irritation around the intravenous line. These effects are monitored in hospital and are less dangerous than an untreated reaction.

- Severe muscle breakdown
- Dangerous potassium levels and abnormal heart rhythms
- Acute kidney injury
- Blood-clotting problems
- Fluid in the lungs or breathing failure

- Brain injury from extreme temperature or reduced circulation
- Return of the reaction after initial improvement

Prevention

The inherited susceptibility cannot currently be removed, but an anaesthetic-triggered episode can usually be prevented by avoiding known triggers.

Tell surgical and anaesthesia teams before any procedure if you or a blood relative has had malignant hyperthermia, an unexplained anaesthetic emergency or a positive susceptibility test. Do this even for a minor procedure.

A medical alert bracelet, card or phone record can communicate the risk in an emergency. Keep copies of genetic results, muscle test reports and specialist letters.

Because susceptibility can run in families, relatives may benefit from assessment. Until their risk is clarified, close relatives may be advised to tell anaesthesia teams about the family history.

Routine vaccinations, ordinary fever medicines and local anaesthetics do not trigger malignant hyperthermia. Susceptible people do not usually need to avoid normal activities solely because of anaesthetic risk.

Living with it and what to expect

Between anaesthetic exposures, most susceptible people have no symptoms. Susceptibility usually remains lifelong, even after previous anaesthesia without a reaction.

Future surgery is possible. The anaesthesia team can choose non-triggering medicines, prepare the anaesthetic machine and monitor you closely. Procedures may need to take place where malignant hyperthermia can be managed.

After a severe reaction, muscle pain, weakness and tiredness may continue for days or weeks. Kidney function and muscle enzyme levels may need follow-up until they recover.

Follow-up may include reviewing hospital records, referral to a specialist testing centre, genetic counselling and discussing testing with relatives. Genetic counselling explains what results may mean for you and your family; it does not require testing.

If you feel anxious about future surgery, ask for a written anaesthesia plan and speak to the anaesthesia service early. Keep your records available if you move or receive care elsewhere.

When to get medical help

During or shortly after general anaesthesia, suspected malignant hyperthermia is an emergency. The hospital team should begin treatment immediately for unexplained rising carbon dioxide, muscle rigidity, rapidly increasing temperature, a severely fast heartbeat or other signs of the reaction.

After leaving hospital, call emergency services for a rapidly rising temperature with severe muscle stiffness, breathing difficulty, fainting, confusion, seizures or dark urine following recent anaesthesia. Do not drive yourself.

Seek urgent medical assessment after recent surgery if you develop dark or sharply reduced urine, worsening muscle pain, marked weakness, persistent fever, palpitations or repeated vomiting. These symptoms may require prompt blood and urine tests.

Arrange non-urgent follow-up if you have a family history of malignant hyperthermia, need help understanding previous anaesthetic records or want to discuss susceptibility testing before a procedure.

Common questions

Is fulminating hyperpyrexia the same as malignant hyperthermia?

The term generally describes a severe, rapidly developing malignant hyperthermia reaction. Malignant hyperthermia is preferred because extreme fever may be a late rather than early sign.

Can I have surgery if malignant hyperthermia runs in my family?

Usually, yes. The team can avoid triggering gases and succinylcholine and use a prepared anaesthetic system. Tell them as early as possible.

Can I have malignant hyperthermia after having safe anaesthetics before?

Yes. Previous uneventful anaesthesia does not exclude susceptibility.

Does a negative genetic test mean I am safe?

Not always. Genetic testing does not identify every susceptible person. A specialist may recommend muscle contracture testing based on your personal and family history.

Can local anaesthetic at the dentist trigger it?

Local anaesthetics are not triggers. Tell the dental team about your history, especially if sedation or general anaesthesia is planned.

Can ordinary fever turn into malignant hyperthermia?

No. Malignant hyperthermia is a specific muscle reaction, usually triggered by particular general anaesthetic drugs. A very high temperature still needs urgent assessment because infections, heatstroke and other conditions can also be serious.

Sources

- European Malignant Hyperthermia Group. Recommendations: Recognising and managing a malignant hyperthermia crisis
- European Malignant Hyperthermia Group. Testing for malignant hyperthermia susceptibility
- Hopkins PM, Girard T, Dalay S, and colleagues. Malignant hyperthermia 2020: Guideline from the Association of Anaesthetists . Anaesthesia. 2021;76:655-664
- Malignant Hyperthermia Association of the United States. Managing a Crisis and Safe and Unsafe Anesthetics
- Rosenberg H, Sambuughin N, Riazi S, Dirksen R. Malignant Hyperthermia Susceptibility . GeneReviews®, NCBI Bookshelf
- Gupta PK, Bilmen JG, Hopkins PM. Anaesthetic management of a known or suspected malignant hyperthermia susceptible patient . BJA Education. 2021;21(6):218-224