CONDITION

Subacute combined degeneration

Subacute combined degeneration is spinal cord damage caused mainly by vitamin B12 deficiency or nitrous oxide exposure.

WHAT IT IS
Spinal cord damage affecting movement and sensation

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Tingling, numbness, unsteady walking, weakness

WHAT CAUSES IT
Vitamin B12 deficiency or nitrous oxide exposure

HOW IT IS DIAGNOSED
Neurological examination, blood tests, and spinal cord MRI

MAIN TREATMENT
Vitamin B12 replacement and removal of the cause

CAN IT BE CURED?
Sometimes - early treatment may reverse damage

IS IT AN EMERGENCY?
Sometimes - rapidly worsening weakness or walking difficulty

LONG-TERM OUTLOOK
Early treatment improves the chance of neurological recovery

Overview

Subacute combined degeneration is damage to certain nerve pathways in the spinal cord. It mainly affects the pathways that carry information about touch, vibration, and body position, as well as pathways involved in movement.

"Subacute" means that symptoms usually develop over weeks or months rather than all at once. "Combined" refers to more than one part of the spinal cord being affected.

The usual cause is a lack of usable vitamin B12. Vitamin B12 helps maintain myelin, the protective covering around nerves. Without enough working vitamin B12, myelin can break down and nerve signals may not travel normally.

Heavy or repeated exposure to nitrous oxide can also cause the condition. Nitrous oxide can

switch off vitamin B12 inside the body, even when a standard blood test shows a normal or near-normal vitamin B12 level.

Subacute combined degeneration matters because untreated nerve damage can become permanent. Prompt assessment and treatment give nerves the best opportunity to recover.

Symptoms

Symptoms often begin in both feet or hands. They may slowly move upward or become more noticeable over time.

Common symptoms include:

Some people develop muscle stiffness, brisk reflexes, or involuntary muscle tightening. Others have reduced ankle reflexes because nerves outside the spinal cord are also affected.

Vitamin B12 deficiency may cause tiredness, shortness of breath, a sore tongue, pale skin, or other signs of anaemia. Anaemia means there are not enough healthy red blood cells. However, neurological symptoms can occur without anaemia or visibly enlarged red blood cells.

Less often, people experience memory problems, mood changes, confusion, visual changes, or problems controlling the bladder or bowel. These symptoms need medical assessment because they can have several causes.

- Tingling, "pins and needles," or burning feelings
- Numbness or reduced awareness of touch
- Poor balance, especially in the dark or with closed eyes
- Unsteady or stiff walking
- Leg weakness or heaviness
- Reduced awareness of where the feet or limbs are positioned
- Clumsy hand movements

Causes and risk factors

Subacute combined degeneration is most often linked to vitamin B12 deficiency. The body cannot make vitamin B12, so it must come from food or supplements. It also needs a healthy digestive system to absorb the vitamin.

Possible causes and risk factors include:

Nitrous oxide deserves special attention because it causes a functional deficiency. This means vitamin B12 is present but cannot work properly. Symptoms can therefore occur despite a vitamin B12 result that appears within the laboratory range.

Copper deficiency can produce a very similar pattern of spinal cord damage. It may be considered when vitamin B12 testing does not explain the symptoms, especially after certain digestive surgeries or with excessive zinc exposure.

- Pernicious anaemia: An autoimmune condition that prevents normal vitamin B12 absorption. The immune system attacks cells or proteins needed to absorb the vitamin.
- Stomach or bowel surgery: Procedures involving the stomach or the final part of the small bowel can reduce absorption.
- Digestive conditions: Coeliac disease, Crohn's disease, and other conditions affecting the small bowel may interfere with absorption.
- Low dietary intake: Vitamin B12 occurs naturally in animal-derived foods. People eating a vegan or very restricted diet may need fortified foods or supplements.
- Certain medicines: Long-term use of metformin or medicines that reduce stomach acid can contribute to low vitamin B12 in some people.
- Nitrous oxide exposure: Repeated recreational use is an important cause. Medical or dental exposure may also be relevant in someone who already has low vitamin B12.
- Rare absorption or metabolism conditions: Inherited problems involving vitamin B12 are uncommon but can cause neurological symptoms.

Diagnosis

There is no single test that confirms every case. Diagnosis is based on your symptoms, a neurological examination, blood tests, and sometimes imaging.

During the examination, a clinician may check strength, reflexes, coordination, walking, and the ability to feel vibration or know the position of a toe or finger.

Blood tests commonly include vitamin B12 and a full blood count. Additional tests may measure:

Recent vitamin B12 supplements can change test results. Nitrous oxide exposure may also make a standard vitamin B12 result misleading. It is important to describe any supplement use and nitrous oxide exposure honestly. This information helps with diagnosis and is treated as part of healthcare.

MRI, or magnetic resonance imaging, may show changes in the back part of the spinal cord,

often in the neck or upper back. A normal MRI does not completely exclude the condition.

Further tests may look for the cause. These can include tests for antibodies linked to pernicious anaemia or investigations for digestive conditions. Nerve conduction studies may be used if damage to nerves outside the spinal cord is suspected.

Other conditions can cause similar symptoms, including spinal cord compression, multiple sclerosis, infection, copper deficiency, and some inherited neurological conditions. Assessment is needed to separate these possibilities.

- Methylmalonic acid: A substance that often rises when cells lack usable vitamin B12
- Homocysteine: Another substance that can rise, although it is less specific
- Folate: A different B vitamin that can also affect blood cells
- Copper: Used when copper deficiency is a possible explanation

Treatment and management

Treatment aims to restore usable vitamin B12 quickly and address the reason it became low or inactive. When neurological symptoms are present, treatment may begin before every test result is available if the clinical concern is strong.

Vitamin B12 can be given by injection or, in selected situations, by high-dose tablets. The route and length of treatment are based on the severity of symptoms and whether the underlying cause can be corrected. People who cannot absorb vitamin B12 normally may need ongoing replacement.

If nitrous oxide is involved, stopping exposure is essential. Vitamin B12 treatment may not work properly if nitrous oxide use continues. Support for substance use can be included without judgment.

Treatment may also involve:

Folate should not be used on its own as a substitute for vitamin B12 treatment. Folate may improve the blood count while vitamin B12-related nerve damage continues.

Recovery is assessed through changes in sensation, strength, balance, and daily function. Blood levels may improve before neurological symptoms do, so follow-up should include how you are feeling and moving, not only laboratory results.

- Physiotherapy to improve strength, balance, and walking
- Occupational therapy to make daily activities safer

- Walking aids when needed
- Treatment of an underlying digestive condition
- Dietary advice when low intake contributed
- Follow-up blood tests and neurological examinations

Complications

Subacute combined degeneration can affect independence and mobility. Poor balance or reduced awareness of foot position can lead to falls and injuries.

Possible complications include:

The risk of lasting problems is greater when treatment is delayed or symptoms are advanced. Even after treatment begins, recovery may be slow because nerves heal more gradually than blood abnormalities.

- Persistent numbness or nerve pain
- Long-term walking difficulty
- Muscle weakness or stiffness
- Reduced hand coordination
- Bladder or bowel problems
- Vision or cognitive changes
- Permanent spinal cord or peripheral nerve damage

Prevention

Not every case can be prevented. Pernicious anaemia and inherited problems affecting vitamin B12 cannot usually be prevented, but their neurological effects may be reduced through recognition and reliable replacement treatment.

If you eat little or no animal-derived food, fortified foods or a suitable vitamin B12 supplement can prevent dietary deficiency. People with digestive conditions, previous stomach or bowel surgery, or medicines linked to low vitamin B12 may need monitoring based on their clinical situation.

Avoiding recreational nitrous oxide prevents the functional vitamin B12 deficiency it can cause. Taking vitamin B12 alongside ongoing nitrous oxide use does not make the exposure safe.

If you have a known absorption problem, following the recommended replacement plan is important even when you feel well. Stopping treatment without review may allow deficiency to return.

Living with it and what to expect

The course differs from person to person. Some people notice improvement within weeks of starting treatment, but nerve recovery often continues over months. Balance, sensation, and fine movement may take longer to improve than tiredness or blood test results.

People treated early may recover substantially. Others are left with numbness, altered sensation, stiffness, or walking difficulty. Symptoms that were severe or present for a long time are less likely to disappear fully.

Rehabilitation can help even when some nerve damage remains. Physiotherapy may improve confidence, strength, and safer movement. Occupational therapy can suggest changes for bathing, dressing, work, or home safety.

During recovery, it may help to reduce fall risks. Good lighting, secure footwear, handrails, and the correct walking aid can make daily activities safer. Reduced feeling in the feet also makes it important to check for cuts, pressure areas, or burns.

Ongoing treatment depends on the cause. A temporary dietary deficiency may be corrected, while pernicious anaemia or permanent malabsorption often requires long-term vitamin B12 replacement. Follow-up should check both symptoms and whether treatment is controlling the underlying deficiency.

When to get medical help

Arrange prompt medical assessment if you develop new tingling, numbness, poor balance, leg stiffness, weakness, or difficulty walking. This is particularly important if symptoms affect both sides, are spreading, or occur after nitrous oxide exposure.

Seek urgent same-day care if weakness or walking difficulty is worsening quickly, or if you develop new problems with bladder or bowel control.

Call emergency services if you:

Sudden one-sided symptoms are not typical of subacute combined degeneration and may indicate a stroke or another emergency.

Routine follow-up is appropriate for monitoring recovery, reviewing vitamin B12 replacement,

checking an ongoing absorption problem, and discussing persistent symptoms that are stable rather than rapidly worsening.

- Suddenly cannot stand or walk
- Develop rapidly increasing weakness
- Lose bladder or bowel control with numbness around the groin
- Have severe confusion, collapse, or difficulty breathing
- Develop sudden facial drooping, one-sided weakness, or speech difficulty

Common questions

Can subacute combined degeneration go away completely?

Sometimes. Early vitamin B12 treatment can lead to major improvement, and some people recover fully. Long-standing or severe nerve damage may not completely reverse.

How quickly does vitamin B12 treatment work?

Blood abnormalities may improve relatively quickly, but neurological recovery usually takes longer. Changes in balance, strength, and sensation may continue over several months.

Can I have this condition without anaemia?

Yes. Spinal cord and nerve symptoms can occur even when the red blood cell count and cell size appear normal. A normal blood count does not rule it out.

Can my vitamin B12 level be normal?

It can be normal or borderline in some cases, especially after taking supplements or when nitrous oxide has made the vitamin inactive. Methylmalonic acid, homocysteine, symptoms, examination findings, and MRI may provide additional information.

Is subacute combined degeneration the same as multiple sclerosis?

No. Both can affect the spinal cord, but they have different causes and treatments. MRI findings, blood tests, symptoms, and the clinical examination help distinguish them.

Can nitrous oxide really damage the spinal cord?

Yes. Repeated or heavy exposure can inactivate vitamin B12 and damage the spinal cord and peripheral nerves. Continuing nitrous oxide exposure can prevent recovery and cause further injury.

Sources

- National Institute for Health and Care Excellence. Vitamin B12 deficiency in over 16s: diagnosis and management . NICE guideline NG239, 2024.
- Devalia V, Hamilton MS, Molloy AM. Guidelines for the diagnosis and treatment of cobalamin and folate disorders . British Journal of Haematology. 2014;166(4):496-513.
- Reynolds E. Vitamin B12, folic acid, and the nervous system . The Lancet Neurology. 2006;5(11):949-960.
- Keddie S, Adams A, Kelso ARC, et al. No laughing matter: subacute degeneration of the spinal cord due to nitrous oxide inhalation . Journal of Neurology. 2018;265:1089-1095.
- Green R, Allen LH, Bjørke-Monsen AL, et al. Vitamin B12 deficiency . Nature Reviews Disease Primers. 2017;3:17040.
- Merck Manual Professional Edition. Subacute combined degeneration . Neurologic disorders reference.