CONDITION

Exogenous Cushing syndrome

Exogenous Cushing syndrome is caused by prolonged exposure to glucocorticoid medicines that act like the hormone cortisol.

WHAT IT IS
Cushing syndrome caused by glucocorticoid medicines

BODY SYSTEM
Hormones and the whole body

MAIN SYMPTOMS
Central weight gain, rounded face, bruising, muscle weakness

WHAT CAUSES IT
Long-term or high-dose glucocorticoid exposure

HOW IT IS DIAGNOSED
Medication history, examination, and cortisol testing when needed

MAIN TREATMENT
Supervised glucocorticoid reduction and complication care

CAN IT BE CURED?
Sometimes - improves after glucocorticoids are safely reduced

IS IT AN EMERGENCY?
Sometimes - adrenal crisis needs emergency treatment

LONG-TERM OUTLOOK
Often improves, but recovery may take months

Overview

Exogenous Cushing syndrome happens when your body is exposed to too much glucocorticoid medicine over time. Glucocorticoids act like cortisol, a hormone made by the adrenal glands above the kidneys.

These medicines include hydrocortisone, prednisone, prednisolone, methylprednisolone and dexamethasone. They are often called corticosteroids or steroids like prednisone or hydrocortisone but are different from anabolic steroids used to increase muscle size.

Glucocorticoids treat serious inflammation, allergic reactions and immune system conditions. They may be given as tablets, injections, inhalers, nasal sprays, creams, eye drops or joint injections. Cushing syndrome is more likely with treatment that reaches the whole body, although high-strength or interacting products can also cause it.

Prolonged exposure can affect weight, muscles, skin, bones, blood pressure, blood sugar, mood and resistance to infection. It can also suppress the adrenal glands, reducing the body's own cortisol production.

"Exogenous" means the excess steroid comes from outside the body. Endogenous Cushing syndrome occurs when the body produces too much cortisol.

Symptoms

Symptoms usually develop gradually and depend on the medicine, dose, route, treatment length and individual sensitivity.

Possible changes include:

Not everyone develops a rounded face or purple stretch marks. High blood pressure, bone loss and raised blood sugar may initially cause no symptoms. The illness being treated can also cause tiredness, weight changes or weakness, making the cause less clear.

- Weight gain around the abdomen, chest, neck or face
- A rounder or fuller face
- A pad of fat at the upper back or base of the neck
- Thinner limbs and weakness in the shoulders or thighs
- Thin skin, easy bruising and slow wound healing
- Wide reddish-purple stretch marks, often on the abdomen
- Acne or increased facial and body hair
- Irregular periods or reduced sexual interest
- Anxiety, irritability, low mood or other mood changes
- Poor sleep, tiredness or difficulty concentrating
- High blood pressure or raised blood sugar
- Frequent or harder-to-clear infections
- Back pain or fractures caused by weakened bones
- Slower growth and increased weight gain in children

Causes and risk factors

The cause is exposure to a glucocorticoid medicine. Risk generally increases with total exposure, but no single dose or treatment length predicts the condition in everyone.

Tablets and repeated injections are common causes because they can affect the whole body. Repeated injections into joints or soft tissues may also have systemic effects.

Strong steroid creams can be absorbed through the skin, especially when used over large or damaged areas or under airtight dressings. Inhaled, nasal and eye preparations can contribute at high doses or when several steroid products are combined.

Some medicines slow glucocorticoid breakdown. These include ritonavir or cobicistat, used with some HIV treatments, and certain antifungal medicines. Interactions can greatly increase exposure to steroids such as fluticasone or budesonide.

Risk may be higher when you:

Herbal, bodybuilding and skin-lightening products can contain undeclared glucocorticoids. Tell your healthcare team about all non-prescription and prescribed products.

- Use more than one glucocorticoid product
- Need treatment for many weeks or months
- Receive repeated courses or injections
- Use a strong skin preparation over a large area
- Have liver or kidney problems that affect medicine handling
- Take another medicine that raises glucocorticoid levels

Diagnosis

Diagnosis begins with a detailed medicine history covering tablets, injections, inhalers, sprays, creams, eye drops and non-prescription products. The timing of symptoms in relation to treatment is important.

An examination may identify thin skin, bruising, central weight gain or muscle weakness. Blood pressure and weight may be checked, along with growth in children.

Exogenous Cushing syndrome often suppresses the body's own cortisol production, so a morning blood cortisol result may be low. An adrenocorticotropic hormone, or ACTH, test may also be used. ACTH is the pituitary hormone that signals the adrenal glands to make cortisol.

Testing may not be needed to identify the cause when glucocorticoid exposure and physical changes are clear. Cortisol testing is often used to assess adrenal suppression and recovery. An ACTH stimulation test can check how well the adrenal glands respond when stimulated.

Tests used to investigate cortisol produced inside the body may not be appropriate while you are taking glucocorticoids. Your healthcare team may also assess blood sugar, cholesterol, blood pressure, bone health and possible infection.

Treatment and management

Treatment aims to reduce glucocorticoid exposure while continuing to control the condition for which it was prescribed.

Do not suddenly stop long-term glucocorticoid treatment. Suppressed adrenal glands may not immediately produce enough cortisol. Abrupt withdrawal can cause adrenal insufficiency and, in severe cases, an adrenal crisis.

A treatment plan may involve:

A gradual reduction is called a taper. It may need to slow as the dose becomes lower. The schedule depends on the underlying illness, previous exposure, symptoms and adrenal recovery.

Some people need a temporary replacement dose after treatment for the original illness ends. During serious illness, surgery or injury, a higher "stress dose" may be needed until adrenal function recovers.

If you are at risk of adrenal insufficiency, you may be advised to carry a steroid emergency card or medical alert identification. Some people also receive an emergency injection kit and instructions for using it.

Surgery is not usually needed because the source of excess steroid is a medicine rather than a tumour.

- Gradually reducing the glucocorticoid under medical supervision
- Changing the steroid's route, strength or type
- Using the lowest exposure that controls the underlying condition
- Considering non-steroid or steroid-sparing treatments
- Reviewing medicines that may interact with the glucocorticoid
- Treating diabetes, high blood pressure, bone loss or other complications

Complications

Prolonged glucocorticoid exposure can cause:

Adrenal insufficiency is particularly important during and after steroid reduction. The body normally releases extra cortisol during illness, injury or surgery, but suppressed adrenal glands may not meet that need.

Some complications improve after exposure is reduced. Others, including fractures or cataracts, may need separate treatment and can have lasting effects.

- Adrenal insufficiency
- Type 2 diabetes or worsening diabetes
- High blood pressure and unhealthy cholesterol levels
- Osteoporosis and fractures
- Muscle loss and reduced strength
- Cataracts or glaucoma
- Increased or masked infection
- Blood clots
- Menstrual, fertility or sexual problems
- Mood disorders, confusion or, rarely, severe psychiatric symptoms
- Slower growth in children

Prevention

Risk can sometimes be reduced by limiting unnecessary glucocorticoid exposure. However, these medicines may be essential for serious conditions, and needing them is not your fault.

Have all steroid products reviewed together. Use them only as directed, and do not increase, repeat or extend treatment without advice. Ensure each prescriber knows about steroid tablets, injections, inhalers, nasal sprays, creams and eye drops prescribed elsewhere.

Interactions should be checked before starting a new medicine, particularly if you use ritonavir, cobicistat or certain antifungal treatments.

Regular follow-up can identify high blood pressure, raised blood sugar, bone loss or growth problems early. Do not stop necessary treatment simply to avoid Cushing syndrome.

Living with it and what to expect

Recovery usually takes time. Facial fullness, bruising, sleep disturbance and central weight gain

may improve after glucocorticoids are safely reduced, but this can take months. Muscle strength often returns gradually and may benefit from paced activity or rehabilitation.

The adrenal glands may remain suppressed after visible features improve. Recovery can take months and sometimes longer than a year. Blood tests may be needed before steroid precautions are stopped.

Weight and blood sugar may improve, while stretch marks may fade without disappearing. Bone loss, fractures, cataracts or diabetes complications may require long-term care.

Reducing steroids can allow the original inflammatory or immune condition to flare. A slower taper or another treatment may be needed. Tiredness, aching and low mood can occur during withdrawal even when cortisol testing is reassuring.

Follow-up commonly covers the underlying condition, adrenal recovery, blood pressure, blood sugar and bone health.

When to get medical help

Seek emergency help if you may have adrenal insufficiency and develop signs of an adrenal crisis, including:

Follow your emergency steroid plan if you have one, but do not delay emergency care.

Get urgent medical advice for fever or signs of infection while using glucocorticoids because steroids can weaken or hide the usual immune response. New severe mood changes, hallucinations, marked confusion, sudden vision changes or symptoms of very high blood sugar also need prompt assessment.

Arrange routine follow-up for gradual weight or facial changes, easy bruising, muscle weakness, irregular periods or slower growth in a child. Also request a review if you use several steroid products or need repeated courses or injections.

- Severe weakness, collapse or fainting
- Repeated vomiting or inability to keep steroid medicine down
- Severe abdominal pain with vomiting or diarrhoea
- Confusion, extreme drowsiness or loss of consciousness
- Signs of very low blood pressure, such as faintness and cold, clammy skin

Common questions

Is exogenous Cushing syndrome the same as Cushing disease?

No. Cushing disease is caused by a pituitary tumour that produces too much ACTH, causing the adrenal glands to make excess cortisol. Exogenous Cushing syndrome is caused by glucocorticoid medicine.

Can an inhaler, nasal spray or skin cream cause it?

Yes, although the risk is usually greater with glucocorticoids that affect the whole body. Risk rises with high-strength products, prolonged use, several steroid products or medicines that slow steroid breakdown.

Can I stop prednisone if I have Cushing symptoms?

Do not suddenly stop long-term prednisone or another systemic glucocorticoid. Your adrenal glands may be suppressed, and the condition being treated could flare. A supervised reduction is usually required.

Will my face and weight return to normal?

Facial fullness and central weight gain often improve after exposure is reduced, but recovery is gradual and varies. Some people have lasting weight or skin changes.

How long does adrenal recovery take?

Recovery may take months and sometimes longer than a year. Appearance alone cannot confirm recovery. Morning cortisol testing and, sometimes, an ACTH stimulation test can assess adrenal function.

Can exogenous Cushing syndrome come back?

Yes. It can return if glucocorticoid exposure increases again. Future treatment may still be possible when medically necessary, but your previous reaction should inform the medicine, route and monitoring plan.

Sources

- National Institute of Diabetes and Digestive and Kidney Diseases: Cushing's Syndrome
- Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology & Metabolism . 2015
- European Society of Endocrinology and Endocrine Society. Diagnosis and Therapy of Glucocorticoid-Induced Adrenal Insufficiency: Joint Clinical Practice Guideline. European Journal of Endocrinology . 2024

- Arlt W. Society for Endocrinology emergency guidance: Emergency management of acute adrenal insufficiency in adult patients. Endocrine Connections . 2016
- Liu D, Ahmet A, Ward L, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, Asthma & Clinical Immunology . 2013
- UK Medicines and Healthcare products Regulatory Agency: Cobicistat, ritonavir and coadministration with a steroid-risk of systemic corticosteroid adverse effects. 2016