A GUIDE TO CUSHING'S DISEASE

Australian Pituitary Foundation

WHAT IS CUSHING'S DISEASE?

Cushing's disease occurs when your body is exposed to high levels of the steroid hormone cortisol. Causes include:

- A pituitary tumour that causes your body to make excess adrenocorticotropic hormone (ACTH), which in turn leads to your adrenal glands producing too much cortisol (called Cushing's disease).
- A tumour from somewhere else in the body e.g. in the lung, that also can produce excess ACTH (called ectopic Cushing's syndrome).
- An adrenal tumour that produces too much cortisol.
- Using steroid medications for a long time.

Cortisol is the main hormone that helps your body deal with physical stress (such as injury or infection), controls blood sugar levels and blood pressure and reduces inflammation.

HOW COMMON IS CUSHING'S DISEASE?

Around 300 to 1,600 Australians are living with Cushing's disease. Each year, about 41 people receive a diagnosis..

WHAT ARE THE SIGNS AND SYMPTOMS?

Cushing's disease can be hard to diagnose as many signs are common in other health issues. Symptoms tend to come on slowly over time.

Physical Signs

- Thin, fragile skin that bruises easily
- Red and purple streaks across the skin
- Muscle loss and weakness
- Weight gain, often around the waist
- Increased back fat between the shoulders (a "buffalo" hump)
- Rounded face
- Irregular or no periods
- Hirsutism in women (excess growth of facial and body hair)
- Reduced growth in children
- Infertility
- Poor wound healing

General Signs

- Fatigue/lethargy
- Poor quality of life
- Poor school/work performance

Emotional changes

- Depression
- Anxiety
- Unable to think clearly
- Mood and behaviour changes
- Increased irritability
- Decreased libido

Other conditions[4]

- Osteoporosis
- Fractures
- High blood pressure
- High blood glucose/diabetes
- Infections e.g skin fungal

DIAGNOSIS

If you have signs of Cushing's disease, you will need tests to confirm a diagnosis. No single test can diagnose Cushing's disease. Common tests include:

- **Blood tests** – to measure hormone levels
- **24-hour urinary free cortisol tests** – to measure daily cortisol production
- **Late night or midnight salivary cortisol tests** – to check for loss of daily cortisol rhythm
- **Overnight dexamethasone suppression tests** – to see if your body can suppress cortisol production normally
- **Scans** – a magnetic resonance imaging (MRI) or computerised tomography (CT) scan can see the pituitary and/or adrenal glands.

Other tests you may need include:

- **Inferior petrosal sinus sampling (IPSS)** – to check whether ACTH is being released from the pituitary gland or elsewhere
- **Visual field test** – to check for vision loss
- **Bone mineral density (BMD) test** – to check your bone health.

If the test results suggest Cushing's disease, your doctor may order more tests to find the reason for high cortisol levels.

Around one in six people with Cushing's disease have cyclical Cushing's syndrome, meaning they have periods of normal or even low cortisol levels and high cortisol production.

If you have cyclical Cushing's syndrome, your results can appear normal, depending on when you have the tests. You may need further tests to catch a period of high cortisol production.

TREATMENT

Treatment aims to restore your cortisol to normal levels, and improve your symptoms and your quality of life. Your medical team will need to tailor your treatment depending on factors such as:

- Age
- Sex
- Tumour size
- Hormone levels
- Fertility concerns
- Medications
- Other medical conditions
- Side effects.

Treatment options include:

- **Surgery** – to remove or reduce the size of the tumour
- **Radiotherapy** – to reduce cortisol levels if surgery does not help
- **Medication** – to control cortisol levels
- **Removal of adrenal glands (bilateral adrenalectomy)** – used when cortisol levels are unable to be controlled adequately by surgery, radiotherapy, medication or all 3; and sometimes if pregnancy is desired when surgery has not been successful.

Medications can reduce high cortisol levels before surgery, between surgery and radiotherapy, and while waiting for radiotherapy to take effect. They

- **Reduce the production of cortisol from the adrenal glands** – osilodrostat, ketoconazole, metyrapone, mitotane
- **Prevent the pituitary gland from releasing ACTH** – cabergoline and pasireotide
- **Block the action of cortisol around the body** – mifepristone.

WHAT HAPPENS AFTER SURGERY?

- **Cortisol levels can remain high (hypercortisolaemia)** – your medical team will determine your next steps
- **Cortisol levels return to normal (eucortisolaemia)** – your doctor will monitor your cortisol levels as they may change over time
- **Cortisol levels can be low (hypocortisolaemia)**, indicating a successful surgery; however, you may need steroid therapy for six to 12 months or longer.

Hormone changes after surgery may cause new symptoms, such as nausea, fatigue, depression and anxiety. You can notice signs even if you are taking cortisol medication. You may need to allow up to a year or more to recover fully. Your medical team will give you information about cortisol replacement medications and how to adjust the dose when stressed or ill. It is also essential to wear a medical alert tag and carry instructions for emergency steroid treatment.

WHAT IS THE LONG TERM PLAN?

There is a high recurrence rate in people with Cushing's disease. Life-long monitoring is essential and therefore you must:

- Check your hormone levels stay within the healthy range (including cortisol and other pituitary hormones)
- Check for tumour regrowth
- Adjust any medication as needed.

Surgery and radiotherapy can cause hypopituitarism in some people, where the pituitary gland can't produce other pituitary hormones. If this occurs, you may need long-term hormone replacement therapy.

COMMON QUESTIONS

Why am I putting on weight?

Cortisol converts proteins, carbs and fats into energy. Your body stores the energy you don't need as fat. High cortisol levels can lead to long-term fat accumulation.

Why am I getting facial hair?

ACTH stimulates the adrenal gland to produce androgens, which promote facial hair growth.

Why do I bruise so easily?

Cortisol increases the breakdown of tissue proteins, causing the tiny blood vessels near the skin (capillaries) to become weak, break easily and cause bruising.

Does Cushing's disease run in families?

Most cases of Cushing's disease are not inherited.

Why do I have stretch marks?

Cortisol causes an increased breakdown of proteins in the skin, which makes the skin more fragile.

Why do I feel so weak?

Muscle wasting, which mainly affects muscles in the upper arms and thighs, can also occur with the breakdown of proteins. You may find it difficult to climb stairs or stand after sitting. Extra weight can also strain your muscles, causing pain and fatigue.

Why am I so moody?

The excess hormone produced by the tumour affects your brain and can cause dramatic mood swings.

Will I be cured after treatment?

Cushing's syndrome can be controlled or put in remission in most cases using either surgery, radiotherapy, medication or a combination. However, Cushing's disease can recur or cortisol levels rise again even after years of followup. Regular follow- up appointments with your endocrinologist are essential.

MORE INFORMATION

The Australian Pituitary Foundation provides social support for patients and carers, and has published a range of patient resources on pituitary conditions and treatments.

For more information, please visit our website: www.pituitary.asn.au

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