

2 THE CAUSES OF ADDISON'S AND RELATED AUTOIMMUNE DISEASES

a) PRIMARY AND SECONDARY ADRENAL DISEASE

Addison's disease is a rare condition where the adrenal glands gradually cease to function. The disease is not usually apparent until over 90% of the adrenal cortex has been destroyed, so that very little adrenal capacity is left. Symptoms of the disease, once advanced, can include severe fatigue and weakness, loss of weight, increased pigmentation of the skin, faintness and low blood pressure, nausea, vomiting, salt cravings, and painful muscles and joints.

The adrenal glands sit at the top of the kidneys, one on each side of the body, and have an inner core (known as the *medulla*) surrounded by the outer shell (known as the *cortex*). The inner medulla produces adrenaline, the 'fight or flight' stress hormone. The outer cortex produces the steroid hormones that are essential for life: cortisol and aldosterone. It also produces sex hormones known as adrenal androgens; the most important of these is DHEA.

Addison's disease is not an 'all or nothing' condition. In the early stages of the disease many individuals are still able to produce some cortisol and enough aldosterone. This is partly why individuals with the disease take varying amounts of medication and why the amount of medication you need may alter over the years.

Dr Thomas Addison first identified the disease in the mid 1800s while working at an inner-city London hospital. Then, the main cause of the disease was as a complication of tuberculosis. In third world countries today, tuberculosis remains an important cause of Addison's. HIV (AIDS) is now becoming another significant infectious disease causing adrenal failure among third world populations.

Among more affluent countries, the main cause of the disease today is *autoimmune adrenalitis*, where an over-active

immune system starts attacking the body's own organs. Autoimmune adrenalitis now accounts for around 70% of all cases, and affects more women than men. The cause of autoimmune adrenalitis is not known, in common with most other autoimmune diseases.

Other, much rarer causes of Addison's include certain fungal infections, adrenal cancer and adrenal haemorrhage (for example, following a car accident). In some cases it can result from the treatment needed for *Cushing's disease* (overproduction of adrenal hormones).

Certain rare hereditary diseases also cause adrenal insufficiency (such as adrenoleukodystrophy and congenital adrenal hyperplasia).

All of the conditions mentioned above are described as 'primary adrenal insufficiency', because they result from a disease process that has directly affected the adrenal glands.

Secondary adrenal insufficiency is sometimes informally described as 'Addison's', although it has a very different cause. Secondary adrenal insufficiency mostly occurs when a pituitary tumour (such as an *adenoma*) forms, although autoimmune destruction of the pituitary gland is also known. Secondary adrenal insufficiency is even rarer than primary Addison's disease.

Secondary loss of adrenal function occurs when the messenger hormone, which stimulates the adrenal glands into action, is no longer produced by the pituitary gland. The pituitary gland is located inside the skull, just behind the eyes and tucked below the grey matter of the brain. This messenger hormone is called *ACTH* and is responsible for the extra pigmentation found in primary Addison's. People with secondary adrenal failure do not experience the increased pigmentation found in primary Addison's, because their ACTH levels are declining.

Long-term use of high doses of steroid drugs to treat other illnesses (such as the high doses of prednisone which may be used to treat bowel disease or asthma) can also cause temporary or permanent loss of adrenal function. This is often referred to as *secondary adrenal suppression*.

b) RELATED AUTOIMMUNE CONDITIONS

Where Addison's disease is autoimmune, around half of those with the condition will develop another autoimmune disorder, usually another endocrine condition.

The most common endocrine disorder associated with Addison's is a thyroid problem, either *hyperthyroidism* or *hypothyroidism*. Most medical studies have found that just over one-fifth of those with autoimmune Addison's are likely to develop a thyroid problem of some kind.

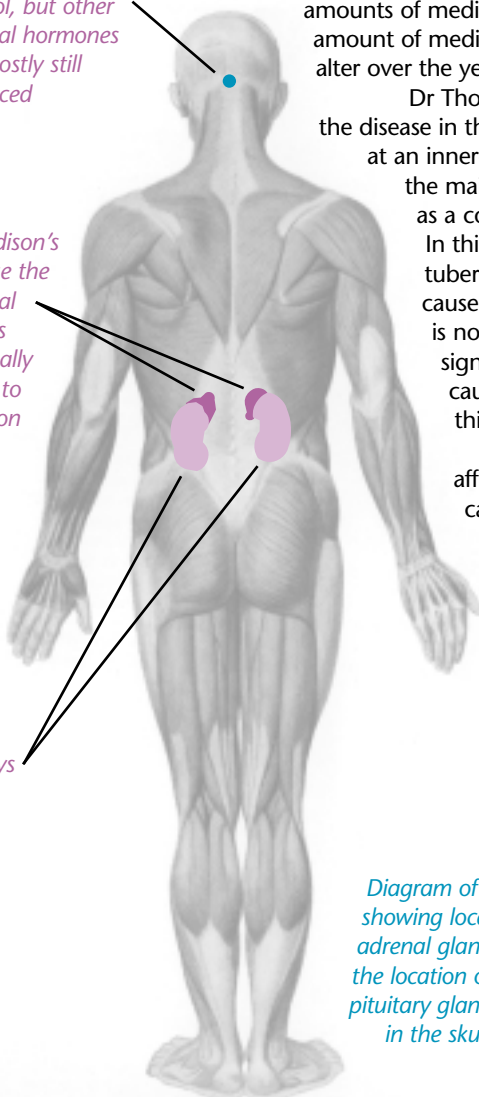
Other recognised associations include premature failure of the ovaries, insulin-dependent diabetes (*type 1 diabetes*) and parathyroid deficiency. These all occur less frequently than thyroid disorders.

In secondary adrenal insufficiency the pituitary gland no longer triggers the adrenals to produce cortisol, but other adrenal hormones are mostly still produced

In Addison's disease the adrenal glands gradually cease to function

Kidneys

Diagram of body showing location of adrenal glands and the location of the pituitary gland in the skull



A few people with autoimmune Addison's develop a combination of related autoimmune conditions, which are known as a *polyglandular autoimmune syndrome*.

Non-endocrine autoimmune diseases sometimes also occur in combination with autoimmune Addison's. Although these are seen less frequently than the endocrine conditions mentioned above, a very small number of people find they develop both endocrine and non-endocrine autoimmune conditions related to their Addison's.

Medical studies estimate that around 5% of individuals with autoimmune Addison's develop *pernicious anaemia* (vitamin B12 deficiency). Much smaller proportions are estimated to develop conditions such as *vitiligo* (loss of pigmentation from parts of the skin), *coeliac disease* (gluten allergy), *alopecia* (hair loss), *myasthenia gravis* (muscle wasting), *thrombocytopenia purpura* (loss of blood

platelets), *Sjogren's syndrome* (dry eyes and mouth) or rheumatoid arthritis.

Autoimmune Addison's is not usually a directly inherited condition. But a tendency to autoimmune diseases does seem to run in some families. Where autoimmune Addison's occurs on its own, some kind of family association with the condition can be traced in about one-third of cases. Where it occurs as part of a polyglandular syndrome, some kind of family history of related autoimmune diseases can usually be found in about half the cases.

Where a tendency to autoimmune endocrine disorders is inherited, it is often not the same condition as the parent/grandparent but some other related autoimmune condition, which appears in the next generation. For example, a grandmother with Addison's disease may see one of her grandchildren develop vitiligo or a thyroid condition.