

Case 109 A girl with hirsutes

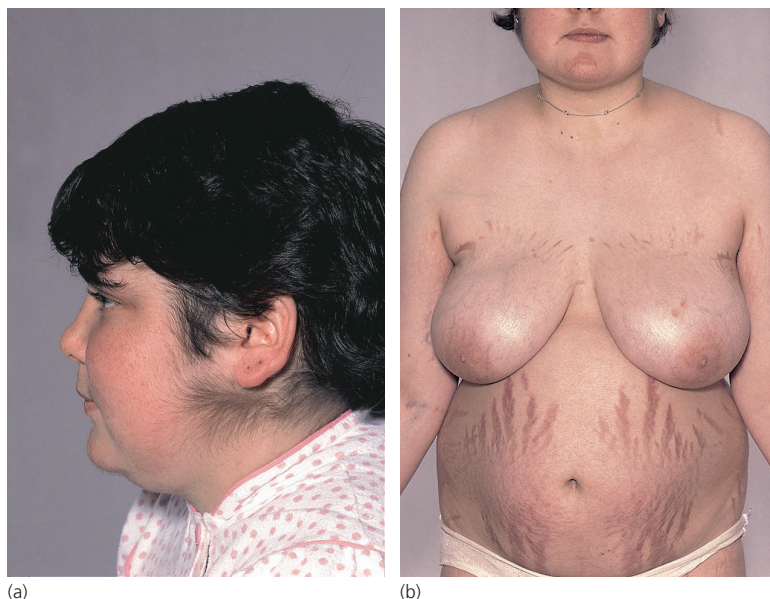


Figure 109.1

Figure 109.1a shows the side view of the face of a 17-year-old school girl who was brought by her mother to the family doctor. She was seriously worried by the growth of hair on her face. When the doctor examined her fully, there were also striking findings on inspection of the abdomen (Fig. 109.1b).

What is the eponymous name of the endocrine disease from which she is suffering?

Cushing's syndrome.*

What are the possible causes of this condition?

Cushing's syndrome occurs when there is prolonged exposure to supraphysiological levels of circulating glu-

corticoids. The aetiology of Cushing's syndrome is most easily considered in terms of whether it is adrenocorticotrophic hormone (ACTH) dependent or independent:

1 ACTH-dependent Cushing's syndrome:

- Pituitary adenoma (the original disease described by Cushing).
- Ectopic ACTH secretion (e.g. from a small cell carcinoma of the lung).

2 ACTH-independent Cushing's syndrome:

- Exogenous steroids.
- Adrenal adenoma or carcinoma.

The effects of oversecretion of adrenal corticosteroids are widespread. Can you list the most important of these?

- Obesity: Principally involving the trunk and neck – so-called centripetal.

*Harvey Cushing (1869–1939), neurosurgeon, Peter Bent Brigham Hospital, Boston.

- Skin changes: Hirsutism, abdominal striae, excessive bruising, thin skin.
- Raised blood pressure.
- Proximal muscle weakness/wasting: Especially of the shoulder and pelvic girdles.
- Glucose intolerance/diabetes mellitus.
- Mental disturbance: Depression or psychosis.
- Growth retardation in childhood.

What laboratory and imaging investigations are useful in such cases?

The investigation of Cushing's syndrome should be considered in two stages.

1 Confirmation of hypercortisolism: Typically two or more of the following tests are used to confirm the diagnosis:

- Elevated 24 h urinary free cortisol (UFC) excretion – a minimum of three collections are required to ensure that mild cases are not missed.
- Failure of cortisol to suppress in response to dexamethasone. An overnight test administering 1 mg dexamethasone is often used for screening purposes, but has a significant false-positive rate, hence the conventional low dose 48 h test (0.5 mg 6-hourly for 48 h) should be used to confirm the diagnosis.

- Loss of circadian rhythm, with elevated midnight cortisol levels.

- Late night salivary cortisol

2 Identification of source: Measurement of the plasma ACTH helps to differentiate ACTH-dependent from ACTH-independent Cushing's syndrome.

- For ACTH-dependent cases, inferior petrosal venous sinus sampling (IPSS) reliably distinguishes pituitary from ectopic ACTH secretion. Pituitary MR imaging identifies approximately 60% of microadenomas. CT imaging, octreotide scintigraphy and positron emission tomography can be used to help localize ectopic tumours.
- For ACTH-independent cases (low/undetectable levels), a CT scan of the adrenal glands is the next appropriate investigation.

What treatment is available for patients with Cushing's syndrome?

In those patients where an adrenal tumour is found, adrenalectomy is performed. Trans-sphenoidal microsurgery is used to remove a pituitary adenoma. Medical pre-treatment with drugs such as metyrapone and ketoconazole can help to control hypercortisolaemia prior to surgery.