Diagnosis of adrenal insufficiency

The short tetracosactrin test can almost always replace the insulin stress test

The clinical diagnosis of adrenal failure is not difficult in patients presenting acutely with features of both glucocorticoid and mineralocorticoid deficiency, such as nausea, vomiting, diarrhea, prostration, hypotension, and pigmentation. Such patients are usually young, and treatment with saline, hydrocortisone, and fludrocortisone is urgent and lifesaving. The results of emergency laboratory tests showing typical hynoponatraemia, hyperkalaemia, moderate ureaemia, and often hypoglycaemia strongly support the diagnosis, which is subsequently confirmed by hypocortisolaemia and the short tetracosactrin (Synacthen) test.1

The short tetracosactrin test is performed once the patient has been stabilised; treatment with hydrocortisone should be stopped for 24 hours, though not that with fludrocortisone. Typically the basal cortisol values are <100 nmol/l, do not rise after giving tetracosactrin, and, together with a plasma concentration of adrenocorticotropic hormone of >200 ng/l (which should always be measured on the basal sample), this pattern establishes the diagnosis.2 3 Most cases of acute adrenal crisis are due to autoimmun or tuberculous adrenitis, but too rapid withdrawal of glucocorticoids or overtreatment with adrenal blocking drugs are other causes. Rifampicin and other drugs that induce cytochrome P-450 enzymes accelerate the metabolism of cortisol1 and can precipitate an adrenal crisis early in the course of antituberculous chemotherapy.5 6

Glucocorticoid insufficiency with normal production of aldosterone is associated with a more insidious clinical onset. The symptoms are fluctuating and non-specific, such as lassitude, weakness, anorexia, abdominal pain, and weight loss. These are common in outpatient practice and often raise the question of adrenal insufficiency, especially in patients coming from communities with a high prevalence of tuberculosis. In most cases, however, adrenal insufficiency is excluded by finding a basal plasma cortisol concentration of >200 nmol/l, rising to >500 nmol/l after giving tetracosactrin. These values are based on cortisol measurement by the old fluorimetric method, but most laboratories now measure cortisol by direct radioimmunoassay, which gives values 20-30% lower.2 Consequently, a peak cortisol value of >400 nmol/l is probably acceptable as normal if found with radioimmunoassay, although there is no published formal evaluation of this.

An absent cortisol response to tetracosactrin with a low basal concentration of adrenocorticotropic hormone (<10 ng/l) points to secondary adrenal failure, which may be confirmed by giving 1 mg tetracosactrin acetate (Synacthen Depot) every day for five days. Because adrenocorticotropic hormone induces cortisol synthesising enzymes the plasma cortisol concentration rises progressively to normal by the end of the test. Nevertheless, difficulty arises when the cortisol response to tetracosactrin is equivocal. Should the clinician invariably proceed to further investigations of hypothalamic-pituitary function? Much will depend on the clinical context, and here additional clinical clues such as signs of other pituitary hormone deficiency or of a pituitary tumour may help. If the clinical index of suspicion is low it is reasonable to wait and repeat the test six to eight weeks later. If the result is then normal the doctor may reassure the patient with confidence; if it is still abnormal an insulin stress test should be considered.

Patients in whom it is essential to assess hypothalamic-pituitary function fall into three broad groups: firstly, those with pituitary tumours and other hypothalamic-pituitary diseases in whom acute adrenal failure may result from severe stress; secondly, those who have had a hypophysectomy or pituitary irradiation, when the test will indicate the continuing need for glucocorticoid replacement treatment; and thirdly, those who are being weaned off long term glucocorticoid treatment for chronic systemic diseases.

The traditional assessment with the insulin hypoglycaemia stress test has the advantage of assessing the integrity of the hypothalamus and the pituitary simultaneously. Unfortunately, it is unpleasant, expensive, and not without risk. The test is contraindicated in those aged 70 and over and at any age in patients with angina, heart failure, cerebrovascular disease, pulmonary disease, and diabetes.7

18 Greenspan D, Greenspan JS, Goldman H. Oral viral lesion (hairy leukoplakia) associated with the acquired immunodeficiency syndrome. MMWR 1985;34:549-50.
or epilepsy, when an alternative such as the metyrapone test may be used. Nevertheless, the metyrapone test relies on measuring serum 11-deoxycorticisol or urinary 17-hydroxycorticosteroid excretion, which is not now commonly performed in Britain. Similarly, the corticotrophin releasing factor test is little used, given that it measures only one component of the axis, the pituitary, and may give normal results in patients with hypothalamic disease. A normal adrenal response to tetracosactrin requires previous exposure of the gland to endogenous adrenocorticotrophic hormone. Hence a normal test result in the short tetracosactrin test suggests that the production of adrenocorticotrophic hormone is normal and the test should be a simple, safe, and cheap means of assessing the hypothalamic-pituitary-adrenal axis. Some have claimed that this suggestion is valid, but others have challenged its reliability. The test has now been re-evaluated in a large number of patients, most of them with pituitary adenomas, and found to be reliable in predicting the requirement for glucocorticoid treatment in patients with hypothalamic-pituitary disease. The short tetracosactrin test also predicts adrenal function early after hypophysectomy and the patients that can stop glucocorticoid replacement after hypophysectomy. Nevertheless, the short tetracosactrin test may not be so reliable in predicting the return of normal hypothalamic-pituitary-adrenal function during the withdrawal of long term glucocorticoid treatment, and when an insulin stress test may be needed.

Given the evidence that the short tetracosactrin test performs as well as the insulin stress test in the vast majority of instances, why do fewer than a quarter of British endocrinologists use it? Stewart and his colleagues did not answer this question, but traditions die hard. Physicians in a district general hospital see few cases in which to compare the two tests, and so they have little chance of becoming confident with the short tetracosactrin test. But they are now justified in sparing most of their patients the discomfort of an insulin stress test, given the knowledge that the short tetracosactrin test will rarely mislead.

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Our children’s teeth

Fluoridation needed to overcome social inequalities in caries prevalence

The dental health of British children has improved dramatically in the past 25 years. In England and Wales the prevalence of dental caries fell in all age groups and in all geographic regions between 1973 and 1983. For example, among 5 year olds the mean number of decayed teeth was 3·4 in 1973 and 1·7 in 1983, while over the same decade the percentage of children in this age group completely free from decay rose from 29% to 52%. A further survey is expected in 1993, and data on caries are currently being collected routinely by health districts in England and Wales. All these surveys will, it is hoped, show further improvement in the dental health of children, but there are some disturbing trends.

Dental caries has become a class related disease that is commoner in poorer communities. This is a recent change as before 1970 the prevalence of decay was similar in all social groups and only its treatment varied: advantaged children received more fillings and fewer extractions than their less fortunate contemporaries. Now children from affluent backgrounds have less decay, producing appreciable national, regional, and local variations.

In 1983 the mean number of decayed teeth in 15 year olds was 5·6 in England, 6·7 in Wales, 8·4 in Scotland, and 9·2 in Northern Ireland. Within England regional differences were striking, with the lowest prevalence in the south and the highest in the north. During 1985-6, 5 year olds in West Essex had only 0·75 decayed teeth on average, whereas in several districts in the north west this value exceeded 3. That such differences are socially determined is shown by the high percentage of decay in several less affluent inner city areas in London.

Changed practices of preventive dental care probably explain this changed pattern in the prevalence of caries. The “rules” for dental health are now well established, and the Health Education Council (now Authority) summarised them in four simple statements: food and drink containing sugar should be restricted to mealtimes; the teeth and gums should be cleaned daily with a fluoride toothpaste; children in areas with suboptimal concentrations of fluoride in the drinking water should take fluoride drops or tablets daily; and everybody should attend the dentist regularly. These rules are now widely used by health educators, and the social gradients that

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