periapical infection.[4] After infection has penetrated the mandible it will follow the line of least resistance, tracking along fascial planes. It may rupture into the adjacent carotid sheath and therefore progress up and down the neck. This may produce pain and tenderness as described in the distribution of the carotid artery, but there are no recent reports of these symptoms in the absence of jaw pain.

Severe spontaneous carotid pain with tenderness along the course of the common carotid artery in the absence of infection or trauma constitutes the syndrome of carotodynia.[5] The clinical picture is similar to that described in our patient. Pain often radiates from the neck to the ipsilateral side of the face and ear. The affected carotid artery is noticeably tender and may be distended and hyperpulsatile. Fever is unusual and a raised erythrocyte sedimentation rate is often the only abnormal laboratory finding. The condition may be a variant of migraine and often responds to ergotamine compounds.[6] The differential diagnosis also includes dissecting carotid artery aneurysms,[7] which are usually seen on a real time ultrasound scan of the neck.

We thank Mr H S Dearing, associate specialist in dental surgery, for his help with this case.

References

1 Stones HH. *Oral and dental diseases*. London: Livingstone, 1957:396.
2 Winstock D. Apical disease: an analysis of diagnosis and management with special reference to root lesion resection and pathology. *Ann R Coll Surg Engl* 1980;**62**:171-9.
3 Price C. Standardized periapical radiographs. *Proceedings of the Royal Society of Medicine* 1975;**68**:126-7.
4 Gold RS. Pansinusitis, orbital cellulitis and blindness as sequelae of delayed treatment of dental abscess. *Journal of Oral Surgery* 1974;**32**:40-3.
5 Davies JVSA. Carotid pain: report of six cases. *Br Med J* 1961;ii:1528-9.
6 Anonymous. Carotidynia, a distinct syndrome [Editorial]. *JAMA* 1967;**199**:21.
7 Beeson PB, McDermott W, Wyngaarden JB, eds. *Textbook of medicine*. 16th ed. Philadelphia: W B Saunders, 1982:2055.

(*Accepted 25 March 1985*)

Biochemical Tests in Medicine

Measurement of urine 17-oxogenic steroids, 17-hydroxycorticosteroids, and 17-oxosteroids has been superseded by better tests

BRIAN T RUDD

It is more than 30 years since reliable colorimetric methods were introduced for the measurement in urine of metabolites arising from steroids secreted by the adrenal cortex. These measurements provided an invaluable replacement for time consuming bioassays and for the first time made it feasible for hospital laboratories to investigate patients with diseases of the adrenal cortex. The elegant innovation that made this possible[1-3] comprised selective oxidation and reduction of the urinary steroids followed by condensation of the products with 1,3-dinitrobenzene—the Zimmerman reaction. This formed the basis of the analysis for urinary 17-oxogenic steroids, 17-hydroxycorticosteroids, and 17-oxosteroids recommended by a working party of the Medical Research Council in 1969.[4] The analytical and interpretative problems associated with these methods have been reviewed.[5]

17-Oxogenic steroids represent metabolites of steroids secreted from the adrenal cortex, while 17-hydroxycorticoids largely represent metabolites of cortisol but also include a minor steroid subfraction (C21 methyl, C20 keto) not measured in the 17-oxogenic steroid assay. The two assays are virtually synonymous and are not distinguished in the rest of this article. 17-Oxosteroids are metabolites of steroids derived from both the adrenal cortex and the gonads. None of these assays is a good index of steroid secretion or reliable indicator of the biological activity of specific steroids secreted by the endocrine glands.

Department of Clinical Endocrinology, Birmingham and Midland Hospital for Women, Birmingham B11 4HL
BRIAN T RUDD, BSC, PHD, top grade biochemist

I believe that urine 17-oxo and 17-oxogenic steroids should be deleted from the clinical chemistry repertoire. Consideration of some individual clinical conditions substantiates this point.

17-Oxogenic steroids/17-hydroxycorticoids

In patients with *Cushing's syndrome* the excretion of 17-oxogenic steroids is not always increased: for example, Crapo[6] found that 56 out of 235 such patients (24%) had normal daily excretion of these steroids. The assay of urine free cortisol or serum cortisol is more useful. Urine free cortisol excretion is of particular value as it parallels the cortisol secretion rate,[7] while measurement of serum cortisol at 0800 and 2400 will often disclose a loss in the circadian rhythm of cortisol. The best first line test for Cushing's syndrome, however, is the single dose overnight dexamethasone suppression test, since this has a low incidence of false negative results.[6]

When adrenal hyperfunction has been established adrenocorticotrophin plasma measurements will help to differentiate adrenal tumours from pituitary and ectopic sources of this hormone.

Measurement of 17-oxogenic steroids after the administration of metyrapone has long been advocated as a useful indirect test of adrenocorticotrophin release.[8] Supporters for retaining this measurement point to the metyrapone test and cite the difficulties and cost of performing assays for adrenocorticotrophin as the direct test of release of this hormone from the pituitary after metyrapone. The specific assay of serum 11-deoxycortisol, however, has been found to be a rapid, useful, and acceptable alternative for the indirect detection of adrenocorticotrophin release after metyrapone administration.[9]

Adrenal insufficiency may be due to destruction of the adrenal cortex or be secondary to impaired pituitary secretion of adrenocorticotrophin. In either case finding low or undetectable basal concentrations of cortisol in serum with absent or poor cortisol response to short term (30 minutes to one hour) administration of tetracosactrin confirms the diagnosis. To achieve comparable diagnostic information when urine 17-oxogenic steroids are measured

Br Med J (Clin Res Ed): first published as 10.1136/bmj.291.6498.805 on 21 September 1985. Downloaded from http://www.bmj.com/ on 10 April 2024 by guest. Protected by copyright.

requires protracted stimulation of adrenocorticotrophin and urine collections on several days.

In patients with *congenital adrenal hyperplasia* in whom 21-hydroxylase deficiency is suspected measurement of 17-hydroxyprogesterone in serum, or its metabolite pregnanetriol in urine, is preferred to measurement of 17-hydroxycorticoids or 17-oxogenic steroids in urine.[10 11]

17-Oxosteroids

The use of 17-oxosteroids for diagnosis is even more questionable than the use of 17-oxogenic steroid or 17-hydroxycorticoid measurements.

Roughly half of patients with *polycystic ovary syndrome* have raised concentrations of serum Δ^4-androstenedione and testosterone, whereas their 17-oxosteroid excretion is normal.[12 13] Δ^4-Androstenedione is secreted from the adrenals and gonads. Stimulation of the adrenal cortex with tetracosactrin increases the serum concentration of testosterone derived from peripheral conversion of Δ^4-androstenedione secreted by the adrenals,[14] while failure to suppress a raised concentration of testosterone in serum suggests an ovarian source for this steroid. Discrimination between an adrenal or gonadal source of the androgens is not possible when 17-oxosteroids are measured.

Serum concentrations of 17α-hydroxyprogesterone, testosterone, and Δ^4-androstenedione are also raised in certain rare diseases associated with *sexual precocity in children*, notably children with congenital adrenal hyperplasia[15] and prepubertal boys with *Leydig cell tumours*.[16] In many of these cases, especially in infancy, raised 17-oxosteroid excretion is not found.

Women with an *adrenal androgen secreting tumour* may present only with hirsutism. On the other hand, prepubertal children may present with advanced bone age and accelerated growth. In these circumstances assay of the adrenal steroid dehydroepiandrosterone or its sulphate is a sensitive index of the underlying disorder, epecially when the concentration is related to age.[17 18] In addition, if testosterone is measured at the same time as dehydroepiandrosterone sulphate raised values are found because of the conversion of dehydroepiandrosterone to Δ^4-androstenedione and testosterone. Less reliance can be placed on the serum testosterone concentration in men suspected of having an *adrenal adenoma* because of the testicular contribution of this hormone. Hence measurement of dehydroepiandrosterone or its sulphate in serum is all that is required.

The adult reference range for serum testosterone shows no overlap between the sexes. By contrast, an overlap in 17-oxosteroid excretion does occur, especially as puberty intervenes. Boys with *primary testicular disease* and *inadequate Leydig cell function* may readily be identified by measurement of serum testosterone concentrations before and after stimulation with human chorionic gonadotrophin.[19] Such patients cannot easily be identified when 17-oxosteroids are measured because testosterone is not detected by this assay and only a quarter of its metabolites appear in the urine.

The diagnosis of *male hypogonadism* is a recurring problem. Rare but well documented[20] gonadal enzyme deficiencies may be the cause. The rare disease of 5α-reductase deficiency, in which there is failure to convert testosterone to the more biologically active metabolite dihydrotestosterone, may be detected by specific measurement of the metabolite,[21] but 17-oxosteroid excretion is not sensitive enough to give any indication of the androgen state of these patients. Phenotypic women with *testicular feminising syndrome* may also be identified by raised serum testosterone and luteinising hormone concentrations, whereas 17-oxosteroid excretion is frequently normal.

Conclusion

17-Oxogenic steroid and 17-oxosteroid assays have been rendered obsolete by specific and sensitive techniques that measure the steroid hormones or their metabolites in urine, serum, and saliva (see table).[22] Measurements of urine 17-oxo and 17-oxogenic steroids have been valuable servants in the past but should now be gracefully retired.

Steroids to measure instead of 17-oxogenic steroids and 17-oxosteroids in different clinical problems

Clinical problem	Assay of choice
Cushing's syndrome	Serum and urine "free" cortisol
Addison's disease or suspected pituitary adrenocorticotrophin deficiency	Serum cortisol
?Congenital adrenal hyperplasia (21-hydroxylase deficiency)	Serum 17α-hydroxyprogesterone, testosterone, urine pregnanetriol
Congenital adrenal hyperplasia (under treatment)	Serum or possibly saliva 17α-hydroxyprogesterone, serum Δ^4-androstenedione
11β-Hydroxylase deficiency	Urine tetrahydro-11-deoxycortisol or serum 11-deoxycortisol
Polycystic ovary disease	Serum dehydroepiandrosterone, testosterone, and Δ^4-androstenedione
Androgen secreting adrenal adenoma	Dehydroepiandrosterone, testosterone (women)
Precocious sexual development in boys	Testosterone (with luteinising hormone), Δ^4-androstenedione, 17α-hydroxyprogesterone
Male infertility	Testosterone, dihydrotestosterone

This is a modified form of a paper prepared at the invitation of The Association of Clinical Biochemists' Scientific Committee Working Party for Clinical Laboratory Investigations, which first appeared in the *Annals of Clinical Biochemistry* (1983;**20**:65-71). One of the remits of this working party is to serve as an avenue for the publication of short, dogmatic, and perhaps provocative articles concerning specific aspects of current clinical laboratory practice.

I thank members of the Clinical Chemistry Laboratory Investigations Working Party of the ACB and many clinical colleagues for helpful advice.

References

1 Norymberski JK. Determination of urinary corticosteroids. *Nature* 1952;**170**:1074-5.
2 Appleby JI, Gibson G, Norymberski JK, Stubbs RD. Indirect analysis of corticosteroids (1). Determination of 17-hydroxycorticosteroids. *Biochem J* 1955;**60**:453-60.
3 Few JD. A method for the analysis of urinary 17-hydroxycorticosteroids. *J Endocrinol* 1961; **22**:31-46.
4 Gray CH, Baron DN, Brooks RV, *et al*. A critical appraisal of a method of estimating urinary 17-oxosteroids and total 17-oxogenic steroids. Medical Research Council memorandum. *Lancet* 1969;i:124-7.
5 Rudd BT. Urinary 17-oxogenic and 17-oxosteroids. A case for deletion from the clinical chemistry repertoire. *Ann Clin Biochem* 1983;**20**:65-71.
6 Crapo L. Progress in endocrinology and metabolism. Cushing's syndrome: a review of diagnostic tests. *Metabolism* 1979;**28**:955-77.
7 Mattingley D, Dennis DM, Pearson J, Cope CL. Rapid screening test for adrenocortical function. *Lancet* 1964;ii:1046-9.
8 Jenkins JS, Pothier L, Reddy WJ, Nelson DH, Thorn GW. Clinical experience with selective inhibition of adrenal function. *Br Med J* 1959;i:398-401.
9 Perry A, Al-Dujaili EAS, Edwards CRW. A direct radioimmunoassay for 11-deoxycortisol. *Steroids* 1982;**39**:115-28.
10 Morris R. Pregnanetriol in urine: determination as a 17-ketogenic steroid. *Acta Endocrinol* 1959;**32**:596-605.
11 Hughes IA, Riad-Fahmy D, Griffiths K. Plasma 170H-progesterone concentrations in newborn infants. *Arch Dis Child* 1979;**54**:347-9.
12 Duignan NM, Shaw RW, Rudd BT, *et al*. Sex hormone levels and gonadotrophin release in the polycystic ovary syndrome. *Clin Endocrinol* 1975;**4**:287-95.
13 Duignan NM. Polycystic ovarian disease. *Br J Obstet Gynaecol* 1976;**83**:593-602.
14 Kandeel FR, London DR, Butt WR, *et al*. Adrenal function in subgroups of the PCO syndrome assessed by a long term ACTH test. *Clin Endocrinol* 1980;**13**:601-12.
15 Rudd BT, Rayner PHW. Androgen levels in plasma and urine of patients with virilising congenital adrenal hyperplasia. *Proceedings of the Royal Society of Medicine* 1970;**63**:1039-40.
16 Root AW, Steinberger E, Smith K, *et al*. Isosexual pseudoprecocity in a 6-year old boy with a testicular interstitial cell adenoma. *J Pediatr* 1972;**80**:264-8.
17 Smith MR, Rudd BT, Shirley A, *et al*. A radioimmunoassay for the estimation of serum dehydroepiandrosterone sulphate in normal and pathological sera. *Clin Chim Acta* 1975;**65**: 5-13.
18 Orentreich N, Brind JL, Rizer RL, Vogelman RL. Age changes and sex differences in serum dehydroepiandrosterone sulphate concentrations throughout adulthood. *J Clin Endocrinol Metab* 1984;**59**:551-5.
19 Rudd BT, Rayner PHW, Smith MR, Holder G, Jivani SKM, Theodoridis CG. Effect of human chorionic gonadotrophin on plasma and urine testosterone in boys with delayed puberty. *Arch Dis Child* 1973;**48**:590-5.
20 London DR. Medical aspects of hypogonadism. In: Butt WR, London DR, eds. *Clinics in endocrinology and metabolism*. London: W B Saunders, 1975:597-618.
21 Savage MO, Grant DB. The incomplete male. *Arch Dis Child* 1978;**53**:701-3.
22 Read GF, Riad-Fahmy D, Walker RF, Griffiths K, eds. *Immunoassays of steroids in saliva*. Vol 9. Cardiff: Alpha Omega Ltd, 1982:101-334.

(Accepted 17 July 1985)

Br Med J (Clin Res Ed): first published as 10.1136/bmj.291.6498.805 on 21 September 1985. Downloaded from http://www.bmj.com/ on 10 April 2024 by guest. Protected by copyright.