labelled with carbon-11 (Tobias *et al.*, 1945) have been employed, again in circulation studies. The use of such gases, combined with external counting over lung, could be complementary to the oxygen-15 technique and broaden the approach to the clinical problems described in this paper.

Summary

The cyclotron-produced radioactive isotope oxygen-15, with a half-life of two minutes, has been used to study regional lung function. There is no intubation of the patient.

Pairs of scintillation counters placed on the chest wall have been used to measure radiation from two regions simultaneously. From observation of counting-rates during breath-holding following a single inspiration of active gas, the relative ventilation and blood-flow of the regions is assessed.

This paper describes the results obtained in selected patients with abnormal lung function.

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REFERENCES

- Brownell, G. L., and Sweet, W. H. (1953). *Nucleonics*, **11**, No. 11, p. 40.
- (1956). *Proceedings of the First International Conference on the Peaceful Uses of Atomic Energy*, Geneva, 1955, **10**, 249. United Nations, New York.
- Clarke, E. R., Martin, C. J., and Politoff, S. (1958). *Dis. Chest*, **34**, 150.
- Dyson, N. A. (1959). *Phys. in Med. Biol.* In press.
- Hugh-Jones, P., Newbery, G. R., and West, J. B. (1958). Second U.N. Conference on the Peaceful Uses of Atomic Energy, Geneva, 1958, Paper 278.
- Gallop, J. W., Vonberg, D. D., Post, R. J., Powell, W. B., Sharp, J., and Waterton, P. J. (1957). *Proc. Instn. elect. Engrs*, Part B, 104, 452.
- Hugh-Jones, P., and West, J. B. (1960). *Thorax*. In press.
- Jaimet, C. H., Tomlinson, R. H., Donato, L., Debus, G., and Nace, P. F. (1958). Second U.N. Conference on the Peaceful Uses of Atomic Energy, Paper 215.
- Knipping, H. W., Bolt, W., Valentin, H., Venrath, H., and Endler, P. (1957). *Münch. med. Wschr.*, **99**, 46.
- Mattson, S. B., and Carlens, E. (1955). *J. thorac. Surg.*, **30**, 676.
- Sanders, R. J., and Morrow, A. G. (1958). Second U.N. Conference on the Peaceful Uses of Atomic Energy, Paper 866.
- Ter-Pogossian, M., and Powers, W. E. (1958). *Radioisotopes in Scientific Research*: edited by R. C. Extermann. Proceedings First (Unesco) International Conference, Paris, 1957, **3**, 625. Pergamon Press, London.
- Tobias, C. A., Lawrence, J. H., Roughton, F. J. W., Root, W. S., and Gregersen, M. I. (1945). *Amer. J. Physiol.*, **145**, 253.

The Indian Government's Central Drugs Laboratory in Calcutta has now found a permanent home, while a new building has been constructed to house an associated chemical laboratory, a library, and a reading-room. The Government has also been approached to provide an air-conditioned animal-house with facilities for keeping all species of animals. The routine analytical work of the laboratory greatly increased during the year under review. (*Annual Report of the Central Drugs Laboratory, April 1, 1955—March 31, 1956*. Ministry of Health, Government of India.)

INTERSTITIAL-CELL TUMOUR OF THE TESTIS IN A CHILD

REPORT OF A CASE AND A REVIEW OF THE LITERATURE

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The rarity of interstitial-cell tumour of the testis in children prompts the following report. The preceding history and the urinary steroid excretion were of particular interest, and these findings are discussed in relation to 25 previously reported cases.

Case Report

The patient, a boy aged 11 years, was referred to us in January, 1956, because of an enlargement of the right testis present for one year. The family history revealed that a female first cousin had an arrhenoblastoma of the ovary at the age of 15.

In November, 1950, when aged 6, he had been sent to the children's department of a psychiatric hospital because of backwardness at school. It was observed at this time that he was nervous and dreamy, disliked his school studies, and became involved in many fights. He had shown intense hostility to his younger brother, and on one occasion had pushed his perambulator in front of a tram. It was noted that the patient's language was aggressive and that he resented authority, but no precocious development was found on physical examination.

Apart from this he was apparently a normal child until the age of 9 years, when he began to develop rapidly and exhibit abnormal physical strength. He became difficult to manage at home because of precocious puberty, and was sent to a children's hospital. Here it was thought that the left testis was underdeveloped. Radiological examination of the skeleton revealed no abnormality, his bone age being in accordance with his chronological age.

From June, 1954, until January, 1956, he continued his abnormal development, but at no time were there any symptoms referable to the right testis, apart from gradual enlargement.

A week after being seen in our out-patient department, he was admitted as an emergency case because of abdominal pain. There were no physical signs of an abdominal lesion to account for this, and his symptoms rapidly subsided.

On examination the patient had the appearance of a rather aggressive youth of about 18 (Fig. 1) because he was very muscular and hirsute. The external genitalia were of adult proportions. The right testis was enlarged, firm, regular, and not tender. The left testis was small and soft. The prostate, as assessed on rectal examination, was considered to be normal. No abnormality was detected in the nervous, respiratory, and cardiovascular systems. The blood-pressure was 110/70.

Investigations.—Radiology: Bone age, approximately 17 years (Fig. 2). Haemoglobin, 17.6 g./100 ml.; packed cell

volume, 50%. Wassermann reaction and Kahn flocculation test were negative. The Aschheim-Zondek test was negative. Pre-operative steroid excretion: (1) Total neutral 17-ketosteroids (M.R.C., 1951), 550 mg./24 hours; corticoids (acid-stable formaldehydogenic substances: Tompsett, 1953; Tompsett and Smith, 1954), 7.9 mg./24 hours. (2) Total neutral 17-ketosteroids, 520 mg./24 hours; ketonic fraction, 394 mg./24 hours; dehydroisoandrosterone (Munson *et al.*, 1948), 11.3 mg./24 hours, 3% of ketonic fraction. These findings are consistent with the marked increase in 17-ketosteroid output being of testicular origin.

Operation.—On February 15, 1956, the right testis was removed *in toto* through a scrotal incision. Extremely large blood-vessels were noted in the spermatic cord. The tumour itself was highly vascular, and no macroscopic trace of the normal testis could be distinguished (Figs. 3 and 4). A biopsy specimen was taken from the left testis through the scrotal septum.

Biopsy Report.—(1) Sections show an interstitial-cell tumour of the testis, with sheets of closely packed cells whose cytoplasm is finely granular and eosinophilic, and also shows some vacuolation (Fig. 5). (2) Sections show a decrease in the diameter of the tubules, together with an increase of interstitial tissue suggesting atrophy of the testis (Fig. 6).

Post-operative Steroid Excretion.—(1) Six days after operation: total neutral 17-ketosteroids, 10 mg./24 hours; corticoids, 6.1 mg./24 hours. (2) Twelve days after operation: total neutral 17-ketosteroids, 3.9 mg./24 hours.

Discussion

Interstitial-cell tumour of the testicle is a rare condition. When it occurs in adults it most often

presents no endocrine features, but on the rare occasions when it does so the most typical is gynaecomastia. The urinary 17-ketosteroid level is apt to be much higher in adult cases than when the tumour develops in childhood, and levels as high as 1 g. per 24 hours have been recorded. In adult cases the tumour may be malignant,

FIG. 1.—Photograph of patient aged 11.

FIG. 3.—Testis and cord (external appearance). (Scale in centimetres.)

FIG. 4.—Testis and cord (bisected). (Scale in centimetres.)

FIG. 2.—Radiographs showing bone age of about 17 years.

though this has not so far been the case when signs have become evident in the first decade. It is possible that the tendency to malignancy, and perhaps also the higher levels of urinary 17-ketosteroids in these adult cases, may be associated with the lack of dramatic somatic and genital changes which occur when the tumour develops in childhood, so that its existence remains unsuspected for a much longer time.

Twenty-five cases of interstitial-cell tumour of the testicle in childhood have so far been reported in the world literature, and details of these are presented in the Table. It will be seen that all these have shown signs of sexual precocity between the ages of 1½ and 9 years, and in 17 of the 25 the onset has been between 3 and 6 years. In only one case (Fraser, 1949) has the enlargement of the testicle been so slight that the diagnosis was difficult to make, and in this case signs of sexual precocity had developed only a few months before the testicle was removed. The unaffected testicle is usually atrophic, but it increases in size after removal of the testicle containing the tumour. The atrophy is due to suppression of the germinal epithelium, though in the case reported by James and

Details of Cases from World Literature

Author	Age at Onset	Age Excision	Size of Testicle	Bone Age	Interval Between Operation and Follow-up	Psycho-sexual Precocity	Physical Development	Penis	Erections	Prostate	Sexual Hair	Acne	Voice	Testes: Germinal Epithelium	17-K.S.	Comments
1. Sacchi (1895)	5½	9½	12 × 10 cm.		10 mts.	Yes R.*	Adult N.R.	Large S.R.	Yes		Beard. Pubic. Axill. S.R. Chest. Pubic. N.R. Beard. Pubic.		Adult S.R.			
2. Rowlands and Nicholson (1929)	6	9	5 × 3½ × 4 cm.		2 yrs.	No	Adult N.R.	Large N.R.					Adult	No development		
3. Sutherland (1932) (Quoted by Somerford, 1941)	5	11	10 × 7 cm.		1½ yrs.		Adult N.R.					Yes				
4. Stewart <i>et al.</i> (1936)	4	5	Twice normal		5 mts.	No		Large S.R. Large			Pubic R. Chest. Pubic. N.R. Pubic. Axill. Face. R.		Adult	To spermatid		Gynaecomastia. N.R.
5. Huffman (1941)	6	6	5 cm.		2 yrs.											
6. Werner <i>et al.</i> (1942) (Quoted by Anderson, 1946)	5½	6½	2½ × 1½ cm.	10-12	3½ mts.	Yes R.	Muscular	Large	Yes	Large			Adult N.R.			
7. Urban (1942)	5	5½	4½ × 3½ × 2½ cm.		9 mts.	No		Large R. Large N.R.	Yes R. Yes R.		Pubic R. Pubic R.		Adult			
8. Sandblom (1948)	2½	3½	Twice normal		1 yr.	Yes R.	Muscular			Large R.		Yes R.	Adult R.	No development	64 17	Adrenal explored owing to misdiagnosis. Testes so slightly enlarged that diagnosis difficult
9. Fraser (1949)	4	4½	Only slightly enlarged	6½	3 mts.	Yes R.	"	Large R.	Yes R.		Slight Pubic R.	No	Adult			
10. Melicow <i>et al.</i> (1949)	4½	5	Enlarged	12	7 mts.		"	Large N.R. Large	Yes	Large N.R.	Pubic N.R. Pubic. Axill. Chest.		Adult N.R. Adult	To spermatogonia		
11. Rezek (1943)	5	6				Yes	"									
12. James and Shupe (1950)	9	14				Yes	"	Large	Yes						9-8	3 mts. post-op. Said to be father of an unborn child!
13. Newns (1952)	1½	2½	4½ × 3 × 3 cm.	6	2 yrs.	Yes R. No	"	Large S.R. Large	Yes	Large	Pubic R. Pubic. Axill. Face. N.R.	Yes	Adult N.R. Adult N.R.	To secondary spermatocytes	13-5 0-9 16-5	Chromotographic separation of 17-ketosteroids
14. Cook <i>et al.</i> (1952)	4½	5½	6 × 4 cm.	13	1 yr.	No	Muscular N.R.		No	Large		Yes				
15. Tavares (1952)																
16. Hertz <i>et al.</i> (1953)	4½	6	Both large. Left grew larger than right		1 yr.		Normal	Large N.R.	Yes N.R.		Pubic					
17. Anagnostou and Frangopoulos (1953)	4½	6½	4 × 4 × 3 cm.	15	2½ yrs.	No		Large R.	No		Pubic. Facial. Limbs. R.		Adult R.			
18. Demetriadis <i>et al.</i> (1948)																
19. Staubitz <i>et al.</i> (1953)	3	20	Bilateral abnormal enlargement	15 at age 6	4 mts.	No	Muscular	Large			Pubic age 3; body age 11	Yes age 11	Adult age 11	Seminal specimens showed no sperms age 20	29 52 74 70-2	α-fraction 72. β-fraction 1-2 mg./24 hr. Bilateral α-fraction 67-6. β-fraction 2-6 mg./24 hr. 4 mts. post-op. Persistently high 17-K.S. suggests adrenocortical rests in testes
20. Thamdrup (1953)	7	7½	Palpably enlarged		1½ yrs.	No	Muscular R.	Large R.	Yes				Adult R.		40 5-3	Pre-op. 10 days post-op. "Oestrogen hormone" >50 <200 M.U. No urinary gonadotrophin 1½ yrs. post-operatively
21. Florentin and Rauber (1954)	9	21	Large: thought to be a hydrocele		19 mts.	Yes	Muscular				Bald and very hairy age 21 N.R. Pubic R.	Yes			182 12-4 16-7	2 mts. post-operatively. 19 mts. post-operatively
22. Jolly (1955)	3½	5½	3 times larger than other testis	11	1 yr.			Large R.	Yes R.						2-9 0-9	Aged 5½, laparotomy to exclude adrenal lesion. Orchiectomy a year later
23. Pomer <i>et al.</i> (1954)	6½	7	2.5 × 2.5 cm.		2 mts.		Muscular N.R.	Large			Pubic. No axill.				4-9	

*R. = Regression. N.R. = No regression. S. = Some regression.

Details of Cases from World Literature—continued

Author	Age at Onset	Age Excision	Size of Testicle	Bone Age	Interval Between Operation and Follow-up	Psycho-sexual Precocity	Physical Development	Penis	Erections	Prostate	Sexual Hair	Acne	Voice	Testes: Germinal Epithelium	17-K.S.	Comments
24. Jungck <i>et al.</i> (1957)		8½	2 × 4 cm.	17	1 yr.	Aggressive	Muscular	Large N.R.			Pubic. Axill. Facial			Atrophic tubules	25.7 6.1 4.5	1 mt. post-operatively 6 mts. post-operatively Gynaecomastia. Regression post-operative
25. " "	5½	6	2 × 3 cm.	13	1½ yr.	No		Large N.R.	Yes	Non-palpable	Pubic					

Shupe (1950) it is said that the child was the father of an as yet unborn child!

In all the cases in which it is recorded the bone age is much in advance of the chronological age. Psycho-sexual precocity occurs in about half the cases and often regresses after removal of the tumour. The child is usually of adult physique, strong and muscular, with well-developed pubic hair, though axillary, facial, and body hair may not be noticeable. Acne is sometimes present, and the voice has broken. The penis is greatly enlarged. These secondary sexual characteristics seldom regress after removal of the tumour. Gynaecomastia, which is so prominent a feature of the adult cases, has been described in only three of the prepubertal cases. Unfortunately, in none of these is the urinary 17-ketosteroid level referred to.

The 17-ketosteroid level has been recorded in 10 of the 25 cases, though in two of them observations were not made until the patients were adult, and in another

only a post-operative figure is given. Of the remaining seven cases for which pre-operative observations were made during childhood the values ranged from 2.9 to 64 mg. per 24 hours. Three of these were grossly increased in relation to age and above the normal adult range (25.7, 40, and 64 mg. per 24 hours), three were clearly increased for the respective ages (7.4 mg. at 5 years, 13.5 mg. at 2½ years, and 16.5 mg. at 5½ years), and three showed levels which might be considered of doubtful significance (2.9 mg. at 5½ years, 3.3 mg. at 5 years, and 4.9 mg. at 6½ years). All cases had normal post-operative levels except that of Sandblom (1948), in which post-operative figures of 10–20 mg. per 24 hours were found over a period of one year, the age at operation being 3½ years. This was, however, a marked fall from the pre-operative level of 64 mg., and in fact there was marked recession of the physical signs as well as complete remission of the psycho-sexual precocity.

In the case recorded by Staubitz *et al.* (1953) three pre-operative 24-hour collections of urine yielded 29, 52, and 74 mg., and four months after operation the value was still 69.6 mg. In this case the total 17-ketosteroids were separated into α and β fractions, and a considerable preponderance of the α fraction was recorded. It is usually considered that the α fractions consist mainly of aetiocholanolone and androsterone, which may be metabolites of testicular or of adrenocortical hormones, and that the β fraction (dehydro-epi-androsterone) is a metabolite of adrenocortical androgens. Nevertheless this is the only case recorded of bilateral tumours occurring in the first decade. Adrenal rests are sometimes found outside the adrenal gland, especially along the course of the spermatic cord and in the epididymis. They may also develop in the testes, and indeed they have been found there in cases of macrogenitosomia praecox, due to congenital adrenal hyperplasia.

Histologically these adrenal rests are extremely difficult to differentiate from interstitial-cell tumours. The one certain distinguishing feature is the presence of "crystalloids of Reinke," which may sometimes be found in Leydig cells (interstitial cells of the testes), but are never to be seen in adrenal rest cells. There is, unfortunately, no mention of their presence or absence in the case of Staubitz *et al.* However, the fact that the tumours were bilateral and the high 17-ketosteroid level was not diminished by their removal leads one to suspect that they were of adrenocortical origin, despite the preponderance of the α fraction.

In the case of Florentin and Rauber (1954) the initial 17-ketosteroid level was 182 mg. per 24 hours, and it fell to normal adult levels after operation. This patient showed signs of sexual precocity at the age of 9, but

FIG. 5.—Section of tumour. (×150.)

FIG. 6.—Section of unaffected testis. (×150.)

was not operated upon until the age of 21, by which time the tumour was large and was thought to be a hydrocele. This may account for the high level of 17-ketosteroids pre-operatively.

A striking feature of the present case is the remarkably high level of 17-ketosteroid excretion. The values found here compare with those from adult cases: for example, Hoffman (1944) obtained from a man aged 41 a ketonic fraction of 374 mg. a day, mainly androsterone and aetiocholanolone, no D.H.A. The present case is, however, the oldest for which pre-operative values have been recorded during childhood. The history is longer; certainly in excess of two years, and possibly (see below) as long as five years, whereas for the rest of the group the range is from 3 to 21 months, with a mean of 11 months. It is perhaps due to this longer history and also to the nearness to the normal age of puberty that the 17-ketosteroid excretion here is so much greater than in the other cases.

When such high figures are found isosexual precocity in male children is likely to be due to interstitial-cell tumour or to tumour of the adrenal cortex. In the absence of physical signs of tumour the estimation of D.H.A. excretion may be of value in indicating the site. Most cases of adrenocortical tumour show gross increase in the excretion of total 17-ketosteroid with a high D.H.A. content (often 80%), whereas with interstitial-cell tumour the excretion of D.H.A. and also of corticoids should be within normal limits. In adrenocortical hyperplasia the total 17-ketosteroid is seldom as high and the increase in D.H.A. is less striking and not invariable, but the positive finding of an increased amount would suggest adrenocortical origin. Furthermore, in those cases the constant suppression of 17-ketosteroid excretion by cortisone is a distinguishing feature which would not be demonstrated if the steroid substances were of testicular origin.

Another point of interest in the case recorded here is the appearance of an aggressive behaviour disorder for which psychiatric treatment was sought five years before the recognition of the tumour. One can only speculate on the possible relation between the two and whether this might mark the onset of symptoms from the tumour as yet impalpable. Psychosexual precocity is seen in about half the cases, but mention of management problems and increased aggression is also found. One child is described as glum and inaccessible (Thamdrup, 1953). That these changes are not only reactive to the difficulties raised by abnormal development but can be due directly to excessive androgen activity is suggested by the early onset of the symptoms. Thus Cook *et al.* (1952) describe increased activity and aggression appearing early with the development of physical signs, and Staubitz *et al.* (1953) refer to difficulties of management following the appearance of physical changes.

More significant are those cases in which abnormal behaviour preceded all physical signs. Werner *et al.* (1942) give the remarkable history of a child smoking 50 cigars between the ages of 2 and 6 years. In two other cases (James and Shupe, 1950; Jungck *et al.*, 1957) marked aggression and antisocial behaviour appear to have antedated the physical precocity. Severe psychiatric disorder is recognized as an occasional association with the adrenogenital syndrome in women

(Broster *et al.*, 1938; Allen *et al.*, 1939; Greene *et al.*, 1945), where the biochemical lesion is similarly an excess of androgens inappropriate to sex rather than to age. It is interesting also to recall the therapeutic trial of dehydroisandrosterone for inadequate psychopaths (Sands and Chamberlain, 1952). Aggressive tendencies were considered to be a contraindication to such treatment, as increased aggression was observed.

The prognosis is dependent on the complete removal of the source of the excessive androgens. The rapid fall in 17-ketosteroid excretion to a normal level within two weeks indicates a satisfactory outcome in the present case. It is probable that premature closure of the epiphyses will occur, and with the abnormal stimulus to growth removed his physique will alter little. As an adult he should appear normal, though rather short, perhaps no more than his present height of 64 in. (162.5 cm.). Problems of personal and social adjustment should become easier as the actual age passes that of normal puberty and approaches that suggested by his present physical state.

Summary

A case is described of an interstitial-cell tumour of the testicle causing precocious puberty, and in which the urinary 17-ketosteroid excretion was strikingly high.

The literature is reviewed, and is discussed with particular reference to steroid excretion and to the occurrence of behaviour disorders.

REFERENCES

- Allen, C., *et al.* (1939). *Brit. med. J.*, **1**, 1220.
 Anagnostou, J., and Frangopoulos, G. J. (1953). *Ibid.*, **1**, 861.
 Broster, L. R., Allen, C., Vines, H. W. C., Patterson, J., Greenwood, A. W., Marrian, G. F., and Butler, G. C. (1938). *The Adrenal Cortex and Intersexuality*. Chapman and Hall, London.
 Cook, C. D., Gross, R. E., Landing, B. H., and Zygmuntowicz, A. S. (1952). *J. clin. Endocr.*, **12**, 725.
 Demitriadis, T., *et al.* (1948). Quoted by Anagnostou and Frangopoulos (1953).
 Florentin, P., and Rauber, G. (1954). *Bull. Ass. franç. Cancer*, **41**, 79.
 Fraser, K. B. (1949). *Aust. N.Z. J. Surg.*, **19**, 48.
 Greene, R., Paterson, A. S., and Pile, G. C. L. (1945). *Brit. med. J.*, **1**, 698.
 Hertz, R., Cohen, M. I., Lewis, L. G., and Firminger, H. I. (1953). *J. clin. Endocr.*, **13**, 1248.
 Hoffman, M. M. (1944). *Endocrinology*, **35**, 215.
 Huffman, L. F. (1941). *J. Urol. (Baltimore)*, **45**, 692.
 James, D. C., and Shupe, R. D. (1950). *Ibid.*, **63**, 718.
 Jolly, H. R. (1955). *Sexual Precocity*. Thomas, Springfield.
 Jungck, E. C., Thrash, A. M., Ohlmacher, A. P., Knight, A. M., and Dyrenforth, L. Y. (1957). *J. clin. Endocr.*, **17**, 291.
 Melicow, M. M., Robinson, J. N., Ivers, W., and Rainsford, L. K. (1949). *J. Urol. (Baltimore)*, **62**, 672.
 M.R.C. Committee on Clinical Endocrinology (1951). *Lancet*, **2**, 585.
 Munson, P. L., Jones, M. E., McCall, P. J., and Gallagher, T. F. (1948). *J. biol. Chem.*, **176**, 73.
 Newns, G. H. (1952). *Brit. J. Surg.*, **39**, 379.
 Pomer, F. A., Stiles, R. E., and Graham, J. H. (1954). *New Engl. J. Med.*, **250**, 233.
 Rezek, P. (1943). Cited by Melicow *et al.* (1949).
 Rowlands, R. P., and Nicholson, G. W. (1929). *Guy's Hosp. Rep.*, **79**, 401.
 Sacchi, E. (1895). *Riv. Sper. Freniat.*, **21**, 149.
 Sandblom, P. (1948). *Acta endocr. (Kbh.)*, **1**, 107.
 Sands, D. E., and Chamberlain, G. H. A. (1952). *Brit. med. J.*, **2**, 66.
 Staubitz, W. J., Oberkircher, O. J., and Blick, M. S. (1953). *J. Urol. (Baltimore)*, **69**, 562.
 Stewart, C. A., Bell, E. T., and Roehlke, A. R. (1936). *Amer. J. Cancer*, **26**, 144.
 Sutherland, D. M. (1932). *Brit. J. Surg.*, **20**, 343.
 Tavares, A. (1952). *Acta gynaec. obstet. hisp.-lusit.*, **2**, 321.
 Thamdrup, E. (1953). *Acta paediat. (Uppsala)*, **42**, 369.
 Tompsett, S. L. (1953). *J. clin. Path.*, **6**, 74.
 — and Smith, D. C. (1954). *J. clin. Endocr.*, **14**, 922.
 Urban, N. (1942). *Mscr. Kinderheilk.*, **90**, 11.
 Werner, A. A., Spector, H. I., Vitt, A. E., Ross, W. L., and Anderson, W. A. D. (1942). *J. clin. Endocr.*, **2**, 527.