Kelly (1961) has shown that the intravenous administration of oestrogen does not affect spontaneous uterine motility. It is likely that it is the concentration of active oestrogen in the uterine muscle which matters. In this event the only effective route of administration may be into the utero-placental space or into the amniotic cavity. The possibility of intra-amniotic injection is foreshadowed by the work of Diczfalussy *et al.* (1961) on the metabolism of intra-amniotic oestrogens, and we propose to extend our trials using this route.

Summary

A controlled trial was done on the effect of oral oestriol or stilboestrol in women who were to be subjected to artificial rupture of the membranes for surgical induction of labour. It was found that these oestrogens had no demonstrable effect on the induction-delivery interval or on the length of labour.

We are grateful to our statistical colleagues Mr. W. Z. Billewicz and Miss R. Holliday for their help in the design of the trial and in dispensing tablets. Our thanks are due to the nursing staff at the Maternity Hospital for their co-operation, and to Dr. C. L. Hewett, of the Organon Laboratories, for the gift of oestrogen and dummy tablets.

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ALBRIGHT'S SYNDROME IN AN ADULT MALE

REPORT OF AN ATYPICAL CASE WITH PSYCHIATRIC SYMPTOMS

BY

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The case of Albright's syndrome reported here is that of a man who at the age of 30 developed psychiatric symptoms culminating in an attempt at suicide. The syndrome consists of unilateral cutaneous melanosis and polyostotic fibrous dysplasia, accompanied by precocious puberty (Albright *et al.*, 1937). It usually occurs in female children, and was probably first reported by Weil (1922). Its aetiology is unknown (Jolly, 1955). Correct differential diagnosis is simple (Cecil and Loeb, 1959) when the syndrome is kept in mind and may save fruitless surgical exploration for parathyroid adenomata. Thus, although the complete syndrome is rare (Murray *et al.*, 1946), it is of practical importance, as well as of considerable theoretical interest. The incidence of other congenital abnormalities is apparently no greater in these patients than in the population at large (Vines, 1952), but many conditions have been found in association with the syndrome, among them coarctation of the aorta (Lichtenstein and Jaffe, 1942), acromegaly (Falconer *et al.*, 1942), diabetes mellitus (Hurxthal and Musulin, 1953), and hyperthyroidism (Sternberg and Joseph, 1942). Some patients have been of subnormal intelligence (Albright *et al.*, 1937). Pritchard (1951) reviews over one hundred papers on the clinical, radiological, and histological features of the condition, but only a small number of male cases have been recorded. Very few of these were adult; fewer still showed the complete syndrome, and none were reported as fertile. Some female patients with Albright's syndrome have borne children (Dockerty *et al.*, 1945). The case reported below is thus in several respects atypical.

Case History

This patient was born on September 16, 1926, with a deformed forehead and a large brown birthmark on his left thigh. He developed normally and was well in every way until 1939, when he complained of a painful limp and a hard swelling on his left thigh. A diagnosis of osteitis fibrosa cystica was made, and a (histologically normal) parathyroid gland was removed. In August, 1940, radiographs

showed small translucent cysts in the neck of the right and lower left femur. There was also a large cyst in the upper left femur. He continued to limp slightly until 1942, when this symptom became worse, and he was found to have developed a pathological fracture of the left femoral neck. An osteotomy was performed, and some months later the parathyroid region was explored again, but no tumour was found.

The patient was employed as a storekeeper with the same firm from the age of 16. He worked regularly until 1956, when he became increasingly depressed and anxious, and unable to work. He became oversensitive about his appearance and would not leave the house. In 1956 he had a course of electric convulsion therapy without much effect. In 1959 his wife gave birth to a son. He had by then been out of work for three years, felt he would be a failure as a father, and just before the birth of his son he made an attempt at suicide with barbiturates. In January, 1961, he was referred to the Sheffield University Department of Psychiatry, and the diagnosis of polyostotic fibrous dysplasia first put forward in 1943 was confirmed radiologically. Psychological testing showed average intelligence (Wechsler), and there was no sign of organic nervous disease.

The patient displayed the features of a chronic anxiety state with depression. His neurotic symptoms appeared to be related to his long-standing selfconsciousness over his deformities. He had the feeling that the two halves of his body were different. He felt his left side to be "all wrong" and his right side "all good." He worried about his facial and testicular asymmetry, spending much time in front of the mirror. He developed a stammer and a left facial tic, and hid in the attic when strangers called. He thought his condition to be unique and possibly even a divine punishment. His mother, an epileptic, had always overprotected him and dominated the household. He and his family lived with her and he felt continually torn between his dependence on her and his responsibilities to his wife and child. He was given psychotherapy over a period of four weeks (twelve sessions of three-quarters of an hour each). In the course of psychotherapy he was able to ventilate his feelings for the first time and he gained considerable insight into them. When he was discharged after seven weeks he was free from psychiatric symptoms. He had found himself a job as a hospital porter and took it up a few days after his

discharge, having been out of work for five years. At the time of the completion of this paper (November, 1961) he was still working despite some pain in his left hip. He planned to look for lighter work.

Physical Examination

The patient was a short (5 ft. 5 in. (165 cm.)) red-haired man, with extensive left-sided pigmentation (Fig. 1) typical in appearance of Albright's syndrome overlying the areas of maximal bony lesion. The pigmentation was sharply restricted to the left lower abdomen, buttock, and thigh (T 10-L2), with one or two small patches on the left side of the head (C2 and C3) and thorax. The left scapula was palpably deformed and expanded, and there was "bossing" of the left forehead, with "leontiasis ossea" and facial asymmetry. The left lower limb was $1\frac{1}{2}$ in. (3.8 cm.) shorter than the right and the left testis was much larger than the right, which seemed somewhat atrophic. Vision was normal but he was partially deaf in the left ear. Despite these changes he had no physical complaints. The patient was an only child, and his son (aged 18 months) showed no features of the condition. His father, however (aged 68), was only 4 ft. 11 in. (150 cm.) tall, and was said to have been "born with a limp" and a badly bowed left thigh. He had fractured this thigh in 1900, aged 7. On examination the father showed gross bowing of both

FIG. 1.—Showing extensive pigmentation.

femora with a few small café au lait patches of pigment over the internal aspects of both thighs. Serum calcium, phosphorus, and alkaline phosphatase levels were normal and radiographs showed no changes in bony architecture. A paternal uncle (who died of pneumonia in 1890) was said to have had "bone disease," and to have broken both legs after allegedly trivial trauma at the age of 2. There was nothing of note on the maternal side of the family.

Investigations

The electrocardiogram, electroencephalogram, and intravenous pyelogram were normal. Cerebrospinal fluid: white-cell count, $<2/c.mm.$; protein, 15 mg./100 ml.; sugar 72 mg./100 ml.; Lange, 0000000000. Urine: culture sterile; no albumin, sugar, or Bence Jones protein; 17-ketosteroids, 14.3 mg./24 hours; 17-hydroxycorticosteroids, 22.3 mg./24 hours; 17-ketogenic steroids, 20.4 mg./24 hours. Total oestrogens, 25 i.u./day; gonadotrophins, 17 mouse units/day; amino-acids—paper chromatography "normal pattern." Calcium, 12.8 mg./100 ml. Blood: Hb, 101%; W.B.C., 7,000 c/mm. (film normal); E.S.R., 21 mm./hr. (Westergren); blood urea, 28 mg./100 ml.; prolonged glucose tolerance curve, normal; W.R. and Kahn negative; serum acid phosphatase, 5 Gutman units; formaldehyde stable acid phosphatase, 4 Gutman units; serum alkaline phosphatase, 61 King-Armstrong units; serum cholesterol, 251 mg./100 ml.; total serum proteins, 7 g.% (increase in α_2 -globulin on electrophoresis); liver function tests normal; thymol turbidity 2 units; thymol flocculation negative; direct van den Bergh, negative; serum bilirubin 0.4 mg./100 ml. Bone biopsy (August 4, 1943): "Young connective tissue with islands of poorly calcified new bone. Suggestive of osteitis fibrosa cystica."

The biopsy was re-examined by Professor D. H. Collins on August 14, 1961: "... a portion of normal and apparently unaffected cortical bone and considerable areas of the medullary tissue, which is osteogenic fibrous tissue and not very highly cellular. Among this bland fibrous tissue are a variable number of trabeculae and islets of coarse-fibred bone and osteoid. The appearance is characteristic of fibrous dysplasia, though a less usual feature is the presence of a small number of osteoclasts along the borders of some of these new bone trabeculae; these giant cells are not anomalous in fibrous dysplasia, but they may have led to the repeated diagnosis of osteitis fibrosa cystica at the time when fibrous dysplasia was only just being identified."

X-ray Appearances. — Radiological examination showed gross thickening of the left side of the calvaria with loss of normal bone structure (Fig. 2). The facial bones were involved in a more sclerotic change. There were widespread extensive cystic lesions in both innominate bones and the upper ends of both femora, with further widespread lesions in ribs, lower limb, left scapula, and vertebral column. There was a large cyst involving the whole body of the fourth lumbar vertebra (Fig. 3).

Chromosome Studies. — Peripheral blood was taken on March 8, 1961, cultured, and examined by Dr. C. E. Blank. No chromosomal abnormality was apparent. It is intended to examine other tissues to exclude, as far as possible, chromosomal mosaicism.

Discussion

This is apparently the first case of Albright's syndrome in

FIG. 2.—Appearance of left side of the calvaria.

FIG. 3.—Showing a large cyst involving the fourth lumbar vertebra.

Chromosomes in 35 Cells

No.	Frequency	45	46	47
1	1	33	1	

Sex chromosome XY.

which chromosome studies have been carried out. The possibility of an unbalanced chromosomal aberration was suggested long ago by Moehlig and Schreiber (1940).

The similarity of the bone changes to the embryonic preformation of membranous bone has been pointed out by Hall *et al.* (1955). It is difficult to see how endocrine dysfunction could be causal unless, as has been suggested (Sternberg and Joseph, 1942), there was also some localized tissue susceptibility. The differentiation between this condition and multiple neurofibromatosis, with which a connexion has often been discussed (Levene, 1959), seems clear in the above case. The only abnormalities in the body fluids examined were the raised E.S.R. and serum α_2 -globulin, apart from the serum alkaline phosphatase, which seems to be the highest yet recorded in the condition. These changes probably indicate the activity of the condition. Fertility in a male case seems not to have been previously reported nor have some of the investigations carried out here—urine paper chromatography and 17-ketosteroid, 17-hydroxycorticosteroid, and 17-ketogenic steroid estimations. No evidence of hepatic damage has been found, although this has also been postulated (Braid, 1939). Unlike a previous case (Helfet, 1939) the patient did not show Bence Jones proteinuria. The abnormalities found in the patient's father are noteworthy as they may be akin to those which form part of Albright's syndrome. Gates (1946) reports that one of Albright's original female cases bore twin boys, one of whom had some pigmentation. It has been pointed out by Sorsby (1953) that an irregular dominant pattern over four generations is on record in facial fibrous dysplasia which shows bone changes similar to those found in the polyostotic form. No evidence has emerged to support theories of a neurological (Thannhauser, 1944) origin or of pituitary dysfunction (Falconer *et al.*, 1942). Thyroid over-activity, reported by Sternberg and Joseph (1942), was neither present clinically nor on radioactive iodine uptake studies. Serum cholesterol and urinary oestrogens which have been reported as high (Dockerty *et al.*, 1945) were normal. Testicular enlargement has been described only twice, either with precocious puberty (Falconer *et al.*, 1942), or associated with feminism and gynaecomastia (Moehlig and Schreiber, 1940). There was no evidence of sexual precocity in this patient who had unilateral testicular atrophy. Sexual precocity (Falconer *et al.*, 1942) is the rule in female cases (Albright *et al.*, 1937), where menstruation may occur as early as at 4 months of age (Pritchard, 1951). Optic atrophy due to bone changes at the optic foramina (Falconer *et al.*, 1942) was absent here but the patient was partially deaf. On the whole, radiographic changes observed in this case are typical of the condition in site and character (Pritchard, 1951), but are unusually extensive. Vertebral lesions are extremely uncommon in the syndrome although they have been recorded (Teng *et al.*, 1951). It has been said that the bony lesions tend to subside at puberty (Dockerty *et al.*, 1945), but in this patient they seem to have become more extensive. Although mental deficiency has been reported in the condition (Albright *et al.*, 1937), as well as neurosis (Falconer *et al.*, 1942), no results of formal psychological testing or of psychiatric examination have appeared previously. The patient's psychiatric symptoms were those of an anxiety neurosis with a tendency to depression. His lifelong awareness of his bony deformities, which made him feel different from other people, played an important part in the aetiology of his neurosis. Bender (1934) made a study of the role of

chronic bone disease in the development of psychiatric symptoms. She regarded the discrepancy between the actual body structure and the socially accepted body image as psychologically pathogenic. The majority of Bender's patients had Paget's disease and the most common psychiatric symptoms were paranoid ideas. The patient described here, whose bony deformities were less severe than those of Paget's disease, reacted with neurotic symptoms only.

Summary

A case of Albright's syndrome with atypical features has been described. The patient was an adult male with skin, bone, and testicular abnormalities. Chromosome studies and certain biochemical investigations have been reported for the first time. Serum alkaline phosphatase levels have been found to be unusually high and radiographs showed vertebral lesions to be present. The patient was disabled by a severe neurosis which responded to psychotherapy. The physical anomalies had played a part in the origin of the neurosis.

I wish to thank Dr. W. L. Tonge for permission to study this patient. I am indebted to Professor E. Stengel for much help and encouragement, to Professor D. H. Collins for advice and the bone-biopsy result, to Dr. C. E. Blank, who carried out the chromosome studies, and to Dr. R. G. Grainger for the radiological reports. Without the great kindness of numerous other colleagues and the staff of their departments in the United Sheffield Hospitals, the non-psychiatric investigation of this case could not have been carried out.

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 Weil (1922). *Klin. Wschr.*, **2**, 2114 (quoted by Pritchard, 1951).

A working party of the British Council of Churches has published a booklet—"as a stimulus to discussion"—called *Human Reproduction: a Study of Some Emergent Problems and Questions in the Light of the Christian Faith*. Its contents include discussions of new techniques in animal reproduction and of whether they are applicable to human beings; the treatment of sub-fertility; developments in contraception; and some legal and theological considerations. Dr. P. L. Backus and Dr. Eleanor Mears were among the members of the working party. (Obtainable from the Publications Department, British Council of Churches, 10 Eaton Gate, London S.W.1. Price 3s.)