patient 70 years old. Secondly, the finding of an easily recognizable and viable chromosome change occurring at an early stage of culture, while it does not detract from the usefulness of this technique, does indicate that results should be interpreted with caution.

Hungerford *et al.* (1959) have published a full study of a true hermaphrodite bearing one testis and an ovotestis, in which the great majority of cells which they examined from the peripheral blood were reported to have 46 chromosomes. The sex chromosomes were interpreted as XX. These findings agree very well with ours, and both results together pose some interesting developmental problems—for example, how can cells which seem genetically determined to form a female organism differentiate into a testis and lead to the formation of a predominantly male phenotype? One must consider the possibility that these patients are mosaics—that is, are made up of two or more clones of cells of different genetic constitution. This has been suggested for true hermaphrodites, but this is not supported by the evidence obtained from observations of the sex chromatin (Grumbach and Barr, 1958). This test, however, would not locate an XX/XXY mosaic, and Hungerford *et al.* do not exclude the possibility that their patient could fall into this category though no XXY cells were found. In our case after examination of bilateral skin biopsies and bone-marrow there is no evidence to suggest that the patient is a mosaic. It would, however, have been very interesting to examine the cells of the right gonad to determine whether the cells which had differentiated into a testis really did have two X chromosomes and no Y, but this is not now possible.

The primary defect in this case is a developmental error which may or may not have been genetically determined. The medullary component of one gonad has somehow become dominant in spite of the presence of two X chromosomes which would normally ensure the dominance of the cortex. The subsequent masculinization of the genital tract is probably a consequence of this primary error. Grumbach and Barr quote several examples of reversal of gonadal development in other vertebrates induced by hormone treatment. Especially interesting is the bovine freemartin, where the presumptive ovary differentiates into a testis under a hormonal influence of unknown origin. It seems reasonable to suggest that some similar, and likewise unknown, hormonal influence may be acting in cases such as the one reported here. This study emphasizes the point, which has been made before but perhaps not sufficiently stressed, that the phenotype of an individual is the resultant of an interplay between several factors, some genetically determined and others probably not. In sex differentiation, as distinct from sex determination, this is of great importance. In this particular case the possession of the female pattern of sex chromosomes has not proved sufficient to determine the phenotype and has not prevented other factors, which may or may not have been genetically determined, causing masculinization of what should apparently have been a female individual.

Summary

The chromosomes of a human true hermaphrodite have been studied and found to be 46 in number, the sex chromosomes being interpreted as XX. There is no evidence of mosaicism. The importance of the interaction of genetic and non-genetic developmental factors in the development of the phenotype is noted.

We thank Dr. D. W. R. Ashby, Dr. C. E. Ford, Dr. J. E. Gray, Miss P. A. Jacobs, and Dr. J. S. S. Stewart, without whose co-operation this work would not have been possible, and Miss C. M. Scammell for her skilful technical assistance.

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UNUSUAL CASE OF GONADAL DYSGENESIS (TURNER'S SYNDROME)

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Turner's (1938) syndrome is characterized by infantilism, shortness of stature, webbing of the neck, and cubitus valgus, but numerous other congenital abnormalities have been described. Turner made no mention of the condition of the gonads. Varney, Kenyon, and Koch (1942) and Albright, Smith, and Fraser (1942) demonstrated in this disorder a high urinary excretion of gonadotrophin, and from this concluded that the infantilism was due to primary ovarian insufficiency. Previous authors, tabulated by Wilkins and Fleischmann (1944), had described similar cases in which rudimentary ovaries had been found at laparotomy or at necropsy. Wilkins and Fleischmann (1944), observing that the "ovary" consisted only of a primitive genital ridge composed of stroma-like cells and showing no proliferation of the epithelium nor primordial germ cells, proposed the term "ovarian agenesis" for this condition.

Subsequently Grumbach, Van Wyk, and Wilkins (1955) showed that most of their patients with this disturbance had a male chromatin sex pattern, and considered that the condition exemplified an extreme form of male pseudohermaphroditism. On this account Wilkins (1957) applied the term "gonadal aplasia" for this disorder, using the wider term "gonadal dysgenesis" for the entire group of defects in the development of the gonads. Ford *et al.* (1959), however, subsequently found that a patient with gonadal dysgenesis and chromatin negative possessed 45 chromosomes instead of the normal 46. They concluded that the sex-chromosome constitution of the patient was XO, and emphasized that such a person should not be referred to as a chromosomal male, as she was a female with an abnormal genotype.

Four cases of gonadal dysgenesis have been reported by Sellheim (1924), Pela (1935), Pich (1937), and Tronci (1938) in which ovarian development had proceeded to a varying degree before arrest took place. In Pela's case, that of a woman aged 36 and 74 in. (188 cm.) in height, the ovaries were "the size of orange seeds," and on histological examination no primordial follicles were seen. In Tronci's case, that of a woman aged 20 and 61 in. (155 cm.) in height, the ovaries measured 6 by 2.5 mm. in diameter; microscopically, germinal epithelium was noted, but there were no primordial follicles. Pich described the case of a woman aged 29 with infantilism, absence of pubic and axillary hair, coarctation of the aorta, and normal stature, whose ovaries measured 28 by 5 by 3 mm. and 30 by 4 by 2 mm.; histological examination revealed proliferative germinal epithelium and fairly numerous primordial follicles. In Sellheim's case, a woman, aged 21 and also of normal stature, the ovaries measured 7.5 by 2.5 mm., and numerous primordial follicles were present. Since the urinary gonadotrophins were not estimated in any of these cases it is impossible to say whether the hormonal deficiency was primarily ovarian or primarily pituitary.

It is the purpose of this paper to record the case of a patient with infantilism, several of the congenital abnormalities of Turner's syndrome, and greatly increased urinary gonadotrophin associated with ovaries which, though of normal size, contained a diminished number of follicles showing no evidence of maturation.

Case Report

A girl aged 17 was admitted to St. Bartholomew's Hospital complaining of amenorrhoea, shortness of stature, and deformity of the spine. Her birth weight was only 4 lb. (1.8 kg.), though the pregnancy had run to full term; delivery was normal. She walked and talked at the usual stages, and at school she was considered to have been above the average intelligence for her age. She had always been small, and for several years her weight has remained unchanged. For many years her parents had observed a deformity of her back. In 1956 she attended a poliomyelitis clinic in Salisbury, Southern Rhodesia, where she lived, but there was a difference of opinion on whether the spinal deformity was due to poliomyelitis: her mother did not know whether she had had poliomyelitis, though there were numerous cases of this disease in Salisbury at the time. She claimed to have menstruated for three days in December, 1957, but apart from this occasion there has been complete amenorrhoea.

During her childhood she contracted chicken-pox and whooping-cough, but had never suffered from mumps. During the two years before her admission to hospital she had recurrent attacks of abdominal colic localized in the right iliac fossa. Her parents and her two brothers are normal and healthy.

Physical Examination (Fig. 1).—She was an intelligent girl with a high-pitched piping voice. Weight 54 lb. (24.5 kg.); height 57 in. (144.7 cm.), span 56½ in. (143.5 cm.), symphysis pubis to the ground 29½ in. (74.9 cm.), symphysis pubis to the vertex 27½ in. (69.8 cm.). (The limb proportions are approximately normal when due account is taken of her severe kyphoscoliosis.)

Musculo-skeletal System.—She was very thin and the musculature was poorly developed. Both deltoid muscles were greatly wasted and she was unable to lift her arms above her head. There was marked webbing of the neck, and the scapulae were winged owing to wasting of the trapezii. The mandible was poorly developed, the hard palate was high-arched and narrow, and the teeth were crowded. The clavicles were increased in length, and the

manubrium sterni was at a lower level than normal so that the clavicles had a marked downward inclination medially. There was bilateral cubitus valgus. The spine showed severe kyphoscoliosis, which had resulted in tilting of the pelvis with apparent shortening of the left leg.

Skin and Hair-growth.—Her colour was somewhat sallow, but there was no abnormal pigmentation. The texture of the skin was normal. The growth of the axillary and pubic hair was normal, and there was a moderate growth of downy hair over the limbs. The scalp hair and hair-line were normal.

Breasts and Genitalia.—There was very slight development of the breasts, and the nipples were small but pigmented. The vulva was infantile. The clitoris was normal.

FIG. 1.—Photographs of the patient.

Other Systems.—The cardiovascular, respiratory, and nervous systems were normal; pulse rate 80; blood-pressure 105/70. There was marked tenderness in the right iliac fossa. The urine contained no albumin and no sugar, and the deposit was normal. In a water-load-excretion test over 80% was excreted within four hours. Laryngoscopic examination (Mr. J. C. Hogg) revealed an infantile type of larynx. The visual fields were full, colour-vision was normal, and there were no lenticular opacities.

Radiological Examinations.—Radiological examination of the skull showed a minor degree of turriccephaly and evidence of premature closure of the coronal and sagittal suture. In the hands there was evidence of early closure of the epiphyses; all the primary epiphyses had united. The secondary epiphyses for the ischium and ilium had appeared. There was no evidence of osteoporosis of the pelvis. The vertebral column showed gross spinal curvature; no vertebral defect was demonstrated, and there was no evidence of osteoporosis. An intravenous pyelogram was normal.

Laboratory Findings.—Blood count: haemoglobin, 92% (13.6 g./100 ml.); white cells, 3,700/c.mm. (neutrophils 52%, eosinophils 5%, basophils 2%, lymphocytes 30%, monocytes 11%). Erythrocyte sedimentation rate, 3 mm.

in first hour (Westergren). Blood group AB, rhesus-positive. Blood urea, 18 mg./100 ml. Chromatography of urinary amino-acids: normal pattern. Serum calcium, 10.4 mg./100 ml.; serum inorganic phosphate, 4.5 mg./100 ml.; serum alkaline phosphatase, 4 King-Armstrong units/100 ml. Serum cholesterol, 258 mg./100 ml. Basal metabolic rate, minus 9%. Glucose-tolerance test: fasting level, 100 mg./100 ml. rising to 145 mg. and falling to 100 mg./100 ml. in one and a half hours. Urinary 17-ketosteroids (M.R.C. method), 3.7 and 6.6 mg. per 24 hours. Urinary 17-hydroxycorticosteroids (Norymberski), 8.4 mg. per 24 hours. Urinary 17-ketogenic steroids (Norymberski), 3.26 mg. per 24 hours. Urinary oestrogens (method of Brown, Bulbrook, and Greenwood, 1957): oestrone, 0.7 μ g. per 24 hours; oestriol, 0.8 μ g. per 24 hours; oestradiol-17 β , nil. Urinary pregnanediol, 0.13 μ g. per 24 hours. Urinary gonadotrophins, more than 150 units of H.M.G. 20* per 24 hours—a very high figure (normal, about 10 units of H.M.G. 20 per 24 hours; post-menopause, about 60 units of H.M.G. 20

FIG. 2.—Section of ovary. ($\times 310$.)

per 24 hours). Vaginal smear showed moderate oestrogenic activity. Nuclear sex of leucocytes: 6 of 312 neutrophil polymorphonuclear leucocytes examined in three blood smears showed nuclear drumsticks—female pattern (Dr. P. Storey). Nuclear sex of skin cells: moderate numbers of female cells were seen in the epidermis (Dr. W. J. Hanbury).

Laparotomy.—During her stay in hospital the patient suffered from an attack of appendicitis, and an acutely inflamed appendix was removed (Mr. N. A. Green). At operation the gonads were inspected, and two ovaries were found that were normal in appearance, measuring 4.5 by 3 cm. in diameter. The uterus measured 3.75 by 3.75 cm. The hymen admitted a little finger.

Histology of Ovaries (Fig. 2).—Dr. W. J. Hanbury reported as follows: "The section shows part of an ovary in which the follicles are diminished in number and show no evidence of maturation into Graafian follicles or corpora albicantia. The tunica albuginea and cortical stroma show normal appearances."

Discussion

The vagaries of the features of gonadal agenesis and dysgenesis have been fully discussed by Hoffenberg and Jackson (1957a, 1957b). We confirm their statements by the following observations: (1) Patients with rudimentary gonads are not always short in stature; for instance, the patient reported by Meyer (1931) was 66.7 in. (169.4 cm.) in height, by Schneider and McCullagh (1943) 62 in. (157.4 cm.), by Greenblatt, Carmona, and Higdon (1956) 70 in. (178.3 cm.), and by Hoffenberg and Jackson (1957a) 66.6 in. (169 cm.). (2) They may have no congenital abnormalities and may

*H.M.G. 20 = Human menopausal gonadotrophin, batch 20 (Organon).

present only with amenorrhoea and infantilism (del Castillo, de la Balze, and Argonz, 1947; Greenblatt *et al.*, 1956; Hoffenberg and Jackson, 1957b; Natoli and de Pedrini, 1957). (3) The breasts may be normal (Hoffenberg, Jackson, and Muller, 1957). (4) Even menstruation may occur (Hoffenberg *et al.*, 1957).

We have not seen any report in the literature of a case of Turner's syndrome in which the ovaries had reached their normal size. The very high urinary excretion of gonadotrophins demonstrated that the ovarian failure was primary and not the result of anterior pituitary deficiency, which may be the cause in some cases in which the urinary gonadotrophins are low. It has been stated by previous authors that an increased excretion of gonadotrophins in the presence of the congenital abnormalities of Turner's syndrome is evidence of rudimentary gonads, but the degree of development of the ovaries in the present case demonstrates that this conclusion is not necessarily true. The ovarian failure probably occurred at the time when puberty should normally have begun; the cause of the failure is unknown. This late ovarian failure, however, was associated with the following congenital stigmata of Turner's syndrome: shortness of stature, webbing of the neck, high-arched palate, poorly developed mandible, elongation of the clavicles, and cubitus valgus.

We consider that the atrophy of the deltoid muscles, limiting the movements of the upper extremities, and the winged scapulae due to paresis of the trapezius muscles are the result of scapulo-humeral muscular dystrophy of the Erb juvenile type. There is no real evidence that the patient had had poliomyelitis; furthermore, it is unusual in poliomyelitis for the muscular wasting to be as symmetrical as in our patient. In the literature on the subject only two cases of muscular dystrophy in hypogonadism have been recorded—namely, those of Bassöe (1956). These patients were a woman with gonadal agenesis and her brother with Klinefelter's syndrome; they both suffered from congenital muscular dystrophy and infantile cataract. In the family there were five other children with muscular dystrophy and infantile cataract, one of whom was found on histological examination to have slight atrophy of the ovaries. Our patient appears to be the third case of muscular dystrophy occurring in a patient with gonadal dysgenesis.

The cause of the severe kyphoscoliosis is uncertain. There is no evidence that it was due to osteoporosis, and it seems doubtful whether poliomyelitis was the cause. It is unlikely that it was due to muscular dystrophy, since in this disease the muscular wasting is usually symmetrical.

Summary

The case is recorded of a girl aged 17 who suffered from infantilism and had the following congenital abnormalities of Turner's syndrome: shortness of stature, webbing of the neck, a high-arched palate, a poorly developed mandible, elongation of the clavicles, and cubitus valgus. There was evidence of early closure of the epiphyses. The nuclear chromatin pattern was female. The urinary gonadotrophins were greatly raised, indicating primary ovarian failure. At laparotomy the ovaries were found to be macroscopically normal, and a section removed for biopsy showed no evidence of maturation of the follicles or corpora albicantia. It is considered that arrest of ovarian development occurred at the time that puberty should normally have taken

place. In addition she had bilateral wasting of the deltoid muscles and winged scapulae, attributed to acquired muscular dystrophy. She also suffered from severe kyphoscoliosis, the cause of which is uncertain: there was no evidence of osteoporosis or definite history of poliomyelitis.

We are indebted to Dr. E. Sanders, of Salisbury, Southern Rhodesia, for referring this patient to one of us (A. W. S.). Our thanks are due to Drs. R. D. Bulbrook and F. C. Greenwood, of the Clinico-Pathological Laboratories, Royal College of Surgeons of England, for their estimation of the urinary oestrogens, pregnanediol, and gonadotrophins, and to the members of the pathological and radiological departments, St. Bartholomew's Hospital, for the other investigations.

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TEMPORAL ARTERITIS IN GENERAL PRACTICE

BY

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Since Horton, Magath, and Brown's (1932) description of temporal arteritis it has been regarded as a rarity and most of the standard textbooks of general medicine give it scant regard.

Cooke, Cloake, Govan, and Colbeck (1946) seem in retrospect as voices crying in the wilderness when they said: "There exists in elderly people a widespread arterial disease, not uncommon, but rarely recognized, in which characteristic arterial and striking local signs occur, and in which inflammatory and degenerative changes in the walls of the affected arteries produce a characteristic histologic picture."

Harrison (1948) reviewed the 75 cases which were all that had been reported in the world literature at that time. Robertson (1952) reported a personal series of 28 cases in the preceding seven years and again suggested that the condition was probably much commoner than had hitherto been suggested. This

contention was supported by the painstaking monograph of Roux (1954), who systematically combed the medical journals and reported 248 published cases.

My present purpose is to report nine cases of this condition occurring in a medium-sized provincial general practice during the period March, 1953, to March, 1959, and thus to bear out the contention that this is probably a much commoner condition than is generally acknowledged.

Nomenclature

Hutchison (1890) first described the condition but did not name it. Horton *et al.* (1934) called the disease "temporal arteritis," but it has since been described as "Horton's arteritis," "giant-cell arteritis," and "cranial arteritis." Martin, Lynn, Dible, and Aird (1956) are in favour of the term "non-specific granulomatous arteritis" with an appropriate prefix, such as "generalized" or "temporal."

Temporal arteritis is a generalized arterial disease almost exclusively affecting elderly people; the average age is about 68 years, and males and females are affected in almost equal proportions (Roux, 1954). From the pathological point of view, temporal arteritis is generally regarded as a collagen disease and, in that cryptogenetic family, a first-cousin to polyarteritis nodosa. The distinction between the two is the basis of the general pattern of the disease rather than on any hard-and-fast dividing line. Broadly speaking, temporal arteritis is a disease of the elderly, is usually relatively benign, and selects the larger arteries. Polyarteritis frequently attacks younger people, tends to run a more acute and malignant course, and selects the medium-sized and smaller arteries of muscles and viscera.

There are other inflammatory vascular conditions related to these two. Zeek (1952) groups these conditions together under the heading "necrotizing angiitis," in all of which there is fibrinoid necrosis and inflammatory reaction involving all three coats of the vascular wall; in her classification five types of necrotizing angiitis could be differentiated (hypersensitivity angiitis, allergic granulomatous angiitis, rheumatic arteritis, periarteritis nodosa, and temporal arteritis).

McCombs, Patterson, and MacMahon (1956) report 30 cases of "allergic" vasculitis, a condition, they maintain, in which vascular changes result from an allergic reaction within the vessel walls, but quite distinct from periarteritis nodosa.

Case 1

A spinster, aged 86, of gentle upbringing was first seen on March 28, 1953. She complained of sudden blindness in the left eye, having suffered for some weeks from increasing headache, nausea, and sporadic vomiting. She was very weak, and for some weeks had had an unexplained low-grade pyrexia.

On examination the left eye had no perception of light, and the fundus appearances were those of occlusion of the central retinal artery. Headache was very severe and the scalp tender to touch, especially in the left temporal area. Both superficial temporal arteries were thickened, tortuous, and tender. The left showed no pulsation. In addition, both occipital arteries were palpable and tender, and both facial arteries could be felt as thickened cords at the point at which they crossed the mandible.

Sight did not return in the left eye, and the patient declined slowly over several months until she died on January 21, 1954.