It should be noted that the earlier conception of histoplasmosis as a rare and inevitably mortal disease is erroneous. Large-scale surveys of the incidence of histoplasmin-sensitivity, especially in parts of the United States of America, have shown that subclinical infections are infinitely commoner than clinically evident disease: most of these benign subclinical infections occur in the lungs. Greater knowledge of the disease has also shown that even severe clinical illness may be followed by recovery. Recent accounts of histoplasmosis to which reference may be made include those by Schwartz (1954), Poles and Lavertine (1954), and Leigh and Thomas (1955).

An unusual feature of the two cases described here was the uncommonly large size of the organisms in the tissues. Organisms of comparable size were characteristic of the lesions in the case studied by Robb-Smith (1943) and Duncan (1946-7): their patient likewise probably contracted the infection in West Africa. Duncan (1946-7) suggested that this large-cell type of histoplasma might be a species distinct from *H. capsulatum*, or a variant of *H. capsulatum*. Dubois, Janssens, Brutsaert, and Vanbreuseghem (1952) found a similar large-cell strain in a patient in the Belgian Congo and cited eight other African infections, including Duncan's (1946-7) case, which were probably caused by this type of organism; they too suggested that the large-cell histoplasma is a distinct species, and they proposed that it should be named *Histoplasma duboisii*.

Clarke, Walker, and Winston (1953) described an extraordinary case of widespread cutaneous histoplasmosis in a Nigerian: their histological findings appear to have been similar to those in the cases reported in this paper; the intracellular organisms were of the large-cell type. They isolated a histoplasma which they described as *H. duboisii*.

The status of the large-cell type of histoplasma as a distinct species has not been finally decided: if not identical with *H. capsulatum* it is at least closely related to it. It is noteworthy that naturally occurring large-cell strains have been recorded so far mainly in the case of infections originating in West Africa; Schwarz (1953), however, observed the development of comparable large forms in tissue explants from organs of mice which had been infected with *H. capsulatum* isolated from patients in the United States of America, and Moore (1955) cited some American cases in which the large forms were present in the tissues.

Summary

Two cases of solitary localized histoplasmic granuloma of the skin are reported. The patients are Nigerians, and were living in England at the time of diagnosis. The infection was contracted in West Africa in each case. The organisms in the granulomas were of the large-cell type which has been described as *Histoplasma duboisii*: their cultural characteristics were typical of *Histoplasma capsulatum*.

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A CASE OF TRUE HERMAPHRODITISM

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[WITH SPECIAL PLATE]

The literature on true hermaphroditism has recently been adequately reviewed by Bromwich (1955) and by Greene *et al.* (1952). From these surveys it appears that at most 60 proved cases have been recorded. The case described here is presented because the diagnosis was made after puberty and because the sex-chromatin findings have a bearing on sex differentiation.

Case Report

The patient, aged 18 years, lived in a remote Jamaican village. Both parents died during his infancy. He has always dressed and behaved as a boy; and, although he had noticed that his breasts were enlarging and his penis was small, he became concerned about his condition only at the age of 15 when he began to bleed from a small orifice in the perineum (Fig. A). The bleeding occurred every month, lasted about five days, and was occasionally accompanied by hypogastric pain.

When first seen he was dressed as a male. On physical examination he appeared to be a well-developed coloured (mixed African and European) youth. His voice was of average male pitch. The scalp and axillary hair were normal, there was little facial and no chest hair, and the abdominal hair was female in distribution. The breasts were well developed and pendulous (Fig. B). The body contours were not strikingly female and the body measurements were as follows: weight, 122 lb. (55 kg.); height, 5 ft. 6½ in. (166 cm.); span, 5 ft. 9 in. (173 cm.); vertex to pubis, 31½ in. (79 cm.); pubis to ground, 35 in. (88 cm.).

The genitalia are shown in Fig. A. There was no pronounced mons pubis. The phallus was more like a penis than clitoris and measured 3.5 by 1.5 cm.; there was a moderate hypospadias. No labial or scrotal swelling was present and no testes could be palpated. There was a small left indirect inguinal hernia. The perineal region was perforated 3 cm. in front of the anus by a small orifice 2 mm. in diameter through which the monthly bleeding occurred and urine occasionally escaped. The anatomy of the vagina and urethra is shown in Fig. C. On abdomino-rectal examination a small uterus could be palpated, but no prostate could be felt.

Contrast radiography with viscous diodone demonstrated a vagina, a long cervical canal, a small, normally shaped uterine cavity, a left Fallopian tube for a distance of about 2.5 cm., and a right Fallopian tube of normal length. There was no peritoneal spill on either side (Fig. D). Radiologically the pelvis was gynaecoid in type. The femoral-head epiphyses were fusing and the flake epiphyses of the pelvis were well advanced for the patient's age. The bone age was thus within the early limits of normal, which is more characteristic of the female than of the male. Urinary oestrogen and 17-ketosteroid excretion was not estimated.

Repeated interviews with the patient confirmed our first impression that he was definitely male in outlook. He was very anxious to be rid of his enlarged breasts and monthly

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FIG. 1.—Internal genital organs at operation.

FIG. 2.—Ovarian component of left gonad. ($\times 480$.)

FIG. 3.—Testicular component of left gonad. ($\times 480$.)

FIG. 4.—Epidermis showing sex-chromatin body on nuclear membrane. ($\times 5,350$.)

FIG. 5.—Interstitial tissue of testis showing sex chromatin. ($\times 5,350$.)

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FIG. 1.—Male nucleus typical of those included. ($\times 1,125$.)

FIG. 2.—Female nucleus typical of those included. ($\times 1,125$.)

FIG. 3.—Nuclei excluded because of bacterial contamination. ($\times 1,125$.)

FIG. 4.—Nuclei excluded because of folding of cell body. ($\times 1,125$.)

bleeding. A psychiatrist reported that there was strong evidence that he was psychologically masculine.

Cystoscopy under general anaesthesia showed the bladder and ureteric orifices to be normal. At laparotomy the internal genitalia were found to be predominantly female. The uterus was 90 mm. in length, with a long, narrow hypoplastic supravaginal cervix measuring 55 mm. The

right tube was long and hypoplastic and measured 90 mm. The left tube was thickened and its fimbrial end was buried amongst peritoneal folds near the brim of the pelvis. The right gonad looked like normal ovary and contained a corpus luteum; biopsy and frozen section confirmed this. The left gonad lay close to the left internal inguinal ring, covered by peritoneal folds. Dissection disclosed that it was made up partly of a testis and partly of an ovary also containing a corpus luteum (Special Plate, Fig. 1). Subsequent histological examination confirmed that the right gonad was an ovary and the left a combined ovary and testis. Total hysterectomy was performed with removal of the upper third of the vagina, both tubes, the right gonad, and the ovarian portion of the left gonad. Convalescence was uneventful.

Fifteen days later bilateral mastectomy was performed through

FIG. A.—View of perineum, showing genitalia. The probe is in the orifice through which menstruation occurred.

FIG. B.—The pendulous breasts.

semicircular incisions in the upper circumference of the areolae, with removal of semilunar pieces of skin and preservation of the nipples and areolae. Eleven days after that operation the hypospadias was repaired, and six days later the perineal orifice was closed in two layers.

Social adjustment of the patient was facilitated by securing him congenial employment as a manservant. He is much happier since his operations and is to all appearances a cheerful, normal young man.

Pathology

The uterus, cervix, right gonad and tube, left gonad and tube, both breasts, and portions of thoracic skin were all examined histologically. The endometrium was in the proliferative phase. The right ovary showed a well-developed corpus luteum with a haemorrhagic centre, the remainder of the section being composed of normal ovarian

tissue. The ovarian portion of the left gonad showed normal ovarian tissue and contained a corpus luteum of later date than the right (Plate, Fig. 2). The small portion of testis removed contained seminiferous tubules and relatively prominent interstitial tissue. The tubules had a thickened basement membrane and the majority of cells appeared to be of Sertoli type. There was no evidence of spermatogenic activity and no definite spermatogenic cells were seen (Plate, Fig. 3). Sections from the isthmus and infundibular portions of the left Fallopian tube were normal. The histo-

FIG. C.—Diagram showing anatomy of urogenital organs.

FIG. D.—Hysterosalpingogram, antero-posterior view. Right posterior oblique view taken few minutes later showed normal right Fallopian tube.

logical features of both breasts were essentially the same and showed marked resemblance to those of the normal adult female. Findings of the sex-chromatin studies are summarized in the Table.

Table Showing Results of Sex-chromatin Studies

Tissue	Female Sex Chromatin Count	Type
Skin of right breast	62%	Female
" " left	69%	"
Testis: Leydig and interstitial cells	56%	"
Seminiferous tubules	No definite female-type sex chromatin demonstrable	"
Smears from oral mucosa	59%	Female
Polymorphs (blood smears) ..	—	"

Discussion

Success in the management of the hermaphrodite depends on early diagnosis, accurate clinical, psychological, and histological evaluation, and the adoption of appropriate surgical, endocrine, and psychotherapeutic measures to adjust the patient as a normal member of society.

Diagnosis

It is extremely difficult to differentiate clinically true hermaphroditism from other types of intersex. The external

genitalia and physical development are variable. By cystoscopy and urography it may be possible to demonstrate accessory structures and communications between the urinary and genital tracts. The presence of a female genital tract and the extent of its development may be demonstrated radiologically, as in this case.

Blood and urine levels of oestrogens, androgens, and ketosteroids are generally unaltered except in the female pseudo-hermaphrodite. The possibility that the gonad of the intersex may be abnormal with regard to hormone production has been suggested by Morris (1953). Descent of the gonad is no indication of its nature. Helpert (1939) and Laycock and Davies (1953) have reported cases of ovotestes in the scrotum. Macroscopic appearances of gonadal tissue have been misleading. Fischer *et al.* (1952) stated that there was an associated inguinal hernia in 21 of 49 cases, and stressed its importance in diagnosis. Diagnosis was made at operation for hernia in 6 of 20 cases studied by Young (1937). The hernial sac often contained a gonad, and in some cases part or whole of the uterus. Giacobine (1946) found 36 male cases of hernia uteri inguinalis in the literature. Accurate diagnosis can be established only by gonadal biopsy, which in most cases involves laparotomy.

Management

As our patient was past puberty, it was assumed that no reversal of psychic sex was likely to occur, and his strongly marked maleness was taken as the guide in our surgical endeavours to render him a more normal person. This procedure has the approval of most modern workers in this field (Creadick, 1953; Greaves, 1954; Wilkins *et al.*, 1955; Barr, 1956). Any attempt to make these individuals behave contrary to their psychological sexual bias, whatever their clinical sex, often gives rise to serious mental conflict and doubtless accounts for many of the suicides common amongst these patients.

Attention has been drawn to the association of malignancy and the cryptorchid testis of the hermaphrodite (Taub, 1954; Gilbert, 1942). Orchidopexy did not significantly lower the incidence in one series of cases (Gilbert and Hamilton, 1940). In our case there was a clear demarcation between the components of the left gonad, and we were able to remove the female component and leave the remainder, since the advantages of preserving the gonad for endocrine function were considered to outweigh the risk of malignancy (Howard, 1951).

Hormone therapy was considered, but it was decided to withhold this until the function of the testis could be evaluated, since substitution therapy may depress gonadal function (Marshall, 1954).

Sex-chromatin Studies

The work of Barr and his associates (1949, 1950) has established that intermitotic nuclei of human tissues bear evidence of the true nature of their sex chromosomes. Sex-chromatin studies were made in this material from three aspects: (1) the type of nuclei present in the tissues; (2) the presence or absence of gynandromorphism; and (3) the nuclear structure of the male components of the reproductive system. All the material except the skin was fixed in 10% neutral buffered formal saline. The skin was preserved in a modified Davidson's solution as recommended by Moore *et al.* (1953). For the sex-chromatin studies sections 5 μ thick were stained with haematoxylin and eosin and Feulgen stains, and the counts made on 100 suitable nuclei in each section (Plate, Figs. 4 and 5). The heavy deposit of melanin in the deeper cells of the negro epidermis increased the difficulty of the counts in this area, but this was overcome by the use of the Feulgen stains. Also the squamous cells around the skin appendages in the dermis were found to be relatively free of melanin, so that the nuclear type could be satisfactorily evaluated.

1. Nuclear Types.—Studies on the nuclear types of true hermaphrodites have previously been completed on nine cases (Barr, 1955a); six of these showed female-type nuclei

and three male-type nuclei. Our case had a nuclear pattern of the female type (see Table).

2. Gynandromorphism.—The phenomenon of gynandromorphism has been shown to occur in insects. In the three cases reported to date (Barr, 1955b; Greene *et al.*, 1952), and in the present case, there was no evidence of gynandromorphism.

3. Nuclear Structure of Male Components.—The presence of female-type nuclei in the interstitial tissue of the testis is an interesting finding. As the small piece of testicular tissue removed at operation was fixed immediately, examination by the squash technique (Greene *et al.*, 1952) was not possible. In the sections the cells within the seminiferous tubules did not show any structure that could be regarded as sex chromatin. However, these cells are unsuitable for cytological study in sections (Barr, 1956).

Of 57 cases of true hermaphroditism the social sex was male in 41, or 72% (Bromwich, 1955). Among 10 similar cases in which the sex chromatin has been studied only three were male in type. This suggests that in the majority of instances of true hermaphroditism the genetic sex, which is usually female, has been suppressed by the social and psychic sex, which is usually male. In our case the hormonal influences must have been strongly female, since the patient had nearly normal female secondary sex characteristics and apparently normal ovarian function. Despite this the psychic sex was male.

Graham (1954a, b) has demonstrated in the cat embryo that the nuclear configuration antedates the sexual differentiation of the reproductive system. Bromwich (1955) has suggested that the apparent sex among intersexes may not be absolutely determined by the sex chromosomes and that the genetic direction of development may be overridden by other factors. In our case, however, the genetic sex and the hormonal sex are female, but the psychic sex is strongly male. It would therefore seem that environmental and psychic influences have successfully suppressed the other factors. This is in agreement with the views of Howard (1951), Creadick (1953), and Greaves (1954), who have all stressed the part played by environment in psychic development.

Summary

A case of true hermaphroditism and its treatment are described. Although in this case the genetic sex and hormonal sex were female, the psychic sex was strongly male, and evidence is put forward to suggest that extra-uterine environmental factors were responsible for this.

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