foreign bodies and the development of the manifestations of systemic sarcoidosis has been recognized (Refvem, 1954; Löfgren *et al.*, 1955). There is no reason to presume any relationship between the old injury in this case and the eventual development of the fungal infection.

It is unlikely that the original illness, believed to be sarcoidosis, was in fact a manifestation of histoplasmosis. The absence of symptoms, the apparently complete recovery, the character of the radiological changes in the lungs and their disappearance without calcification, the clear-cut histological picture of sarcoidosis, and the failure to find parasites in the original biopsy and in the siliceous granuloma are all features which favour the diagnosis of sarcoidosis. However, none of these observations is incompatible with the diagnosis of histoplasmosis, and therefore the latter cannot be altogether excluded in considering this earlier phase in the patient's history.

There does not appear to be any record of histoplasmosis occurring in a patient who at that or any other time showed evidence of any illness which could reasonably be interpreted as sarcoidosis. There have been a few cases in which histoplasmosis mimicked sarcoidosis histologically, but none of these showed anything like the apparently clear picture of sarcoidosis in the case described here (Reimann and Price, 1949; Pinkerton and Iverson, 1952; Israel *et al.*, 1952; Binford, 1955; Crispell *et al.*, 1956).

The association of sarcoidosis with other fungal infections, particularly torulosis, is discussed briefly elsewhere (Plummer *et al.*).

Summary

A case of histoplasmosis is described. The only manifestations of the infection have been enlargement of two cervical lymph nodes and a positive histoplasmin skin reaction. Fungi were found in sections of one of the lymph nodes. The diagnosis was proved by the isolation of *H. capsulatum* in cultures from the second node. The patient is without symptoms 16 months after the mycotic lymphadenitis appeared.

The patient had never been out of the British Isles before he developed histoplasmosis. His case is believed to be the first unequivocal instance of mycologically proved histoplasmosis in which the infection was contracted in Britain.

He had previously had sarcoidosis, the course of which was benign. The first manifestation of sarcoidosis was probably the development of a siliceous granuloma at the site of an old injury.

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LOCALIZED CUTANEOUS HISTOPLASMOSIS

BY

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Two cases of localized cutaneous histoplasmosis, confirmed by isolating *Histoplasma capsulatum*, are described in this communication. Both patients are Nigerians. The diagnosis was made while they were living in England; it is clear that the infection was acquired before they came here. Their cases were referred to as "unpublished observations" in an earlier paper (Symmers, 1953), and were listed in a more recent paper (Symmers, 1956) in a table of 13 acceptable cases of histoplasmosis which have been recognized in this country. A mycologically proved histoplasmic infection has only once been reported in a patient who had never been out of Britain (Symmers, 1956).

Case 1

A Nigerian man, aged about 28, came to England at the end of 1951. He had not been away from Nigeria before. His health had always been good. He travelled to England by sea from Lagos, where he lived, calling ashore at Accra on the Gold Coast, Freetown in Sierra Leone, and Bathurst in Gambia. Two days after sailing from Bathurst he developed a pustule on one cheek; thinking that this might be due to a bite by a tumbu-fly (*Condylobia anthropophaga*) he incised it carefully with a sterile scalpel and evacuated its purulent contents—no larva was present. The lesion healed over quickly, but a little painless nodule remained at its

site. Eighteen months later the nodule became slightly itchy and began to enlarge, and within a few weeks a small ulcer appeared at its centre.

Examination showed a shallow ulcer, 0.5 cm. in diameter, with a thin dry crust and a firm, slightly raised, rolled, pearly marginal zone about 0.2 cm. wide. The lesion was indistinguishable from a rodent ulcer. Films of fluid expressed from it contained a few leucocytes and some Gram-positive cocci; culture of the fluid yielded *Staphylococcus albus* and a diphtheroid bacillus.

The lesion was excised along with a 0.5 cm. rim of healthy skin. An immediate frozen section showed a giant-cell granuloma containing large yeast-like intracellular organisms; cultures were at once set up from the fresh specimen. After eight days' incubation at 37° C., on blood-agar and on Sabouraud's medium, a sparse growth of a yeast-like organism was present. This was subcultured at room temperature and at 37° C.: at room temperature a mycelial growth gradually appeared, with eventual formation of tuberculate chlamydospores. The cells of the yeast-like form, which grew only at 37° C., were of practically uniform size, not exceeding about 4 by 2 μ . The cultural characteristics were typical of *H. capsulatum*. Animal inoculation was not carried out.

Paraffin sections of the skin lesion confirmed that it was a tuberculoid giant-cell granuloma, with central ulceration and no caseation; histologically it resembled any other simple foreign-body reaction, except that the foreign bodies were clearly yeast-like fungi. The organisms were present only within the giant cells (see Fig.): most of the organisms were

Facial lesion in Case 1. Multinucleated giant cell containing many large histoplasmas. The organisms appear as round or oval double-contoured bodies, sometimes with a broad pale surrounding zone. They are much less intensely stained than the giant cell's nuclei, which they resemble in size. (Haematoxylin-eosin. $\times 435$.)

large (about 10–12 by 8–10 μ), although many giant cells also contained some small forms (about 4 by 2 μ). The organisms had a double-contoured "capsule"; many were birefringent. Periodic-acid/Schiff was the most satisfactory stain for demonstrating them, although they were clearly visible in haematoxylin-eosin preparations. Some organisms stained poorly, and some appeared to be disintegrating.

Investigations and Progress.—The operation wound healed quickly and cleanly. The patient had no other symptoms. Investigations showed no sign of disease clinically. The rest of his skin and the mucosae were healthy. There was no lymphadenopathy; the liver and spleen were not palpable. Chest radiographs were normal. Haematological examination, including sternal marrow, showed nothing abnormal; no parasites were found in films of marrow, and marrow cultures were sterile. Wassermann reaction was negative. Serum albumin was 4.3 g. per 100 ml., globulin 2.1 g. Histoplasmin skin tests were repeatedly negative with concentrations up to 1:10.

The patient returned to Nigeria in 1954; he has remained perfectly fit. No treatment was given. When last heard from (December, 1955) he had no symptoms.

Case 2

A Nigerian woman, aged 23, left her home for the first time in September, 1952, and came direct to England. She had a routine medical examination soon after arrival here and was found to have an annular skin lesion, 2 by 1 cm., over the lower end of the sternum. This lesion consisted of an irregularly ovoid ring of induration, about 0.4 cm. wide, slightly raised, sharply outlined at its periphery, and less clearly demarcated at its inner margin. The normal skin markings were smoothed out over the indurated area, but elsewhere were unaffected. The skin within the ring was healthy, but very slightly less pigmented than that around the ring. The appearances were reminiscent of Majocchi's erythema annulare centrifugum (illustrated by Andrews, 1954). The patient said that this skin lesion had been present for two years, slowly enlarging for the first 18 months and then remaining stationary. No other abnormality was found; her health had always been good. The chest radiograph was normal.

Six months later, when a fellow-student (Case 1) was found to have a histoplastic lesion, she raised the possibility of this diagnosis in her own case. A histoplasmin test was positive (induration 2 cm. in diameter 48 hours after intradermal injection of 0.1 ml. of 1:100 histoplasmin). She asked for a biopsy of the skin lesion, which remained unchanged: this request was agreed to, as it was remembered that the multiple skin lesions in an earlier case of histoplasmosis* seen in this country resembled her lesion.

Part of the indurated ring was excised; the wound healed uneventfully. The biopsy showed a histological picture identical with that in Case 1, except that there was no ulceration. As in Case 1, a typical strain of *H. capsulatum* was cultivated from the biopsy specimen: no large yeast-like cells were formed in the cultures, although they predominated in the lesion.

No other abnormality has been found in this patient. Marrow examination was not undertaken. She has remained in this country and her health is excellent: the skin lesion gradually disappeared completely during the year following the biopsy. No treatment was given.

Comment

The infection in each of these patients appears to have been confined to the single skin lesion. The source of their infection is unknown. The first patient had no knowledge of having been bitten by any insect: he merely mentioned his awareness of the possibility of early dermal myiasis as the cause of the pustule, particularly as he was not liable to boils; he had seen several tumbu-flies in the neighbourhood of Freetown. There is as yet no evidence that histoplasmosis can be transmitted by insects or other vectors.

Cutaneous lesions in histoplasmosis are not uncommon; when they occur they are usually multiple and are part of a disseminated infection, with visceral involvement (Miller, Keddie, Johnstone, and Bostick, 1947). Occasionally the infection is seemingly confined to the skin, and recovery takes place (Curtis and Grekin, 1947), as in the cases described above. Poles and Lavertine (1954) stated that signs of dissemination of the infection have been noticed on several occasions to follow a biopsy; it is not apparent, from what I have read, that this is a substantial risk, but it is obviously prudent to keep the possibility in mind until enough observations are available for the risk to be assessed, particularly as no dependable treatment is known yet. In many cases biopsy is likely to be essential for diagnosis.

*The case of Robb-Smith (1943). This is the case mentioned by Duncan (1945, 1946–7); it was previously described briefly by Carleton (1942–3).

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

BY

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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