

and it is necessary in order to help to assess the significance of radiological changes found in the chest or bones. As in everything else, experience of the relative advantages of different methods is required.

The test gives a positive result four to six weeks after primary infection, and thereafter a positive reaction means simply that a child has undergone primary infection. It does not mean that any particular illness is tuberculous in origin, but it emphasizes the possibility, or indeed with a young child the probability, that it is so.

A negative reaction is important, for the presence of tuberculosis is practically dismissed unless the child is very ill, when other physical signs are almost certainly present.

Two tests are in general use—the percutaneous (jelly) and intradermal (Mantoux). In the jelly test the skin is carefully cleaned with acetone or ether, and a petroleum jelly ointment containing Old Tuberculin is placed on the skin; usually the child's initial or a "v" mark is outlined with the jelly, to the length of about 1 in. (2.5 cm.). This is covered with a piece of strapping without any intervening lint. After 48 hours the strapping is removed and the skin examined 72 hours later—that is, after five days. This interval allows any strapping reaction to fade and gives a delayed tuberculin reaction time to appear. The result is not often in doubt. There is either no reaction whatsoever or, if positive, a reddish-brown slightly raised area; or sometimes a line of papules, not indurated or oedematous, will show on the skin in contact with the jelly. It is best to regard any reaction as positive until proved otherwise, but sometimes if only two or three papules are present the intradermal test will be necessary. We do not recommend the use of flourpaper (very fine sandpaper) in testing children under 5 years of age. The jelly test is roughly equivalent to 0.1 ml. of 1:1,000 Old Tuberculin by intradermal injection. It is most useful in clinic work where repeated tests are necessary and time is not important. Avoiding a prick, the doctor retains the child's confidence. But it takes five days, and occasionally an intradermal tuberculin test is necessary afterwards. So if there is any urgency, if the child is ill and tuberculosis seems likely, an intradermal (Mantoux) test should be used. The intradermal test consists of the intradermal injection of 0.1 ml. of 1:1,000 Old Tuberculin; 48 hours later a weal or area of induration more than 5 mm. in diameter indicates a positive reaction. Redness without induration is ignored, and redness surrounding a weal is not included in measurement.

The reactions of the tests are therefore very different and should not be compared. That of the jelly is on the skin—a series of small spots, papules, or vesicles which sometimes coalesce; that of the intradermal test is oedema in the skin at the site of injection. Every child with a positive reaction should be known to his family doctor, and it is most important that the results of tuberculin tests done in clinics or elsewhere should be communicated to him. It is also important that he should recognize the significance of the information and its value if the child becomes ill.

#### Why is this Urgency Necessary?

Almost all deaths from tuberculosis in infancy are the result of tuberculous meningitis or miliary tuberculosis. Both conditions are now treatable. In the early stages of tuberculous meningitis (uncomplicated by radiological miliary spread) there is a 75% chance of survival and a 50% chance of complete recovery; in the later stages 30% survival and only 10% complete recovery (Lorber, 1954). In meningitis alone the results are better than if miliary is also present. Relapse may occur, but it is unlikely after two years: the results depend almost entirely upon the stage at which diagnosis is made and treatment started. In the great majority of cases the first person to see the ill child is the family doctor, and his is the most difficult role of all. He must suspect and seek confirmation of his suspicions: early diagnosis depends upon the use of the tuberculin test, radiology, lumbar puncture, and bacteriological proof.

#### Summary

In this paper we have dealt with the recognition of tuberculosis in young children, arguing that diagnosis by clinical signs is outmoded and that early recognition requires above all suspicion, followed by tuberculin-testing, radiology, or other investigation.

One-third of 150 ill children presented with illnesses caused by lung primary lesions or miliary tuberculosis: one-third with tuberculous meningitis; one-fifth with superficial lymphadenitis. Bone lesions are relatively uncommon and sensitivity phenomena quite uncommon at this age.

The techniques and relative roles of the tuberculin jelly test and Mantoux test are considered.

We wish to thank our colleagues who allowed the use of records of children under their care, Dr. George Brewis, Dr. Donald Court, Dr. George Davison, and Dr. G. A. Nølgan; and the late Professor Sir James Spence for his constant encouragement of our work on childhood tuberculosis.

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## HISTOPLASMIN SENSITIVITY IN UGANDA

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Histoplasmosis was first known as a rare severe generalized infection, but during the past ten years American workers have shown that there is also a benign and usually symptomless form producing pulmonary infiltration followed by calcification. It is commonest in the United States, between the Mississippi and the Arkansas Rivers, where incidences of up to 80% of positive reactions to the intradermal injection of histoplasmin have been recorded. The geographical distribution of cases of proved histoplasmosis and of histoplasmin sensitivity have been ably reviewed by Mochi and Edwards (1952).

A few cases of the generalized disease have been diagnosed in Africa. In the Union of South Africa Simson and Barnettson (1942) encountered one, Lurie (1949) two, Murray and Brandt (1951) three, and B. A. Dormer one (Mochi and Edwards, 1952); in French and Anglo-Egyptian Sudan Catanei and Kervran (1945), Kervran and Aretas (1947), and Jelliffe (1949) found other cases, while one has been reported from Senegal by Friess and Delvoye (1947) and from Belgian Congo by Dubois *et al.* (1952). *Histoplasma capsulatum* in Africa may be a different and unusually large form, as in the cases of cutaneous disease seen by Duncan (1947) in a man who had been in West Africa. In another British case the patient had been in Sudan, as well as in

India (Derry *et al.*, 1942). There is thus no doubt that the organism occurs in Africa, and it is likely that the benign form of the disease may be found there.

Several surveys have been made in Africa. In the Nile delta no positive skin reactions were obtained in 380 persons (Mochi and Edwards, 1952). Jackson (1952) found three reactors in about 200 tested in South Africa. In Natal none were positive in the high mountainous Drakensberg, 1.6% were positive on the coast, and 5.9% were positive in Durban (Mochi and Edwards, 1952). In Transvaal, Lurie (1949) found as many as 8% positive, and in Kenya, Stott (1954) found 14.6% of a group of miners and 5.3% of prisoners with positive reactions. Twenty-three of the tuberculin-negative prisoners were x-rayed, and two had pulmonary calcification—one of them had a positive and the other a minimal reaction to histoplasmin. Among the remaining 21 prisoners there were only three who reacted at all to histoplasmin. The incidence of calcification in men who were x-rayed was four times as high in those with both tests positive as in those with positive tuberculin but negative histoplasmin reactions.

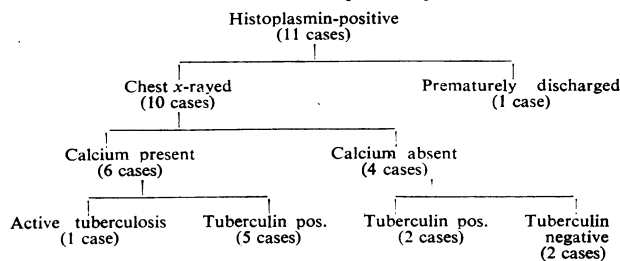
#### Uganda

"A broad view of the districts, where sensitivity is found suggests that priority in the search for new endemic centres might be given to low-altitude regions along large rivers" (Mochi and Edwards, 1952). Uganda lies at a high altitude, the area from which most of our patients came being about 4,000 feet (1,220 metres) above sea-level and consisting chiefly of rolling cultivated land near swamps or lakes. We tested 175 persons, all being native Africans. Of these, 145 were adults, often of indeterminate age (76 men and 69 women), and 30 were children under 12 years. All were patients in the medical or paediatric wards except 11 who were members of medical or nursing staff.

Injections of 0.1 ml. of histoplasmin equivalent to a 1/100 concentration were made into the volar aspect of the forearm, care being taken to avoid any possibility of contamination with tuberculin, and results were read three days later. Lesions with induration 5 mm. or more in diameter were counted as positive reactions; these were found in 11 individuals (6.3%). In about 10% of the total there were similar reactions measuring less than 5 mm.

Ten of the 11 patients who had positive histoplasmin reactions were examined for calcification in the lungs by chest x-ray examination, and for tuberculous infection by Mantoux tests. The results, shown in the diagram, indicate

Diagram Showing Results of Chest X-ray Examinations and Tuberculin Tests in 11 Histoplasmin-positive Cases



that all patients with pulmonary calcification had evidence of past or present tuberculous infection. In five cases the calcium was in the hilar glands; in one it was in the lung parenchyma at the right base.

Of our 11 histoplasmin-positive patients, 8 were men, 2 were women, and 1 was a child (giving incidences of 10.5% in men, 3% in women, and 3.3% in children). These observations suggest that histoplasmosis will probably not be found commonly in Uganda, but may have to be taken into account in considering the aetiology of unusual pul-

monary infiltration and calcification. A probable example of such a case was seen at Mulago Hospital in 1951 and 1952.

An African student, an Acholi from North Uganda, was found to have some abnormal shadows in the lungs on routine x-ray examination. He had no symptoms or abnormal signs referable to the lungs, and no history of any chest disease; his physique and general health were excellent. Gastric resting juice was examined on four occasions for acid-fast bacilli and none was found. The abnormal x-ray appearances consisted of small mottled shadows, fairly sharply defined in places, scattered over both bases and mid-zones, more marked on the left; several showed a strong suspicion of calcification. These shadows were watched over a period of ten months and showed no change. After this he proceeded to the U.S.A. for higher studies, and while he was there investigation of histoplasmin sensitivity in Uganda raised the possibility of his having this condition. Contact with Dr. R. A. Snyder produced this report:

"We had been thinking along the lines of histoplasmosis . . . and had done skin tests for histoplasmosis and coccidioidomycosis in October, 1953, with negative results. Following your letter, I repeated the histoplasmin skin tests and must report the result as rather equivocal. In other words, there seemed to be no angry reddening of the skin, but there was a definite swelling about 1 cm. in diameter, and I believe that I would interpret the test as mildly positive. We, here at Northwestern University, see a fair number of students each year with healed histoplasmosis. The usual x-ray finding is one of scattered small hard calcifications throughout both lung fields, but we have seen some cases with x rays that resemble this patient's."

#### Summary

Histoplasmin skin tests were performed on 175 native Africans in Uganda, with positive results in about 10% of men and about 3% of women and children. Pulmonary or hilar calcification was seen in 6 of 10 patients with positive reactions, but in five of them tuberculin tests were also positive and the sixth had active tuberculosis.

A case of probable pulmonary histoplasmosis is briefly described.

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The seventh series of the *Scottish Chemists' Index of Modern Remedies*, recently published, lists about 3,000 proprietary and other preparations. A vitamin mineral chart has been added to facilitate the location of products containing vitamins and minerals in the proportions required, and the list of antibiotics has been much expanded. The *Index* may be obtained from Messrs. H. K. Lewis and Co., Ltd., 136, Gower Street, London, W.C.1, price 7s. 6d.