

HISTOPLASMOSIS

A pilot survey

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Introduction

Though Histoplasmosis was first recognized as a disease entity in 1905 by Darling in the Panama Canal Zone, it was still considered a rarity up till 1945. It was only when the frequency of the positive skin reaction to the histoplasmin test was reported first by Palmer (1945), and then by Christie and Petersen (1945), that the disease acquired epidemiological and clinical importance, with the result that it is currently estimated that 40 million people have been infected by the fungus, *Histoplasma capsulatum*, and that a significant proportion of the 500,000 annual infections are severe enough to require medical treatment (Chick, 1971).

Histoplasmosis is endemic only in the Eastern Central United States of America but cases have been reported in various parts of the World including some European countries, such as the Netherlands, England, France and Italy (Tassinari, 1948) as well as places in the Mediterranean.

In view of the presence of the disease along the Southern shores of nearby Italy where the fungus was cultivated from the soil (Murray, 1969), it was considered worthwhile to carry out a pilot survey to ascertain the local histoplasmin reactivity, even though so far no case of histoplasmosis has been diagnosed in Malta.

Methods

The population chosen to be tested consisted of a selected group having the following characteristics:

- a) All had pulmonary tuberculosis, with the disease healed or in the inactive stage — thus having a pulmonary pathology similar to that of histoplasmosis;
- b) All came from a rural or former rural area, and therefore were more likely to have come in contact with a possible source;
- c) All belonged to the age-group 40-60 years, i.e. had already been born when a larger part of Malta could be described as rural.

A Histoplasmin Skin Test was carried out by the Mantoux Method in 461 persons (315 men, 146 women) coming from 30 rural areas and from 14 towns, the area representation being quite comprehensive; all the tests were carried out and read by the same individual.

The antigen used was a standardized sterile filtrate from cultures of *Histoplasma capsulatum* grown on liquid synthetic medium, equal in potency to Reference Histoplasmin; 0.1cc of this antigen was injected intradermally in the volar surface of the left fore-arm, the test being read 48 hours later. A positive reaction was taken as an induration of 5 mm or more; as with the Tuberculin Test, erythema without induration was not taken as a positive response.

All tests gave negative results.

Discussion

Systemic *primary* fungal infestation is rare in Malta. As far as could be ascertained only four cases of this type of fungal disease have been seen or reported locally: a Cryptococcal meningitis in a mid-

dle-aged man, a diffuse Nocardiosis in a young boy, localised pulmonary Nocardiosis in another case and a pleural effusion caused by *Penicillium lilacinum* (Fenech and Mallia, 1972) in a fourth.

No case of pulmonary aspergillosis, diffuse or localised, has been seen locally in spite of a careful look-out extending over 20 years, and no other fungi have been isolated at the Bacteriological Laboratories of the Health Department except those already mentioned (Agius, 1973; Spiteri, 1973).

It had been suggested that the best condition for the growth of *H.capsulatum* in nature include (a.) red-yellow podzolic soil under certain conditions of temperature (16° — 32°C) and humidity (relative humidity 50% or more), enriched by bird manure, and (b.) elevation above sea-level of from 500 to 1,000ft. (Addington, 1967; Manos *et al.* 1956); but it now appears that such soil is not indispensable for the growth of the fungus. In fact Chick *et al* (1972) have isolated the *H.capsulatum* from bat manure obtained from the concrete block wall of an abandoned building, and this was the source of infection in at least one case reported by them. There is no red podzolic soil in Malta, but bats are prevalent.

There is no evidence of direct spread from animals to humans or from humans to animals or that histoplasmosis is a contagious disease (Addington, 1967). Prior (1951) has however suggested that there may be transmission from animal to animal (dog), in fact in certain areas of the U.S.A. up to 50% of dogs are serologically positive, and the majority culturally positive on autopsy (Chick, 1971). The mode of infection is by inhalation of airborne spores, and the natural reservoir of the fungus is its saprophytic growth in nature from where it is spread to humans (Grayston and Furcolow, 1953; Furcolow, 1960; Lash, 1960).

Histoplasmosis has a clinical and pathological similarity to many diseases. It may be confused with Kala-azar (irregular fever, splenomegaly, leucopenia, inclusion bodies in endothelial cells), the Reticuloses (enlargement of liver, spleen, glands, leucopenia and anaemia), and, because of

the pulmonary changes, with tuberculosis. In fact it can simulate any illness, but it is primarily granulomatous in nature and the fungus is highly invasive to the reticulo-endothelial system.

As the disease is acquired by way of the respiratory tract, almost without exception the respiratory organs are the most common site of the primary infection, mimicking tuberculosis very strongly. Four types of pulmonary lesions are recognized:

1. A primary complex — having the same size, shape and localization as in tuberculosis.
2. Miliary lung — the most common.
3. Coin lesions, multiple or single, simulating malignancy.
4. Cavity formation, especially in adults.

Because of the multiplicity of the clinical manifestations, a diagnosis of histoplasmosis can only be confirmed by special laboratory investigations i.e. serology, mycology, and skin sensitivity tests.

Conclusion

The findings of the present pilot survey indicate that one is unlikely to come across endogenous histoplasmosis, yet, in view of the rapid increase in travel throughout the World, the possibility of meeting with imported disease has to be seriously considered.

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