NEUROSURGICAL ASPECTS OF CRYPTOCOCCOSIS*

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Cryptococcosis, sometimes called torulosis, or European blastomycosis, is a fungous disease caused by Cryptococcus neoformans.† The disease is rare, but has shown a surprising increase in incidence in the past decade, undoubtedly concomitant with increasing clinical awareness on the part of the physician.‡

CAUSATIVE ORGANISM

The causative organism is a small, yeast-like spherule, approximately the size of a red blood cell, which reproduces by budding, and which has neither mycelia nor ascospores. It is surrounded by a mucinous capsule, frequently twice the diameter of the cell, seen as a wide, clear area around the organism, and best demonstrated in India-ink preparations. The fungus grows readily at room or body temperature, ferments no sugars, nor liquefies gelatin. The cryptococci are widespread in nature, occurring with great frequency on the skin and in the intestinal tract of normal individuals. There are several strains, both pathogenic and non-pathogenic, which can be identified by cultural characteristics, agglutination reactions, and animal toxicity experiments. Recently it has been demonstrated that the capsules of cryptococci contain serologically reactive substances, so that specific antisera reacting with the organisms produce a capsular swelling, akin to the Quellung reaction seen between pneumococci and specific antisera.25 These antigenic properties, however, have been of little use in diagnosis and treatment in human cases. The cryptococci can be distinguished mycologically from Blastomyces dermatitidis, the causative organism of American blastomycosis, since the latter, although the same size and possessing a budding stage as well, has no capsule and produces mycelia.

GEOGRAPHICAL DISTRIBUTION

Although cryptococcosis has been called European blastomycosis, having first been described in Germany, the great majority of cases have occurred in the United States, with only 30 cases recorded from the European continent.

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† There has been much discussion concerning the mycological nomenclature of this organism, the subject being authoritatively reviewed by Benham.2

‡ In a recent review of the literature, 220 published cases of cryptococcosis have been found. In addition, there are more than 30 other known but unreported cases (personal communications), primarily with central nervous system involvement.
Cryptococcus neoformans is unique among the fungi in its predilection for invasion of the central nervous system. This readily becomes apparent when it is noted that of a total of 220 reported cases recently reviewed, 178 (81 per cent) exhibited central nervous system involvement. There was a two-to-one preponderance of the male sex in this group.

Study of these 178 cases with central nervous system involvement revealed only 1 case, that of a cryptococcic meningitis, in which the patient could be considered cured, with sulfadiazine the therapeutic agent employed. The majority of these patients (86 per cent) were dead within 1 year, and 70 per cent of these within 3 months of onset. The central nervous system disease is, therefore, a virulent one, although there are several patients reported alive after 2½, 7 and 9 years; these still have evidence of disease activity, indicating a more indolent, but rarer, type of infection.

**DIAGNOSIS**

The diagnosis during life in cases of central nervous system involvement was made primarily by observation or isolation of the organism from the cerebrospinal fluid. Thereafter, in order of decreasing frequency, diagnosis was made by biopsy (both local and during exploratory craniotomies) and by culture of blood, urine, and sputum, and of material from nasopharynx, rectum, vagina and pleural cavity. Biopsy or culture established the diagnosis during life in 69 per cent of the central nervous system cases.

**PATHOLOGY**

The organisms most likely reach the central nervous system by way of the blood stream, producing three varied types of pathological reaction.

(1) **Meningitis.** Grossly the exudate is found most often at the base of the brain and diffusely in the spinal subarachnoid space. It may vary from rather delicate opacities to dense masses of yellowish-white material primarily in the basilar cisterns and often in the lumbar sac. Where the organisms are concentrated, gelatinous, sometimes amber-colored exudate is encountered.

Histologically, the findings in the leptomeninges are those of a granulomatous meningitis, resembling those seen in tuberculous meningitis, as well as in other fungous infections. It is characterized by chronic inflammation, necrosis of exudate, angiitis, and granulation tissue. In other areas there may be a striking paucity of inflammatory changes, although many organisms may be present, either lying free in the tissues, or phagocytized by Langhans giant cells. This is far more frequent, however, in the meningoencephalitic form of the infection.

(2) **Meningoencephalitis.** In addition to the changes in the leptomeninges described above, a honey-combed appearance of the cerebral cortex, basal ganglia, and thalamus may be encountered, as well as of the roof nuclei of the cerebellum and much of the brain stem. These changes are almost wholly confined to the gray matter.