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Experimental Studies on Bronchomonoliasis.

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Infection of the respiratory tract by pathogenic monilia gives rise to the disease entity designated bronchomonoliasis. The first report on record of this disease was given by Castellani[1] from Ceylon. In this country it was primarily reported by Boggs and Pincoffs.[2] Flinn[3] reported 9 cases. Monoliasis is no longer considered endemic in the tropics since it is now being reported with increasing frequency from all parts of the world.

With a strain of *Monilia albicans* isolated from a proven case of bronchomycosis we injected rabbits intravenously, intraäbdominally, intratracheally and directly into the lung parenchyma with varying doses of the recovered culture. The routes, other than intravenous, proved either inconsistent in their effects or the animals remained apparently normal. As the intravenous method of inoculation yielded constant results, this route was employed as the method of choice. The dosage was measured according to the method of Stovall.[4]

No lesions have been described which are specific or pathognomonic of bronchomonoliasis. It is, however, generally agreed that the gross appearance of the lesions resembles tuberculosis. Mendelson[5] pointed out that the lesions are, in reality, mycotic tumors and as a rule show no signs of breaking down. Ikeda[6] found miliary cortical abscesses of the kidney to be the most conspicuous finding in animals injected by various routes.

In the present work the injected rabbits were divided into 2 series.

Series I: These animals were given the lethal dose of *Monilia albicans* intravenously as established by Stovall,[4] and died within 24

1 Castellani, A., *Fungi and Fungous Diseases,* Chicago, American Medical Association, 1927, p. 121.

2 Boggs, T. A., and Pincoffs, M. C., *Bull. Johns Hopkins Hosp.*, 1915, **26**, 407.

3 Flinn, John W., Flinn, Robert S., and Flinn, Z. Mackay, *Ann. Int. Med.*, 1935, **9**, 42.

4 Stovall, W. D., and Pessin, S. B., *Am. J. Clin. Path.*, 1933, **3**, 347.

5 Mendelson, R. W., *J. A. M. A.*, 1921, **77**, 110.

6 Ikeda, Kano, *Arch. Path.*, 1936, **22**, 63.

to 48 hours. The lesions found at autopsy were usually in the periphery of the liver, kidney or lung. While the gross appearance of the small nodules resembled miliary tubercle formation, the histopathology, however, consisted of central necrosis with polymorphonuclear neutrophilic and slight lymphoid cellular reaction at the periphery.

The tendency to peripheral location in the organs was striking. In the instance of the kidneys an embolic formation of mycotic microörganisms might form an explanation; this interpretation would not apply, however, to the blood circulatory arrangement of the liver or lung.

Series II: These rabbits were injected with only approximately 5% of the dose administered in series I. Death did not take place for 10 days to 3 weeks. In these animals we found the typical mycotic tumors, resembling miliary tubercles, in all the parenchymatous organs. Microscopically the lesions showed peripheral lymphocytic infiltration, epithelioid proliferation and giant-cell formation, thus simulating the histopathology of a miliary tubercle.

In the lesions of both series of animals monilia occasionally can be noted with hematoxylin-eosin staining but it is usually necessary to resort to the Gram-Weigert method to demonstrate the microorganisms.

While the gross lesions present in both series of animals revealed some similarity to miliary tubercles, in that they were rounded, white and firm, the histopathologic aspect varied according to the period of survival of the animal. In those animals wherein the dosage employed killed in 24 to 48 hours, the changes produced were analogous to early abscess formation *i. e.* predominant necrosis and peripheral polymorphonuclear neutrophilic cellular response. On the other hand the reduced dosage provoked changes conforming to those noted in miliary tuberculosis, namely, epithelioid cell proliferation, giant cell formation and peripheral lymphoid cell infiltration.

The results of our experiments show, as has the work of others, that experimental bronchomonoliasis can readily be produced in the rabbit by the intravenous injection of *Monilia albicans*. Furthermore the pathological features conform to the disease in man. We have shown further, however, that the histopathological changes produced in the rabbit present variants in the tissue reactions conforming regularly to the duration of the experimental disease as controlled by the dosage employed. Herein there is presented further analogy to the acute and chronic types as seen in man.