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Studies in glandular fever (infectious mononucleosis).

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(Introduced by Fred M. Smith).

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Acutely hyperplastic lymphatic tissue from many causes, for example, scarlet fever,[1] whooping cough, typhoid fever, secondary syphilis, etc., has been known to result in an absolute increase in lymphoid cells in the circulating blood. This study is based on cases of apparently specific lymphadenopathy called glandular fever,[2] a condition characterized by general enlargement of the lymphatic glands, an absolute mononucleosis and the presence in the blood of abnormal mononuclear cells.[3] Our study is based on the findings in fifty clinical cases of glandular fever or infectious mononucleosis and in fifty-five medical students in whom the symptoms were so mild as to be negligible but in most of whom there was evidence of glandular enlargement and mononucleosis. Glands were removed from six patients.

Our purposes are: (1) to determine the etiology, (2) to ascertain whether or not the pathological changes in the glands are characteristic, (3) to establish the origin of the abnormal mononuclear cells, (4) to determine whether the mononucleosis is a specific response to the etiological agent, a response peculiar to certain individuals, or a compensatory reaction in individuals in which the granulocytic apparatus is rendered impotent by the infection.

[1] Tilestone, W., and Locke, E. A., *J. Inf. Dis.*, 1905, ii, 375.

[2] Pfeiffer, E., *Jahrb. f. Kinderh.*, 1889, xxix, 257.

[3] Sprunt, T. P., and Evans, F. A., *Johns Hopkins Hosp. Bull.*, 1920, xxi, 410.

(1) Blood cultures were done on fourteen cases, thirteen of which remained sterile. In one culture diphtheroids were obtained both from bouillon and blood agar plates. Glands removed from six patients were cultured and diphtheroids[4] were obtained in pure culture from four, one of which was removed six months after the acute symptoms had subsided. The organisms grew best in veal bouillon and four to seven days were required for clouding the media. One cc. of a five day old bouillon culture either subcutaneously or intraperitoneally in guinea pigs caused mild fever of three to five days duration but no special symptoms nor distinctive adenopathy. Organisms were not recovered from the lymph glands of injected guinea pigs. Injections of gland emulsion in guinea pigs and rabbits were without effect. Suspensions of organisms were not agglutinated by the serum of convalescent patients. Dark field illumination of tissue fluid from the excised lymph nodes showed no spirochetes nor other organisms. Seventy-four of the eighty-four mouth smears studied for Vincent's organisms were positive.

(2) Pathology—All of six glands studied were very similar both in gross and microscopic appearance. All were axillary glands and were removed from four days to six months after the onset of illness. The size varied from 2 to 3 cm. in diameter and the glands were soft and spongy. They were kidney shaped with distended white capsules and cut sections were uniformly gray and granular. Histologically, the architecture was for the most part discernable though there was much distortion by a marked lymphoid hyperplasia which compressed the sinuses and stretched the capsules. Some germinal centers were replaced by uniform lymphoid hyperplasia. Mitoses were present in the germinal centers and lymph sinuses. Many very large lymphoid cells with irregular nuclei were found in the lymphatic cords and sinuses. An occasional eosinophile was also seen.

(3) All types of abnormal mononuclear cells appearing in the blood stream were found in the lymph sinuses of the glands. Blood smears stained by the method of McJunkin showed only a small percentage of the abnormal mononuclear cells to have the staining characteristics of endothelial cells.

The mononucleosis seemed to be directly dependent on the lymphoid hyperplasia. The lymphoid hyperplasia was very much

[4] Coon, H. M., and Thewlis, E., *Wis. Med. J.*, 1922, xxi, 191.

more marked and generalized than is usually seen in a localized infection with drainage to regional nodes as, for example, in streptococcic sore throat. The epidemic nature of the condition is also in favor of a specific etiological agent. In order to demonstrate the ability of the granulocytic apparatus to respond, four patients were given a foreign protein (typhoid vaccine) intravenously. All patients responded with a leukocytosis, the increase being entirely confined to the polymorphonuclear leukocytes.

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Chronic benzol poisoning.

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Our purposes were to verify in human pathology, the morbid anatomical changes described in animals poisoned with benzol, and to observe the effects of benzol medication on patients with chronic myelogenous leukemia.

The first studies were on a patient occupationally exposed to the fumes from a vat of benzol from January 6, 1925, to March 20, 1925. The symptoms, findings and course including a terminal sepsis were typical of chronic benzol poisoning. Entrance to the hospital was on May 27, 1925, and death on June 7, 1925.

Blood: R.B.C. 860,000; W.B.C. 1400; Hb. 20 per cent. Differential. Polymorphonuclear neutrophiles 13 per cent; lymphocytes 48 per cent; endothelial leucocytes 39 per cent. No normablasts were seen. Blood platelets 70,000. Coagulation time 9 minutes. Bleeding time 13 minutes.

Necropsy showed hemorrhages into the skin, mucous membranes and meninges. The lungs had the gross appearance of broncho-pneumonia. Microscopically the alveoli were plugged with fibrin which contained many organisms but no inflammatory cells. Numerous areas of focal necrosis were present in the liver. Organisms were plentiful in these areas but no inflammatory