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Giant-Cell Inclusions in Cicatrizing Enteritis.

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The cause of cicatrizing enteritis (regional ileitis) remains unknown. Similar lesions have been produced experimentally by injections of sclerosing solutions into the mesenteric lymphatics of dogs.[1] Various lipids introduced parenterally provoke granuloma formation such as characterizes cicatrizing enteritis.[2,3] In this disease giant cells in the granulomas stain for fat,[4] and in addition occasionally contain crystalloid inclusions.[5,6] As part of a study of etiologic factors in cicatrizing enteritis, investigation of the origin and significance of these inclusions appeared worthwhile.

Two specimens among a group of 138 cases of cicatrizing enteritis contained numerous enough inclusions to make detailed study possible. The patients were women aged 19 and 26 years, who had portions of the small intestine removed surgically. The gross appearance of the resected specimens was characteristic of cicatrizing enteritis, with pronounced edematous and inflammatory thickening of the intestinal wall and mesentery. A fine stippled gray line near the serosal surface of each sectioned bowel marked the location of most of the inclusions. Histologically, there were many of these colorless rounded objects with smooth surfaces within the giant cells, measuring up to about 45 μ in diameter, and varying two-fold or more in size (Fig. 1). Some showed concentric laminations. They did not stain with any of the usual reagents, were strongly doubly refractile in polarized light, and remained unaffected by heat sufficient to char the tissue. Regional lymph nodes contained similar inclusions. They were not found extracellularly, and did not resemble any living organism.

Physical and chemical properties investigated were identical for the inclusions of both cases. The objects were slowly soluble in distilled water over a period of approximately 48 hours. They were easily soluble in dilute hydrochloric acid and ammonium chloride, insoluble in sodium hydroxide, acetic acid, glycerine, alcohol and dioxane. The refractive index by the immersion method was 1.65 or higher.

By means of a micropipette many of these objects were freed from paraffin tissue sections under polarized light and dissolved in small amounts of water. Qualitative tests made separately on the two cases by the micromethods of Chamot and Mason[7] gave strong reactions for calcium. Attempts to identify the anions by similar methods were unsuccessful. Presence of bismuth and silicates appeared to be excluded by these experiments.

The origin of the inclusions has been frequently discussed.[4] Their localization in the subserosa of the intestine and its regional lymph nodes argues against a dietary source. In morphology and chemical properties they resemble the psammoma bodies of meningiomas. Bailey's theory that certain types of cell necrosis attract calcium salts[8] may serve to explain both psammoma formation

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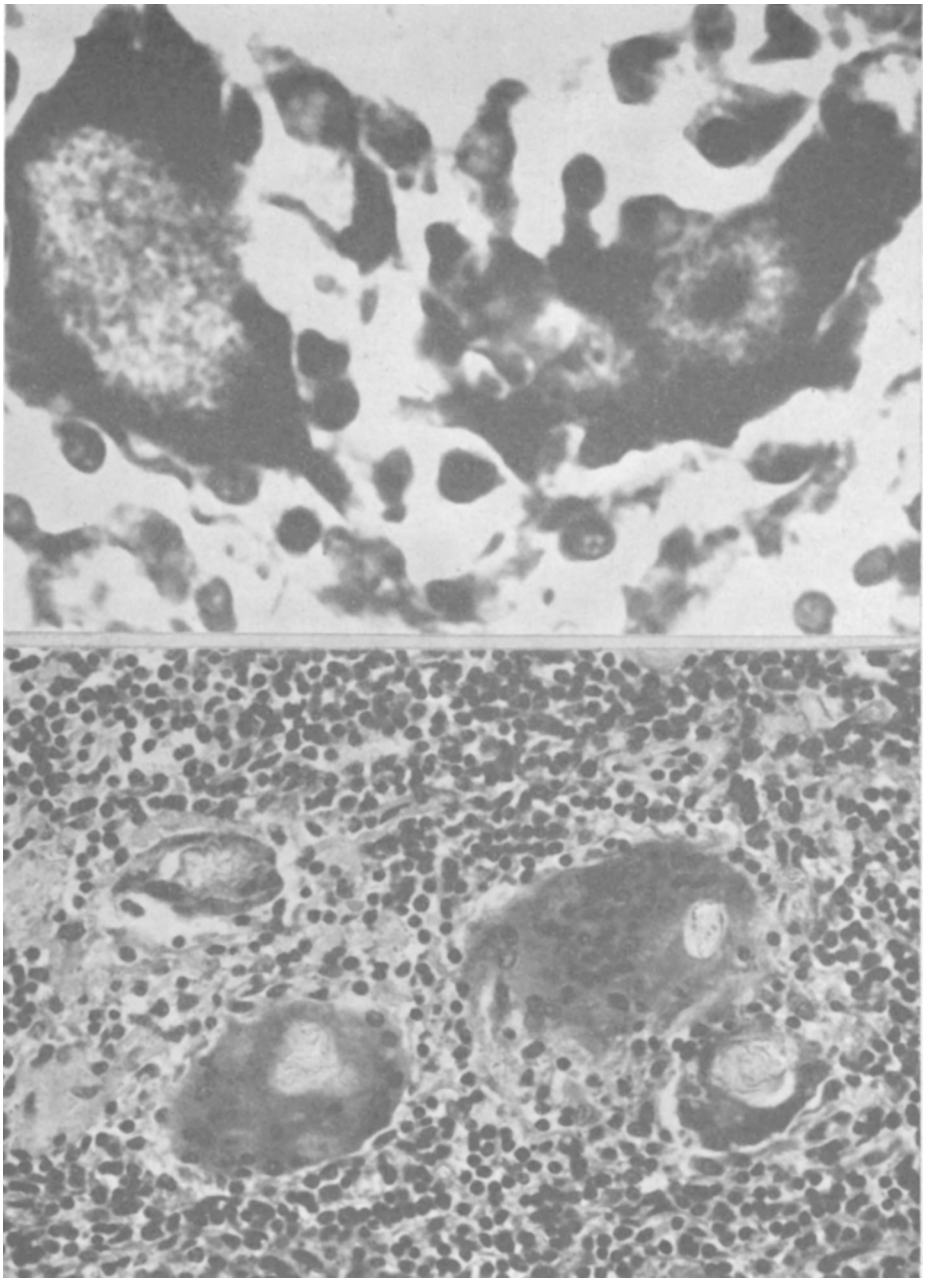

FIG. 1.

Several giant cells in cicatrizing enteritis are shown with laminated refractile inclusions. Eosin methylene blue. ×375.

FIG. 2.

Two giant cells, one containing a central area of cytoplasmic concentration suggesting an early stage of inclusion formation. Iron hematoxylin. × 1500.

and the development of these inclusions. An early stage of an inclusion is suggested by a focal abnormal concentration of cytoplasm of a giant cell observed in cicatrizing enteritis (Fig. 2). Absence of organic material from the fully developed inclusions is responsible

for their failure to take the usual stains.

These giant-cell inclusions are therefore considered to be a byproduct of granulomatous inflammation in cicatrizing enteritis.

Summary. Inclusion bodies in the giant cells of 2 cases of cicatrizing enteritis (regional ileitis) were investigated. By physical and chemical methods they were found to be inorganic calcium salts. The anions were not identified. Their origin is attributed to focal abnormalities of the cytoplasm of giant cells found in this type of granulomatous inflammation, which attract calcium salts. In their development they somewhat resemble psammoma bodies.

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Effect of Strophanthin and Quinidine upon Conduction and Electrical Systole (Q-T Interval) of the Rabbit Heart.*

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Previous studies from this laboratory[1,2] noted the effects on conduction of varying rates of stimulation, and of the use of strophanthin and quinidine, upon the isolated rabbit ventricles. Intraventricular conduction times (QRS widths) increased markedly at extremely high (300 and over) rates of stimulation. Strophanthin, and particularly quinidine, prolonged the QRS intervals at all rates of ventricular contraction.[1] The electrical systole or Q-T interval showed a more gradual decrease with increasing ventricular contraction rates. Small doses of strophanthin, of the order of 0.006 mg/kg, in general prolonged the Q-T interval; larger doses, *e.g.* 0.018 mg/kg, uniformly shortened it,[2] in line with its known clinical effect. Quinidine consistently prolonged the ventricular electrical systole or the Q-T interval, as it delayed intraventricular conduction.

The isolated rabbit ventricles were a useful instrument of study for two reasons. First, they could be driven at much faster rates than the whole heart. Secondly, we were able to elicit the effects of various drugs upon the ventricular musculature without the complicating interconnected influences upon the atria and the A-V junctional tissues. The following presentation is of similar studies made with the isolated whole rabbit heart.

Method. The procedure was essentially the same as in the previous experiments. The perfusion fluid best adapted for the whole heart we found to be the one used by Calder[3] under similar conditions. The atria were left on and the electrodes of the thyrotron stimulator applied usually to the right atrium. The electrocardiographic records were made as before, approximately at 10 minute intervals after the introduction of the drugs into the rubber tube leading to the aortic cannula. Control measurements similarly spaced and rest periods between salvos of rapid stimulation excluded the effects of fatigue. Oxygenation and a constant 37°C temperature of the perfusing fluid were provided as before by means of continuous bubbling of 5% CO_2 in oxygen and a heated water jacket respectively.

Results. Effect of varying rates. Lengthening of the P-R interval occurred, gradually as a rule, at increasingly fast rates of stim-

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