

of 6 animals with or without irritation of the nerves, no histologic evidence of its presence was found on the proximal side a scant inch beyond the injection. When Fairbrother and Hurst<sup>1</sup> injected virus into the sciatic nerve, there was a local reaction, but the nerves were negative a short distance beyond the injection. This observation was confirmed by us in 3 animals. Thus, there is an interval elapsing between the injection of virus and the onset of symptoms of the disease. It is clear that the approximate interval after injection before symptoms appear and the length of time before there is histologic evidence of the disease probably coincide.

During the summer of 1935 44 animals were injected subserosally in the manner previously described.<sup>2</sup> Sections of the central nervous system were cut, stained in various ways and studied. It was found that, after the introduction of the virus by way of the gastrointestinal tract, histopathologic evidence of disease was regularly found in the lumbar area of the cord within 24 hours after injection. The first reaction seen was destruction of neurons in the cord. Marked increase in microglial elements (Wickman's Polyblasts) followed so soon after this reaction that it seemed to be almost coincidental. In from 3 to 4 days increase and dilatation of capillaries began. In many animals, neuronophagic plaques surrounded practically all of the cells in a field, and, in others, this change was accompanied by the usual perivascular cuffing and round cell infiltration, which never occurred prior to the 5th day after injection.

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### **Significance of Carbohydrate Metabolism and Local Acidosis in Inflammation.\***

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Earlier studies by one of the writers have indicated that the cytological sequence in inflammation, characterized by primary

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<sup>2</sup> Toomey, John A., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **31**, 1015.

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TABLE I.  
The Relationship between Glycolysis and the Cytological Picture in Acute Inflammation.

Dog No.	Amount of turpentine injected	Total duration of inflammation hrs.:mins.	Sugar mg./100 cc.		Lactic Acid mg./100 cc.		pH		Cytology of Exudate	
			Blood	Exudate	Blood	Exudate	Blood	Exudate	% of polymorphonuclear phagocytes	% of mono-nuclear phagocytes
9-2	1.5 cc.	0:0	100.0	—	—	—	7.5	—	—	—
		19:10	88.1	96.0	10.8	54.6	7.45	7.43	—	—
	2.0 cc. (reinjecte d on third day)	47:10	111.9	57.9	13.0	27.0	7.48	7.33	85	15
		68:00	145.5	116.8	16.0	27.8	7.48	7.33	74	26
		96:15	81.2	13.9	21.9	135.8	7.43	6.5	15	85
		115:00	138.6	6.4	38.4	248.6	7.43	6.5	2	98
167:00	138.6	34.7	14.7	217.1	7.45	6.5	2	98		

infiltration of polymorphonuclear leucocytes followed by mononuclear phagocytes, seems to be conditioned by the local hydrogen concentration of the exudate.<sup>1</sup> With the developing local acidosis in an area of inflammation polymorphonuclear cells degenerate and are replaced by macrophages. If the pH is maintained above 7.0 the polymorphonuclear cells predominate. The cytological picture can be fairly well predicted from the pH of the exudate and vice-versa. In many cases the pH changes appear to precede the cytological shift which, however, invariably follows. Further studies show that the mechanism of local acidosis in inflammation is referable to a disturbance of local carbohydrate metabolism. With impairment in the local circulation, as indicated by lymphatic blockade and thrombosis of small vessels, it is conceivable that a state of relative anoxemia develops.<sup>2</sup> Anaerobic glycolysis follows. Lactic acid is found to increase two to fourfold as the inflammation progresses. The sugar in the exudate correspondingly falls sharply, revealing a conversion into lactic acid. Most of the inflammatory exudates studied were induced by the injection of small amounts of turpentine, administered sometimes in divided doses, into the pleural cavity of dogs. With the progress of the inflammatory reaction the local alkali reserve soon becomes depleted, as determined by the volume percent of CO<sub>2</sub> content. An uncompensated acidosis follows; the volume percent of CO<sub>2</sub> falling in some instances from 40 to 29 and even to lower levels. The pH falls and the polymorphonuclear cells are replaced by macrophages. Below a pH of 6.8 or 6.7 most types of leucocytes are damaged and frank pus results. The observations indicate that the cytological picture in inflammation seems to be conditioned by the pH, which in turn is referable to the increased rate of glycolysis and the local depletion of the alkali reserve. These studies have obvious implications in regard to the factors determining various histological manifestations of inflammatory lesions. Their bearing on the mechanism of suppuration is likewise evident and is being studied in the case of lesions induced by various pyogenic and non-pyogenic organisms. The present conclusions are based on results obtained with 7 dogs. For the purpose of illustration a type experiment is presented in Table I. The details of this investigation will form the subject of a separate communication.

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<sup>1</sup> Menkin, V., *Am. J. Path.*, 1934, **10**, 193.

<sup>2</sup> Menkin, V., *Arch. Path.*, 1931, **12**, 802.