described by Davies(3) and Véghelyi(4), all have a nutritional basis as a common denominator. Although it is not the purpose of this paper to discuss the similarities between this lesion and the ones found in celiac disease, fibrocystic disease of the pancreas, and sprue, it would seem worthwhile to consider a common etiology for all.

Summary. A degeneration of the acinar cells of the pancreas as the result of a nutritional deficiency has been described. The microscopic lesion was characterized by increased acidophilia and vacuoles within the cytoplasm of the acinar cells, pyknosis and karyorrhexis, which were followed by disintegration of the acinar structure and infiltration by fibroblasts. Finally, there was an increase in the perilobular and periacinar fibrous stroma and in some areas, large amounts of the parenchymal tissue were replaced by fibroblastic material. No changes were observed in the islet cells.

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Changes in Distribution of Potassium and Sodium in Rabbit Muscle Following Cold Injury.* (19558)

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Several observations may be found in the literature reporting alterations in the distribution of potassium and sodium in muscles of experimental animals following various forms of injury as prolonged ischemia, burns and trauma(1-4). Crismon and Fuhrman(5) observed, in the rabbit's muscle exposed to severe cold, a significant gain of sodium in the injured tissue ranging from 30 to 697% with an accompanying increase of extracellular water. In our experiments, the alterations in potassium and sodium distribution in relation to morphological changes in rabbit muscles subsequent to cold injury, were investigated.

Material and methods. Seven adult albino rabbits weighing 2350 to 2800 g were anesthetized with pentobarbital sodium. A standard injury was produced on one of the depilated hind legs by immersing for 4 minutes in a medium previously cooled by solid carbon dioxide to a temperature of —35°C to —37°C (6,7). The muscle biopsies for chemical analysis and cytological study were taken from anterior tibial muscle of both the exposed and unexposed leg under light ether anesthesia, using aseptic technic. The first group of animals (No. 15, 16, 17, 18) was sacrificed at 48 hours, the others (No. 1922, 2023, 2124) 24 hours after exposure to cold and portions of the same muscle were removed. The muscle tissue to be investigated was free from fat, tendons, larger blood vessels and nerves. Muscle specimens were dried to constant weight at a temperature of +105 to +110°C and digested in nitric acid. Sodium and potassium concentrations were determined by means of an internal standard flame photometer. The specimens for morphological study were preserved in Carnoy's fluid, embedded in paraffin and stained with hematoxylin and eosin and van Gieson stain.

Results in electrolyte alterations. The resulting changes are tabulated in Table I and

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TABLE I. Redistribution of Potassium Contents in Injured and Uninjured Muscle Tissue After Exposure to −35°C to −37°C for 4 Min (mEq/100 g Dry Tissue).

	Hr after exposure						% loss of K after		
	6 hr		24 hr		48 hr				
Rabbit	Uninj.	Inj.	Uninj.	Inj.	Uninj.	Inj.	6 hr	24 hr	48 hr
15	40.30				39.52	15.92			59.8
16	43.77	31.55			47.51	11.20	27.9		76.5
17	37.87	27.77			40.48	20.5	26.9		49.3
18	39.3	20			41.57	16.99	49.1		59.2
1922	45.5	6.48	41.1	9.61			85.7	76.7	
2023	38.2	9.15	35.1	31.4			76.3	10.5	
2124	45	19.25	37.3	37.6			57.2	+.8	

TABLE II. Redistribution of Sodium Contents in Injured and Uninjured Muscle Tissue After Exposure to −35°C to −37°C for 4 Min (mEq/100 g Dry Tissue).

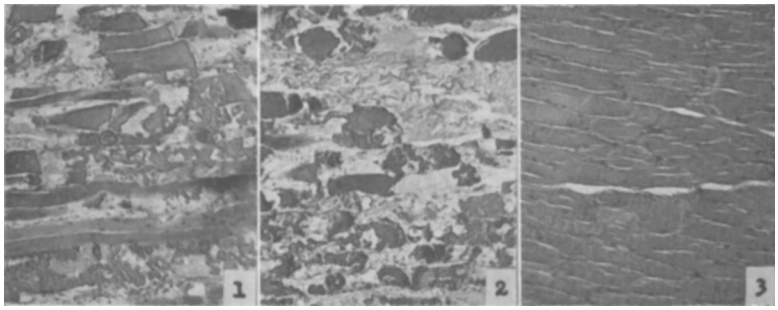
	Hr after exposure						% gain of Na after		
	6 hr		24 hr		48 hr				
Rabbit	Uninj.	Inj.	Uninj.	Inj.	Uninj.	Inj.	6 hr	24 hr	48 hr
15					6.77	55.80			724
16					10.52	103.12			879
17					11.39	54.25			377
18					8.28	72.78			779
1922	12.30	71.9	9.68	74			485	664	
2023	18.90	93	12.5	34			392	172	
2124	13.60	76.7	15.58	19.02			465	22.1	

II. All terms are expressed in mEq per 100 g dry tissue. Six hours after exposure to cold there is a significant loss of potassium from the injured tissue ranging from 26.9 to 85.7% in all experiments. On the other hand, the sodium content in the injured muscle tissue increases considerably from 392 to 485%. A similar decrease in potassium concentration can be observed in animals sacrificed 24 hours after injury, except in experiment No. 2124, in which the potassium content in the injured tissue remains unchanged as compared to the uninjured musculature. There is also a further gain of sodium in the frostbitten tissue except in the above mentioned experiment in which only a slight increase can be noted. The potassium concentration in the injured tissue decreases progressively during the 48-hour period showing a further loss up to 76.5%. At the same time, *i.e.*, at the end of the 48-hour period, the sodium content rises significantly up to values of 879%. The opposite uninjured muscle tissues in the same animal, show uniform losses in sodium concentration during the whole experimental period except in animal No. 2124, in which a slight increase can be observed. On the other hand, there is a decrease in potassium in the unexposed tissue in animals sacrificed 24 hours after cold injury. The other group of animals presents a gain in potassium in uninjured musculature 48 hours after cold injury.

Microscopic findings. The sections taken from the muscles 6 hours after exposure to cold (Fig. 1) show uniform changes consisting of primary damage to the tissue as shown by extensive degeneration of the muscle cells. It is represented by disruption, shrinkage, vacuolization and fenestration of portions or of whole cells. The cell membranes are ruptured or broken and the nuclei undergo pyknosis and karylosis. Edema fluid containing debris of sarcoplasm and nuclei distends the interstitial spaces.

More advanced degenerative changes and further disintegration of muscle cells can be seen in the sections taken 24 hours after cold injury (Fig. 2). At this time, the resorptive activity of phagocytic elements is evident and the proliferating connective tissue starts to replace necrotic muscle cells. Interstitial spaces contain less edema fluid.

Identical degenerative changes can be observed in the muscle tissue 48 hours after exposure to cold. The activity of phagocytic elements absorbing and removing the disin-



Sections taken from anterior tibial muscle at different intervals after exposure to cold. H. and E. × 72.

FIG. 1. Extensive degeneration of muscle tissues 6 hr after injury. Rabbit #2023.

FIG. 2. Further disintegration and resorption of injured cells 24 hr after injury. Rabbit #2023.

FIG. 3. Control section taken from unexposed muscle 6 hr after injury. Rabbit #17.

tegrated muscle cells predominates. Proliferating connective tissue replaces areas of the necrotic tissues. There is evidently less edema in the interstitial spaces.

In rabbit No. 2124, similar pathological alterations can be seen in the musculature. Most of the muscle fibers, however, are intact in the sections taken 24 hours after exposure to cold.

The sections taken 6, 24, and 48 hours after exposure to cold from uninjured anterior tibial muscle of the corresponding animals (Fig. 3), do not show any pathological changes in the structure.

Discussion. The exposure of living muscular tissue to cold of —35 to —37°C results in irreversible damage to the cells similar to that in trauma and burns. The injury is morphologically evidenced by breakdown of the cellular membranes and of cell protoplasm. The immediate changes appearing after injury (7-9) are most marked in sections taken from 6 to 8 hours after exposure to cold(7). At this time, the potassium concentration in the injured tissue is significantly reduced, corresponding in a degree to the microscopic findings. The loss of potassium from injured tissue increases progressively and corresponds to the concomitant disintegration of the damaged cells with the subsequent absorption of necrotic material in the course of 48 hours. A similar release of potassium from injured muscle cells has been observed in burns(1), in experimental traumatic shock(1,2), and in ischemic tissue (1,3,4), as well as in liver tissue after anoxia(10).

The distension of the interstitial spaces by edema in injured muscles indicates an accumulation of extracellular fluid in the injured region. Correspondingly, the sodium concentration of the injured tissue increases markedly. The injured tissue, however, gains more sodium than could be accounted for on the basis of increased water content of the tissue (1,4). Crismon and Fuhrman found an accumulation of more sodium in frostbitten(5) and ischemic musculature(4) than calculated on the basis of addition of extracellular fluid. This accumulation of "excess sodium"(1,4) in the injured tissue, *i.e.*, sodium not present in extracellular fluid, can be partially due to replacement of intracellular potassium by sodium(1,3,4). The combination of the loss of potassium from injured tissue and accumulation of extracellular fluid as edema in the region of injury, are partially reflected in the uninjured tissue by their increase in potassium and their decrease in sodium contents. Histologically, a decrease of edema in the injured region occurs in the course of the experiments, while a progressive rise in sodium concentration indicates a probable exchange of intracellular potassium for sodium. It seems that the redistribution of electrolytes between intra- and extracellular phase does not depend upon the amount of edema in the injured tissue. The concentration of potassium in the injured tissue depends on the number of cells involved in the process of necrosis. On the

other hand, with more extensive necrosis there is less uninjured tissue to absorb the additional potassium released from injured cells(1). More marked electrolyte changes therefore, seem to be related to the greater extent of the injury.

In rabbit No. 2124, there is an evident rise in sodium and a decrease in potassium concentration in injured tissue 6 hours after injury. After 24 hours, however, the damaged tissue shows values different from those in other experiments indicating that the analyzed tissue was limited to only a small number of injured cells, which can be confirmed in the histological sections. These experiments show the alterations in electrolyte distribution similar to the changes in electrolyte concentration in edema fluid subsequent to injury.

Finally, it is possible that the larger variations in electrolyte distribution in injured tissue might be influenced by the increased permeability of cell membranes in the adjacent, functionally damaged but morphologically intact, cells; further, varying degrees of re-establishment of circulation in injured areas and different levels of protein content in edema fluids, might accentuate or mask changes in local electrolyte concentrations.

Summary and conclusions. The redistribution of potassium and sodium in anterior tibial muscles of adult rabbits was investigated at different times after cold injury. The pathological changes were observed simultaneously by means of routine histological technics. Six hours after injury, an extensive necrosis in muscle tissue was observed with a simultaneous release of potassium from injured cells. The loss of potassium was progressive and parallel to the breakdown and subsequent disintegration of the cells during the 48-hour experiment. Conversely, the injured tissue progressively gained sodium despite the diminishing edema fluid. An increase of potassium and a decrease of sodium concentration in uninjured muscle tissues were observed. These events indicate the exchange of intracellular potassium for sodium in injured tissues. The variations in the electrolyte redistribution in injured tissues may be due to such factors as re-establishment of adequate circulation, protein content of edema fluid and ability of uninjured cells to absorb the additional potassium. The severity of the injury is apparently directly related to the electrolyte changes.

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Fluid and Electrolyte Shifts in the Hydrated Adrenalectomized Rat After Nephrectomy.* (19559)

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The normal diuresis which follows hydration is greatly impaired during adrenal insufficiency. This retention of water in the adrenalectomized rat is due in part to a decreased emptying time of the stomach and an impaired intestinal absorption of ingested water(1,2). Primarily, however, it is caused

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