

sodium by re-immersion for 2 h at room temperature in Ringer-Conway fluid containing 104 mM sodium and 10 mM potassium. As already described for rat<sup>7</sup>, one muscle of each pair was cut free of the nerve before re-immersion in recovery fluid and the sodium ion excretion and potassium ion uptake by innervated and denervated muscles were compared. The results are shown in Table 1.

Table 1. FINAL CONCENTRATIONS OF SODIUM IONS AND POTASSIUM IONS IN MUSCLES AFTER RECOVERY AND  $E_m$  MEASURED 10 MIN AFTER RE-IMMERSION OF SODIUM-RICH MUSCLES AND 5 MIN AFTER DENERVATION

Muscles with nerve			Denervated muscles			$E_K$
Na <sup>+</sup> (m.equiv./kg)	K <sup>+</sup> $E_m$ mV	$E_m$	Na <sup>+</sup> (m.equiv./kg)	K <sup>+</sup> $E_m$ mV	$E_m$ mV	
33.1±2.9	87.9±2.5	63.6±0.9	45.9±2.3	78.9±2.4	72.0±0.9	59.2±3.2

In another series of experiments the mean membrane potential of innervated sodium-rich sartorii was measured about 10 min after re-immersion in recovery fluid. The muscle was then cut free of the nerve and the potential measurements resumed after an interval of about 5 min. One of the innervated companion muscles was analysed for sodium ions and potassium ions immediately after enrichment with sodium ions, while the other in each case was analysed after the potential measurements described. The mean value of  $E_K$  for the set of muscles was then calculated and compared with the measured potentials. From the results (Table 1) it appears that the membrane potential of innervated muscles is much closer to  $E_K$ , while sodium ion excretion is stimulated at the same time. The sodium pump clearly becomes more electrogenic following denervation of the muscle. The increase in potential observed on denervation is associated with reduction of sodium ion excretion, which might be explained on the basis of reduced potassium ion uptake or permeability. This view is in keeping with the poor accumulation of potassium ions observed in denervated rat muscles during sodium ion excretion as compared with innervated ones<sup>7</sup>. The lower  $E_m$  of innervated muscles might be expected to facilitate excretion of sodium ions by reducing the energy barrier to this process<sup>8</sup>. A similar stimulation of excretion of sodium ions has been observed by Horowicz and Gerber<sup>9</sup> when  $E_m$  of muscles was reduced by treatment with azide.

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### Transaminase Deficiency in Alcoholics and Cases of Peptic Ulcer

DURING vitamin treatment of ten male and five female alcoholics it was found that, in the majority of cases, internal rate of conversion of vasodilating nicotinic acid to non-vasodilating nicotinamide was much slower than with controls, as manifested by the incidence of flushing with low doses (50–75 mg nicotinic acid). Very similar results were obtained with five non-alcoholic peptic ulcer cases, duration of flushing being of the order of 30 min and extending over face, neck, arms and sometimes as far as the legs.

Six controls who had not suffered any chronic gastric abnormalities or from alcoholism required doses of

150–200 mg of nicotinic acid to produce similar flushing, but it was further noted that, with both experimental and control subjects, ingestion of food a short time after administration of nicotinic acid induced flushing with lower doses than when fasting. For example, a control subject who required 200 mg to produce a marked flush when fasting needed only 150 mg if food was taken 10–15 min after administration.

The findings suggest that the same enzymes are implicated in the metabolism of foodstuffs and nicotinic acid, food taking the priority of use. In view of present theories of enzyme defects in alcoholics<sup>1</sup> and the frequent occurrence of peptic ulcers in alcoholics, a common enzyme defect is possible. Whatever intermediate steps may be involved, transamination is necessary for conversion of nicotinic acid to nicotinamide, and involvement of a transaminase such as pyridoxal-5-phosphate appears probable.

Preliminary findings from an investigation in progress suggest that in many alcoholics and peptic ulcer cases there is a defective utilization of vitamin B<sub>12</sub>, lack of which can lead to deficiency of transmethylase<sup>2,3</sup>, ribonuclease<sup>4</sup>, cytochrome-oxidase<sup>5</sup> and various dehydrogenases<sup>6</sup>. Defective transmethylation could result in deficiency of synthesized pyridoxal-5-phosphate and consequently impaired transamination.

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### Actinomycin D and the Regulation of Apoferritin Synthesis in Rat Liver

IRON administration increases the net synthesis of apoferritin in rat liver *in vivo*<sup>1</sup>. Correspondingly, liver slices prepared from rats dosed with iron incorporate <sup>14</sup>C-leucine into apoferritin *in vitro* more readily than do slices from untreated controls<sup>2</sup>. The mechanism by which the iron acts is unknown, although it has been postulated that intracellular iron in erythroblasts may influence genetic loci<sup>3</sup>. In the following experiments actinomycin D, an inhibitor of DNA-dependent RNA synthesis<sup>4</sup>, was administered to rats prior to a dose of iron, and liver slices were later tested *in vitro* for incorporation of <sup>14</sup>C-leucine into apoferritin. Actinomycin D inhibited the stimulatory effect of iron, indicating that derepression of genes and the synthesis of messenger RNA are involved in the regulatory response to the metal.

Male albino rats of the Sherman strain weighing 150–250 g were fasted for 18 h in metabolism cages, lightly anaesthetized with ether, and given 7 mg iron intravenously as iron dextran ('Imferon', Lakeside Lab., Milwaukee). At various intervals thereafter livers were removed from groups of four rats, sliced with a Stadie-Riggs microtome, and 2.0 g of pooled slices incubated in 15.0 ml. medium at 37° C with continuous shaking and gassing with 95 per cent oxygen–5 per cent carbon dioxide. The incubation medium described by Matioli and Eylar<sup>5</sup> was used except that 3.3 μc. of <sup>14</sup>C-L-leucine (222 mc./mmole, New England Nuclear Corp., Boston) and 1 μmole carrier L-leucine were added to 15 ml. medium along with 3.0 ml. normal rat serum in place of serum albumin and transferrin. After 3 h of incubation, 1.5 g slices were homogenized in 10 volumes of 0.01 M sodium chloride, the homogenate heated to 72° C for 10 min, and precipitated