Correlation Between Lactate Levels and pH in Discs of Patients with Lumbar Rhizopathies

In a recent report NACHEMSON[1] found that the intradiscal pH in patients explored at surgery for lumbar rhizopathy varied between 5.7 and 7.5. No significant difference was found in pH between lumbar discs with prolapses and those without visible pathology (range 6.6–7.5 and 6.8–7.4, respectively).

In the prolapsed discs, however, there was a statistically significant correlation between low pH and visible connective tissue reaction around the nerve root as well as the preoperative impression of pain. In 4 additional patients with severe pain but without prolapses the nerve root was found to be surrounded by dense fibrous scars and adhesions. In these discs the pH was remarkably low (5.7–6.3).

The morphological events of disc degeneration have been described among others by SAUNDERS and INMAN[2] and HIRSCH and SCHAJOWICZ[3]. The first-mentioned authors demonstrated an increasing amount of necrotic tissue inside the disc and the latter authors could demonstrate some attempts at reparation by granulation tissue via ruptures in the annulus fibrosus. In the poorly vascularized disc it is possible that the anaerobic metabolism of the remaining fibroblasts and other cells could in some instances increase the lactic acid concentration and thus lower the pH.

In the present investigation we have correlated the lactate levels in biopsies from nucleus pulposus of lumbar discs with the intradiscal pH measured during surgery.

Methods and materials. During surgery for lumbar rhizopathy the pH was measured in the nucleus pulposus of the discs in 9 patients. One additional patient (No. 9) was measured during instrumental correction for idiopathic scoliosis. Pertinent data on these patients are presented in the Table. The needle type pH electrode constructed for this purpose consisted of antimony and was described in a previous paper[1]. Prior to pH measurement the disc was explored in a routine fashion, care being taken to obtain a dry field. The disc prolaps, when present, was not removed until after the measurements which were performed through a larger bore needle inserted into the nucleus pulposus. Using a concotome, small pieces of tissue from the nucleus pulposus were removed and immediately (within less than 5 sec) frozen in liquid nitrogen and stored in dry ice until the lactate analyses were performed.

Treatment of the biopsies with perchloric acid and lactate determinations (see DIAMANT et al.[4]) follows in general procedures given by LOWRY et al.[5].

Results and discussion. The results are presented in the Figure. It is evident that there exists a correlation between the pH of the nucleus pulposus as measured in vivo and the lactate concentrations in the frozen biopsies.

Assuming a linear relationship between lactate concentration and pH, the equation of the regression line is $Y = 8.05 - 0.10 \times X$. The correlation coefficient is 0.82.

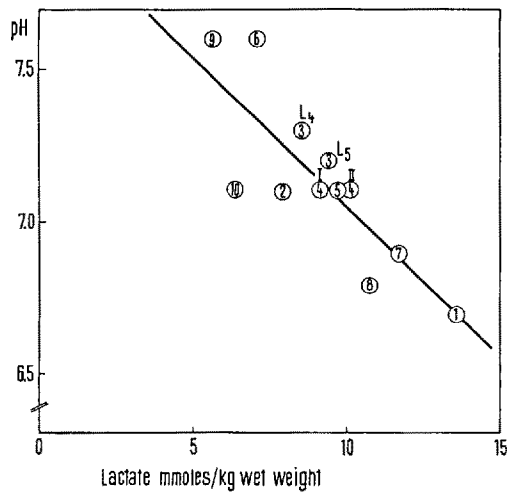
In comparison with human muscle tissue (M. vastus lat.) the lactate levels are remarkably high in the nucleus pulposus. Recent determinations in the resting muscle showed values of lactate amounting to 1–3 mmoles/kg wet weight which rose to 19–23 mmoles/kg wet weight after short term maximal work loads[4,6].

It can be assumed that lactate is formed within the nucleus pulposus since preliminary experiments have shown measurable amounts of lactic dehydrogenase.

It is known that the direct blood supply to the intervertebral discs is occluded at the age of 15–20[2,3]. Little is known about the nutrition of discs after that age but it has been assumed that diffusion through the end plates occurs. The relatively rapid degeneration of the discs has been discussed in terms of defective diffusion through the end plates[2,3,7]. It seems therefore possible that the increased lactate levels observed in the present material are due to enhanced anaerobic glycolysis within the nucleus pulposus in order to counteract a decreased nutritional diffusion.

It is possible that the connective tissue reactions that were found[1] around the nerve roots in cases with low pH somehow is related to an increased production and leakage of lactic acid from the discs through the ruptures in the posterior part of the annulus fibrosus. In this way

Patient No.	Sex	Age	Operative finding
1	F	36	free prolaps, L5
2	M	41	covered prolaps, L5
3	M	28	covered prolaps, L4 covered prolaps, L5
4	M	52	negative (2 biopsies taken), L4
5	F	36	free prolaps, L5
6	M	30	negative, L4
7	F	40	covered prolaps, L5
8	M	64	negative, L4
9	F	17	negative (scoliosis), L3
10	M	50	free prolaps, L4



Intradiscal pH and lactate concentration of nucleus pulposus. Figures denote patient number from the Table. If one assumes a linear relation the equation of the regression line: $Y = 8.05 - 0.10 \times X$. Coefficient of correlation = 0.82.

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sensitive structures like the dorsal longitudinal ligament[8], the dura and the nerve root could be irritated by the leakage of acid metabolites. It is documented that pain will arise in tissues showing low pH[9–12].

It is thus possible that some cases of lumbar rhizopathy could be due to the demonstrated increase in lactic acid.

Zusammenfassung. An 10 Patienten wurde das während der Operation im Discus gemessene pH mit dem Laktatspiegel des in derselben Zeit entfernten Nucleus pulposus in Korrelation gebracht. Mit absteigenden pH-Werten war der Laktatspiegel höher. Es wird dem erhöhten Laktatspiegel der lumbaren Bandscheiben eine mögliche Rolle in der Pathologie einiger lumbarer Rhizopathien zugeschrieben.

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Uptake of some Amino Acids by Rat Brain Slices: Effect of Various Substrates

The studies of STERN et al.[1], ABADOM and SCHOLEFIELD[2], and NEAME[3] have established that cerebral slices incubated in a suitable medium are able to concentrate amino acids against a concentration gradient, as do other tissues[4]. Several distinct transport systems have been described for neutral, acid, basic and heterocyclic amino, acids of similar charge and structure[5]. The extent to which rat cerebral slices can actively concentrate glycine has been shown to correlate with concentration of adenosine triphosphate present in the tissue[2].

The present paper examines the effects of glucose and glycolytic and citric acid cycles intermediates on the rate of accumulation of some amino acids. The levels of adenosine triphosphate and phosphocreatine have been measured in the presence of the same substrates; the effects of anoxia and of metabolic inhibitors have also been investigated.

Methods. Cortical brain slices (0.35 mm thick) were prepared from adult Sprague-Dawley rats which were rapidly decapitated without anaesthesia; the slices were incubated in the Krebs-Ringer bicarbonate saline medium previously described[6]. In the anaerobic experiments Krebs-Ringer phosphate buffer was used under 100% N_2 atmosphere with yellow phosphorus in the centre well of the conical Warburg vessels. Substrates were neutralized with *N* NaOH, if necessary, and the corresponding amount of Na^+ was omitted from the saline. After incubation, the slices were picked up with a bent silver wire, drained on glass until no more clear fluid came off, weighed on a torsion balance, and homogenized in 2 ml of 6% cold trichloracetic acid (TCA). They were then dried at 105 °C for 6 h, and the tissue water content calculated. L-tryptophane[7], L-histidine[8], L-arginine[9] and L-proline[10] (Calbiochem, Los Angeles) were analyzed colorimetrically after centrifugation. All results were corrected with blanks of tissues containing no amino acids in the suspending medium. 1-C^{14}-L-glutamic acid, 1-C^{14} glycine, 1-C^{14} γ-amino-butyric acid (Calbiochem) were determined by addition of 0.5 ml deproteinized supernatant to 7 ml of liquid scintillation fluid[11] and counted for 7 min in an Elliot I.D.L. liquid scintillation spectrometer. Internal standards were used to correct for sample quenching. Calculations were based on measurements of total tissue radioactivity, and no correction was made for $^{14}CO_2$ evolution, or the possible presence of other labelled metabolites. As brain slices accumulate water and electrolytes during incubation, results were expressed as mmoles of amino acid/l tissue water, all amino acids being assumed to be evenly distributed throughout the tissue water.

Results and discussion. It has previously been shown that amino acid concentration reaches a constant level after 40 min incubation in Krebs-Ringer bicarbonate glucose saline[12]. In the present study active concentration can be seen to occur in cerebral slices under similar conditions of L-glutamic, L-histidine, glycine and γ-aminobutyric acid (Table I). This accumulation was much diminished in the absence of substrate (Table I). Substrates could be divided into 2 groups by their effect: (1) maximum accumulation of amino acids occurred in the presence of glucose, pyruvate, lactate and oxaloacetate, (2) succinate and fumarate always gave the lowest amino acid levels not significantly higher than in the absence of substrate. The levels of energy-rich phosphate maintained by rat brain slices during incubation with different substrates are shown (Table II), and there appears to be a correlation between the total amount of labile phosphate and the rate of amino acid accumulation. During hypoxia, and in the presence of metabolic inhibitors, there was a marked decrease or lack of accumulation of amino acids (Table I). The uncoupling agent 2-4 DNP also strongly diminished the uptake. All these experimental conditions are known to reduce the levels of phosphocreatine[13]. These results confirm the dependence of this process on cellular stores of energy-rich com-

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