difference: during the last week, the rats were treated with the following vitamins: Vitamin B_1, 40; lactoflavin, 23; niamid, 160; pyridoxin, 16; panthothenic acid, 240; biotin, 2 mg/kg, and cyanocobalamin, 80 γ/kg body weigth (BVK[6]). Group 6. Procedure differed from that used in group 5 only in one respect: instead of Vitamin B, coumarin[7] was given (25 mg/kg/day). Group 7. Procedure differed from that used in group 6 by injecting troxerutin[8] (500 mg/kg/day) instead of coumarin. Data were analysed statistically by variance analysis.

Results. After cervical lymphatic blockage, permeability of the BBB increases significantly in rats fed the normal diet. Complex vitamin B defiency had the same effect. By combining Vitamin B deficiency and lymphostatic encephalopathy, the lesion of the BBB was the most pronounced. This combined effect could be influenced therapeutically not only by the administration of the Vitamin B drug BVK, but also by the 2 members of the 'vitamin P-family', coumarin and troxerutin.

Zusammenfassung. Die bereits bekannte Permeabilitätszunahme der Blut-Hirnschranke bei der lymphostatitischen Enzephalopathie wurde mittels einer neuen Methode bestätigt: i.v. infundiertes PVP, mit einem Molekulargewicht von 40.000, drang bei normalen Kontrollratten in die Hirnsubstanz nicht ein; bei Tieren mit einer lymphostatischen Enzephalopathie war PVP in der Hirnsubstanz nachweisbar. Eine komplexe B-Avitaminose führt ebenfalls zum Eindringen von PVP in die Hirnsubstanz; eine Kombination zwischen lymphostatischer Enzephalopathie und komplexer B-Avitaminose hat eine Addition der Permeabilitätsstörung zur Folge. Zwei in die «Vitamin P-Familie» gehörende Stoffe, Cumarin und Troxerutin, übten einen weitgehenden protektiven Effekt gegen die Zunahme der Permeabilität der Blut-Hirnschranke aus.

ETHEL FÖLDI-BÖRCSÖK and M. FÖLDI

Research Laboratories, Schaper und Brümmer, P.O. Box 1160, D-3324 Salzgitter-Ringelheim (Germany).
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[6] BVK Roche®, Hoffmann-La Roche AG, Grenzach/Baden (Germany).
[7] A component of Venalot®, Schaper and Brümmer, Salzgitter-Ringelheim (Germany).
[8] A component of Venalot®, Schaper and Brümmer, Salzgitter-Ringelheim (Germany).

Myocardial Concentrations of High Energy Phosphates in Normal Mini-Pigs and Dogs[1]

In recent years evidence indicating that the use of mini-pigs and swines might offer distinctive advantages in comparative cardiovascular research has accumulated[2,3]. In this paper we report on the normal myocardial concentration and distribution of ATP, ADP, creatine (Cr) and creatine phosphate (CrP) in mini-pigs, comparing the results with values obtained in dogs. As the myocardial stores of high energy phosphates are of primary importance for the mechanical performance of the heart[4–9], this work will serve as a basis to study hemodynamic and metabolic alterations during a controlled reduction of coronary flow.

Materials and methods. 6 mini-pigs (27–39 kg) of the Göttinger breed, premedicated with 0.5 mg/kg azaperon (Stresnil®), 3 mg/kg phencyclidin-HCl (Parkesernyl®) and 0.1 mg/kg atropine-sulfate were connected to a respirator (Bird-Mark IX) and ventilated initially with 1 vol.% and after reaching surgical tolerance with 0.5 vol. % of methoxyfluran (Pentrane®) in 50 vol. % oxygen and 50 vol. % air at 20 cycles/min. The pO_2, pCO_2 and pH of the arterial blood were controlled during the experiments and constantly readjusted to preoperative values. Details of the anaesthesia will be published elsewhere[10].

Eight mongrel dogs (18–24 kg) premedicated with 1.25 mg/kg methadon-HCl (Polamivet®) and 0.5 mg/kg propionyl-promazin (Combelen®) were anaesthetized with 25 mg/kg pentobarbital-sodium (Vetanarcol®). They were connected to an Engström-respirator and ventilated with a mixture of 50 vol. % O_2 and 50 vol. % air at 20 cycles/min.

After a thoracotomy on the left side, the heart was exposed. Proceeding from the apex to the base of the left ventricle, two to four biopsies were obtained at intervals of 30–60 sec. We used a small WOLLENBERGER-tong[11] with cutting edges (details of construction on request) precooled in liquid nitrogen. Slices of tissue with a thickness of less than 1 mm weighing between 40–120 mg were obtained.

The frozen tissue was freeze-dried, pulverized in a mycrodysmembrator (Braun, Melsungen) and extracted with freezing 0.6 M $HClO_4$ under constant stirring in an alcohol bath of −70 °C. The suspension was centrifuged for 3 min at −4 °C. The sediment was re-extracted with 0.45 M $HClO_4$ under the same conditions. The combined extracts were neutralized to pH 6 with 54 mM triethanolamine in 2 M K_2CO_3. The supernatant obtained after centrifugation was kept at 0 °C and used for analysis.

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Myocardial (left ventricle) concentrations (μmol/g wet weight) of ATP, ADP, ATP + ADP, creatine (Cr), creatine phosphate (CrP) and Cr + CrP

Spezies	n	ATP	ADP	ATP + ADP	ATP/ADP
Mini-pigs	6	4.51 ± 0.34	0.94 ± 0.20	5.44 ± 0.35	5.10 ± 1.22
Dogs	8	6.15 ± 0.67	0.85 ± 0.16	7.02 ± 0.81	7.61 ± 1.14
p		< 0.0005	> 0.15	< 0.0005	< 0.0025
Spezies	n	CrP	Cr	CrP + Cr	CrP/Cr
Mini-pigs	6	10.70 ± 1.17	10.84 ± 1.59	21.57 ± 1.90	1.03 ± 0.23
Dogs	8	14.09 ± 1.74	11.52 ± 2.67	25.68 ± 2.72	1.37 ± 0.51
p		< 0.0025	> 0.25	< 0.005	< 0.05

Data from 6 mini-pigs (23 biopsies) and 8 dogs (23 biopsies). The mean values of each ventricle were used for the statistical analysis with an unpaired t-test[24]. Values in the table are $\bar{x} \pm s_{\bar{x}}$.

ATP[12], CrP[13], ADP[14] and Cr[15] were determined according to published methods. All enzymes, coenzymes and substrates were from Boehringer and sons.

Results and discussion. The results obtained in 6 mini-pigs (23 biopsies) and 8 dogs (23 biopsies) are compiled in the Table. The concentrations in the dog heart agree well with results published by others under comparable conditions[5–9,16,17]. High levels of CrP[5–7] are correlated with a low oxygen consumption of the heart[6,7]. With the exception of ADP and Cr all values differ significantly in the two species. Species differences and possible analytical errors have been repeatedly reviewed[4,9,17–22]. We do not know if the different coefficients (ATP/ADP and CrP/Cr) are due to the anaesthesia. An average value of 6.24 for ATP/ADP is commonly found in dogs under aerobic conditions[9]. However, NÄGLE et al.[23] and KÜBLER[7] did not find a change in total creatine (CrP + Cr) during ischemia and anoxemia lasting 1 h. According to SPIECKERMANN[9], the sum of the adenine nucleotides is identical in pentobarbital and halothan anaestheisa and the concentrations of ATP are equal in pentrane and pentobarbital anaesthesia. We believe therefore that, assuming identical coefficients of ATP/ADP and of CrP/Cr in both species, all metabolites have a lower concentration in the mini-pig.

Using a t-test to analyse differences of paired samples[24], the concentrations of all metabolites in the most distal (apex) biopsies were compared with those of the most proximal ones. No significant differences could be found at a confidence level of $P < 0.05$. A random distribution of ATP, CrP and lactate in left ventricles of dogs under aerobic conditions has been reported by BRAASCH et al.[6,25].

Zusammenfassung. Die Gewebskonzentrationen an ATP, ADP, ATP + ADP, Kreatinphosphat, Kreatin und Kreatinphosphat + Kreatin sind unter vergleichbaren Bedingungen im linken Ventrikel von Mini-pig-Herzen kleiner als im Hundeherzen. Die Unterschiede in den Koeffizienten (ATP/ADP und Kreatinphosphat/Kreatin) dürfen narkosebedingt sein. Sämtliche Messgrössen sind nicht mit dem Entnahmeort der Biopsien (apikal, basal) korreliert.

S. RODENROTH[26], R. LERCH[26], W. RUTISHAUSER[26] and E. JENNY[27]

Kardiologische Abteilung, Departement für innere Medizin, Rämistrasse 100, CH–8006 Zürich (Switzerland) and Institut für Pharmakologie und Biochemie, Winterthurerstrasse 260, CH–8057 Zürich (Switzerland), 4 April 1973.

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[26] Kardiologische Abt., Dept. für innere Medizin, Rämistr. 100, CH–8006 Zürich, Switzerland.
[27] Institut f. Pharmakologie und Biochemie, Winterthurerstr. 260, CH–8057 Zürich, Switzerland.

Effect of Lithium on the Blood and Intestinal Serotonin Contents of Rats

Lithium salts are widely used as a specific remedy for manic states[1]. Recently they have been reported to accelerate the synthesis rate of serotonin in the brain[2,3]. Early side effects commonly associated with lithium treatment are a variety of gastro-intestinal discomforts, such as nausea, vomiting, diarrhea and stomach pain[4]. It seemed possible that these symptoms were associated with disturbance of serotonin metabolism in the blood and