cause a generalized vascular lesion followed by platelet adhesion and aggregation, such as endotoxin[13], produce dramatic platelet consumption, i.e. severe thrombocytopenia.

Zusammenfassung. Die Innenseite von Kaninchenaorten wurde durch selektive Endothelentfernung in vivo in eine thrombogene Oberfläche verwandelt. Trotz Akkumulation von mehr als 10^9 Plättchen in 10 min an subendothelialen Strukturen konnte keine Veränderung der Zahl, Volumenverteilung oder Faktor-3-Freisetzung von Plättchen im Blut vor und nach Passage dieser Oberfläche gemessen werden.

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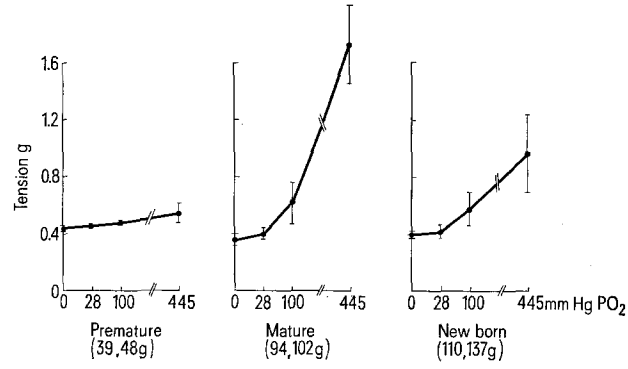
Development of the Q_2 Induced Contractions in the Ductus Arteriosus of the Guinea-Pig

The ductus arteriosus of several animals and man contracts when the PO_2 of the supporting medium is increased. This response constitutes a possibly essential step in the physiological ductal closure after birth and initiation of breathing[1]. The extent of the contraction[2] and the sensitivity to the increase in the O_2 concentration[3] vary among species. Even within the same species, variability in the response to O_2 has been reported[3]. We have attempted to analyze this problem of differences in responsiveness by studying the fetal age dependence of the reactivity to O_2 and norepinephrine (NE) in isolated ductal rings of the guinea-pig.

The vascular segments were isolated from newborn animals and fetuses of different gestational age. The latter was estimated from the body weight, the degree of hair growth and the somatic response to sensory stimulation, e.g. pinching. The mothers were lightly anesthetized with pentobarbital sodium, supplemented by infiltration of lidocaine into the abdominal wall, and the fetuses were delivered by cesarean operation. The fetus or newborn animal was rapidly decapitated; the chest opened; the heart, lungs, and great vessels removed en masse; and the ductus quickly dissected. A ductal ring, approximately 2 mm long, was excised and mounted between two fine wires, to record isometric tension changes (Statham UC2 load cell transducer and Grass Model 5 polygraph) while superfused with Krebs-bicarbonate solution maintained at 37 °C in an organ bath[4,5]. The resting tension was adjusted to 400 mg by varying the distance between the supporting wires with a micrometer. This level was below the in situ wall tension (300 mg/mm or 600 mg for a 2 mm segment) calculated using a simplified Laplace relationship. Changes in tension were evoked by increasing stepwise the PO_2 in the perfusing medium from 0 to 28 (the usual fetal level) to 100 and finally to 445 mm Hg, and also by adding NE (10^{-10} g/ml) to the superfusate.

The graded responses to changes in O_2 increased with the gestational age (Figure) from a very small tension development in the immature fetus to a marked contrac-



Progressive contractile response to increasing O_2 concentration (mean ± S.E.) in the ductus arteriosus of the guinea-pig. Repeated tests (3) were performed in 2 ductal segments from animals at different stages of development. Numbers in parentheses indicate the weight of the fetuses (premature or mature) and the newborn animals. Resting tension, at 0 mm Hg PO_2, was set in all cases at 0.4 g.

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Ductal contraction to NE as a function of PO_2 and maturation

Developmental stage	Premature			Mature			Newborn		
PO_2 (mm Hg)	28	100	Δ	28	100	Δ	28	100	Δ
Change in tension (mg)	45	60	15	75	210	135	60	130	70
to norepinephrine (10^{-10} g/ml)	55	120	65	105	220	115	75	140	65

Change in tension of 6 ductal rings in response to NE. Resting tension in all cases was set at 400 mg. Each ring was tested at low (28 mm Hg and high (100 mm Hg) PO_2. Δ = difference between responses at the two PO_2 levels.

tion in the mature one, followed by a decrease in the response to the higher PO_2 levels in the newborn animal.

The response to NE, tested at two levels of PO_2 (28 and 100 mm Hg), varied also as a function of the age of the animal (Table). The greater response was observed in the mature fetus at both low and high PO_2. The difference between the responses to NE at 100 and 28 mm Hg PO_2 (Δ) was also significantly larger in the mature fetus.

Our results are comparable with the report that the ductus of the fetal lamb increased its responsiveness to O_2 as a function of developmental age[6]. However, that preparation showed a distinct threshold for the response at a PO_2 of 65 mm Hg. In contrast, in our experiments, the guinea-pig ductus contracted gradually in response to any increase in O_2 above 0 mm Hg (95% N_2 and 5% CO_2) as shown in the Figure.

The temporal changes in ductal responsiveness to O_2 were characterized by a progressive increase with fetal maturation followed by a decline after birth. The increased responsiveness during the fetal period could depend upon maturation of a) specific receptors for O_2 or b) the ductal vascular smooth muscle. The first possibility was suggested in the report[7] describing dissociation of responses to O_2 and NE with advancing fetal age. Thus, oxygen receptors, with maturational characteristics different from those of NE receptors were postulated. Our results, without disputing the notion of differentiated receptors, support the second possibility namely, that the age dependent increase in responsiveness reflects the graded maturation of the vascular smooth muscle. This notion is based on our observation of a parallel increase in the contractile changes to O_2 and NE during fetal growth. The gradual decrease in the responses observed after birth may depend on involution of the ductal wall starting shortly after birth, as has been shown in the lamb ductus arteriosus[8].

Zusammenfassung. Die Wirkung von Sauerstoff und Norepinephrin auf die Kontraktionen des isolierten Ductus arteriosus des Meerschweinchens nimmt mit zunehmendem Alter des Feten bis zur Geburt zu und verschwindet kurze Zeit hernach wieder.

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Effect of Lithium on Brain Aconitase Activity

Although lithium salts are known to be effective agents against mood disorders[1,2], an explanation of lithium's mechanism of action in the treatment of manic-depressive psychosis is still lacking[3,4].

FORN and VALDECASAS[5] observed that a wide range of Li^+ concentrations inhibits rat and rabbit cerebral cortex adenyl cyclase in vitro. Recently, ABREU and ABREU[6] reported a highly significant in vivo activation of brain succinate dehydrogenase in mice treated with Li_2CO_3. The object of the present work was to find out whether any significant differences in brain aconitase (aconitate hydratase, E.C. 4.2.1.3) activity occur in mice on long term treatment with Li_2CO_3.

Material and methods. Male Swiss mice (26 g mean body weight) maintained in a standard balanced diet ad libitum were used throughout the experiment. One group of mice received as drinking water a solution containing 100 mg of Li_2CO_3/l. To the control group distilled water was given. After 108 days of treatment the animals were killed by cervical dislocation and the brains removed quickly. 10% brain homogenates were prepared immediately in ice cold distilled water and the aconitase activity was determined by a modification of the spectrophotometric method of RACKER[7]. The final volume was 3.0 ml including 1.5 ml of 0.06 *M* sodium citrate in 0.1 *M* phosphate buffer at pH 7.4 and 0.1 ml of brain homogenate added to start the reaction. After 10 min of incubation at 37 °C the reaction was stopped by the addition of 3.0 ml of 0.5 *M* $HClO_4$. A control was prepared for each sample by the addition of $HClO_4$ anf homogenate to the buffered substrate at time zero. Spectrophotometric determinations in the supernatants were made at 240 nm in a Shimadzu QV-50 spectrophotometer equipped with cells of 10 mm light path. The enzymatic activity follows a zero order kinetics and 1 unit is equivalent to a change in optical density of 0.001 in 10 min at 37 °C. Total proteins in the homogenates were determined by the biuret method of GORNAL, BARDAWILL and DAVID[8] using

Effect of Li^+ on mouse brain aconitase activity

Treatment	No. of mice	Body weight (g)	Aconitase (units/mg of protein)
Li_2CO_3	19	30 ± 0.7	218 ± 16
Controls	19	31 ± 0.6	233 ± 17

Each value represents the mean $\pm$ standard error of the mean.

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