fibres are summarized in Figure 2. While tidal volumes large enough to yield end-tidal carbon dioxide concentrations between 2.5 and 3.3 vol% were compatible with a slight hypotensive reaction, a progressive decrease in ventilation such as to give 3.8 and 4.8 vol% of end-tidal carbon dioxide, changed the depressor into a pressor response of increasing amplitude. To sum up, it seems that pulmonary ventilation is without any important action upon the reflex effect of low threshold 'pressoceptive' afferents, while strongly influencing that of the intermediate threshold 'chemoceptive' fibres. Potentiation of this effect during hypoventilation appears to overwhelm also the depressor activity of high threshold pressoceptive afferents, at least when submaximally activated.

It should be recognized that most, though by no means all, of the animals behaved according to the pattern reported above. A limited number of spontaneously ventilating preparations (2 out of 33) responded with blood pressure falls of increasing size (up to a given maximum) and with decreased respiration to any type and strength of aortic stimulation. These hypotensive responses could never be changed into pressor reactions by any degree of artificial hypoventilation. The lack of hyperpnoea after left aortic excitation suggests that the intermediate threshold 'chemoceptive' component was absent or inconspicuous in the left aortic nerve of these animals.

Various mechanisms whereby ventilatory changes might affect blood pressure reactions to aortic stimulation have also been considered and subjected to experimental testing. Basal blood pressure levels are unlikely to be the crucial factor, as ventilation could influence the circulatory reflex responses even when no considerable change of the basal arterial pressure was observed. The pulmonary reflex, which has been shown by DALY et al.[3,4] to have a marked interaction with the cardiac response to natural chemoceptive stimulation, does not seem to play a fundamental role in our experimental conditions, as reversal of hypotensive to hypertensive reactions has also been observed after bilateral vagotomy. We have no data, however, as to the possible contribution of this reflex to the whole effect. Hypercapnia and hypoxia can each play an important role in the modification of the circulatory reflex response, as in 14 preparations where their effect was tested, either high carbon dioxide (5–7% CO_2 in O_2) or low oxygen mixtures (5–8% O_2 in N_2) could always shift a depressor into a pressor reaction, provided the appropriate intermediate stimulating voltage was used. The level at which both hypercapnia and hypoxia affect the circulatory response to aortic stimulation can only be surmised: the well-known excitatory effect of hypercapnia[5], and probably of hypoxia as well[6], on the vasomotor centre suggests that the excitatory state of the nervous centres controlling the circulation may be of some importance, but a peripheral action of carbon dioxide and oxygen tension on blood vessels or heart performance cannot be excluded.

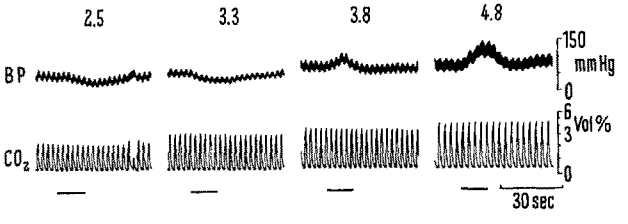

Fig. 2. Blood pressure responses to electrical stimulation of the left aortic nerve with stimuli of intermediate strength (2 V, 1 msec), during artificial ventilation at decreasing amplitudes. BP: blood pressure, CO_2: continuous records of carbon dioxide concentration in the expired air. The number on the top of each figure indicates the value of end-tidal (alveolar) carbon dioxide concentration during each stimulation trial, thus testifying that ventilation volume is decreasing from the first to the fourth trial. Decerebrate animal with both carotid sinus nerves and the right vago-aortic trunk severed.

Riassunto. Le risposte circolatorie alla stimolazione elettrica del nervo aortico sono notevolmente modificate dalla ventilazione polmonare. In particolare le risposte a stimoli di intensità intermedia ed elevata, che attivano oltre a fibre pressocettive anche fibre chemocettive, divengono da ipotensive ipertensive durante ipoventilazione. Gli effetti dell'ipoventilazione sono sempre riprodotti sia dall'ipercapnia (respirazione con CO_2 5–7% in O_2) sia dall'ipossia (respirazione di O_2 5–8% in N_2).

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The Permeation of Drugs Across the So-called Blood-Brain-Barrier at Low Temperature

The close correlation between lipid solubility of a drug and its rate of permeation from the blood into the cerebrospinal fluid (CSF) led to the assumption that the so-called blood-brain-barrier is lipoid in character[1]. The drugs are considered to penetrate passively by diffusion through a lipid layer of the membrane according to their lipid/water partition coefficients. The question arises whether the normal function of the cell is necessary to maintain these properties of the membrane or not. In order to prove this, we minimized the metabolism of cells by studying the permeation of drugs into the CSF at low temperature.

The heads of dogs weighing about 15 kg were perfused with isotonic salt solution[2] *via* the carotid arteries at a rate of 90 ml per min. The solution was saturated with oxygen and adjusted to a pH of 7.4. Haemoglobin was added in a concentration of 1% as an indicator in order to detect a leakage of the blood-brain-barrier by the appearance of a reddish tint of the CSF. The drugs investigated were added in the following concentrations: aniline

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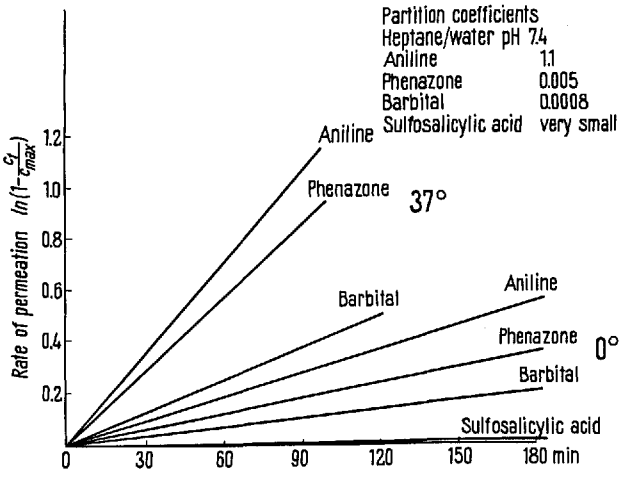
50 µg/ml, phenazone 100 µg/ml, barbital 1 mg/ml, sulfosalicylic acid 1 mg/ml. The temperature of the perfusion fluid was 0° or 37°C. In the experiments at 0°C, the perfused head of the animal was covered with crushed ice. In the experiments at 37°C, the head was heated slightly by a lamp. At various intervals after starting the perfusion, samples of CSF were collected *via* a cannula placed in the cisterna magna. The concentrations of the drug in the perfusion fluid and in the samples of CSF were determined using methods previously described[1]. The partition coefficients of the drug were calculated from the distribution of the substance between heptane and an aqueous phase at pH 7.4.

The results are shown in the Figure. As demonstrated by the graph, a dependence of the rate of permeation on the partition coefficient is found not only in the head perfused at 37°C but also in the experiments made at the low temperature of 0°C. In both experiments aniline with the highest partition coefficient permeates most quickly. This drug is followed by the less lipid-soluble phenazone and barbital. The sulfosalicylic acid with its very low partition coefficient hardly enters the CSF. This suggests that the lipoid character of the membrane between blood and CSF does not require a normal function of the cells. Therefore it seems improbable that the barrier hindering the free exchange of substances between blood and CSF has to be maintained by energy.



Rate of permeation of aniline, phenazone, barbital and sulfosalicylic acid into the cerebrospinal fluid in the perfused dog head (mean values from 3–4 experiments). c_t = concentration of the drug in the CSF at the time t, c_{max} = maximum concentration of the drug.

The graph demonstrates also an overall difference in the rate of permeation from the experiments made at 37°C and 0°C. This seems to be understandable because diffusion in the aqueous phase is slowed down as the temperature decreases. If this were the only factor involved, the temperature coefficient calculated from the experimental results should be equal to the temperature coefficient for the diffusion in water. The comparison of these values in the Table shows no such coincidence. The temperature coefficients for the diffusion in the aqueous phase are smaller than the corresponding coefficients calculated from our experiments. This points to a further factor being involved. RENKIN[3] found that decreasing the temperature decreases the rate of diffusion through the lipid layer more strongly than the rate of diffusion in the aqueous phase. He suggests that this is because the increase in the viscosity of the lipids with decreasing temperature is greater than the corresponding increase in the viscosity of the water. This might also be true for the blood-brain-barrier and would give additional evidence of its lipoid character.

	Blood/brain	Agar-gel
Aniline	4.49	2.08
Phenazone	3.92	1.92
Barbital	3,73	1.97
Temperature coefficients: $Q_{37°}$		

Zusammenfassung. Zur Erhaltung der lipoiden Eigenschaften, welche die sogenannte Blut-Liquor-Schranke permeierenden Arzneistoffen gegenüber besitzt, ist keine Stoffwechseltätigkeit erforderlich.

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Etat hygrométrique, coloration et résistance chez l'imago de *Locusta migratoria migratorioides* (R.F.)

Il résulte d'un travail récent[1] que la résistance des nouveau-nées à des conditions de vie difficiles est accrue, chez les Acridiens migrateurs, par le groupement des parents. Les recherches sur les fluctuations d'effectifs devaient conduire à explorer, du même point de vue, le stade imaginal.

Les faits rapportés ci-dessous concernent *Locusta migratoria migratorioides*; ils précisent le déterminisme de la coloration, brune ou verte chez les solitaires, ainsi que les conditions d'adaptation chromatique, en approfondissant les observations de FAURE[2] et de BURTT[3].

Les larves nouveau-nées de filiation solitaire et grégaire sont respectivement brunes et noires. L'élevage à 100% d'humidité relative conditionne, dans tous les cas, le verdissement des isolées au 2e âge. A 50–80% d'humidité relative, ce virage se fait essentiellement au 3ème ou au 4ème âge, sauf une minorité de larves qui ne réagissent pas (5 à 10%). A 30–50% d'humidité relative, *les formes vertes sont fortement minoritaires*. Aucun individu ne verdit à 15–30% d'humidité. Le virage au vert se produit dans

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