Table II. Tissue/medium ratio (relative initial uptake from the medium after 10 min incubation at 25 °C) for taurine, glycine and Gaba in rat cortex slices (calculated as cpm per 100 mg slices/cpm per 100 µl initial incubation medium)

		N	Tissue/medium ratio
^{35}S-taurine	1.0×10^{-5} M	7	0.73 ± 0.14
^{3}H-glycine	4.5×10^{-7} M	5	3.38 ± 0.36
^{3}H-Gaba	4.5×10^{-7} M	5	11.59 ± 0.75

Table III. Subcellular distribution of taurine, glycine and Gaba in rat cerebral cortex slices after 10 min uptake at 25 °C

		N	Fraction 1–7	Fraction 8–23	Fraction 24–27	Fraction 28–30
^{35}S-taurine	1.0×10^{-5} M	7	2.1 ± 0.5	27.4 ± 0.5	13.1 ± 1.3	57.3 ± 2.4
^{3}H-glycine	4.5×10^{-7} M	5	1.6 ± 0.3	40.6 ± 1.3	19.7 ± 1.1	38.0 ± 1.9
^{3}H-Gaba	4.5×10^{-7} M	5	1.4 ± 0.1	39.8 ± 1.2	19.1 ± 0.9	38.7 ± 1.0

Fractionation of homogenized slices (after sedimentation of cell nuclei at 184 g/10 min) on a 10-step discontinuous sucrose density gradient[7]. Figures give the precent of total cpm's applied to the gradient found in the 4 regions containing different subcellular structures.

Zusammenfassung. Die Kinetik der Aufnahme von S^{35}-Taurin in Rattencortex-Schnittchen wird im Konzentrationsbereich von 9×10^{-8} M bis 5×10^{-3} M untersucht. Nach Abzug des Transportes durch Diffusion ($K_D \times S$) findet man einen Mechanismus, der Michaelis-Menten Kinetik folgt (v_{sat}), mit $K_m = 1{,}73 \times 10^{-4}$ M. Ein solcher Transport liegt nicht im Bereich des spezifischen «uptake» der Neurotransmitter. Auch die sehr niedrige Aufnahme-Rate und die subzelluläre Verteilung nach «uptake» sprechen gegen eine Neurotransmitter-Funktion von Taurin.

mitter role for taurine. Furthermore, the subcellular distribution patterns of the 3 amino acids (Table III) shows that, while about 40% of glycine and Gaba are found in fractions 8–23 (synaptosomal), only 27% of the taurine label appears there. Most of the taurine remains in the supernatant (57%) compared with only 38% for glycine and Gaba.

Taurine is present in unusually high concentrations in mammalian brain[9] and retina[10]. In chicken retina, uptake kinetics have an apparent $K_m = 1.53 \times 10^{-3}$ M, falling into the low-specificity range[11], as we have found for rat cortex. Our preliminary experiments on rat retina and spinal cord slices (unpubl. observations) have shown even lower uptake rates than those in cortex. There are 3 lines of physiological evidence pointing to a transmitter function of taurine: (a) it inhibits neurones when applied to brainstem and spinal cord[12]; (b) it is released from chicken retina in response to light stimulation[13]; (c) it is released from cortex slices upon electrical stimulation[2]. In spite of this evidence, biochemical studies on a neurotransmitter role of taurine have so far had conflicting results[2, 4, 5, 14]. Our analysis of the kinetics and subcellular distribution of taurine uptake speaks against a neurotransmitter role for this amino acid.

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The Mechanics of Breathing in Respiratory Acidosis

The effect of respiratory acidosis on the airway diameter during bronchial contraction has not yet been sufficiently clarified. For this reason investigations on the influence of CO_2 and H^+ion concentration in the blood on the mechanical properties of the respiratory system were undertaken. Since it cannot be assumed, a priori, that the action of these two substances on the lungs and bronchial tree is the same, the influence of CO_2 and H^+ions was tested separately.

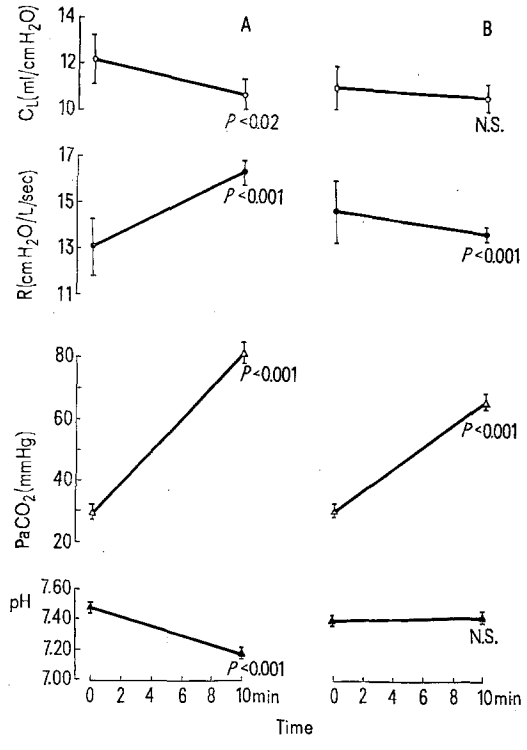
Material and methods. 22 rabbits weighing 2.60–3.25 kg were used. After immobilization, the animals were placed under light ether anesthesia and the trachea cut and connected to a Fleisch pneumotachometer. The jugular vein and carotid artery were cannulated with heparinized polyethylene catheters. A balloon was inserted into the oesophagus to record intraoesophageal pressure. 30 min after cessation of the anesthesia, the animal was placed in a body plethysmograph and gallamine triethiodide (Flaxedil) was injected into the jugular vein (4 mg/kg body wt.) to paralyze the respiratory muscles. As soon as respiratory movements ceased, controlled ventilation was started with a bellows connected to the plethysmograph. The velocity of respiratory air flow and changes of oesophageal pressure were measured for calculation of lung compliance (C_L) and total lung resistance (R). At the same time, a sample of arterial blood was taken for measurement of acid-base balance parameters. Then the animals were given an inspired gas mixture containing 10% CO_2 and 21% O_2, and after 10 min, the same measurements as those before inhalation were taken again. In 11

of the rabbits 0.6 *M* trihydroxymethylaminomethane (THAM) was injected during inhalation at a rate of 0.6 ml/kg/min^{-1} to maintain blood pH at the control level.

Results. The Figure shows that during 10 min of inhalation of a 10% CO_2 gas mixture not only $PaCO_2$ but also blood pH changed considerably. These changes were accompanied by an increase of total lung resistance and a decrease of lung compliance. All these changes were statistically significant (A). Infusion of THAM simultaneously with the administration of the CO_2 mixture prevented the drop of blood pH. In consequence, 'pure' hypercapnia developed, which was accompanied by a decrease of total lung resistance. At the same time lung compliance did not change (B). Thus, when hypercapnia was accompanied by lower blood pH, total lung resistance increased and lung compliance decreased. On the other hand, when the arterial blood pH was maintained at the control level during inhalation of the CO_2 mixture, total lung resistance decreased and lung compliance did not change.

Discussion. The mechanism of this phenomenon is probably complex. Data from literature indicate that, in vitro, both CO_2 and H^+ions increase the bronchial diameter[1–3]. Thus, it appears that both substances decrease bronchial muscle tonus if they act directly on the bronchi. In contrast to the in vitro results, in experiments in vivo bronchial contraction was usually observed when the vagus nerves were intact[4–9]. It appears that during hypercapnia in vivo vagus nerves are stimulated and the bronchial diameter decreases. This observation was supported by WIDDICOMBE[10], who found an increased impulses traffic in vagal efferent nerve fibres to the lungs and trachea during inhalation of a 5% CO_2 mixture in anesthetized cats. From the result of the present study, however, it seems more reasonable to conclude that CO_2 dilates the bronchi in vivo as well as in vitro. This conclusion is supported by the finding that total lung resistance decreases during CO_2 inhalation when blood pH remains at the control level. The observation from the present study that CO_2 is associated with a decrease in total lung resistance is supported by observations of NEWHOUSE et al.[11] and SCHONER et al.[12] that, during a drop of CO_2 partial pressure in the blood, there is a rise in flow resistance[11] and in slowly adapting pulmonary stretch receptor activity[12]. In addition, the results of the present study indicate that blood pH plays an important role in the control of bronchial diameter. A drop of blood pH in the presence of elevated CO_2 exerts an opposite effect on the bronchial diameter to elevated CO_2 alone. It seems that the final effect depends upon the relationship between CO_2 and H^+ion action on the bronchial muscle tonus. Since the influence of H^+ions is much stronger than that of CO_2, inhalation of the 10% CO_2 mixture causes bronchial construction, consequently total lung resistance increases. It is probable that the opposite effect exerted by H^+ions on the bronchial muscle tonus in vivo is due to the influence of these ions on the vagus nerve activity.

It appears that during impairment of the ventilatory function of the lungs, elevated CO_2 level suppresses bronchial contraction and improves pulmonary gas exchange by improving conductance and reducing the work required for maintaining gas exchange at a desirable level.



The relationship between mechanical properties of the lung and arterial blood pH in respiratory acidosis. On the left side of the Figure (A) are data obtained during inhalation of a 10% CO_2 mixture alone. On the right side of the Figure (B) are changes which appear after THAM injection during inhalation of CO_2. Vertical bars represent the standard error of the mean /n = 11/. N.S. means not significant at $p < 0.05$.

Zusammenfassung. Nachweis, dass Inhalation von Luftgemisch mit 10% CO_2 bei wachen Kaninchen eine bronchiale Konstriktion verursacht, wenn die Lungendehnung selbst von niedrigem Blut pH begleitet ist. Erhöhung von CO_2 allein erschlafft die Bronchien und unterdrückt teilweise die Bronchienkontraktion, was mit dem niedrigen Blut pH zusammenhängt.

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