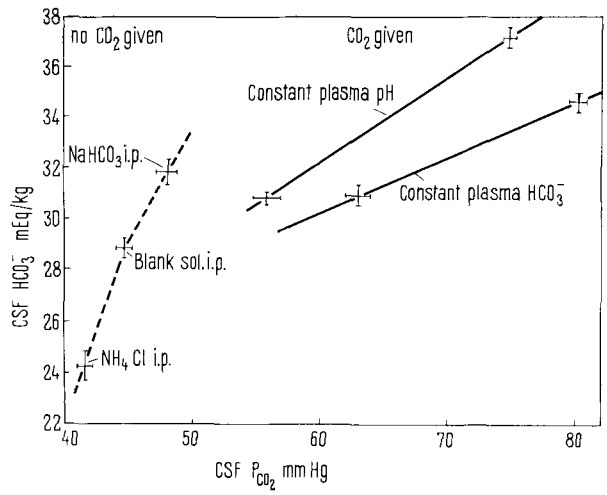
Factors Affecting the Cerebrospinal Fluid (CSF) Bicarbonate Concentration

The cerebrospinal fluid (CSF) pH remains essentially constant even in chronic non-respiratory acid-base disturbances (for ref., see [1]). The mechanisms behind this pH regulation are unknown but probably include passive as well as active factors. Thus, there may be passive exchanges of H^+ and HCO_3^- ions between CSF and plasma due to chemical or electrical diffusion gradients, but actual differences in the electrochemical potentials between the two compartments also suggest the presence of an ionic pump[2,3]. In the present paper the effect of varying the chemical and the electrical diffusion gradients were studied. This was accomplished by combining varying degrees of hypercapnia with i.p. injections of $NaHCO_3$ or NH_4Cl solutions so that either the plasma pH or the plasma bicarbonate was held constant.

Methods. The experiments were performed on rats weighing 250–400 g. The rats were exposed to the acid-base shifts while unanaesthetized. 4–10% CO_2 was administered for 6 h and during this period 3 injections were given of an isotonic NH_4Cl or $NaHCO_3$ solution. After the set equilibration period the animals were anaesthetized with phenobarbital and a tracheal cannula was inserted to allow continuous exposure to the gas mixture. Arterial blood samples were drawn from an indwelling catheter in the femoral artery. CSF samples were drawn from the suboccipital cistern. In blood, pH and P_{CO_2} were measured with microelectrodes. In the CSF the total CO_2 content was measured with a microdiffusion method. The plasma bicarbonate concentrations were calculated from standard nomograms. The CSF bicarbonate concentrations were calculated from the T_{CO_2} values, using the appropriate solubility factor and the CSF CO_2 tension, as derived from the arterial P_{CO_2}. For details of techniques and calculations the reader is referred to previous papers[4–6].

Results. The Table gives the measured and the directly derived acid-base parameters in arterial plasma and CSF. The values were compared with those of a group of rats injected with a simulated extracellular fluid ('blank')[6]. In the groups given the NH_4Cl solution the dose injected and the CO_2 concentration administered were matched so as to give a constant plasma bicarbonate concentration. In these groups the CSF bicarbonate concentration varied inversely with arterial pH, but thus also directly with the CO_2 tension. In the corresponding experiments in which $NaHCO_3$ was administered, the plasma pH was kept constant. In these groups the CSF bicarbonate concentration varied directly with the plasma bicarbonate, but also with the CO_2 tension.

In order to compare the effects of plasma pH and plasma bicarbonate the values must be compared at the same CO_2 tensions. The Figure clearly shows that at identical CO_2 tensions there is a higher CSF bicarbonate when the plasma pH is kept constant than when the plasma bicarbonate is fixed. Moreover, the change in HCO_3^- per unit change in CO_2 tension is less at constant plasma bicarbonate than at constant plasma pH. It can also be seen that the CSF HCO_3^- changes per unit change in P_{CO_2} in the combined respiratory and non-respiratory acid-base shifts (unbroken lines) were much smaller than the corresponding CSF HCO_3^- changes in pure non-respiratory acid-base shifts (broken line). The baseotic and the



Relation between the CO_2 tension and the bicarbonate concentration in CSF in non-respiratory (data from [6], broken line) and combined respiratory and non-respiratory acid-base shifts (unbroken lines). In these latter experiments either the plasma pH or the plasma bicarbonate concentration was kept constant.

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Relation between the plasma and the CSF acid-base parameters in combined non-respiratory and respiratory acid-base changes. The values were compared with the blank group taken from a previous paper[6]. In the groups given NH_4Cl the dose injected and the CO_2 concentration were matched so as to give a constant plasma bicarbonate concentration, while in the groups given $NaHCO_3$ the plasma pH was kept constant. Number of experiments within paranthesis.

Type of experiment	Arterial plasma pH	Arterial plasma P_{CO_2} mm Hg	Arterial plasma HCO_3 mEq/l	CSF P_{CO_2} mm Hg	CSF HCO_3 mEq/l	CSF pH
Blank (12)	7.43 ± 0.01	39.9 ± 0.6	25.8 ± 0.5	44.6 ± 0.2	28.9 ± 0.3	7.44 ± 0.01
$NH_4Cl + CO_2$ (6)	7.29 ± 0.01	57.8 ± 0.9	27.0 ± 0.9	63.0 ± 0.9	31.0 ± 0.4	7.32 ± 0.01
$NH_4Cl + CO_2$ (5)	7.16 ± 0.02	76.3 ± 0.5	26.4 ± 1.4	80.2 ± 0.5	34.7 ± 0.5	7.27 ± 0.01
$NaHCO_3 + CO_2$ (7)	7.43 ± 0.01	50.2 ± 0.9	32.8 ± 0.6	55.8 ± 0.9	30.9 ± 0.2	7.37 ± 0.01
$NaHCO_3 + CO_2$ (6)	7.41 ± 0.01	70.6 ± 1.1	43.5 ± 1.0	74.8 ± 0.4	37.2 ± 0.4	7.33 ± 0.02

acidotic groups of the latter study[6] had plasma HCO_3^- values of 35 and 17 mEq/l and plasma CO_2 tension of 43 and 36 mm Hg, respectively.

Discussion. Although there are good indications that the CSF possesses effective homeostatic mechanisms for keeping the pH constant, the present experiments have shown that factors such as the plasma pH and the plasma bicarbonate influence the resulting acid-base changes in the CSF. Apparently, the regulation of CSF pH towards normal values in hypercapnia will be less effective in the absence of a chemical diffusion gradient for bicarbonate.

There is a clear difference in the effectiveness of the CSF pH regulation in respiratory and non-respiratory acid-base shifts. In non-respiratory acid-base shifts this regulation appears almost perfect (maximal CSF pH change 0.05 pH units, see [6]). Since this difference was observed in the same species exposed to the acid-base shifts for an identical period it would appear that the mechanisms behind the acid-base changes in the CSF were different in respiratory and in non-respiratory conditions[7].

Zusammenfassung. Es wurde nachgewiesen, dass die Zunahme des HCO_3^--Gehaltes in der Cerebrospinalflüssigkeit bei konstantem Plasma-pH unter Hyperkapnie grösser als bei konstantem Plasmabikarbonatgehalt und wesentlich anders als bei der nicht respiratorisch bedingten Säurebaseänderung ist.

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Gustatory Responses to Anomeric Sugars

Differences in taste between D- and L-enantiomorphs of amino acids[1] and between α- and β-configurations of carbohydrates have interested investigators from many disciplines. CAMERON[2] was among the first to report that a freshly prepared solution of 10% α-D-glucose was noticeably sweeter than a solution at equilibrium. This was later confirmed by others[3,4]. TSUZUKI and YAMAZAKI[5] observed that the linear relationship of the sweetness of fructose with temperature corresponded to the linear variation of its specific rotation with temperature. The sweetness intensity of α-fructose was estimated to be one-third of that of β-fructose. With L-rhamnose, the sweetness of the α-form was less than $^2/_5$ that of the β-form[6]. As early as 1939, BLAKESLEE[7] collected 25 different combinations of taste responses to mannose tablets from 3121 untrained volunteers. More recently, D-mannose was again referred to as an ambiguous taste stimulator[8,9] as the α-anomer is sweet and the β-anomer is bitter. BOYD and MATSUBARA[10] prepared the 'unnatural' L-forms of glucose and mannose; the former was slightly salty and the latter gave inconclusive results due to lack of agreement among the subjects.

Attempts have been made to correlate the taste of anomers with their chemical configuration, but few reliable generalizations have evolved. TSUZUKI[11] stated that sweeter sugar anomers had *cis*-hydroxyl groups on the carbonyl and adjacent carbon atom, while in the less sweet isomer the hydroxyls on the two carbon atoms were in the *trans* position. This relationship was confirmed for fructose[5] and rhamnose[6], but not for lactose, as the β-form is sweeter[4], yet has the *trans* configuration[12]. Measuring hydrogen-bonding, molecular models, and tasting of crystals of 7 sugars, SHALLENBERGER[13] concluded that sweetness varied with hydrogen bonding of hydroxyl groups. It is difficult to assume that a single hydroxy group – as in ordinary alcohol – can 'cause' sweetness. As pointed out by NICOL[14], the gustatory function of a single group can no more be solely responsible for evoking sweetness, than can hydrogen ion content be the sole cause of sourness. Relative to sugar alcohols, CARR et al.[15] found no relation between the number of carbon atoms, hydroxyl groups, molecular arrangement or spatial configuration and sweetness.

We noted that most investigators tasted the sugars in the crystalline form. STEINHARDT et al.[9] administered samples in the solid state due to the mechanical difficulties of comparing equilibrated solutions with freshly-prepared samples which are rapidly undergoing mutarotation. Their preliminary experiments with mannose had indicated little effect of concentration. Since our previous work had shown marked influence of concentration[4,16], we undertook the present study to determine the effect of concentration on both taste quality and intensity of the α- and β-configurations of fructose, mannose,

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