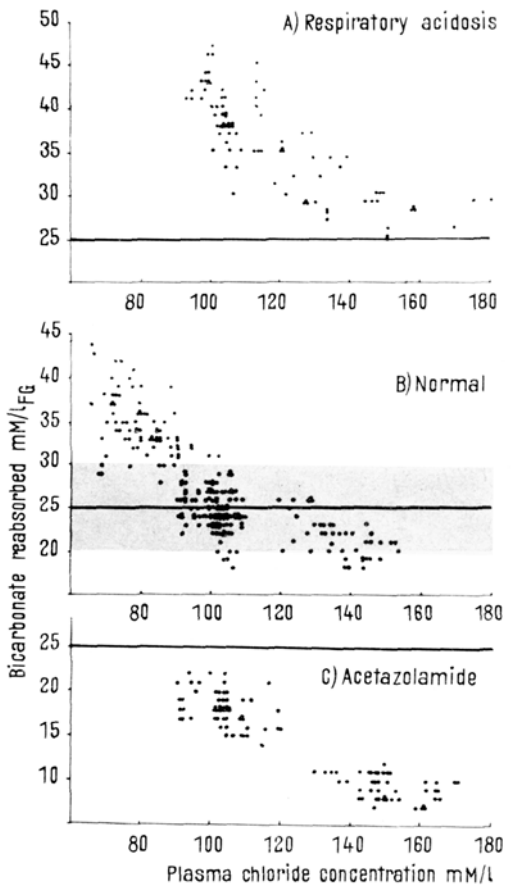
Experimental procedures. 1. *Normal dogs.* Bicarbonate reabsorption rate ($BHCO_3R$) was measured a) at normal P_{Cl} values (29 experiments on 17 dogs, 134 clearance periods), b) at high P_{Cl} values (8 experiments on 7 dogs, 43 clearance periods) and c) at low P_{Cl} values (13 experiments on 10 dogs, 84 clearance periods).

2. *Respiratory acidotic dogs.* While blood pCO_2 values were maintained between 132 and 164 mm Hg by the inhalation of CO_2 20% in O_2, $BHCO_3R$ was measured a) at normal P_{Cl} values (11 experiments on 9 dogs, 43 clearance periods) and b) at high P_{Cl} values (10 experiments on 9 dogs, 45 clearance periods).

3. *Acetazolamide-treated dogs:* During continuous infusion of acetazolamide (30–55 mg/kg/h, preceded by a priming dose of 10 mg/kg), $BHCO_3R$ was measured a) at normal P_{Cl} values (8 experiments on 7 dogs, 65 clearance periods) and b) at high P_{Cl} values (5 experiments on 5 dogs, 46 clearance periods).

Results. 1. *Normal dogs* (Fig. B). The respective values of the slope of the regression lines calculated for the relation between $BHCO_3R$ and P_{Cl} in the 3 groups of normal animals are: 0.295 in hypochloremia, 0.167 in normochloremia and 0.130 in hyperchloremia. Thus, the effect of Cl on $BHCO_3R$ is progressively diminishing as P_{Cl} values are increasing so that the relation between $BHCO_3R$ and P_{Cl} is truly a curvilinear one.



Bicarbonate reabsorption rate values plotted with plasma chloride concentration values in respiratory acidosis A, in normal dogs B, and during acetazolamide treatment C.
The horizontal lines drawn at $BHCO_3R$ values of 25 mM/L_{GF} represent the mean value of $BHCO_3R$ during $NaHCO_3$ infusion in normal dogs. The hatched zone in B represents the 4 σ range of the mean value of $BHCO_3R$.

2. *Respiratory acidotic dogs* (Fig. A). As for the normal animals, the depression induced by Cl on $BHCO_3R$ is of greater magnitude at normal than at high P_{Cl} levels: the values of the slope of the regression lines calculated for the relation between $BHCO_3R$ and P_{Cl} are 0.276 for the normochloremic, and 0.169 for the hyperchloremic respiratory acidotic animals.

3. *Acetazolamide-treated dogs* (Fig. C). Despite the profound inhibition of $BHCO_3R$ produced by acetazolamide, this tubular transport is further depressed (to the extremely low level of 7.0 mM/L_{GF}) by NaCl administration. As was noted for normal and for respiratory acidotic animals, the influence of Cl on $BHCO_3R$ is diminishing as P_{Cl} is progressively rising: the regression line has a slope of 0.114 at normal, instead of 0.055 at high P_{Cl} levels. Both values differ significantly from zero ($P < 0.001$).

Comment. Although the depression of $BHCO_3R$ produced by Cl was previously noted in normal[6] and in respiratory acidotic[7] dogs, our data further show that the magnitude of the influence of hyperchloremia is primarily affected by the initial level of $BHCO_3R$ itself. This phenomenon is demonstrated by the fact that, for any given value of P_{Cl} increment, the intensity of Cl influence on $BHCO_3R$ is diminishing in the following order: respiratory acidotic, normal and acetazolamide-treated animals. The values of the slope of the regression lines calculated for the relation between $BHCO_3R$ and P_{Cl} in the three conditions investigated, differ significantly in the sole case of respiratory acidotic versus acetazolamide-treated animals ($0.02 < P < 0.05$ in normochloremia and $0.001 < P < 0.01$ in hyperchloremia).

Finally, our data on respiratory acidotic dogs loaded with $NaHCO_3$ alone demonstrate that, contrarily to a recently held view[8], the increase in $BHCO_3R$ observed at high plasma bicarbonate concentration values is readily explained by the spontaneous reduction in P_{Cl} which follows acute $NaHCO_3$ loading.

Résumé. L'intensité de la dépression qu'entraîne l'hyperchlorémie sur la réabsorption tubulaire du bicarbonate chez le chien paraît être essentiellement déterminée par le niveau initial de la réabsorption du bicarbonate.

CH. TOUSSAINT and P. VEREERSTRAETEN

Laboratoire de Médecine expérimentale, Université libre de Bruxelles et Fondation médicale Reine Elisabeth, Bruxelles (Belgium), October 14, 1960.

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Effects of Stimulation and Inhibition of Bicarbonate Reabsorption on the Renal Tubular Transport of Sodium and Chloride in the Dog

The numerous observations[1-3] demonstrating the influence of changes in plasma chloride concentration (P_{Cl}) on tubular bicarbonate reabsorption rate ($BHCO_3R$) have led us to investigate the tubular transport of Na and Cl in

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dogs submitted to two experimental procedures affecting primarily $BHCO_3R$: acute respiratory acidosis and acetazolamide treatment.

Experimental procedures. In each experiment, hypertonic NaCl was infused to raise P_{Cl} and P_{Na} to 170 and 210 mM/l, respectively.

1. *Respiratory acidosis* (17 experiments performed on 16 dogs, 94 clearance periods): respiratory acidosis (blood pCO2 134–174 mm Hg) was maintained throughout each experiment by the inhalation of CO_2 20% in O_2. In 7 experiments, P_{BHCO_3} ranged from 19.5 to 24.7 mM/l so that $BHCO_3$ excretion rate was negligible. In 10 experiments, P_{BHCO_3} was maintained between 27.5 and 45.0 mM/l by adding $NaHCO_3$ to the saline infusion, so that $BHCO_3$ excretion rate exceeded 5.0 mM/l glomerular filtrate in 26 clearance periods.

2. *Acetazolamide treatment* (6 experiments performed on 6 dogs, 49 clearance periods): acetazolamide[4] was infused throughout each experiment at a rate of 30–45 mg/kg/h, after a priming dose of 10 mg/kg. P_{BHCO_3} ranged from 10.6 to 22.3 mM/l and $BHCO_3$ excretion rate exceeded 5.0 mM/l glomerular filtrate in 38 clearance periods.

be noted that, in the dog[7] as well as in the rat[8,9] submitted to prolonged CO_2 exposure, without NaCl loading, Cl excretion rate has been regularly found to be increased during the first two days of CO_2 exposure. Our negative findings in acute respiratory NaCl-loaded dogs would suppress one of the objections raised against PITTS's theory[10] which assumes a primary role to active Na transport in the genesis of an electrochemical potential responsible for the passive reabsorption of $BHCO_3$ and Cl.

Acetazolamide treatment markedly reduces NaR and ClR. Similar results were obtained by SCHWARTZ and RELMAN[11] and by WESSON[12], although smaller doses of acetazolamide are devoided of any significant effect[12]. This lack of action of small doses on ClR, despite their effect on $BHCO_3R$, affords evidence, but no proof, that the chloruretic effect of large doses is independent of the action of the drug on hydrogen secretion. Such an interpretation would stand against the second objection opposed to PITTS's theory[10], for, according to this conception, if the action of acetazolamide on ClR was dependent on $BHCO_3R$ inhibition, ClR would be increased rather than decreased by the drug.

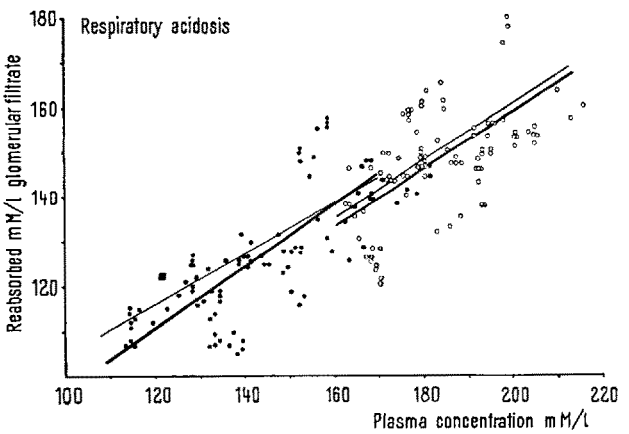

Fig. 1. Relation between Cl (black circles) and Na (open circles) reabsorption rate and plasma concentration values during respiratory acidosis. The thick line represents regression during acidosis and the thin line regression previously calculated for normal dogs.

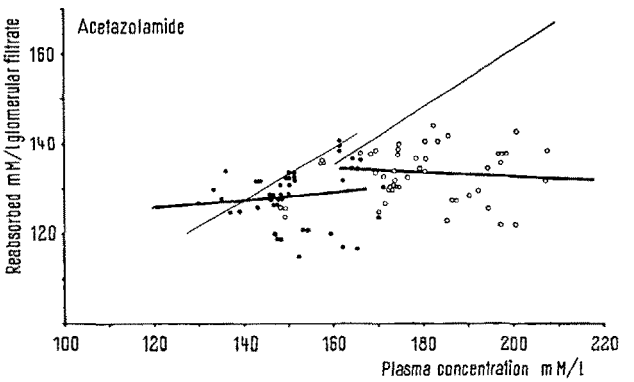

Fig. 2. Relation between Cl (black circles) and Na (open circles) reabsorption rate and plasma concentration values during acetazolamide infusion. The thick line represents regression during acetazolamide treatment, and the thin line regression previously calculated for normal dogs.

Results. 1. *Respiratory acidosis.* In Figure 1, the values of Na and Cl reabsorption rate have been plotted with the corresponding values of P_{Na} and P_{Cl}. It is obvious that NaR and ClR rise linearly with P_{Na} and P_{Cl}. The slopes of the regression lines calculated for the relation between reabsorption rate and plasma concentration values are 0.655 for Na and 0.674 for Cl. Both values are significantly different from zero, but they do not differ from the slopes calculated in normal dogs[5]. Increase in P_{BHCO_3} during respiratory acidosis did not affect the relation between NaR and P_{Na} or between ClR and P_{Cl}.

2. *Acetazolamide treatment.* Figure 2 presents in a similar manner the data obtained in acetazolamide-treated dogs. The values of the slope of the regression lines calculated for the relation between reabsorption rate and plasma concentration values are -0.030 for Na and 0.089 for Cl. These values are not significantly different from zero, but they differ from the slopes obtained in normal dogs[5].

Comment. The lack of stimulation of respiratory acidosis on ClR in our experiments is in marked opposition with the findings of WESSON[6] in similar experiments. It should

Résumé. L'acidose respiratoire aiguë n'affecte pas significativement la réabsorption tubulaire du Na et du Cl, alors que celle-ci est déprimée par l'administration d'acétazolamide.

CH. TOUSSAINT and P. VEREERSTRAETEN

Laboratoire de Médecine expérimentale, Université libre de Bruxelles et Fondation médicale Reine Elisabeth, Bruxelles (Belgium), November 3, 1960.

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