

Quantitative Acid-Base Dynamics in Chronic Pulmonary Disease

Defense of pH During Acute Respiratory Acidosis Superimposed upon Chronic Hypercapnia

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SUMMARY The defense of the extracellular pH was evaluated in 17 patients with chronic obstructive lung disease and chronic hypercapnia during superimposed acute respiratory acidosis. In group I the chronic stable state P_{aCO_2} -pH-HCO₃⁻ was not defined; in groups IA and II the stable state was defined. Duration of acute acidosis in groups I and IA was 16 and 23½ hr, respectively; in group II, 30 min.

The defense of pH in groups I and IA was greater than acute hypercapnia in normal man but less than chronic stable hypercapnia ($P < 0.05$). The pH in group II approached that of normal man during acute respiratory acidosis. Plasma bicarbonate concentrations paralleled the (H⁺) responses. A wide confidence band based on these observations overlapped the previously established bands for acute and chronic hypercapnia.

In the clinical situation, variable P_{aCO_2} exposures create variable in vivo carbon dioxide titration curves. Thus, the defense of the extracellular pH during acute respiratory acidosis superimposed upon chronic hypercapnia is related temporally to renal buffering mechanisms. Under these circumstances, prediction bands for steady state acute or stable chronic hypercapnia are not valid for the interpretation of coexisting metabolic disorders.

RECENTLY THE QUANTITATIVE relationships of the defense of extracellular pH during acute hypercapnia in normal man and dogs have been defined (1, 2). Similar responses during steady-state chronic hypercapnia have been established for the dog (3). However, experimental studies of chronic hypercapnia in man have been difficult to perform because of the limited tolerance of normal man to such chronic exposures. Thus, the carbon dioxide titration curves of patients with chronic pulmonary disease have been compiled statistically,

based upon numerous in vivo observations (4, 5). Such observations have been made under chronic steady-state conditions, thereby permitting near or maximal renal buffering responses. The quantitative acid-base dynamics during transient acute hypercapnia occurring in chronic lung disease patients have not been clearly delineated from the above cited steady-state studies. This paper reports the hydrogen ion activity and plasma bicarbonate responses to acute increments in carbon dioxide tension superimposed upon chronic hypercapnia in patients with chronic obstructive lung disease. These patients were in acute ventilatory failure, and steady-state conditions were not present.

METHODS

Serial arterial blood gas (PO_2 and P_{CO_2}) and pH studies were performed on 17 patients with established chronic obstructive lung disease

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TABLE 1. Patient Profile: Arterial Blood Data for Chronic

Patient* Group† (Mean Age, yr)	Number Patients (No. Samples)	Mean and Range Values	Chronic Stable State				
			Paco ₂	pH	(H ⁺)	HCO ₃ ⁻	Pao ₂
			mm Hg		nmoles/ liter	mEq/liter	mm Hg
I (58)	7 (59)	Mean Low High			Not defined		
IA (67)	4 (35)	Mean Low High	56.3 49.2 61.0	7.37 7.39 7.35	42.9 40.7 44.7	31.7 29.2 35.1	54.5 32.0 79.0
II (61)	9 (18)	Mean Low High	53.9 47.0 65.0	7.35 7.29 7.40	44.7 40.0 52.0	29.9 26.5 35.5	62.5 46.0 90.2

* Average for each group and range values.

† I: acute ventilatory failure: previous chronic stable data not defined. IA: acute ventilatory failure: previous chronic stable data defined. II: chronic stable state with oxygen-induced hypercapnia.

under two circumstances: group (I) (IA) during a clinical period of acute respiratory failure, group (II) during controlled administration of oxygen (Table 1). The major pulmonary diagnoses were chronic pulmonary emphysema, chronic bronchitis, bronchiectasis, chronic asthmatic bronchitis, and pulmonary tuberculosis. All patients were carefully selected as having "pure" respiratory acidosis with no complicating metabolic disorders. This selection was based upon clinical information, electrolyte status, hepatic and renal status, and use of therapeutic agents (diuretics, sodium bicarbonate therapy, nasogastric suction, etc.). Patients of group I were those with chronic obstructive lung disease in acute ventilatory failure in whom defined prior stable Paco₂ and pH data were not available. Group IA includes four patients with *known* preexisting stable chronic hypercapnia who were in acute ventilatory failure. For groups I and IA changes in Paco₂, Pao₂, pH, and HCO₃⁻ were followed during progressive stages of respiratory acidosis (decompensation) and during assisted or controlled ventilation (recompensation) (6) to clinical and blood gas stability. In groups I and IA the causes for superimposed acute ventilatory failure were exacerbation of primary disease, pneumonia, depressant drugs, bronchospasm, secretions, inadvertent oxygen depression of ventilation, and cardiac failure. In group I acute respiratory failure was judged clinically and confirmed by arterial blood Pco₂ and pH and in group IA as any acute change from the chronic stable state. The patients of group II

were clinically stable and had chronic stable hypercapnia for at least several weeks. These patients were given 100% oxygen for 30 min under controlled conditions with confirmation of hypoventilation over their chronic base-line levels by changes in Paco₂ and alveolar ventilation.

Arterial blood was obtained anaerobically and immediately analyzed in the Instrument Laboratories blood gas analyzer (model 102) for Po₂, Pco₂, and pH at 37 C. Blood exposed to known gas concentrations (analyzed in a Scholander apparatus) was tonometered in a water bath at 37 C and used for calibration of the Po₂. Dry gas was used for the Pco₂ calibration slope. All duplicate samples were required to check within 5 mm for Po₂ (within the 50- to 100-mm ranges), 2 mm for Pco₂, and 0.005 units for pH. The remainder of the sample was analyzed for plasma sodium, potassium, chloride, blood urea nitrogen, and total protein. Oxygen saturation was calculated from the Po₂ and pH measurements, using the standard dissociation curve for oxyhemoglobin at 37 C and 7.40 pH. Plasma bicarbonate was calculated from the independently measured Pco₂ and pH by means of the Henderson-Hasselbalch equation using a pK of 6.10 and a solubility coefficient of 0.0301.

RESULTS

DECOMPENSATION AND RECOMPENSATION PACO₂-(H⁺) RELATIONSHIPS

Regression analysis for Paco₂-(H⁺) during the decompensation and recompensa-

Stable State, Peak Ventilatory Failure, and Recovery State*

Peak Decompensation					Recovery State				
Paco ₂	pH	(H ⁺)	HCO ₃ ⁻	PaO ₂	Paco ₂	pH	(H ⁺)	HCO ₃ ⁻	PaO ₂
mm Hg		nmoles/ liter	mEq/ liter		mm Hg		nmoles/ liter	mEq/ liter	mm Hg
102.4	7.17	58.6	37.2	137.7	44.0	7.41	41.1	26.6	95.7
60.0	7.05	50.1	29.0	34.0	31.0	7.28	25.7	19.5	31.0
140.0	7.26	89.1	43.0	283.0	57.0	7.59	52.5	32.4	300.0
108.8	7.15	71.7	37.9	106.0	47.0	7.36	46.5	25.1	166.5
67.0	7.05	52.5	31.0	34.0	31.0	7.28	40.7	19.5	33.0
140.0	7.28	89.1	43.0	178.0	57.0	7.42	52.5	29.2	300.0
62.1	7.30	50.1	29.6	330.0	Not available				
54.0	7.22	42.0	27.5	58.0					
74.0	7.38	60.0	33.0	574.0					

tion phases of acute respiratory acidosis were analyzed separately and found not to be significantly different at the $P = 0.05$ level; namely for group I decompensation $(H^+) = 0.48 \text{ Pco}_2 + 15.4$, recompensation $(H^+) = 0.47 \text{ Pco}_2 + 17.9$. Based upon this observation all of the individual data were pooled for the statistical analysis of regression equations for each of the individual subgroups presented below.

RELATIONSHIPS BETWEEN PACO₂ AND (H⁺) IN PATIENT GROUP I WITH CHRONIC STABLE STATE DATA NOT DEFINED *

In this patient group with acute uncomplicated respiratory acidosis a linear relationship was observed between Paco₂ and (H⁺) over the ranges Paco₂ 31 to 140 mm Hg with a regression expression of $(H^+) = 0.48 \text{ Pco}_2 + 17.3$. Values of Paco₂ less than

* See Table 2.

TABLE 2. Acute and Chronic Hypercapnia. Comparison of Regression Equations Pco₂-(H⁺): This Study Versus Literature Observations

Type of Hypercapnia (Induced By)	Group	Prior Chronic Hypercapnia	Species	First Author	Regression Equation
Acute (chamber)		No	Normal man	Schwartz	$H^+ = 0.77 \text{ Pco}_2 + 8.0$
Acute (chamber)		No	Normal dog	Schwartz	$H^+ = 0.77 \text{ Pco}_2 + 14.0$
Chronic (intrinsic chronic disease)		Stable state only	Chronic obstructive lung disease man	van Ypersele de Strihou	$H^+ = 0.30 \text{ Pco}_2 + 26.8$
Chronic (chamber)		Stable	Dog	Schwartz	$H^+ = 0.32 \text{ Pco}_2 + 26.9$
Acute (acute ventilatory failure)	I	Not defined	Chronic obstructive lung disease man	This study	$H^+ = 0.48 \text{ Pco}_2 + 17.3$
Acute (acute ventilatory failure)	IA	Yes	Chronic obstructive lung disease man	This study	$H^+ = 0.49 \text{ Pco}_2 + 16.6$
Acute (100% oxygen depression of ventilation)	II	Yes	Chronic obstructive lung disease man	This study	$H^+ = 0.62 \text{ Pco}_2 + 11.3$

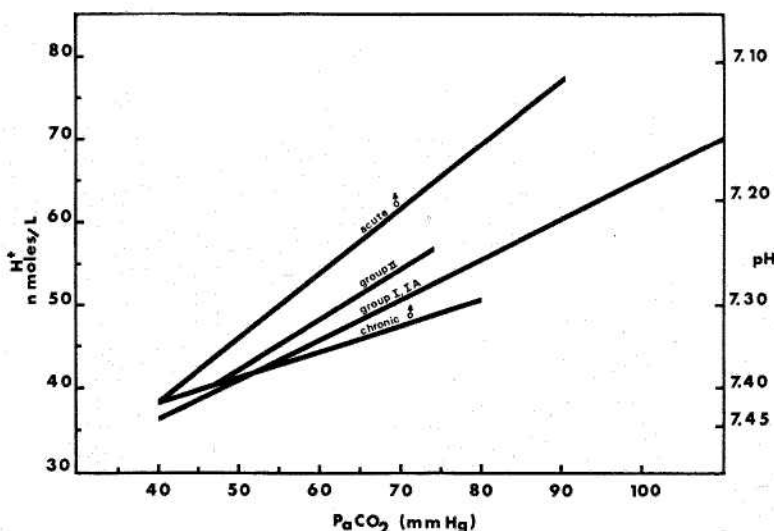


FIGURE 1. Relationship between hydrogen ion concentration and P_{aCO_2} during acute hypercapnia in patients with chronic obstructive lung disease. The acute carbon dioxide titration curve in man is based on the data of Brackett, Cohen, and Schwartz (1); the chronic curve is that reported by van Ypersele de Strihour, Brasseur, and De Coninck (4); groups I and IA (present study) represent the response to acute hypercapnia occurring in chronic obstructive lung disease patients in whom the chronic stable P_{aCO_2} -pH relationships are not defined (group I) and those in whom the chronic stable P_{aCO_2} -pH were known (IA). The changes in pH to acute alveolar hypoventilation induced by 100% oxygen for 30 min in patients with chronic hypercapnia are shown by group II. The limits of reported observations are indicated by the lengths of the regression lines. See text for details.

40 mm Hg are the result of data observed during the recompensation phase that were included for statistical analysis of the regression equation.

RELATIONSHIPS BETWEEN P_{aCO_2} AND (H^+) IN WHICH CHRONIC STABLE STATE DATA WERE DEFINED (GROUP IA)

This subgroup developed acute respiratory acidosis upon a known level of pre-existing chronic stable hypercapnia. All had P_{aCO_2} -pH data that fit the chronic confidence band (4), thereby confirming uncomplicated chronic stable hypercapnia. In these patients superimposed acute hypercapnia yielded a linear regression equation of $(H^+) = 0.49 P_{aCO_2} + 16.6$, similar to that observed in group I.

The present data were compared with the previously established regression equations for acute hypercapnia in normal man (1) and chronic hypercapnia in man (4) and

dogs (3) and found to be significantly different from all three at the $P < 0.05$ level (Table 2). Furthermore, the responses to acute hypercapnia in our patients in groups I and IA were between the pure acute and chronic state P_{aCO_2} - (H^+) relationships as previously defined (Figure 1).

The average time elapsing between the clinical presentation and recovery to arterial blood and clinical stability was 16 hr in group I and $23\frac{1}{2}$ hr in group IA with a range of 30 min to 96 hr.

PLASMA BICARBONATE RESPONSE *

The plasma bicarbonate relationships to increasing hypercapnia in patient groups I and IA were curvilinear, as reported with previous data for man and dogs. Similarly, those HCO_3^- - P_{aCO_2} responses fell between those established for pure acute and

* See Figure 2.

chronic hypercapnia in man and dogs under steady-state conditions.

"CONFIDENCE" BAND FOR PURE RESPIRATORY ACIDOSIS *

Within the established relationships for $(H^+)-P_{aCO_2}$ and $HCO_3^--P_{aCO_2}$, a significance band was constructed (1) from all the data of patient groups I and IA to test the hypothesis that a new (H^+) or HCO_3^- response was significantly different from the estimated mean response at the 0.05 level. This confidence band for $(H^+)-P_{aCO_2}$ in comparison with the bands previously established in normal man with acute hypercapnia (1) and for man with chronic hypercapnia (4) is very wide and overlaps the other bands in the ranges of clinically encountered hypercapnia (namely, P_{aCO_2} , 50 to 100 mm Hg).

* See Figure 3.

A confidence band for $HCO_3^--P_{aCO_2}$ (not shown) revealed a similar wide overlapping of the responses established for man and dogs with acute and chronic hypercapnia.

PATIENT GROUP II: (H^+) AND HCO_3^- RESPONSES DURING ACUTE ALVEOLAR HYPOVENTILATION INDUCED BY 100% OXYGEN

These patients had chronic stable hypercapnia with no complicating acidosis or alkalosis and demonstrated alveolar hypoventilation after 30 min of 100% nasal oxygen. A linear relationship of $(H^+) = 0.62 P_{CO_2} + 11.3$ was observed. The plasma bicarbonate responses were curvilinear and intermediate to the acute and chronic hypercapnia responses in dogs and man (Figures 1, 2). Moreover, the hypercapnia in this group II was more acute than that of groups I and IA, providing insight into the temporal relationships of hypercapnia to

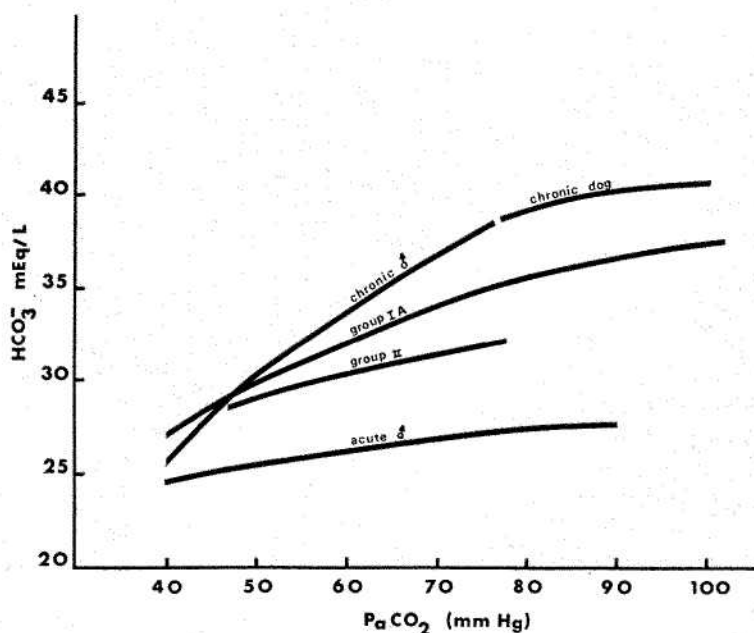


FIGURE 2. Relationship between plasma bicarbonate concentration and P_{aCO_2} during acute hypercapnia in patients with chronic obstructive lung disease. See Figure 1 for definition of terms. The extension of the chronic HCO_3^- response curve is based upon data in the dog reported by Schwartz, Brackett, and Cohen (3). The intermediate vectors in chronic obstructive lung disease groups I, IA, and II are to be contrasted with acute hypercapnia in man and chronic stable hypercapnia in chronic obstructive lung disease patients.

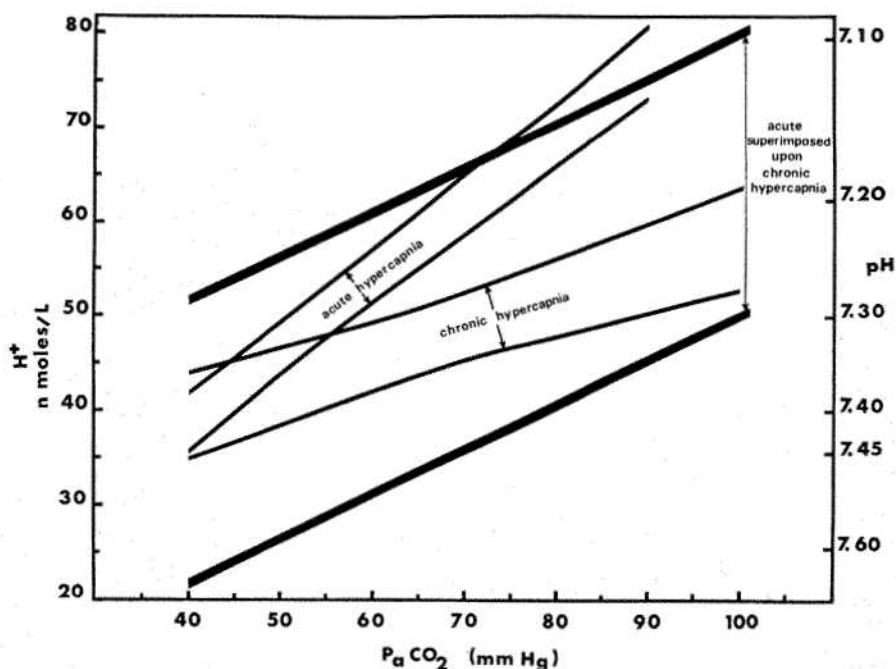


FIGURE 3. Significance band for plasma hydrogen in concentrations in acute hypercapnia occurring in patients with chronic obstructive lung disease. For the patients reported in this study, a 95% probability of falling within the respective zones of the wide significance band would overlap those bands established for acute hypercapnia in normal man and chronic stable hypercapnia in chronic lung disease. The band width suggests a family of P_{CO_2} -pH response relationships thereby limiting the interpretation of complicating metabolic acid-base disorders in the chronic obstructive lung disease patient with superimposed acute respiratory acidosis. The band was constructed by methods reported by Brackett and associates (1).

the hydrogen ion activity and bicarbonate responses.

EFFECT OF OXYGEN

The incorporation of variable P_{aO_2} tensions into the analysis presented here did not significantly alter the P_{aCO_2} -(H^+), P_{aCO_2} - HCO_3^- relationships observed.

DISCUSSION

The definition of predicted responses in (H^+) and HCO_3^- to increments in P_{aCO_2} by Brackett, Cohen, and Schwartz (1-3) has contributed significantly to present understanding of acid-base dynamics in man under steady-state conditions (1-3). However, the patient with chronic obstructive lung disease and superimposed acute res-

piratory failure is a particular problem since these responses may not reflect the steady state of normal man or dogs and are difficult to measure under controlled conditions. The clinical importance of predicted values is clear where pure respiratory acidosis must be distinguished from the multiple extrapulmonary metabolic disturbances that may influence the arterial pH (7, 8).

The final arterial pH in uncomplicated acute respiratory acidosis in nephrectomized dogs or in normal man under acute steady-state conditions is dependent upon bicarbonate generation by body buffers (1, 9). Such defense is entirely extrarenal and incomplete. During chronic steady-state hypercapnia additional defense of the extra-

cellular pH occurs by the renal mechanisms of increased acid excretion and reabsorption of bicarbonate (3, 4). The renal responses are more effective in buffering blood pH but are significantly slower. In man, the quantitative hydrogen ion activity changes to stepwise increments in $Paco_2$ during acute and chronic exposure to carbon dioxide (Figure 1) reveal two discrete linear (H^+) relationships during acute and chronic steady-state hypercapnia reflecting in the former the blood pH change without, and in the latter with, near or maximal renal compensation. The increase in plasma bicarbonate parallels these (H^+) changes but is curvilinear in nature (Figure 2).

The results of our data show a pH response between the pure acute and chronic hypercapnic states; namely, in the acute hypercapnia of normal man for each millimeter rise in a $Paco_2$ the hydrogen ion concentration rises 0.77 nmoles/liter; for chronic hypercapnia in man, 0.33 nmoles (H^+) per liter; and for acute respiratory acidosis superimposed upon established chronic obstructive lung disease (this study), 0.48 nmoles (H^+) per liter for prolonged exposures (groups I, IA) and 0.62 nmoles (H^+) per liter for exposures limited to 30 min (group II). In our patients, as with previously reported data, the (H^+) activity was related linearly to the $Paco_2$ increments. Concurrently, bicarbonate concentrations rose in a curvilinear fashion (up to observed $Paco_2$ levels of 75 and 129 mm Hg). However, the bicarbonate increments were greater than acute hypercapnia but less than chronic hypercapnia, indicating an intermediate response. Furthermore, the group I and IA patients had a greater defense of pH than those in group II. Is this bicarbonate rise solely accountable by tissue bicarbonate mechanisms, or are added renal factors present? Over the $Paco_2$ range of 40 to 53 mm Hg, a rise of 13 mm Hg $Paco_2$ produces the following increments in plasma HCO_3^- in man: 1.5 mEq/liter

for acute hypercapnia, 5.8 mEq/liter for chronic hypercapnia, 3.6 mEq/liter for groups I and IA, and 2.0 mEq/liter for group II (acute superimposed upon chronic hypercapnia). In group II the duration of superimposed acute hypercapnia was 30 min, thus no renal factors could influence the pH. This would indicate that the tissue defense during superimposed acute respiratory acidosis occurring from states of chronic hypercapnia is approximately similar to that seen during acute respiratory acidosis occurring from the normocapnic state. With the addition of variable degrees of renal buffering in groups I and IA, the pH is partially defended.

Any quantitative definition of expected compensatory mechanism during respiratory acidosis will depend on the existing clinical conditions, that is, a patient with normocapnia, stable chronic hypercapnia, or, as emphasized here, hypercapnia *superimposed* acutely upon the chronic hypercapnia of chronic obstructive lung disease. Here, the following variables may influence the final blood pH: [1] the level of chronic stable hypercapnia, [2] the level of $Paco_2$ in acute hypercapnia, [3] the degree of tissue buffering, and [4] the duration of exposure to carbon dioxide increase, which would influence the degree of renal compensation. This latter time factor is obviously difficult to define in the context of a dynamically changing $Paco_2$. With the pulmonary patient we have described, the level and *rate* of $Paco_2$ increase (decompensation) as the result of disease, or the decrease (recompensation) via assisted or controlled ventilation is variable and would complicate the stimulus to renal retention of bicarbonate. In dogs exposed to 10 to 13% inspired carbon dioxide, plasma HCO_3^- concentration rises abruptly during the first day accounting for about 50% of the total increase with little or no increase in renal acid excretion. Thus, the initial pH defenses result from tissue buffering mechanisms. Thereafter, gradual renal

adaptation occurs over a 5- to 6-day period with a final HCO_3^- concentration of 35 to 38 mEq/liter (10). Additionally, studies in dogs (2) reveal variation in slope and intercept of PCO_2 -(H^+) responses to acute hypercapnia that are attributed to differences in initial plasma HCO_3^- concentrations and quantity of HCO_3^- generated by each animal. Related to this is the observation of Dorman, Sullivan, and Pitts (11) that the tissue Paco_2 change is one of the effective stimuli for renal bicarbonate reabsorption.

The intermediate (H^+) and HCO_3^- responses observed in this study must be viewed as variable depending upon the intensity and duration of carbon dioxide exposure and concomitant renal compensation. Another group of patients with different temporal exposures may well produce different results. This is emphasized by the fact that our 95% confidence band is extremely wide. While this may reflect our small population sample, it may also suggest a family of titration curves between the state of acute respiratory acidosis and that of chronic stable hypercapnia. Support for this interpretation is obtained from our observation that the acute hypercapnia of patient group II with no possibility of renal compensation (duration of exposure, 30 min) had lower HCO_3^- levels than group I, IA (average duration of exposure 16 and 23 hr, but some cases up to 96 hr) where comparable degrees of acute hypercapnia resulted in greater plasma HCO_3^- concentrations. Similarly, Schwartz, Brackett, and Cohen (3) compared the maximum renal compensation to different steady-state levels of Paco_2 in dogs and found a curvilinear rise in plasma bicarbonate concentration with each increment of inspired carbon dioxide tension. In Figures 1 and 2, a summary of the sequence of responses as a function of duration of carbon dioxide exposure reveals a progressive defense of pH and rise in plasma HCO_3^- from acute hypercapnia in normal man and group II, to groups I and IA, and finally to chronic

stable-state hypercapnia. In fact, such intermediate responses have been alluded to in dogs (12). Thus, our extremely wide band indicates the variety of time-dependent Pco_2 -pH responses that occurred during acute respiratory acidosis superimposed upon chronic hypercapnia. It should be noted that the narrow significance band created for chronic hypercapnia in man (4) is based on the assumption that the confidence limits around the mean bicarbonate response curve were the same as dogs made chronically hypercapnic. While this might appear to be a reasonable approach, the data are lacking on the point.

Thus, under controlled steady-state conditions renal buffering responses are definable, and acute and chronic confidence bands developed for definition and prediction of complicating metabolic acid-base disorders are valid. However, during the clinical period of acute respiratory acidosis superimposed upon chronic obstructive lung disease patients with chronic hypercapnia, rapid progression of disease or therapeutic intervention will create non-steady-state conditions. Here, predicted responses will be difficult to define since dynamic Paco_2 changes will alter the time-dependent renal compensatory mechanisms. Under these circumstances, intermediate (H^+) and HCO_3^- concentrations may occur, and the decision regarding which band to have "confidence in" to define a coexisting metabolic disorder may become a problem. These metabolic acid-base complications occurring during pure acute respiratory acidosis superimposed upon the chronic hypercapnia of chronic obstructive lung disease will require a clinical approach based upon physiologic data for definition.

Statistical evaluation of the effect of variable oxygen tensions in the range of 31 to 575 mm Hg upon the Pco_2 -(H^+) and HCO_3^- responses in our patient population failed to reveal any significant effect, a point we reported previously and that has also recently been documented in dogs (13, 5).

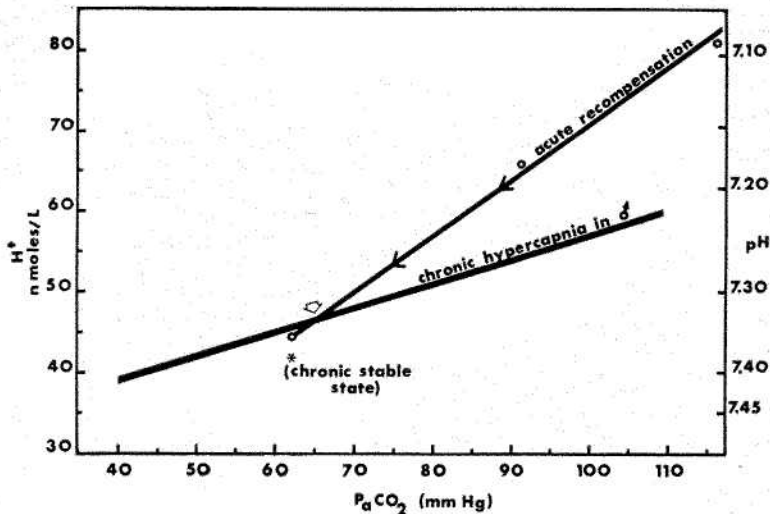


FIGURE 4. Graphic application of any acute decompensation, or recombination data, or both. This case demonstrates the potential application of the observation that acute Pco_2 - (H^+) decompensation and recombination slopes are similar, in establishing the chronic stable state Paco_2 -pH range from which acute respiratory acidosis starts. A 67-year-old negro man with chronic bronchitis and emphysema and chronic stable hypercapnia was given 100 mg meperidine (Demerol®) intramuscularly before bronchography. Alveolar hypoventilation occurred in several hours and was managed by intravenous nikethamide (Coramine®). Three Paco_2 - (H^+) points were available during this 12-hr period. Extrapolation of the line formed by these points intercepts the chronic hypercapnia line (4) at a theoretical Paco_2 of 64 mm Hg and pH of 7.34 (arrow). In fact, his previously known chronic stable Paco_2 was 62 mm Hg and pH, 7.38 (asterisk). See text.

In our patient population, Paco_2 values rose as high as 140 mm Hg with mean values at peak decompensation of 102.4 mm Hg in group I and 108.8 mm Hg in group IA. The relation of (H^+) and Paco_2 was linear by statistical analysis and suggests that during superimposed acute hypercapnia, Pco_2 s greater than 70 mm Hg are associated with equally effective buffering mechanisms that are not defined by this study (4, 14).

Finally, we should like to draw attention to the observation that the in vivo carbon titration curves were similar in the decompensation (progressive increase in Pco_2) and recombination (progressive decrease in Pco_2) period, namely, decompensation $(\text{H}^+) = 0.48 \text{ Pco}_2 + 15.4$, and recombination $(\text{H}^+) = 0.47 \text{ Pco}_2 + 17.9$. Individual cases demonstrating a recovery different from decompensation did occur with

our patients based upon variable temporal and therapeutic factors. These individual variations were minimized by the pooling of upgoing and downgoing data for purposes of statistical analyses. Nevertheless, it is suggested that changes in alveolar ventilation occurring too rapidly to significantly influence renal defenses will result in pH buffering at similar slopes during hypoventilation and hyperventilation from high Paco_2 levels. A practical application of this is demonstrated in Figure 4 when one is confronted with a chronic lung disease patient whose chronic hypercapnia levels are unknown but in whom an uncomplicated respiratory acidosis supervenes within a limited time period (namely, 12 to 24 hr) and in whom serial Pco_2 -pH observations are available. A plot of these points should establish a linear response. Extrapolation of this line to an intersection

established for chronic hypercapnia could indicate a region (based upon the chronic confidence band) representative of the chronic stable state P_{CO_2} -pH from which the acute alveolar hypoventilation began. This requires that several observations are made and that no metabolic complications occur during this period of acute respiratory acidosis.

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