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Research Article

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INTRODUCTION

The blood vessels supplying the villi of the small bowel form a hairpin curve, so that the arterial and venous vessels run in close proximity for a relatively long distance. This arrangement has stimulated the idea that substances with high permeabilities for the vessel wall diffuse between these vessels, resulting in countercurrent exchange (1–4).

An effect of such an exchange would be to slow the rate of delivery via the blood of highly diffusible materials to the villus tip, since these substances would diffuse between the arterial and venous limbs of the exchanger, short-circuiting the villus. A second effect would be to slow absorption of diffusible substances from the lumen, since these substances would diffuse from the veins draining the villus into the arterioles supplying the villus. The concentration of the material in the venous blood leaving the villus would therefore be reduced and their absorption rate would be diminished.

In the present study, we attempted to quantitate the importance of this exchange process in the small bowel of rabbits by comparing the absorption rate of carbon monoxide with that of four other gases: hydrogen, helium, methane, and ^{133}xenon. Since absorbed CO becomes tightly bound to hemoglobin, it should not dif-

fuse between the limbs of the exchanger. The other four gases, which are unbound and have appreciable solubility in both lipid and water (5), should exchange freely. Therefore, the degree to which the observed absorption of the unbound gases falls below that predicted by CO absorption should provide a quantitative estimate of countercurrent exchange. As will be demonstrated, no such discrepancy existed between the observed and predicted absorption rates, suggesting that countercurrent exchange does not influence absorption in the rabbit small intestine.

METHODS

The rates of absorption of the five gases (CO, CH_4, H_2, He, and ^{133}Xe) were measured from closed loops of rabbit jejunum. Adult New Zealand rabbits were fasted for 24 h and were anesthetized with intravenous Valium (diazepam, 10 mg, Roche Laboratories, Division of Hoffmann-La Roche Inc., Nutley, N. J.) and pentothal (15 mg/k). During each experiment, the rabbit's temperature was maintained at 37–39°C with an electric heating pad controlled by a thermostat connected to a rectal temperature probe. Through a midline abdominal incision, a 10-cm segment of midjejunum was delivered and tied off at both ends with umbilical tape. The blood supply to the segment was carefully preserved. Small-bore cannulas connected to three-way stopcocks were inserted into the lumen through a stab wound at both ends of the gut segment and secured with two layers of sutures to prevent leaks. The segment was carefully washed clean of all contents by perfusing it several times with warm saline and then was emptied by careful stripping. Initial studies showed that this procedure reduced production of H_2 and CH_4 in the gut segment to negligible levels ($< 1 \times 10^{-4}$ ml/20 min).

Absorption period and test gases. Studies to determine the relation between P_{CO} and CO absorption rate were carried out with two test gas mixtures which had an initial P_{CO} of 760 and 570 mm Hg. In studies comparing the absorption of CO with that of the unbound gases, a mixture was employed which contained 90% CO, with the remainder consisting of equal parts of H_2, He, CH_4, and tracer quantities of ^{133}Xe. Most studies were carried out for 20 min. A few studies were carried out for 40–60 min to verify the accuracy of the measured absorption rates for the more slowly absorbed gases during the shorter test period. The uptake rates for the longer periods were virtually identical with those obtained in the 20-min runs.

At the beginning of each timed absorption period, 5 ml of the mixture of test gases was instilled into the segment. This volume of gas filled but did not overly distend the segment. The stopcocks were closed, the gut segment was placed back into the peritoneal cavity, and the abdominal wound was closed with towel clips.

At the end of the absorption period, the loop was brought out through the abdominal incision, all gas remaining in the lumen was carefully stripped into a 10-ml syringe, and the volume of gas was measured to the nearest 0.1 ml. Studies indicated that 96±2.5% of the gas could be removed from a loop in this fashion. This gas was quantitatively transferred to a 100-ml syringe and, to insure complete washout of residual gas in the loop, about 95 ml of air was perfused through one cannula and then collected in the 100-ml syringe. Initial studies in which the loop was first washed in this manner and then washed out with another 100 ml of gas indicated that less than 1% of the test gases remained after the initial washout. Lastly, a sample of blood for hemoglobin determination was obtained by cardiac puncture.

The fractional absorption rate (percent per minute) for each gas was calculated from the volume of the gas absorbed, divided by the logarithmic mean volume of the gas present in the lumen and the time interval of the study. The gas volume of the loop was calculated as the logarithmic mean of the initial volume (assumed to equal the 5 ml instilled) and the final measured volume.

Determination of relative diffusion rates of the gases through tissues. The relative rates of diffusion of the unbound gases through small intestinal tissue of the rabbit were determined by a method previously described (5). An 8–10-cm segment of rabbit jejunum was washed out with saline and one end was then ligated. A polyethylene tube was inserted into the lumen through the opposite end and secured in place with suture. The segment was rapidly dissected from the rabbit, 5 ml of a test gas mixture was instilled into the segment, and the polyethylene tube was sealed. The gut was placed in a sealed 250-ml flask containing 100 ml of Krebs-Ringer bicarbonate previously gassed with 95% O_2-5% CO_2. The flask was maintained at 37°C and the fluid in the flask was vigorously stirred with a mechanical shaker. At 20 min, 50 ml of gas was withdrawn from the flask through the gas chromatograph gas-sampling valve into a syringe. This 50 ml of gas was displaced by Krebs-Ringer bicarbonate. 4 ml of gas was removed from the syringe for ^{133}Xe determination and the gas in the syringe was then reinjected into the flask, displacing Krebs-Ringer bicarbonate. The gas remaining in the gas-sampling valve was injected into the chromatograph. A second analysis of gas concentrations was made at 40 min.

Analytical techniques. ^{133}Xenon concentration was determined by injecting 2 ml of gas (ambient temperature [26°–27°C] and pressure, dry) into an evacuated, stoppered glass test tube. The test tube was counted in a scintillation counter [1] to at least ±2% accuracy.

The concentration of each of the other four gases was determined with a gas chromatograph [2] equipped with a 2-ml gas-sampling valve, a thermal conductivity detector (for H_2, He, and CO), and a hydrogen flame detector (for CH_4) in series. Adequate separation of these gases was achieved with a 9′ × ⅛″ column packed with molecular sieve at an oven temperature of 105°C. Argon was used as the carrier gas at a flow rate of 30 ml/min.

Blood hemoglobin concentrations were determined by the cyanmethemoglobin method of Drabkin (6).

RESULTS

Relation of CO absorption to luminal P_{CO}. The absorption of CO at a mean luminal P_{CO} of 640 mm Hg (initial P_{CO} 760) and 455 mm Hg (initial P_{CO} 570) were virtually identical, averaging 1.53±0.10 and 1.48±0.12 (SEM) ml/min/100 g respectively, in eight studies. All simultaneous studies of the absorption of CO and the unbound gases were carried out at a mean luminal P_{CO}

[1] Packard Auto-Gamma Spectrometer, Series 410A, Packard Instrument Co., Inc., Downers Grove, Ill.

[2] Beckman GC-6, Beckman Instruments, Inc., Fullerton, Calif.

of greater than 500 mm Hg. To demonstrate that CO absorption would increase with increasing P_{CO} in a diffusion-limited case, similar studies were carried out in the stomach, an organ that shows marked diffusion limitation during absorption (5). As expected, CO absorption increased from 0.31±0.03 to 0.52±0.04 (SEM) ml/min/100 g, when the mean P_{CO} was increased from 430 mm Hg to 672 mm Hg.

Measurement of the absorption rates and diffusion rates of the test gases. The observed absorption rates of the five test gases are shown in Table I. The absorption of CO (Q_{CO})[3] is expressed as milliliters per minute per 100 grams of intestine, and for the unbound gases, absorption is given as the fractional absorption rate (C), and expressed as per cent per minute per 100 grams of intestine. To determine if the presence of CO influenced the absorption rate of the other four gases, two studies were performed substituting room air for CO. The results of these studies did not differ significantly from the results obtained in the presence of 90% CO.

Table I also indicates the measured diffusion rates of the gases in rabbit intestinal tissue expressed as the ratio of the diffusion rate of each gas relative to CH_4 (k_x/k_{CH_4}).

Calculation of blood flow from the absorption rate of CO. 1 g of hemoglobin binds 1.36 ml of CO (STP) (7). Assuming that the hemoglobin of the equilibrating blood flow becomes saturated with CO and that the hemoglobin of the villus blood equals central hemoglobin, the blood flow that absorbed CO (F_{CO}) is calculated as follows:

$$F_{CO} = \frac{Q_{CO}}{1.36 \times [Hgb]} = 7.24 \pm 0.12 \text{ (SEM) ml/min/100 g.} \quad (1)$$

The amount of the unbound gases that would be absorbed if these gases equilibrated with F_{CO} and if there were no countercurrent exchange is given by:

$$Q_x = F_{CO}\alpha_x P_x, \quad (2)$$

where Q_x is the expected absorption rate of gas x, F_{CO} is calculated from Eq. 1, α_x is the solubility coefficient of the gas in blood (5), and P_x is the partial pressure of the gas in the lumen.

Expression of this relation in terms of fractional absorption rate (C_x) of a gas rather than absolute absorption rate (Q_x) requires the following manipulation. The total amount (A_x) of a gas in the lumen equals $VP_x/P_B - 47$ where V is the total volume (STP) of gas in the loop and P_B is barometric pressure. Therefore the predicted fractional absorption for gas x can be calculated[4] from:

$$C_x = \frac{Q_x}{A_x} = \frac{(P_B - 47)\alpha_x F_{CO}}{V} \quad (3)$$

The expected fractional absorption rate of each of the unbound gases (arbitrarily set at 1.0) is compared with their observed fractional absorption rates in Fig. 1A. It is apparent that the gases were absorbed much more rapidly than predicted. This result is the opposite of what would be expected with countercurrent exchange.

Calculation of blood flow from the absorption rate of the unbound gases. In Fig. 2, the fractional absorption rate of each gas relative to CH_4 (C_x/C_{CH_4}) is plotted against the blood solubility of each gas (5) relative to CH_4 (α_x/α_{CH_4}). If uptake was entirely blood flow limited, the uptake rate of each gas should be proportional to its solubility in blood and all points should fall on the line of identity. Instead the more rapidly diffusing, low molecular weight gases (H_2 and He) are absorbed faster than predicted and ^{133}Xe, a large, slowly diffusing gas, is absorbed more slowly than predicted. We have previously shown that absorption of gases from the rat small intestine is well described by a model that assumes that functionally there are two absorptive flows (5). One flow, in close proximity to the lumen, perfectly equilibrates with luminal gases. A second flow maintains a negligible concentration of the luminal gases and therefore absorbs with diffusion-limited kinetics. It can be shown that if this model is correct, the uptake of gas x relative to CH_4 should be described by the following equation (5)

$$\left(\frac{F\alpha_{CH_4}}{k_{CH_4}} + 1\right)\left(\frac{C_x\alpha_{CH_4}}{C_{CH_4}\alpha_x} - 1\right) = \frac{k_x\alpha_{CH_4}}{k_{CH_4}\alpha_x} - 1 \quad (4)$$

where C_x/C_{CH_4} is the ratio of the fractional absorption

TABLE I

Absorption Rate and Relative Diffusion Rate of Gases

Gas	Fractional absorption rate (C)	Diffusion rate in tissue relative to CH_4 (K_x/K_{CH_4})
	%/min/100 g	
He	5.48±0.65 (18)	1.14±0.04 (8)
H_2	8.37±1.02	1.52±0.03
^{133}Xe	45.25±2.18	1.81±0.47
CH_4	11.90±0.75	
	Absorption rate (Q) *(ml/min/100g)*	
CO	1.52±0.08	

Data expressed as ±1 SEM; ( ), number of observations.

[3] *Abbreviations used in this paper:* C, fractional absorption rate; F_{CO}, the flow that equilibrates with CO; Q, absorption.

[4] The values employed for α were 0.0088, 0.0149, 0.120, and 0.032 for He, H_2, ^{133}Xe, and CH_4, respectively (5).

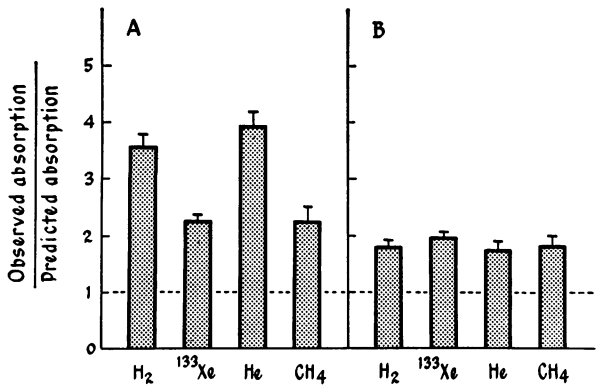

FIGURE 1 Comparison of the observed absorption rates of H_2, ^{133}Xe, He, and CH_4 with the absorption rates predicted from CO absorption. In (A) the total observed absorption rate is compared with the predicted rate. In (B) the fraction of the observed uptake calculated to have been absorbed into an equilibrating flow is compared with the predicted rate.

rates of the two gases, k_x/k_{CH_4} is the relative diffusion rates of the two gases (experimentally determined in vitro) and F is the equilibrating flow. If this model is correct, a plot of $(C_x\alpha_{CH_4}/C_{CH_4}\alpha_x) - 1$ vs. $(k_x\alpha_{CH_4}/k_{CH_4}\alpha_x) - 1$ should give a straight line passing through the origin. Fig. 3 shows that when plotted in this form, the observed data very nearly fall on a straight line passing through the zero intercept, indicating that this model accurately predicts the absorption of gases from the rabbit as well as the rat small bowel. The slope of this plot is 0.23±0.008 (±1 SD), the intercept is 0.088 and $r = 0.99$.

It can be shown (5) from Eq. 4 that the slope (S) of the line in Fig. 3 is described by:

$$S = \frac{k_{CH_4}}{k_{CH_4} + \alpha_{CH_4}F} \quad (5)$$

= fraction of total CH_4 uptake that is diffusion limited.

An S of zero indicates complete blood flow limitation and as the slope increases, there is increasing diffusion limitation until, when $S = 1$, diffusion limitation becomes complete. The percentage absorbed by a diffusion-limited mechanism was 23% for CH_4, and 49%, 55%, and 12% for H_2, He, and ^{133}Xe, respectively. The 95% confidence limit for the slope shown in Fig. 3 was 0.23±0.016 and thus the 95% confidence limit for the percentage of CH_4 absorbed by a diffusion-limited mechanism is 21.4%–24.6%. The percentage of the total uptake absorbed into the equilibrating flow equaled 51%, 45%, 77%, and 88% for H_2, He, CH_4, and ^{133}Xe, respectively, with 95% confidence limits of about ±2% above and below these values. The value of the equilibrating blood flow (F) can be determined from the value of the slope and the fractional absorption of CH_4:

$$F = \frac{C_{CH_4}V(1 - S)}{\alpha_{CH_4}(P_{B-47})}. \quad (6)$$

The equilibrating flow calculated from Eq. 6 averaged 13.2 ml/min/100 g, about 1.8 times greater than F_{CO}. Fig. 1B compares the uptake rate of the unbound gases calculated to have been absorbed into this equilibrating flow (F) with the uptake rate predicted from F_{CO} (Eq. 3). As would be expected from the discrepancy between the flows, the observed rate was about 1.8 times faster for each of the gases than would be predicted from F_{CO}.

DISCUSSION

The technique employed in this paper to quantitate the influence of countercurrent exchange is based on the following rationale: Coburn demonstrated that the rate of CO absorption from the ileum of rabbits (8) rises linearly with increasing luminal P_{CO} until P_{CO} reaches a level of about 400 mm Hg. Above this level absorption remains constant despite further increments in P_{CO}. This finding was confirmed in the present study. Thus, absorption of this gas at high luminal P_{CO} is entirely accounted for by a flow that becomes saturated with CO. Uptake by a partially saturated blood flow must be negligible, since the absorption of CO by such a flow would rise when the luminal P_{CO} was increased.

If the hemoglobin concentrations of villus and central blood are identical, the flow that equilibrates with CO(F_{CO}) can be calculated from Eq. 1 and equaled 7.24±0.12 (SEM) ml/min/100 g. Employing roughly comparable methodology, Coburn measured a flow of 8 ml/min/100 g for the rabbit ileum (8).

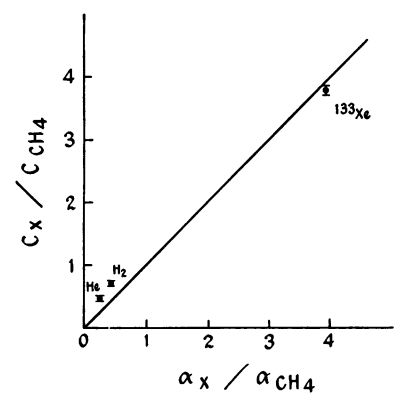

FIGURE 2 Relation of the absorption rates of H_2, He, CH_4, and ^{133}Xe to their solubilities in blood. The observed absorption rate of each gas relative to CH_4 (C_x/C_{CH_4}) is plotted against the ratio of the solubility of the gas in blood to that of CH_4 (α_x/α_{CH_4}). If the absorption rate is determined solely by the solubility of the gas in blood, all points should fall on the line of identity.

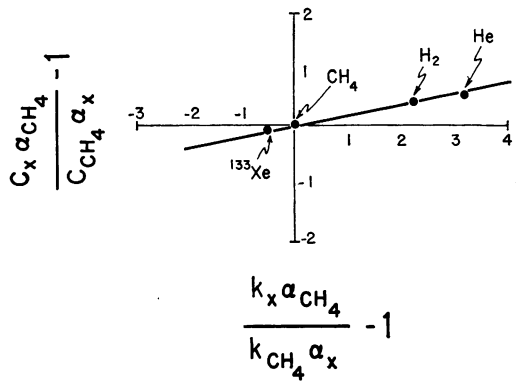

FIGURE 3 Fit of the observed absorption rates of H_2, He, CH_4, and ^{133}Xe to the two-flow model. If this model accurately predicts the absorption rates of the gases, all points should fall on a straight line with an intercept of zero. A slope of zero indicates complete blood flow limitation and a slope of 1 indicates complete diffusion limitation.

The rate of absorption of the unbound gases by F_{CO} should be predicted by Eq. 3 if there is no countercurrent exchange. This equation assumes complete equilibration for these gases between lumen and F_{CO}. While difficult to verify experimentally, this assumption seems almost certainly correct, since the half-time for equilibration of the blood with luminal gases is proportional to $\alpha_B/\alpha_T D$ where α_B and α_T are the blood and tissue solubilities and D is the diffusion coefficient in the tissue. CO and the unbound gases have roughly the same values of D; thus the relative equilibration times of the gases is proportional to α_B/α_T. This ratio is about 1 for the unbound gases and 20 for CO. Since it was demonstrated that there was equilibration of CO, the unbound gases should also equilibrate with F_{CO} and the rate of absorption of the unbound gases by this flow (if there is no countercurrent exchange) should be described by Eq. 3.[5]

As can be seen in Fig. 1A, the experimentally observed absorption rates for the unbound gases were from two to four times greater than the rates predicted from Eq. 3. This result is the opposite of what would be expected if countercurrent exchange influenced absorption, since the unbound gases should exchange and reduce their observed absorption rates below that predicted by the CO uptake data. Coburn, Swerdlow, Luomanmäki, Forster, and Powell (9), in an extensive study of gas absorption from the canine urinary bladder, similarly observed that unbound gases (N_2O and C_2H_2) were absorbed more rapidly than could be attributed to equilibration with a mucosal flow calculated from CO uptake.

Part of the difference between the observed and predicted absorption rates of the unbound gases is explained by the finding that the uptake of unbound gases, unlike CO, involves both diffusive and flow-limited components. A simple model, previously employed with success to distinguish between the flow and diffusive components of gas absorption in the rat intestine (5), was also found to accurately predict the absorption rates of gases from the rabbit jejunum (see Fig. 3). This model assumes that, functionally, two flows are involved in gas absorption. One flow equilibrates with the lumen and absorbs with perfect flow-limited kinetics, and the second flow is sufficiently rapid and distant from the lumen that it absorbs with perfect diffusion-limited kinetics. Failure to observe the diffusive component for CO results from the high "solubility" of CO in blood relative to tissue. The equilibrating blood flow acts as a sink and obscures the relatively minor diffusive component for CO, even though the absolute value of the diffusive component may be as large as the diffusive component for the unbound gases.

The flow (F_{CO}) which equilibrates with CO should account for only that fraction of the total uptake of unbound gases that is absorbed into an equilibrating flow. Fig. 1B compares the uptake of unbound gases predicted by F_{CO} with the uptake calculated to have been absorbed into the equilibrating flow of the two-flow model. It is apparent that each of the four gases was still absorbed about 1.8 times faster than predicted by F_{CO} and clearly there was no evidence to support the hypothesis that countercurrent exchange retarded the absorption rate of readily diffusible substances. This discrepancy between observed and predicted uptake may possibly be explained by the fact that F_{CO} was calculated on the assumption that blood perfusing the villi has a hemoglobin concentration identical to that of central blood. However, Jodal and Lundgren have demonstrated in the cat that plasma skimming results in a villus hemoglobin concentration only about 60% of that of central blood (10). Thus, the villus blood flow required to absorb CO would be about 1.7 times greater than that initially calculated from central hemoglobin measurements. With this correction factor, the absorption of unbound gases predicted by CO measurements is roughly comparable to the uptake of these gases by the equilibrating flow.

What are the assumptions involved in the present study which, if incorrect, might have resulted in failure to demonstrate a functioning countercurrent exchange? Failure of CO to fully saturate the absorbing flow would

[5] It should be noted that a maximal P_{CO} gradient between lumen and blood would be maintained until saturation of the blood was essentially complete, while partial pressure differences between lumen and blood would drop as the unbound gases entered the blood. However, the tissue: blood "solubility" for CO is roughly 1:20, while that of the other gases is about 1:1. Therefore, the unbound gases would equilibrate more rapidly than would CO until 95% equilibration between blood and lumen was reached (i.e., 1/20 of the initial partial pressure differences remained).

result in an underestimation of F_{CO}. As previously discussed, this possibility seems to be ruled out by the constant absorption rate of CO at luminal P_{CO} values above 400 mm Hg. F_{CO} would also be underestimated if plasma skimming was greater than assumed. It seems unlikely, however, that the villus hematocrit could be appreciably less than 60% of the central hematocrit without resulting in ischemia of the villi and in an extraordinarily high hematocrit in the nonvillus flow.

The flow measurement based on CO absorption would also be underestimated if CO was able to exchange. However, the tight binding of CO to hemoglobin appears to rule out this possibility. The rate of exchange of a gas will be directly proportional to the partial pressure differences for the gas between the two limbs of the exchanger. The small amount of unbound, dissolved CO would diffuse between the limbs of the exchanger with kinetics roughly comparable to the diffusion of the unbound gases. The P_{CO} in the efferent blood would then fall to a very low level but the blood would remain nearly saturated with CO. Thus, further exchange would take place at a very slow rate relative to the amount of CO present in the blood draining the villous. In contrast, the concentration of the unbound gases in blood is directly proportional to their partial pressures. Hence, relative to the quantity of gas present in venous blood, the unbound gases would diffuse at a rate several orders of magnitude faster than CO. For example, venous blood equilibrated with H_2 and CO at a partial pressure of each gas of 2 mm Hg would contain about 400 times as much CO as H_2 (assuming a P_{O_2} of 30 mm Hg and a normal hemoglobin concentration). Since the diffusivities of CO and H_2 are roughly similar, the rate of fall of the venous H_2 concentration by diffusion to the arteriole would be roughly 400 times faster than the fall in the bound CO. Thus, countercurrent exchange of CO should be negligible relative to the exchange of the unbound gases.

A model consisting of a flow-limited and a diffusion-limited component has been used to represent the mechanism of absorption of unbound gases in the present study. This model employs no correction for countercurrent exchange subsequent to the uptake of gases by the two absorptive streams. The concept of a discrete flow that equilibrates with the lumen is supported by the CO data, which indicate that a flow equilibrates with the lumen at high luminal P_{CO}, while the remainder of the perfusion is sufficiently distant from the lumen that it has negligible uptake of CO. The major support for the accuracy of the model, however, is that the observed absorption rates of the gases from the small bowel of both the rat and the rabbit are almost perfectly predicted by the model.

Countercurrent shunting should be largely diffusion limited. Therefore the most diffusible gas would be shunted the most rapidly, and hence have the greatest retardation of absorption. In most cases, such an effect results in absorption data that do not accurately fit the model. In addition, with the model it was observed that the flow calculated to equilibrate with unbound gases was similar to the equilibrating flow for CO. The most likely interpretation of these findings is that the model employed to describe the absorption of the unbound gases is correct and there is no appreciable countercurrent exchange. Similarly, the same flow rate appears to equilibrate with CO and the unbound gases because there is such an absorptive flow, whose gas content is not subsequently influenced by countercurrent exchange.

However, the possibility cannot be excluded that unbound gases diffuse to a greater blood flow than indicated by the model, and subsequent exchange fortuitously reduces the observed gas absorption to values that exactly fit the model. The similarity between the equilibrating flow for CO and that calculated for the unbound gases would likewise have to be dismissed as a fortuitous occurrence.

While the present study does not provide incontrovertible evidence against the existence of countercurrent exchange, it suggests that exchange did not have a major influence on the absorption of the unbound gases under the conditions of this study. The possibility certainly remains that in animals with different villus architecture or at very slow linear rates of blood flow, a countercurrent mechanism might well be important.

The results of this investigation are at variance with a variety of carefully conducted studies (1–4) interpreted as demonstrating the existence of countercurrent exchange. The explanation of these disparate findings is not entirely apparent, although different techniques and experimental animals were employed.

It should also be noted that a theoretical case can be made for the existence of exchange. From knowledge of diffusion distances and diffusion rates, and with favorable assumptions concerning transit time in the limbs of the exchanger and villus-lumen equilibration, it can be argued that appreciable exchange should occur (11). However, data on the above assumptions seem insufficient to allow for reliable theoretical calculations concerning the existence of countercurrent exchange. For example, if the entire villus equilibrates with the lumen, venous blood draining the villus will be equilibrated with the lumen and there will be no countercurrent exchange. Thus it seems necessary to base the major arguments for or against the existence of exchange upon experimental observations, which at present both support and refute the importance of this mechanism. Additional studies will be required to resolve these differences.

Haglund has proposed that ischemic necrosis of the villi observed in low perfusion states is a result of a

slow linear rate of villus blood flow with efficient exchange of O_2, rather than a manifestation of low volume flow per se (12). Because of the high affinity of hemoglobin for oxygen (analogous to the situation with CO), the rate of countercurrent exchange of the unbound gases should be many times faster than the rate for oxygen. Thus, if this explanation for the necrosis is correct and there is a significant shunt for oxygen, one would expect to find almost complete shunting of the unbound gases, which should be readily detected by the technique described in this paper.

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