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Research Article

PULMONARY TRANSCAPILLARY EXCHANGE OF Na^{24} AND P^{32}-LABELED PHOSPHATE IN PULMONARY EMPHYSEMA*

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In previous studies it was observed that 5 to 20 per cent of intravenously administered Na^{24} and P^{32}-labeled phosphate and other electrolytes escaped from the circulation during a single transit through the cardiopulmonary pool (1). The relatively small transcapillary exchange of electrolytes in the lungs as compared with skeletal muscle and certain other viscera was attributed to a lesser permeability of the pulmonary capillaries (1). The fraction of intravascular tracer electrolyte transferred across the pulmonary capillaries during pulmonary transit was diminished in the presence of a rapid circulation time and increased in patients with congestive heart failure and a prolonged circulation time (1). The present study extends these observations in patients with pulmonary emphysema where the problem of structural and physiological alterations of the pulmonary vascular tree is of particular interest.

METHODS

Subjects. The control subjects were adult patients, without evidence of pulmonary, cardiovascular or hematological disturbances, of the First Medical Service, Bellevue Hospital. Emphysematous patients without anemia or heart failure were selected from the Emphysema Section of the Chest Clinic, Bellevue Hospital. These patients had been observed for a period of years and their disease confirmed by pulmonary function tests and roentgenographic examination. The present study compares the exchange of Na^{24} ions in 11 control and seven emphysematous subjects and the exchange of P^{32}-labeled phosphate in six control and six emphysematous subjects.

The techniques employed in this laboratory have been described previously (1). Briefly, a solution containing either Na^{24} or P^{32}-labeled phosphate, together with a reference material (in these studies albumin-I^{131}), to which the capillaries are relatively impermeable, is injected rapidly into a peripheral vein and samples of arterial blood are obtained at two second intervals from an indwelling arterial needle previously inserted in the brachial artery of the opposite arm. The doses of the various isotopes used were as follows: Na^{24}, 40 to 80 μc.; P^{32}-labeled phosphate, 10 to 20 μc.; and albumin-I^{131}, 5 to 40 μc. The methods employed in assaying these isotopes have been described previously (1).

If a tracer electrolyte leaves the circulation during passage through the lungs the dilution curve shows concentrations which are lower than those for the reference substance on the ascending portion, owing to loss of electrolyte into the lungs during the initial transit. On the descending limbs of the curves the electroyte concentrations frequently approach or even exceed those of the reference material. This has been interpreted as being due to the return to the blood stream of some of the tracer electrolyte which has previously diffused out (1). At any time during the first circulation the net loss of the tracer electrolyte may be determined by comparing the areas under the curves up to that time. Since in many instances the descending portions of the curves reflect reentry of the electrolyte, it was felt that by comparing the areas under the ascending portions to the peak concentration (A%) a closer approximation of the magnitude of transfer would be obtained. However, both these ascending areas (A%) and the total extrapolated curve areas (T%) were used in the calculations (Table I).

All curves were plotted on semilogarithmic paper; the initial exponential portion of the descending limb was extrapolated to the baseline to exclude recirculation and the first circulation curve replotted on linear paper. Area measurements were made with a rotary planimeter. The difference in areas beneath the electrolyte and albumin curves was expressed as percentage of the albumin curve area. The mean circulation time was determined by the method of Hamilton, Moore, Kinsman and Spurling (2). Cardiac outputs were calculated by means of the arterial dilution technique (3, 4).

RESULTS

The mean net loss of Na^{24}, calculated from the ascending portion of the curves (A%) for seven emphysematous patients, was 3.8 ± 1.2 per cent (S.E.), while the mean loss for 11 control patients was 12.9 ± 1.6 per cent (S.E.) (Table I, Figures

* This material was presented in part at the Third World Congress of Cardiology, Brussels, Belgium, September 1958.

TABLE I

Pulmonary transcapillary exchange of Na^{24} and P^{32}-labeled phosphate

	Na^{24}			$P^{32}O_4$	
Subjects	A%*	T%*	Subjects	A%	T%
Control			Control		
Ni.†	21.3	6.0	Fi.†	6.0	12.0
Jo.†	19.4	12.0	Pa.†	20.0	19.3
Si.†	13.0	19.3	He.	10.9	9.0
Ki.†	6.0	5.0	Ju.	8.1	4.7
Hu.†	6.0	9.0	Ca.	12.1	8.4
Lo.	10.0	5.5	Re.	11.4	8.1
Co.	8.0	7.0			
Wa.	16.9	10.4			
Ro.	10.0	7.0			
Cas.	16.0	8.0			
Va.	15.5	12.3			
Mean values‡	12.9±1.6	9.2±1.5	Mean values	11.4±1.9	10.3±2.1
Emphysema			Emphysema		
Go.	0.4	6.0	Mo.	0.0	0.0
Ma.	1.3	3.3	Lu.	5.8	5.3
Su.	8.2	7.7	Mi.	5.4	3.9
Ba.	3.3	3.6	Ch.	4.1	3.9
Ron.	0.0	0.0	Tu.	0.0	0.0
Sh.	6.0	6.0	Mc.	0.0	0.0
Sc.	7.4	5.2			
Mean values	3.8±1.2	4.5±0.9	Mean values	2.6±1.2	2.2±1.0

$$*\,A\% = \frac{I^{131}\text{ albumin ascending area} - \text{electrolyte ascending area}}{I^{131}\text{ albumin ascending area}} \times 100;$$

$$T\% = \frac{I^{131}\text{ albumin total area} - \text{electrolyte total area}}{I^{131}\text{ albumin total area}} \times 100.$$

† Previously reported (1).

‡ Mean values expressed as mean ± standard error of the mean.

1, 2). The difference between the means is significant according to the "t" test (5) ($p < 0.01$).

Six studies were performed on emphysematous patients using P^{32}-labeled phosphate and albumin-I^{131}. Three of these subjects demonstrated no loss of phosphate during the entire first circulation, and the mean value for the group determined from the ascending curve areas (A%) was 2.6 ± 1.2 per cent (S.E.). The mean loss for P^{32}-labeled phosphate in six control subjects was 11.4 ± 1.9 per cent. These differences are also significant ($p < 0.01$).

In control subjects and in emphysematous patients the total Na^{24} curve areas (T%) were 9.2 ± 1.5 per cent (S.E.) and 4.5 ± 0.9 per cent (S.E.), respectively, less than the albumin curve area. The difference between the means is significant, the p value being between 0.05 and 0.01. In the control group the mean difference in areas beneath the total albumin-I^{131} and total P^{32} curves (T%) was 10.3 ± 2.1 per cent (S.E.), while in the emphysematous patients the mean difference was only 2.2 ± 1 per cent (S.E.). The difference between the means is statistically significant ($p < 0.01$).

The mean circulation time determined in 10 of the control subjects was 18.5 ± 0.9 seconds (S.E.) while that for all 13 emphysematous patients was 21.4 ± 1.2 seconds (S.E.) (Table II). The difference is of questionable significance, the p value being between 0.1 and 0.05.

The cardiac index for 12 of the control subjects in whom data were available was 3.99 ± 0.36 L. per minute per $M.^2$, while that for the 13 emphysematous patients was 3.69 ± 0.30 L. per minute per $M.^2$. The mean values do not differ significantly ($p > 0.1$). These values (particularly in Co., Mi. and Ron.) are somewhat higher than those reported by others (6, 7) for normal subjects. The explanation probably lies in the fact that no attempt was made to conform to basal resting conditions in either the control group or the emphysematous patients.

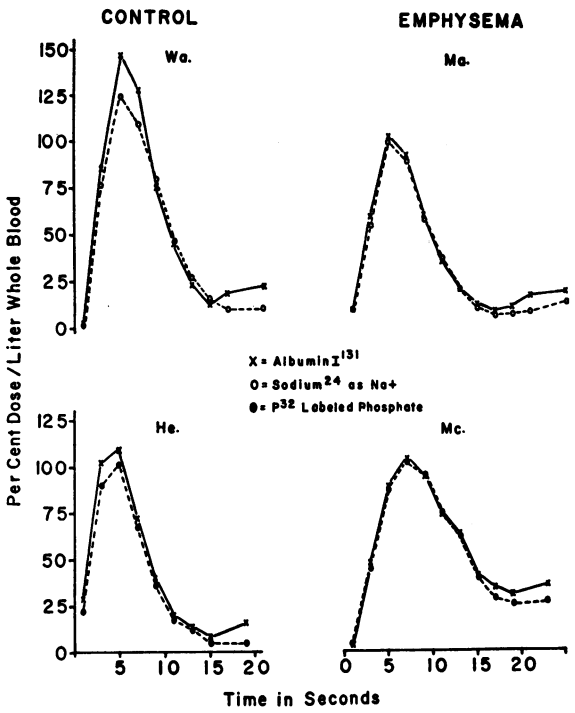

FIG. 1. SIMULTANEOUS ARTERIAL DILUTION CURVES

Albumin-I^{131} and Na^{24} as Na^+ in control and emphysematous patients (upper curves) and albumin-I^{131} and P^{32}-labeled phosphate in control and emphysematous patients (lower curves).

DISCUSSION

The results of the present study again indicate that the ion curves differ from the albumin curves in normal subjects. This difference partially or completely disappears in patients with pulmonary emphysema, indicating a decrease in the fraction of Na and phosphate transferred out of the blood during circulation through the lungs. Transfer of the tracer out of the circulation is primarily a function of capillary transit time, capillary surface area and capillary permeability. Although it is not possible to identify exactly alterations in any of these factors, it is interesting to speculate as to the mechanism involved in causing the diminished outflux in emphysema.

Although the capillary transit time was not determined in the present study, previous studies have demonstrated a correlation between circulation time and the fractional loss of plasma electrolytes (1). The calculated mean circulation time for the emphysematous patients was slightly longer than in the control subjects which would, if anything, tend to augment this fractional loss of plasma electrolytes (1). However, the capillary transit time has been calculated to be approximately one second (8) and alterations in the rate of blood flow through the capillaries could take place without being reflected in the calculated mean circulation time. On the other hand, it is unlikely that the lack of any detectable transfer could be accounted for solely by reduction in capillary transit time.

The effect of pulmonary emphysema on the capillary surface area is not known, but disruption and obliteration of the smaller blood vessels have been described (9–11) and a significant diminution in total capillary surface area would result in a decrease in outward movement of the tracer ions. Likewise, the diminished gas-diffusing capacity observed in emphysema has been partially attributed to a decreased membrane surface area (12–15). However, the finding of McNeil, Rankin and Forster (12) that the capillary blood volume remains essentially unaltered in emphysematous patients offers no support to the possibility that the capillary surface area is diminished but does not, of course, exclude it.

Capillary permeability remains to be considered. Alterations in the characteristics of the membrane have been discussed as another factor limiting gas exchange (12, 14) and it is possible that the decreased electrolyte transfer in emphysema could result from alterations in capillary permeability.

In addition to the three factors just discussed, other alterations in the emphysematous lung should be considered. The presence of right to left shunts bypassing the capillary bed could obviously limit outflux. However, such shunts are not characteristic of the emphysematous lung and, furthermore, would appear to be excluded by the absence of a rapid initial appearance of both tracer electrolytes and albumin-I^{131}. Bronchial arterial anastomoses with the pulmonary vessels have been described in chronic pulmonary disease (16–18), but since blood flow through these channels is from left to right no effect on the first circulation transfer would be expected.

Finally, it is conceivable that capillary permeability is so altered in pulmonary emphysema as to allow the tracer electrolytes and albumin-I^{131} to exchange at the same rate, thus eliminating any

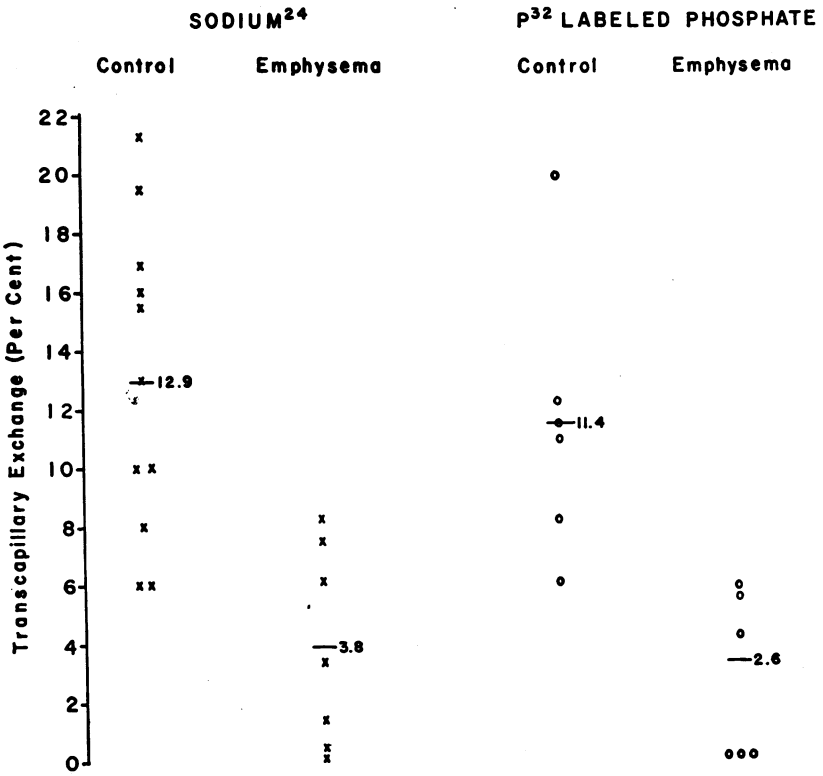

FIG. 2. TRANSCAPILLARY EXCHANGE OF Na^{24} AS Na^{+} AND P^{32}-LABELED PHOSPHATE

Exchange in control and emphysematous patients, expressed as per cent of plasma sodium and phosphate leaving the circulation in a single passage through the lungs.

difference in the curves. Although this possibility cannot be excluded, there is no evidence to support it.

The statements made in the discussion above are based on certain assumptions for which data are not available. Capillary transit time and capillary

TABLE II

Circulatory data

Control subjects	M.C.T.*	C.I.†	Emphysematous patients	M.C.T.	C.I.
	sec.	*L./min./M.²*		*sec.*	*L./min./M.²*
Ni.		3.30	Go.	19.4	4.17
Si.		3.84	Ma.	19.5	3.43
Lo.	17.9	4.67	Su.	17.6	3.63
Co.	14.0	6.70	Ba.	20.1	3.61
Wa.	17.3	3.40	Ron.	14.5	5.70
Ro.	24.2	3.40	Sh.	20.4	3.40
Cas.	17.5	3.92	Sc.	27.4	2.29
Va.	17.0	3.79	Mo.	18.0	3.34
He.	16.1	3.82	Lu.	28.2	2.49
Ju.	22.6	3.30	Mi.	24.7	6.00
Ca.	17.5	4.54	Ch.	26.4	2.84
Re.	21.0	3.21	Tu.	23.2	3.77
			Mc.	19.4	3.25
Mean values‡	18.5±0.9	3.99±0.36		21.4±1.2	3.69±0.30

* M.C.T. = mean circulation time.
† C.I. = cardiac index.
‡ Means expressed as mean ± standard error of the mean.

surface area are not known and the factors limiting gas exchange may not effect electrolyte transfer in a similar fashion.

Although it is recognized that no final conclusions as to mechanism may be drawn, the fact remains that electrolyte transfer as measured here is markedly reduced in emphysema.

SUMMARY

1. The pulmonary transcapillary exchange of Na^{24} and P^{32}-labeled phosphate was determined in 17 control subjects and in 13 patients with pulmonary emphysema.

2. Exchange of both ions is markedly reduced or practically abolished in emphysema. Factors causing this diminished transfer are discussed.

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