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Lung Tissue Resistance in Diffuse Interstitial Pulmonary Fibrosis *

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Summary. *1*) **Measured during spontaneous breathing in ten patients with diffuse interstitial lung disease, total pulmonary resistance averaged 3.53 ± 1.56 cm H_2O per L per second; airway resistance, 1.63 ± 0.79 cm H_2O per L per second; and lung tissue resistance, 1.90 ± 0.95 cm H_2O per L per second (range, 0.89 to 3.96). The lung tissue resistance was on an average about four times higher in patients with lung fibrosis than in ten healthy persons of the same age. No significant difference in airway resistance was found between healthy subjects and patients.**

2) **In three patients the lung tissue resistance was measured during spontaneous breathing and during panting. Much higher values were found during spontaneous breathing.**

3) **In patients with lung fibrosis and also in healthy subjects, there seems to have been an inverse correlation between the vital capacity, or the compliance, on the one hand, and the lung tissue resistance on the other. Nevertheless, in patients with lung fibrosis the lung tissue resistance was more increased than could be attributed to the loss of normally compliant lung tissue only.**

4) **No correlation was found between the lung tissue resistance and severity of impairment of pulmonary gas exchange; especially no relationship appeared to exist between the lung tissue resistance and the alveolar-end capillary P_{O_2} gradient during hypoxia. This result indicates that the pathological alterations producing a measurable end gradient in hypoxia may be independent of the augmentation of the fibrous framework responsible for the stiffening of the lung.**

Introduction

The disturbances of the mechanics of breathing and pulmonary gas exchange have been extensively studied in patients with diffuse interstitial fibrosis [(1–9) and many other more recent authors]. Nevertheless, little attention has been paid to the viscous properties of lung tissue in this disease. Marshall and DuBois (10) observed a slight increase of lung tissue resistance by a plethysmographic method. Possibly owing to the small number of patients examined (three cases), or to their experimental procedure (all measurements were made in panting subjects), no success was achieved in demonstrating any relationship between values for lung tissue resistance and other data of lung function. This study is a further attempt to illuminate the problem of lung tissue resistance and its correlation to other figures of pulmonary function tests in diffuse interstitial lung disease. In contrast to the method of Marshall and DuBois, the total pulmonary, airway, and lung tissue resistance was measured during spontaneous breathing in our experiments.

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Methods

Subjects. Ten patients were studied. For the selection the following points were decisive:

1) The histories (progressive exertional dyspnea, nonproductive cough), clinical signs (persistent moist rales over both lungs), and radiological appearances were characteristic. There was no evidence of bronchopulmonary infection.

2) The clinical status showed relative stability; for several weeks at least there were no noticeable changes of signs, symptoms, or X-ray findings.

3) Lung volume measurements by spirometry gave a purely restrictive pattern; in all patients who were cooperating well, the forced expiratory volume over 1 second was 75% or more of the vital capacity.

4) The alveolar-arterial P_{O_2} difference during hypoxia (fractional concentration of O_2 in inspired air, $F_{I_{O_2}} = 0.154$), from which the components induced by shunts and distribution inequalities were subtracted, was remarkably increased. This alveolar-end capillary gradient seemed to us to be more reliable a criterion for the degree of impairment of diffusion than the O_2 or CO diffusing capacity, considering the various hypotheses involved in the Bohr integration and trial and error procedure for calculating the O_2 diffusing capacity (11) on the one side, the difficulties in estimating the CO diffusing capacity in patients with unequal distribution (12, 13) on the other side.

Of course, the clinical, roentgenological, and physiological alterations mentioned above are not specific signs of "fibrosis," but may also include interstitial pneumonitis (14) and granulomatosis. However, the prolonged histories (2 months to 15 years), the marked decrease of lung volumes, and the stability of the clinical status point to rather fibrotic and advanced forms of diffuse interstitial pulmonary disease designated in this paper as "diffuse interstitial pulmonary fibrosis."

Physical data, duration of symptoms, and results of lung volume measurements are given in Table I.

Technics. The lung volumes were determined by spirometry, and the functional residual capacity was calculated with a helium dilution technic.

Total pulmonary resistance (R_p) and airway resistance (R_a) were measured with subjects sitting and breathing spontaneously [a moderate hyperventilation could not be avoided because of the rebreathing system used (15)]. R_a was determined with a volume displacement body plethysmograph of the type designed by Mead (16) and modified by Jaeger and Otis (15, 17–19). The changes of temperature and water content of respiratory gases during spontaneous breathing were eliminated by having the subjects rebreathe from a bag containing gas at BTPS (body temperature and pressure, saturated with water) conditions. R_p was obtained by simultaneous recordings of intraesophageal pressure and rate of air flow. Intraesophageal pressure was measured with a thin-walled rubber balloon (length, 10 cm; perimeter, 3.5 cm) similar to that described by Schilder, Hyatt, and Fry (20). With a polyethylene tube (length, 65 cm; i.d., 0.1 cm) the balloon was connected to a Statham pressure transducer (model PM 131 TC ± 5-350) equipped with a special pressure adapter having a small chamber volume on the positive side of the gauge. The balloon-tubing-gauge system had a natural frequency of 30 cycles per second. All variables (intraesophageal pressure, volume fluctuations of the plethysmograph, rate of air flow, tidal volume, and mouth pressure) were plotted simultaneously on photographic paper by an Electronics for Medicine multichannel recorder. After the balloon was passed by the nasal route into the esophagus until the tip of the tube was lying about 40 cm from the nares, the balloon system was emptied, then filled again with 6 ml air. Finally enough air was extracted that only 0.8 ml remained in the system (between tube and transducer a three-way stopcock was connected). The computation of R_p was based upon pressure volume loops that were plotted from the photograph recordings, each loop determined by 14 points. For each of these points the corresponding alveolar pressure was calculated from the photograph and added to (inspiration) or subtracted from (expiration) the proper value of intraesophageal pressure. Thus, by

TABLE I

*Physical data, duration of symptoms, and lung volumes in ten patients with diffuse interstitial pulmonary fibrosis (mean age, 55 years)**

Name	Sex	Age	Height	Weight	Duration of symptoms	Vital capacity		Residual volume		$FEV_{1.0}/VC$
		years	*cm*	*kg*	*years*	*ml*	*% predicted*	*ml*	*% of TC*	*%*
1. C.E.	♀	71	160	67	5	2,130	69	910	30	66†
2. S.A.	♀	34	148	65	2	1,500	53	630	30	55†
3. B.G.	♂	28	163	57	18 months	3,180	68	790	20	82
4. H.G.	♂	56	176	65	4	2,680	60	990	27	82
5. Z.R.	♀	56	165	63	15	1,130	32	850	43	88
6. R.D.	♂	58	161	63	5 months	2,200	59	560	20	76
7. L.R.	♂	48	173	75	10 months	2,900	62	780	21	83
8. M.M.	♀	58	151	59	2 months	1,570	56	960	38	66†
9. R.W.	♂	72	172	71	15 months	2,860	69	1,720	38	76
10. G.J.	♂	72	172	60	3 months	3,150	75	1,370	30	82

* TC = total capacity; $FEV_{1.0}/VC$ = timed vital capacity.
† The poor cooperation of the three patients accounts for these low values.

connecting these 14 new points, a smaller loop could be drawn in the center of the intraesophageal pressure-volume loop (Figure 1). Whereas the area of the latter corresponded with the work done against the total viscous resistance of the lung, the area of the former (small) loop was proportional to the work done against the viscous lung tissue resistance. The areas of both loops were measured with a planimeter, and R_p, as well as R_t, was computed with the area formulas indicated by Nisell and Ehrner (21). Dynamic lung compliance was obtained by dividing the tidal volume by the change in the esophageal pressure between points of zero flow. The values of R_p, R_a, and R_t are averages of at least three measurements, that of the dynamic compliance of at least five measurements. For calculating these mean values only those cycles of respiration were evaluated during which the functional residual capacity and the tidal volume remained nearly constant.

In all subjects the gas exchange was analyzed with the subjects supine and breathing spontaneously. The alveolar-arterial P_{O_2} difference ($A\text{-}aD_{O_2}$) was determined at normal oxygen ($F_{I_{O_2}} = 0.21$), hypoxia ($F_{I_{O_2}} = 0.154$), and hyperoxia ($F_{I_{O_2}} = 0.95$) under steady state conditions. The patients breathed each gas mixture during 15 to 20 minutes from the closed circuit of the metabographe designed by Fleisch (22). The $F_{I_{N_2}}$ was continuously measured and held constant by Lundin and Åkeson's (23) nitrogen meter (24). The deflections of the nitrogen meter were calibrated by analyzing samples of inspired air for O_2 by a Haldane apparatus. Ventilation, O_2 uptake, CO_2 output, and respiratory quotients were measured with the metabographe. The arterial P_{CO_2} was calculated by the formula of Henderson-Hasselbalch, with the pH and the plasma CO_2 content of the arterial blood obtained by an indwelling needle. The arterial O_2 content and capacity were determined by the Van Slyke technique, and the arterial P_{O_2} was determined by an O_2 electrode of the Clark type immediately after sampling the blood in syringes warmed up to 37° C. The electrode was calibrated in each case with the patients' blood equilibrated at three different levels of P_{O_2} (50, 100, and 600 mm Hg) at 37° C. With an assumed arteriovenous O_2 difference of 5 ml per 100 ml, the anatomical shunt was calculated by the $A\text{-}aD_{O_2}$ during hyperoxia (the absence of any signs of heart disease suggested that there was no important increase or decrease of pulmonary blood flow or arteriovenous O_2 difference). On the assumption that there was no gradient due to diffusion at normal oxygen, the venous admixture due to ventilation-perfusion or other distribution inequalities was calculated with the $A\text{-}aD_{O_2}$ at normal oxygen, from which the true shunt component had already been subtracted. Then, the $A\text{-}aD_{O_2}$ in hypoxia was corrected also by subtracting the anatomical shunt and distribution component, assuming that there was no change in venous admixture during the whole procedure. The correction of the $A\text{-}aD_{O_2}$ from true shunt and distribution effects was performed with individual *in vivo* O_2 dissociation curves extrapolated from the two arterial points measured during normal oxygen and hypoxia. The remaining P_{O_2} gradient in hypoxia was considered as an alveolar-end capillary P_{O_2} gradient, i.e., a gradient mainly due to diffusion (25–27). It should be emphasized that the most questionable assumption made by Riley and Lilienthal—constant O_2 diffusing capacity in normal oxygen and hypoxia—was not involved in these calculations. Our new assumption that there is no diffusion gradient at normal oxygen may be incorrect in patients with severe "alveolar-capillary block." However, the only consequence of neglecting this possibility is that the end gradients obtained by this method must be considered as minimal values, i.e., that a much increased end gradient could possibly be larger, but in no case smaller.

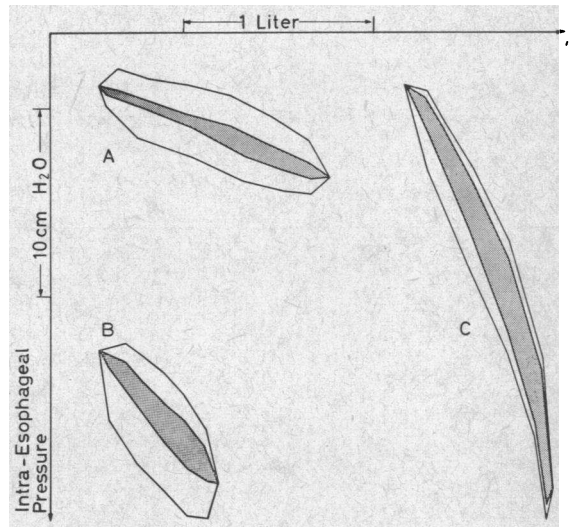

FIG. 1. VOLUME-PRESSURE LOOPS A) IN A HEALTHY ADULT, B) IN A HEALTHY CHILD (11 YEARS OLD), AND C) IN A PATIENT WITH DIFFUSE INTERSTITIAL PULMONARY FIBROSIS. The stippled areas correspond with the work done against the viscous lung tissue resistance.

Normal values. Normal values were obtained with the technics described above and have been published in part elsewhere (19, 28). The mechanics of breathing were also studied in five healthy children. They were asked to hyperventilate to reach breathing patterns similar to those registered on adults during plethysmographic measurements. The mean values found in the different age groups of healthy subjects are plotted at the bottom of Table II.

Results

Measured during spontaneous breathing in ten patients with diffuse interstitial lung fibrosis, total pulmonary resistance (R_p) averaged 3.53 ± 1.56 cm H_2O per L per second, the mean airway resistance (R_a), 1.63 ± 0.79 cm H_2O per L per second, and the lung tissue resistance (R_t), 1.90 ± 0.95 cm H_2O per L per second, or 54% of R_p. Compared with values in a group of healthy persons showing a similar age and sex distribution (Table

TABLE II

*Dynamic compliance of the lung and total pulmonary, airway, and lung tissue resistance in ten patients with diffuse interstitial pulmonary fibrosis and in 34 healthy subjects**

Name	Respiratory rate	$\dot{\bar{V}}$	Cdyn(l)	Resistance: Total pulmonary R_p	Resistance: Airway R_a	Resistance: Lung tissue R_t	Lung tissue as % R_p	$R_t \cdot Cdyn(l)$ (time-constant)
	rpm	*L/sec*	*ml/cm H₂O*	*cm H₂O/L/sec*			*%*	*sec*
1. C.E.	21	0.70	58	3.61	2.15	1.46	40	0.085
2. S.A.	21	0.40	37	4.15	2.16	1.99	48	0.073
3. B.G.	25	0.65	90	2.40	1.51	0.89	37	0.080
4. H.G.	19	0.51	36	3.06	0.66	2.40	78	0.086
5. Z.R.	30	0.69	18	7.23	3.27	3.96	55	0.071
6. R.D.	18	0.41	50	3.64	1.84	1.80	50	0.090
7. L.R.	23	0.67	66	2.71	1.31	1.40	52	0.092
8. M.M.	26	0.55	37	4.54	1.71	2.83	62	0.105
9. R.W.	35	0.84	61	1.89	0.81	1.08	57	0.066
10. G.J.	30	0.70	56	2.10	0.87	1.23	59	0.069
Mean	24.8	0.61	50.9 ±20.0†	3.53 ±1.56	1.63 ±0.79	1.90 ±0.95	54	0.097
Healthy subjects								
5 children (mean age 10 years)		0.64	83 ±10.2†	3.57 ±0.98	2.26 ±0.73	1.31 ±0.37	37	0.108
7 females (mean age, 25 years)		0.64	160 ±50	1.96 ±0.45	1.46 ±0.47	0.50 ±0.15	26	0.080
12 males (mean age, 32 years)		0.65	260 ±60	1.25 ±0.28	0.96 ±0.27	0.29 ±0.12	23	0.076
10 elderly persons (4 females, 6 males; mean age, 52 years)		0.60	226 ±91	1.62 ±0.47	1.20 ±0.38	0.42 ±0.14	26	0.096

* $\dot{\bar{V}}$ = mean flow rate; Cdyn(l) = dynamic compliance of the lung. Sequence of the patients analogous to Table I.
† Standard deviation.

II), total pulmonary and lung tissue resistances were significantly increased ($p < 0.001$). On the other hand, no significant difference of airway resistance ($p > 0.05$) between patients with lung fibrosis and normal persons was found. Considering these results, the increase of total pulmonary resistance in lung fibrosis is mainly due to the marked increase of lung tissue resistance. In Figure 1 the volume-pressure relationship of a healthy adult, of a child (11 years old), and of a patient with interstitial lung disease (HG, Table I) is plotted. The ratio of the dotted area (corresponding with the work done against lung tissue resistance) to the whole area of the volume-pressure loop is much larger in patients with lung fibrosis than in the healthy subjects. Furthermore, the horn-like configuration of the volume-pressure loop is a typical finding in lung fibrosis; neither in healthy adults nor in children with a vital capacity of the same order as that measured in patients with lung fibrosis could a pressure-volume relationship of such a shape be found during spontaneous breathing.

The figures characterizing the gas exchange are plotted in Table III. The $A\text{-}aD_{O_2}$ in hypoxia was clearly above the normal limits. The alveolar-end capillary P_{O_2} gradient in hypoxia amounted to 13.3 ± 9.2 mm Hg, significantly higher ($p < 0.02$) than that determined in healthy 70-year-old men [1.6 ± 1.3 mm Hg (28)].

Discussion

In ten patients with diffuse interstitial pulmonary fibrosis the lung tissue resistance varied between 0.89 and 3.96 cm H_2O per L per second (mean value, 1.90 ± 0.95); on an average it was even higher than the airway resistance. However, although a major part of total pulmonary resistance, the lung tissue resistance is of minor importance in the total (viscous and elastic) work of breathing.

TABLE III

Ventilation, arterial blood gases, alveolar-arterial P_{O_2} differences, and alveolar-end capillary P_{O_2} difference during hypoxia in ten patients with diffuse interstitial pulmonary fibrosis

Name	Minute ventilation	Respiratory rate	Arterial oxygen saturation: At normal oxygen	Arterial oxygen saturation: At hypoxia ($F_{I_{O_2}}$=0.154)*	Arterial carbon dioxide tension (at normal oxygen)	Alveolar-arterial P_{O_2} difference: Normal oxygen ($F_{I_{O_2}}$ = 0.21)	Alveolar-arterial P_{O_2} difference: Hypoxia ($F_{I_{O_2}}$ = 0.154)	Alveolar-arterial P_{O_2} difference: Hyperoxia ($F_{I_{O_2}}$ = 0.95)	Alveolar-end capillary P_{O_2} difference (hypoxia)
	L/min	*rpm*	*%*	*%*	*mm Hg*	*mm Hg*	*mm Hg*	*mm Hg*	*mm Hg*
1. C.E.	17.2	22	93.1	89.4	24.5	21	24	46	21
2. S.A.	11.7	28	91.6	87.6	29.4	11	13	24	9
3. B.G.	7.4	15	94.6	87.2	46.9	2	2	26	1†
4. H.G.	13.7	18	90.8	54.5	38.6	46	34	11	29
5. Z.R.	10.2	25	91.9	84.5	40.5	27	15	37	11
6. R.D.	13.2	16	86.2	76.4	48.4	19	17	−16	13
7. L.R.	8.7	15	95.8	80.5	37.5	31	18	33	14
8. M.M.	6.8	28	90.5	79.6	39.9	36	17	55	6
9. R.W.	13.3	28	69.2	42.8	43.6	52	41	357	25
10. G.J.	12.6	19	94.9	89.8	31.9	21	13	44	4
Mean	11.5	21.4	89.9	77.2	38.1	27	19.4	61.7	13.3
SD						±15	±11.2	±105.7	±9.2

* $F_{I_{O_2}}$ = fractional concentration of O_2 in inspired air.

† In this patient no disturbance of the pulmonary gas exchange could be detected at rest, but a marked arterial normocapnic hypoxemia was present at exercise (O_2 saturation, 84.2%).

Studying panting subjects with lung fibrosis, Marshall and DuBois (10) found the values of lung tissue resistance to be much lower (0.32, 0.42, and 0.83 cm H_2O per L per second) than our results. The question may arise whether this discrepancy has to be attributed to a methodological error involved in the plethysmographic technique used. We measured airway resistances with the volume displacement plethysmograph of Mead (16), ingeniously modified by Jaeger and Otis (15) so that one can determine the airway resistance at any breathing pattern. Considering the theoretical basis (15) and the results of the extensive preliminary studies (15, 19), there seems to be no reason to assume that this new technique gives less accurate values of alveolar pressure than the original method developed by DuBois, Botelho, and Comroe (29), i.e., our high values of lung tissue resistance are hardly ascribable to incorrect measurements of airway resistance. Furthermore, it would seem unlikely that the reason for this considerable difference is due only to the individual variations of lung tissue resistance in the patients examined. More probably, the discrepancy is related to the different breathing patterns. To confirm this hypothesis, we made repeated parallel measurements on three patients during spontaneous breathing and during panting. The results are given in Table IV. In all cases much higher values of lung tissue resistance were obtained during spontaneous breathing, whereas there was only a slight change in airway resistance. The explana-

TABLE IV

*Influence of the breathing pattern on the lung tissue resistance in three patients with diffuse interstitial pulmonary fibrosis**

Name	Spontaneous breathing: FRC	f	$\dot{V}$	Cdyn(l)	R_p	R_a	R_t	Panting: FRC	f	$\dot{V}$	Cdyn(l)	R_p	R_a	R_t
	ml	*rpm*	*L/sec*	*ml/cm H_2O*	*cm H_2O/L/sec*			*ml*	*rpm*	*L/sec*	*ml/cm H_2O*	*cm H_2O/L/sec*		
6. R.D.†	1,900	15	0.5	63	3.09	1.37	1.72	2,100	90	0.9		2.33	1.68	0.65
7. L.R.	2,100	23	0.67	66	2.71	1.31	1.40	2,100	100	0.75		2.10	1.24	0.86
Z.RU.‡	3,000	21	0.57	101	1.69	1.02	0.67	3,100	86	0.68		1.12	0.85	0.27

* Same symbols as in Table II; also FRC = functional residual capacity, and f = respiratory rate.

† These results were obtained by a re-examination about 3 months after the first measurements shown in Tables I–III (after corticosteroid treatment).

‡ Z.RU. was not listed in Tables I–III.

tion of this phenomenon can only be a hypothetical one. On the one hand, it is possible that, by the procedure of panting, only those parts of the fibrotic lung with a low tissue resistance, probably identical with the most compliant parts, are ventilated. On the other hand, keeping in mind the phenomenon of static hysteresis shown by Mead, Whittenberger, and Radford (30) to be dependent on the size of volume change, similar factors may be involved in decreasing lung tissue resistance when subjects pant or breathe with small tidal volumes. It might be possible that with increased stretching of the compliant elements the viscous tissue resistance increases, i.e., that the lung tissue resistance is also a function of the degree of elongation of the compliant elements. This hypothesis would agree with the observation that in persons having small lung volumes (females, children), higher tissue resistances were found than in subjects with large lung volumes (males), although the tidal volumes in all three groups were of the same order.

Reduced lung volumes and a decreased compliance on the one side and a much increased lung tissue resistance on the other are the typical alterations of lung mechanics in our cases of advanced interstitial lung disease; a close interrelationship between the two former and the latter figures seems to exist. The result given in Table II, the product

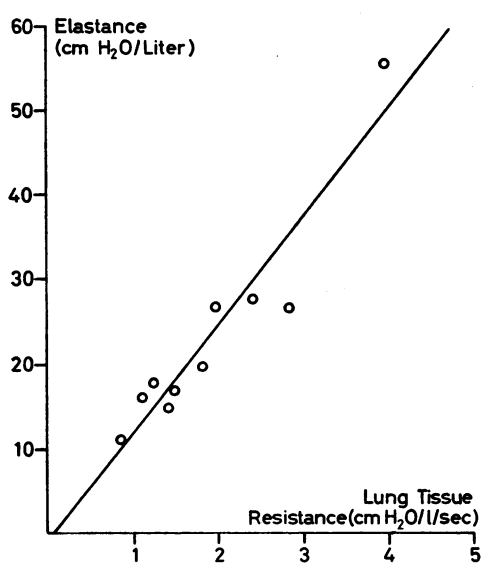

FIG. 2. RELATIONSHIP BETWEEN THE ELASTANCE AND THE LUNG TISSUE RESISTANCE (R_T) IN TEN PATIENTS WITH LUNG FIBROSIS. The regression line is elastance $= -1.15 + 12.7\ R_t$; $r = 0.95$.

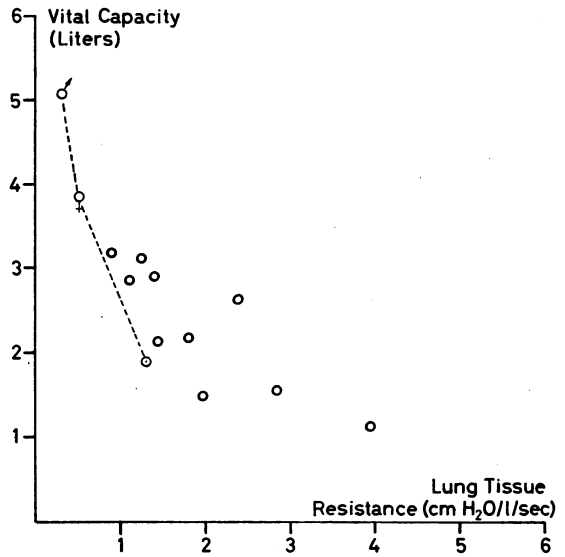

FIG. 3. RELATIONSHIP BETWEEN THE VITAL CAPACITY AND THE LUNG TISSUE RESISTANCE IN HEALTHY SUBJECTS AND IN PATIENTS WITH LUNG FIBROSIS. The lung tissue resistance increases with decreasing vital capacity. ○, patients with lung fibrosis. ♂, mean value of 18 healthy males; ♀, of 11 females; and ⊙, of 5 normal children.

of R_t and Cdyn(1) [i.e., the time constant (10)] being of the same order in all cases, points out a reciprocity between R_t and Cdyn(1). By a graphical analysis wherein the elastance substituted for the compliance in order to obtain linearity, a very good correlation between elastance and R_t can be shown (Figure 2). Likewise, an inverse nonlinear relationship was found between the lung tissue resistance and the vital capacity, showing an increase of R_t with decreasing vital capacity. These observations suggest the interpretation that the increase of R_t as well as the decrease of Cdyn(1) is mainly due to the same cause, the diminution of compliant lung tissue, as mentioned by Marshall and DuBois (10). Moreover, this interpretation is also in good agreement with the observations made in healthy subjects; by likewise plotting the mean values of vital capacity and lung tissue resistance obtained in 18 healthy males, 11 females, and 5 children, we found a vital capacity-R_t relationship quite similar to that obtained in patients with lung fibrosis (Figure 3). Nevertheless, although we have taken into account the influence of decreased lung volumes, the lung tissue resistance in pulmonary fibrosis appears to be higher than in healthy subjects with small lung

volumes (children). This result becomes apparent in Figure 3 if the vital capacity-R_t relationship of patients is compared with that of normal persons; the lung tissue resistance obtained in children is significantly lower ($p < 0.01$) than that in patients having a vital capacity of the same order (CE, HG, RD, and MM in Table I). Therefore, the following conclusions seem to be justified: The increase of lung tissue resistance is mainly due to a diminution of compliant lung tissue, but in addition, other factors, such as the pathological alteration of tissue viscosity caused by the augmentation of connective tissue and the infiltration of cells, seem to have a part in increasing lung tissue resistance in diffuse interstitial pulmonary fibrosis.

On the assumption that the increase of R_t was due to a diminution of normally functioning lung tissue, an augmentation of interstitial tissue, and thickening of the alveolar membranes, one would expect a relationship between the lung tissue resistance and the impairment of O_2 diffusion (due to the decrease of the capillary blood volume and to the membrane thickening). By a statistical comparison, however, no correlation was found between R_t and the alveolar-end capillary Po_2 gradient in hypoxia nor between other figures characterizing the disturbances of pulmonary gas exchange. With regard to the parallel variations of R_t and the elastance shown in Figure 2, our results are in accord with previous studies in which no close correlation, either between the compliance of the lung and the arterial desaturation (2) or between the compliance and the diffusing capacity measured by the single breath CO method, could be obtained (31). On the one hand, we have shown patients (ZR, MM in Tables II and III) with most severe disturbances of the mechanical properties of the lung accompanied by an only slightly increased end capillary gradient; on the other hand, moderate mechanical disorders may be combined with a severe impairment of diffusion (CE), as can be seen in Figure 4. Although it is possible that the end gradient may be due in part to a decrease of capillary volume, the membrane thickening appears to be a more important factor, for, in our experiments, the influences of the possibly altered circulatory dynamics are probably of little importance considering the methodological procedure (all patients were studied at rest) and the absence of any clinical sign pointing to a considerable pulmonary hypertension, which would be present in cases with a marked decrease of capillary volume. Therefore, based upon the results of Figure 4 and provided that the alveolar-end capillary Po_2 gradient in hypoxia reflects essentially the membrane component limiting the O_2 diffusion, the hypothesis suggested by West and Alexander (2) seems to be reasonable, namely, that the pathological changes influencing the mechanical properties and the pulmonary gas exchange may act at different planes, i.e., the thickening of the blood-gas barrier may be independent of the increase and thickening of the fibrous framework responsible for the stiffening of the lung.

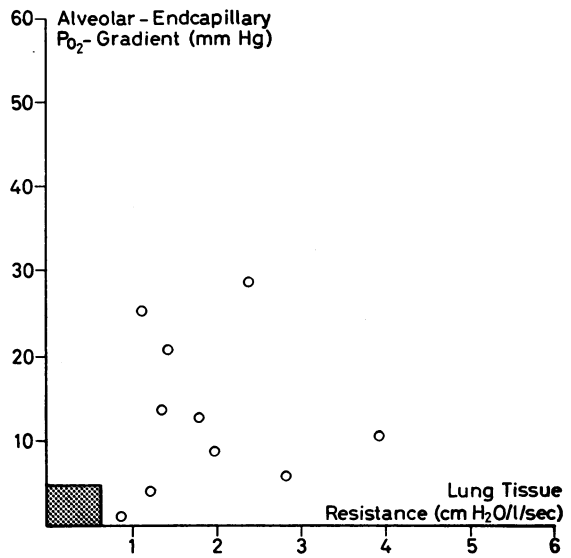

FIG. 4. LUNG TISSUE RESISTANCES AND ALVEOLAR-END CAPILLARY Po_2 DIFFERENCES DURING HYPOXIA IN TEN PATIENTS WITH DIFFUSE INTERSTITIAL PULMONARY FIBROSIS. No close correlation was found between these two figures. Stippled area = normal subjects.

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