Respiratory Dysfunction Following Acute and Chronic Pump Failure of the Heart

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In order to explore pulmonary dysfunction originating in cardiac decompensation, acquired heart diseases were classified into three selected categories; chronic compensated heart, chronic decompensated heart and acute decompensated heart with severe alveolar edema. Pathophysiology in each category was investigated. Hemodynamic variables were measured by cardiac catheterizations and a variety of pulmonary functions based on respiratory physiology were studied. Severe alveolar edema due to acute pump failure of the heart revealed a significant inverse correlation between PaO_2 and PaCO_2 indicating the appearance of decreased effective alveolar ventilation with markedly decreased PaO_2 . A-aDO_2 remained still high despite a complete resolution of alveolar edema. There are some possibilities that pulmonary dysfunction might be accelerated by repetition of acute cardiac decompensation in chronic heart diseases. Chronic pulmonary involvements caused by chronically decompensated heart must be stressed most important for comprehensive treatments of cardiac pump failure. Lung volumes considerably decreased but ordinarily there was no obvious airflow obstruction in the large central airways. Chronic compromised lung with giant left atrium, however, showed appreciable decrease in $\text{FEV}_1\%$ (FEV_1/FVC), MMF, $\dot{V}_{50}$ and $\dot{V}_{25}$, indicating an apparent evidence of both central and peripheral airway obstructions. Patients with CTR over 70% were more seriously involved with a significant reduction in lung volumes in addition to total airway obstructions. Under these situations an inverse correlation between PaO_2 and PaCO_2 in chronic decompensated heart was observed showing a contrast difference in chronic compensated heart.

It has been well recognized that cardiac decompensation gives rise to secondary pulmonary involvements leading to respiratory dysfunction.¹⁻³ Respiratory dysfunctions caused by acute cardiac decompensation apparently differ from those of chronic functional and

structural alterations of the lung caused by chronically compromised heart. Recent therapeutic progress for serious pump failure of the heart which was fatal before has conversely increased the population of the patients with chronically compromised heart. The gas exchange in the lung is known to be seriously impaired in acute parenchymal pulmonary edema following acute left sided heart failure,⁴ whereas, in patients with chronically compromised heart or chronically decompensated heart, arterial blood oxygen tension could be well preserved in

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Fig.1. Classification of 4 grades of pulmonary edema according to the extent of pulmonary parenchymal infiltrates on plain chest roentgenogram.

appearance, even though it might be true only at resting conditions. There was, however, an ample evidence for disturbed gas exchange in the lung demonstrated by increased oxygen tension difference between alveolar gas and arterial blood^{5,6}. Pathophysiologic consequence to the lung involved chronically by hemodynamic and mechanical abnormalities of the heart has been recently emphasized potentially hazardous for comprehensive medical and surgical treatments of cardiac pump failure. Some abnormalities of gas exchange function in the lung carry grave prognosis in patients with chronically severely compromised heart. The current study was undertaken to elucidate the clinical and physiological significance of respiratory dysfunction following acute and chronic cardiac decompensations.

MATERIALS AND METHODS

For the purpose of studying physiopathology of the lung after decompensated heart, various stages of acquired heart disease were intentionally selected and classified into three categories of chronic compensated heart, chronic decompensated heart, and acute decompensated heart with parenchymal pulmonary edema. The heart diseases which were considered to be complicated with any primary lung disease on the examinations including chest roentgenogram were excluded for the study.

193 patients with acquired heart disease ranging in age from 20 to 65 years were employed for the current study. 74 patients were in chronically decompensated heart (vide post). 56 of them were in valvular disease; 36 with mitral, 8 with aortic, and 12 with combined valvular

disease. Remaining 18 patients were in dilated cardiomyopathy composed of 8 with idiopathic and 10 with secondary cardiomyopathy possibly derived from myocarditis or coronary ischemic disease. From the difference in elevated mechanism of pulmonary venous pressure, 74 patients with chronic heart failure also were divided into two different etiological groups; 27 with dominant mitral stenosis primarily disturbing left ventricular filling and 47 with left ventricular failure primarily disturbing left ventricular emptying. 20 of 74 patients were diagnosed to have CTR over 70% and 54 patients were in CTR under 70%. 9 of 27 patients with mitral valvular disease were echocardiographically evaluated the patients with a giant left atrium (GLA),⁷ while 18 of 27 patients did not have GLA. 53 patients with chronic compensated heart disease (vide post) were used for controlled study. 19 patients of them were in mitral valvular disease and 14 patients were in aortic valvular disease, and the remaining 20 patients were in combined valvular disease. Other 66 patients consisting of 27 with acute myocardial infarction, 17 with previous myocardial infarction, 12 with valvular heart disease, 6 with arterial hypertension and 4 with cardiomyopathy were in acute parenchymal pulmonary edema with grade 4 (severe) assessed by chest roentgenogram (Fig. 1) representing acute left ventricular failure.

Hemodynamic variables were measured by combined right and left heart catheterizations and left ventriculography in both chronic compensated and chronically decompensated patients at routine cardiac catheterization laboratory. Cardiac output was measured by thermodilution technique using Waters Instruments COR-100A and the intravascular pressures

TABLE I PULMONARY FUNCTIONS IN CHRONIC DECOMPENSATED HEART

a)	VC (%pred)	FEV ₁ (%pred)	MMF (%pred)	$\dot{V}_{50}$ (%pred)	$\dot{V}_{25}$ (%pred)	FEV ₁ % %	CV/VC (%pred)	D _{LCO} (%pred)	ΔN_2 %	A-aDO ₂ torr	a-ETDCO ₂ torr
MS (N = 27)	73 ± 13.4	68 ± 19.2	49 ± 22.5	56 ± 33.9	42 ± 24.8	77 ± 8.4	149 ± 39.5	61 ± 17.8	1.8 ± 1.17	25 ± 10.9	1.65 ± 1.88
LVF (N = 47)	83 ± 16.9	79 ± 20.0	63 ± 24.8	65 ± 30.3	58 ± 33.0	80 ± 7.7	124 ± 22.3	81 ± 24.0	1.5 ± 0.91	27 ± 7.6	1.70 ± 1.56
p	< 0.05	< 0.05	< 0.05	NS	< 0.05	NS	< 0.001	< 0.001	NS	NS	NS
b)	VC (%pred)	FEV ₁ (%pred)	MMF (%pred)	$\dot{V}_{50}$ (%pred)	$\dot{V}_{25}$ (%pred)	FEV ₁ % %	CV/VC (%pred)	D _{LCO} (%pred)	ΔN_2 %	A-aDO ₂ torr	a-ETDCO ₂ torr
GLA (-) (N = 18)	75 ± 14.1	72 ± 20.0	56 ± 22.0	67 ± 35.1	50 ± 25.8	80 ± 7.1	144 ± 39.5	62 ± 17.4	1.9 ± 1.30	26 ± 12.5	1.67 ± 1.90
GLA (+) (N = 9)	70 ± 12.1	60 ± 15.6	34.8 ± 16.7	35.2 ± 19.3	25 ± 11.0	70 ± 6.7	159 ± 40.6	60 ± 20.5	1.6 ± 0.89	22 ± 6.5	1.62 ± 1.86
p	NS	NS	< 0.05	< 0.05	< 0.01	< 0.005	NS	NS	NS	NS	NS
c)	VC (%pred)	FEV ₁ (%pred)	MMF (%pred)	$\dot{V}_{50}$ (%pred)	$\dot{V}_{25}$ (%pred)	FEV ₁ % %	CV/VC (%pred)	D _{LCO} (%pred)	ΔN_2 %	A-aDO ₂ torr	a-ETDCO ₂ torr
CTR < 70% (N = 54)	86 ± 13.7	82 ± 17.2	65 ± 22.3	70 ± 31.3	61 ± 32.1	81 ± 6.6	131 ± 31.5	81 ± 22.7	1.6 ± 1.01	26 ± 9.2	1.67 ± 1.68
CTR > 70% (N = 20)	65 ± 12.7	57 ± 15.4	37 ± 19.7	41 ± 22.4	30 ± 13.0	72 ± 8.6	142 ± 35.2	55 ± 15.1	1.7 ± 1.05	27 ± 9.3	1.69 ± 1.59
p	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	NS	< 0.001	NS	NS	NS

mean ± 1SD

Abbreviations: VC = vital capacity; FEV₁ = forced expiratory volume in 1 second; MMF = maximum midexpiratory flow; $\dot{V}_{50}$ and $\dot{V}_{25}$ = maximal expired flow rates at 50%VC and 25%VC in maximal expiratory flow volume curve, respectively; FEV₁% = FEV₁ divided by forced vital capacity (FVC), expressed as %; CV/VC = closing volume divided by vital capacity; D_{LCO} = lung diffusing capacity by CO gas; ΔN_2 = increase in N₂ concentration from 750 ml expired volume to 1250 ml expired volume (BTSP) in single breath N₂ washout test; A-aDO₂ = alveolar arterial O₂ tension difference; a-ETDCO₂ = arterial endtidal CO₂ tension difference. VC, FEV₁, MMF, $\dot{V}_{50}$, $\dot{V}_{25}$, CV/VC, and D_{LCO} were divided by their predicted values and expressed as %; MS = dominant mitral stenosis; LVF = left ventricular failure; GLA (-) = absence of giant left atrium; GLA (+) = presence of giant left atrium; CTR = cardio-thoracic ratio.

Fig.2. Relationship between %VC (VC/pred VC) and FEV₁% (FEV₁/FVC) in patients with chronically decompensated heart disease. Shaded area indicates 95% confidence band in chronic compensated heart disease obtained from our previous extensive study concerning various compensated heart diseases. %VC is equal to VC (%pred).

were measured by Gould-Statham P23ID strain gauge transducer. Hemodynamics and some pulmonary functions were serially studied during breathing air at bed side under Swan Ganz cardiac catheterization at the onset and after the successful disappearance of grade 4 of parenchymal pulmonary edema in 7 patients with acute cardiac decompensation caused by acute myocardial infarction without any previous complications of heart and lungs.

The differentiation between chronic compensated and chronic decompensated heart was made from the etiologic, anatomic and physiologic diagnoses under careful considerations of both hemodynamic abnormality and functional disability indicating physical work capacity depending on cardiac reserve, according to a revised classification, cardiac status and prognosis, extended by the New York Heart Association.⁸ Patients with decompensated heart disease were all determined to be in cardiac status 3 to 4, moderately to severely compromised, with a prognosis guarded despite medical therapy, on the other hand, patients with compensated heart disease were assessed their cardiac status 1 to 2 indicating fairly good prognosis with medical therapy. According to the previous functional classification of NYHA,⁹ chronic compensated patients were in class 1 to 2 in functional classification, and chronic decompensated patients belonged to all in class 3 to 4 and they did not improve their functional disabilities much

more than those in class 3 with further medical therapy. The lung volumes and forced expiratory functions were measured by Benedict Roth spirometer calculating vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁) and maximum midexpiratory flow (MMF) which is flow rate measured over the middle half of the forced expiration, and maximal expiratory flow volume curves calculating maximal expiratory flow rates at 50%VC and 25%VC ($\dot{V}_{50}$, $\dot{V}_{25}$) were measured by electrospirometer equipped with pneumotachography. Expired gas was sampled continuously at mouth level by a mass spectrometer (Perkin Elmer MGA 1100B) to study closing volume (CV) and an indicator of uneven distribution of inspired gas in the lung (ΔN_2) by the single breath test¹⁰ using wedge spirometer (Med Science 570) through the bag-in-box system. Arterial blood gas was sampled at the supine bed rest and analyzed by an IL meter 813. The alveolar arterial O₂ tension difference (A-aDO₂) was calculated by using an alveolar air equation with the actual measurement of gas exchange ratio from the analysis of expired gas sampled in a Douglas bag, and arterial endtidal CO₂ tension difference (a-ETDCO₂) was simultaneously measured by continuous tracing of expired CO₂ under resting tidal breaths. Pulmonary carbon monoxide diffusing capacity (DLCO) was measured by single breath technique.¹¹ All pulmonary function data except FEV₁% (FEV₁/FVC), ΔN_2 , A-aDO₂ and a-ETDCO₂ were expressed as a percentage of the predicted value for convenience.

RESULTS

Respiratory Dysfunction Caused by Chronically Compromised Heart

Pulmonary functions in patients with chronic decompensated hearts which were compared between the groups with different circulatory disturbances were listed in Table I. They, compared with their normal values, showed significant reduction in VC, FEV₁, MMF, $\dot{V}_{50}$, $\dot{V}_{25}$ and DLCO, and significant elevation in CV/VC (closing volume divided by vital capacity), ΔN_2 , A-aDO₂ and a-ETDCO₂. Our normal values (mean $\pm$ 1SD) of ΔN_2 , A-aDO₂ and a-ETDCO₂ were 0.80% $\pm$ 0.20%, 13.3 torr $\pm$ 1.6 torr, and 0.1 torr $\pm$ 1.5 torr, respectively. Normal value of FEV₁% (FEV₁/FVC)¹² is generally accepted more than 70% and so FEV₁% showed normal range. VC (%pred) and FEV₁% in 74 patients

TABLE II HEMODYNAMIC VARIABLES IN CHRONIC DECOMPENSATED HEART

a)	PAm mmHg	PCm mmHg	LVEDP mmHg	CI l/min/m ²	EF %	CTR %
MS (N = 27)	38 ± 14.1	23 ± 8.3	9.9 ± 6.3	2.42 ± 0.66	50 ± 10.3	69 ± 12.4
LVH (N = 47)	21 ± 9.7	12 ± 6.3	14.2 ± 7.9	2.74 ± 0.76	51 ± 12.3	60 ± 9.3
<i>p</i>	< 0.001	< 0.001	< 0.05	NS	NS	< 0.001
b)	PAm mmHg	PCm mmHg	LVEDP mmHg	CI l/min/m ²	EF %	CTR %
GLA (-) (N = 18)	39 ± 16.2	22.2 ± 9.3	9.7 ± 7.1	2.44 ± 0.66	52 ± 10.7	66 ± 13.7
GLA (+) (N = 9)	36 ± 7.8	24.7 ± 5.5	10.4 ± 4.2	2.38 ± 0.79	46 ± 8.7	75 ± 6.9
<i>p</i>	NS	NS	NS	NS	NS	NS
c)	PAm mmHg	PCm mmHg	LVEDP mmHg	CI l/min/m ²	EF %	
CTR < 70% (N = 54)	24 ± 11.2	14 ± 9.2	12.2 ± 7.9	2.73 ± 0.71	52 ± 11.7	
CTR > 70% (N = 20)	43 ± 13.4	22 ± 7.7	13.9 ± 6.3	2.31 ± 0.71	48 ± 10.1	
<i>p</i>	< 0.001	< 0.001	NS	< 0.05	NS	

mean ± 1SD

Abbreviations: PAm = pulmonary artery mean pressure; PCm = pulmonary capillary mean pressure; LVEDP = left ventricular enddiastolic pressure; CI = cardiac index, cardiac output/body surface area; EF = ejection fraction of left ventricle measured by left ventriculography; CTR = cardio-thoracic ratio; MS = dominant mitral stenosis; LVF = left ventricular failure; GLA (-) = absence of giant left atrium; GLA (+) = presence of giant left atrium

with chronic decompensated heart averaged 80% ± 16.3%, 1SD and 79% ± 8.1%, 1SD, respectively. These data were plotted on the co-ordinate of VC (%pred) and FEV₁% as shown in Fig. 2. Shaded area represents 95% confidence interval band depicted by our previous study¹³ for the patients with chronic compensated heart disease (see discussion). Difference in pulmonary pathophysiology of decompensated heart between dominant mitral stenosis (MS) and left ventricular failure (LVF) was studied; pulmonary functions were listed in Table Ia and hemodynamic variables were listed in Table IIa. MS had significantly increased vascular pressures of pulmonary artery mean pressure (PAm) and pulmonary capillary mean pressure (PCm), while LVF had significantly increased left ventricular enddiastolic pressure (LVEDP). MS group showed significantly decreased VC, FEV₁, MMF, V₂₅, and DLCO with a significant increase in

CV/VC. Similar comparison between mitral valvular diseases with and without giant left atrium (GLA) was made. Although there was no significant difference in hemodynamic variables between them (Table IIb), forced expiratory functions such as MMF, V₅₀, V₂₅, FEV₁% were significantly decreased in patients with GLA (Table Ib). Effect of enlarged heart size on pulmonary functions was also studied, and chronically decompensated patients with cardio-thoracic ratio (CTR) over 70% showing significantly increased vascular pressures with low cardiac output (Table IIc) showed significant reduction in VC, FEV₁ and DLCO associated with impaired forced expiratory functions (a significant decrease in MMF, V₅₀, V₂₅, FEV₁%), (Table Ic). Relationship between alveolar-arterial O₂ tension difference (A-aDO₂) and pulmonary intravascular pressures was demonstrated in Fig. 3, and increased A-aDO₂ was not affected by

Fig.3. Relationship between alveolar arterial O₂ tension difference (A-aDO₂) and pulmonary intravascular pressures of pulmonary artery mean pressure (PA_m) and pulmonary capillary mean pressure (PC_m) in patients with chronically decompensated heart disease. Comparison of two major groups with left ventricular failure (LVF) and with dominant mitral stenosis (MS).

TABLE III ARTERIAL BLOOD GAS AND A-aDO₂

	PaO ₂	PaCO ₂	A-aDO ₂
a) Chronic Decompensated Heart (N = 74)	83.5 ± 10.6	38.5 ± 5.1	26.2 ± 9.1
Chronic Compensated Heart (N = 53)	81.3 ± 8.7	36.0 ± 3.9	28.2 ± 10.4
b) Acute Pulmonary Edema Grade 4 (N = 66)	52.6 ± 8.5	35.3 ± 6.5	54.6 ± 10.1
c) Normal Subjects (N = 25)	96.3 ± 5.2	37.3 ± 2.9	13.3 ± 1.6

mean ± 1SD (torr)

Abbreviations: PaO₂ = arterial O₂ tension; PaCO₂ = arterial CO₂ tension;

A-aDO₂ = alveolar arterial O₂ tension difference.

the magnitude in pulmonary vascular pressures of pulmonary artery mean pressure (PA_m) and of pulmonary capillary mean pressure (PC_m).

Respiratory Dysfunction Caused by Acutely Compromised Heart

Pulmonary functions were studied in only the patients with grade 4 of acute parenchymal pulmonary edema. Arterial blood gas was analyzed during breathing air at the bedside and A-aDO₂ was calculated from actual measurement of gas exchange ratio (R). The data from 66 acute patients were listed in Table IIIb. PaO₂ was markedly depressed to 52.6 torr on the average,

and PaCO₂ was also decreased to 35.3 torr on the average. This resulted in increased A-aDO₂ of 54.6 torr ± 10.1 torr, 1SD. In 7 patients examined serially at the onset and after the disappearance of grade 4 of acute parenchymal edema of the lung by Swan Ganz flow directed catheter, the increase in A-aDO₂ was lowered concomitantly with the decrease in intravascular pressures (PA_m, PC_m) shown in Fig. 4. However, despite the complete resolution of pulmonary parenchymal edema some of patients were evidenced to hold their A-aDO₂ still abnormal high. Increased CV/VC was also lowered but remained still elevated after the complete resolu-

Fig.4. Alveolar arterial O₂ tension difference ($A-aDO_2$) and pulmonary intravascular pressures of pulmonary artery mean pressure (PAm) and pulmonary capillary mean pressure (PCm) in patients with grade 4 of acute pulmonary edema originally caused by acute myocardial infarction. Effect of complete resolution of pulmonary parenchymal infiltrates was demonstrated.

Fig.5. Effect of complete resolution of grade 4 of acute pulmonary edema on alveolar arterial O₂ tension difference ($A-aDO_2$) and closing volume divided by vital capacity (CV/VC) in patients with acute myocardial infarction. CV/VC was expressed a percentage of the predicted value as CV/VC (%pred).

tion as shown in Fig. 5. Alterations of blood gas by the full recovery from parenchymal edema in serial observations were shown in Fig. 6. $A-aDO_2$ were dramatically decreased with concomitant increase in PaO_2 . $A-aDO_2$ in two thirds of the patients remained still high after the

disappearance of alveolar infiltrates on chest roentgenogram. $Paco_2$, however, was centered around 40 torr after the recovery in compensation with slight decrease in elevated $Paco_2$ and slight increase in depressed $Paco_2$.

Blood Gas Abnormality and Disturbed Gas Exchange in the Lung

Blood gas data obtained from 74 chronic decompensated patients, 53 chronic compensated patients, and 66 patients with grade 4 of acute pulmonary edema were summarized in Table III. Arterial blood gas and $A-aDO_2$ between chronic decompensated heart disease and chronic compensated heart disease did not make any difference (Table IIIa). However, a striking difference was observed as shown in Fig. 7, 8, when individual data were plotted on the coordinate of PO_2 and PCO_2 . There was a significant positive linear correlation between PaO_2 and $Paco_2$ in 53 patients with chronic compensated heart disease ($r = +0.44$, $p < 0.001$) as shown in the right of Fig. 7. Whereas patients with chronically decompensated heart disease did not show a positive correlation but showed an inverse linear correlation between PaO_2 and $Paco_2$ (Fig. 8), especially there was a significant inverse correlation ($r = -0.68$, $p < 0.001$) between them as shown in the left of Fig. 8. Surprisingly approximately 30% of 74 chronically decompensated patients held their blood gas quite

Fig.6. Arterial O₂ tension (PaO₂), arterial CO₂ tension (PaCO₂) and alveolar arterial O₂ tension difference (A-aDO₂) at the onset and after the complete resolution of pulmonary parenchymal infiltrates on plain chest roentgenogram.

Fig.7. Relationship between PaO₂ and PaCO₂ in patients with grade 4 of acute pulmonary edema and with chronic compensated heart disease.

normal at supine resting condition and also one third of them (approximately 10% of 74 patients) revealed supernormal PaO₂ (above 100 torr). Grade 4 of pulmonary edema following acute cardiac decompensation revealed marked reduction in PaO₂ which was less than 60 torr in 72% of the patients and showed a significant inverse correlation between PaO₂ and PaCO₂ ($r = -0.35$, $p < 0.005$).

To study an etiological basis of normal arterial

blood gas level in some patients of chronically decompensated heart, hemodynamic and physiologic parameters were analyzed by using A-aDO₂ as a representative parameter of pulmonary gas exchange. No significant correlations between A-aDO₂ and the hemodynamic variables were detected. However, chronically decompensated patients with normal A-aDO₂ was evidenced to have decreased cardiac index (CI), although there were a number of patients with decreased CI

CHRONIC DECOMPENSATED HEART DISEASE

Fig.8. Relationship between PaO_2 and PaCO_2 in patients with chronically decompensated heart disease. Comparison between two major groups with left ventricular failure and with dominant mitral stenosis, which were classified with etiological difference in the elevation of pulmonary venous pressure.

Fig.9. Relationship between alveolar arterial O_2 tension difference (A-aDO_2) and cardiac index (CI) in patients with chronically decompensated heart disease.

without normal A-aDO_2 (Fig. 9). Pulmonary gas exchange in chronic decompensated heart was studied by measurements of both A-aDO_2 and a-ETDCO_2 to be independent parameters of low and high ventilation to perfusion ratios, respectively. It was shown that chronic decompensated patients with normal A-aDO_2 possessed decreased a-ETDCO_2 as shown in Fig. 10, although there was no essential correlation between A-aDO_2 and a-ETDCO_2 .

DISCUSSION

Functional abnormality of the lung following cardiac decompensation was analyzed on the basis of acute and chronic pump failure of the heart. Some patients with chronically decompensated heart might be derived from accumulating several mild to severe episodes of acute cardiac decompensation and others to the contrary might continue to have insidiously decompensated cardiac state without apparent episodes of acute decompensation of the heart for a number of years. Naturally some may well have both combined states. Pulmonary involvements in chronically decompensated heart were more or less influenced by various degrees of episodes of acute cardiac decompensation.

First of all to study the effect of acute cardiac pump failure on the lung, respiratory dysfunction in grade 4 of acute parenchymal pulmonary edema which is the most typical pulmonary manifestation due to acute cardiac decompensation⁴ has been analyzed. Severe arterial hypoxemia reflecting gas exchange abnormality in the lung was observed as shown in Table IIIb and in the left figure of Fig. 7. PaO_2 averaged $52.6 \text{ torr} \pm 8.5 \text{ torr}$, 1SD associated with rather decreased average PaCO_2 which was $35.3 \text{ torr} \pm 6.5 \text{ torr}$, 1SD. However the relationship between PaO_2 and PaCO_2 in grade 4 edema did not show such a linear correlation as that in chronic com-

pensated heart disease did (Fig. 7). PaCO_2 was inversely correlated with PaO_2 significantly ($r = -0.35$, $p < 0.005$). Grade 4 edema with markedly decreased PaO_2 had increased PaCO_2 . This indicates severe alveolar flooding must play a role to decrease the effective alveolar ventilation. Resolution of parenchymal edema in

Fig.10. Relationship between alveolar arterial O_2 tension difference (A-aDO_2) and arterial-entidal CO_2 tension difference (a-ETDCO_2) at supine rest in patients with chronically decompensated heart disease.

the lung permitted the great improvement of PaO_2 and A-aDO_2 as shown in Fig. 6. However even complete disappearance of alveolar infiltrates on chest roentgenogram keeps A-aDO_2 and closing volume (CV/VC) still increased (Fig. 4, 5, 6). There are some possibilities that interstitial edema which might be left for a considerable period of time after the disappearance of florid parenchymal pulmonary edema leads to the organized interstitial fibrosis^{14,15} and to the thickening of alveolo-capillary membranes and that the repetition of such acute decompensation of the heart ultimately leads to further advanced structural changes of the lung with respiratory dysfunction.

Chronic decompensated heart disease has considerable decrease in VC , FEV_1 , MMF , $\dot{V}_{50}$, $\dot{V}_{25}$ and DLCO and also has the increase in closing volume (CV/VC), ΔN_2 , A-aDO_2 and a-ETDCO_2 . These functional abnormalities basically lie in cardiac decompensations, because the patients with primary lung disease are to be excluded from the present study. $\text{FEV}_1\%$ (FEV_1/FVC) as a representative indicator of large airway obstruction in chronic decompensated heart was mostly within normal ranges the value of which is 70% and above.¹⁶ Decreased VC (%pred) and normal $\text{FEV}_1\%$ show restrictive ventilatory impairment!¹⁷ Individual data plotted on the co-ordinate of VC (%pred) and $\text{FEV}_1\%$

Fig.11. Relationship between %VC (VC/pred VC) and $\text{FEV}_1\%$ (FEV_1/FVC) in chronic compensated heart diseases. The band showing 95% confidence interval indicating $\pm 2\text{SEE}$ was obtained from 392 cardiac catheterized patients with various chronic compensated heart diseases. SEE = standard error of the estimate. %VC is equal to VC (%pred).

were all inside the shaded area as shown in Fig. 2. Shaded area was originally made to know characteristic features of ventilatory capacity in chronic heart disease. This band was statistically depicted by our previous study¹³ with 95% confidence interval based on $\pm 2\text{SEE}$ (standard error of the estimate) as shown in Fig. 11, using 392 patients with chronic compensated heart disease among the patients who were catheterized at our routine cardiac catheterization laboratory, which were composed of 216 patients of acquired valvular heart disease, 97 patients of ischemic heart disease and 79 patients of congenital left to right shunt disease. Surprisingly there was no essential difference in VC (%pred) and $\text{FEV}_1\%$ between chronically decompensated heart disease and chronic compensated heart disease. VC (%pred) and $\text{FEV}_1\%$ averaged $82.3\% \pm 19.3\%$, 1SD and $79.5\% \pm 8.0\%$, 1SD in 392 compensated patients, respectively, while $80\% \pm 16.3\%$, 1SD and $79\% \pm 8.1\%$, 1SD in 74 decompensated patients currently studied, respectively. Dominant mitral stenosis (MS) with significantly increased intravascular pressures (Table IIa) among chronically decompensated patients showed further significantly reduced VC, FEV_1 , MMF, $\dot{V}_{25}$ and DLCO with a significant increase in CV/VC (Table Ia). A-a DO_2 did not make any difference between MS and left ventricular failure (LVF) (Table Ia). This also indicates gas exchange abnormality was not explicable with the elevated intravascular pressures (Fig. 3). Decompensated patients with giant left atrium (GLA) which was assessed by the length of the postero-basal portion of left ventricle compressed by enlarged left atrium being 30 mm or longer by real time cross-sectional echocardiography⁷ had a significant reduction in forced expiratory flow and volume such as MMF, $\dot{V}_{50}$, $\dot{V}_{25}$ and $\text{FEV}_1\%$ (Table Ib), although there was no obvious difference in hemodynamic parameters between with and without giant left atrium (Table IIb). Decreased $\text{FEV}_1\%$ ¹² is usually considered an indicator of airway obstruction in relatively large central airways up to the seven generation which play a major part in elevating total airway resistance. So the compression to the large airways from main bronchi to subsegmental bronchioles by enlarged left atrium must be responsible for decrease in $\text{FEV}_1\%$. MMF must decrease accordingly. It is generally accepted that static lung elastic recoil pressure is the principal driving force for maximal expiratory

flow at relatively low lung volumes up to about 80% of VC and that $\dot{V}_{50}$ and $\dot{V}_{25}$ derived from effort independent portion of maximal expiratory flow-volume curve are determined by static elastic recoil pressure of the lung divided by the resistance of upstream airway segment from alveoli to collapsed point¹⁸ which was considered to represent flow resistance of peripheral airways. There is no evidence for decrease in elastic recoil pressure which is to be rather increased in chronic heart failure on theoretical grounds.¹⁹ So $\dot{V}_{50}$ and $\dot{V}_{25}$ are known to be decreased characteristically in peripheral small airway obstruction. Thus it was concluded that GLA involved whole conducting airways with increasing airway resistance from central to peripheral airways. Effect of enlarged heart size in chronically decompensated heart was listed in Table Ic and IIc. Abnormalities of both pulmonary functions and hemodynamic variables in patients with CTR over 70% were more serious than those of the patients with the giant left atrium alone. Enlarged heart over 70% of CTR with significantly increased vascular pressures (PAm, PCm) and with decreased cardiac output (CI) had decrease in VC, FEV_1 and DLCO in addition to the respiratory dysfunction of giant left atrium. Cardiac enlargement over 70% of CTR had a prominent decrease in VC (%pred) of 65% on the average indicating the development of restrictive ventilatory impairment. DLCO was decreased to 55% on the average indicating impaired carbon monoxide transfer with the chronicity and severity of the disease.²⁰ Decreased diffusing capacity of the lung theoretically does not imply arterial hypoxemia at supine resting condition, because arterial O_2 tension is determined by only endcapillary O_2 tension, not reflecting oxygen uptake along pulmonary capillaries.

Averaged values of arterial blood gas and A-a DO_2 obtained from 74 chronic decompensated patients and from 53 chronic compensated patients were listed in Table IIIa. There was no obvious difference in these parameters between both groups. PaO_2 and PaCO_2 at supine rest in chronic cardiac patients of both groups were rather well preserved although slight average decrease in PaO_2 was detected. Alterations of PaO_2 and PaCO_2 in chronically compromised heart must be still a controversial issue.^{21,22} However our data exhibited in Fig. 7 and 8 clearly showed a fundamental difference between chronic compensated patients and chronically decompensated patients. Chronic compensated

Fig.12. Schema showing gas exchange mechanism in the lung when cardiac output considerably decreased. Explanation of condition I, II and III in terms of $A-a D_{O_2}$ as an indicator of low $\dot{V}_A / \dot{Q}$ and $a-ET D_{CO_2}$ as an indicator of high $\dot{V}_A / \dot{Q}$, using O_2-CO_2 diagram.

v = mixed venous blood; a = arterial blood; i = ideal point; A = alveolar gas; E = expired gas; I = inspired gas; ET = endtidal gas; V_T = tidal volume; $phys V_D$ = physiological dead space; V_D = anatomical dead space; $alv V_D$ = alveolar dead space; $\dot{Q}$ = pulmonary blood flow or cardiac output; $\dot{V}_A$ = alveolar ventilation; effective $\dot{V}_A$ = effective alveolar ventilation; alveolar $\dot{V}_D$ = the ventilation of alveolar dead space

heart disease showed a linear correlation between P_{aO_2} and P_{aCO_2} (the right figure of Fig. 7), while chronically decompensated heart disease showed an inverse correlation between them, especially such an inverse correlation between P_{aO_2} and P_{aCO_2} was more prominent in chronic decompensated patients with left ventricular failure ($r = -0.68$, $p < 0.001$) than in those with dominant mitral stenosis ($r = -0.23$, ns) (Fig. 8). Chronic compensated heart diseases include the diseases with or without previous episodes of cardiac decompensation and the magnitude and duration of cardiac derangements varies depending on the course of the disease. The insidious changes arising in the lung in chronic compensated patients tend to increase transpulmonary pressure of the lung required to effect respiration,

thereby increasing the work of breathing.²³ The patients endeavor to compensate for the increased work by decreasing the tidal volume and by elevating respiratory frequency and result in hyperventilation leading to decreased P_{aCO_2} . Despite the hyperventilation induced, P_{aO_2} remained lowered reflecting the disturbed gas exchange in the lung evidenced by increased $A-a D_{O_2}$ of $28.2 \text{ torr} \pm 10.4 \text{ torr}$, 1SD on an average. In decompensated patients, however, the mechanism leading to alveolar hyperventilation in depressed case of P_{aO_2} does not work properly as shown in Fig. 8. It was demonstrated that patients with decreased P_{aO_2} revealed a reduction in effective alveolar ventilation, probably reflecting the increase in total airway obstruction involved. It was fascinating that

approximately 30% of the patients showed normal PaO_2 more than 90 torr, regardless of the presence of chronic cardiac decompensation. We studied the basic mechanism producing arterial blood gas normal using A-aDO_2 as a physiologic indicator of pulmonary gas exchange and found from simultaneous hemodynamic study that these patients were in low cardiac output state. Patients with A-aDO_2 less than 15 torr exclusively showed cardiac index (CI) under 2.5 l/min/m^2 (Fig. 9), although decreased CI did not necessarily associate decreased A-aDO_2 . Patients with decreased A-aDO_2 less than 15 torr were evidenced to have decreased a-ETDCO_2 as shown in Fig. 10. Pathophysiology in decompensated hearts with low cardiac output was analyzed in terms of ventilation-perfusion relationship. If the relatively sufficient O_2 delivery might be assured with O_2 uptake and CO_2 production depressed less than normal in tissues at basic supine resting conditions and also if the steady state gas exchange between the alveolar to capillaries and the capillaries to tissue might be established, mixed venous O_2 and CO_2 tensions may possibly remain within normal limits or only slightly disturb. In this particular situations arterial blood gas is to be governed by ventilation to perfusion ratio in each respiratory units throughout the lung. The lung with overall pulmonary blood flow decreased less than normal induces relatively hyperventilated state, which results in relative "alveolar" hyperventilation unless ventilatory pattern is altered. Increased alveolar ventilation must be divided into 3 different pathophysiologic conditions of I, II and III as illustrated in Fig. 12. Condition I shows increased effective alveolar ventilation without any increase in alveolar dead space, condition II was in slightly to moderately increased effective alveolar ventilation (alveolar $\dot{V}_A$) with slightly to moderately increased alveolar dead space ventilation (alveolar $\dot{V}_D$), and condition III did not show any increase in effective alveolar $\dot{V}_A$ but show increased alveolar $\dot{V}_D$. These conditions could be separated by simultaneous measurement of A-aDO_2 and a-ETDCO_2 as shown in Fig. 12. It is clear that condition I lowers increased A-aDO_2 , which once might be caused by secondary pulmonary involvements, thereby showing normal arterial blood gas tensions at rest. That is why some patients with decreased cardiac output show normal or supernormal of PaO_2 . Supernormal PaO_2 more than 100 torr was seen in 10% of the decompensated patients. This

is not the case, if O_2 delivery extremely decreased with low cardiac output compared with amount of O_2 consumption in tissues or O_2 demand increased in the situations other than at supine resting state. These chronically decompensated patients could not compensate for increased oxygen demand in tissues produced by increased physical work during exercise. Their PaO_2 must be decreased when exposed over the extent to which patients might be allowed to extend their physical work capacity.

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