Physiopathology and Treatment of Chronic Cor Pulmonale Due to Dysventilation Syndrome

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133 patients with chronic cor pulmonale due to dysventilation syndrome were studied. Chronic obstructive pulmonary disease (COPD) was found, possibly for the first time in Japan, to be the most common etiological condition, occurring in 54% of the patients. Chronic cor pulmonale was clinically diagnosed as the appearance of right heart failure on admission. Patients were divided into two groups depending on clinical state, compensated and decompensated. There was a marked difference in arterial blood gases and electrocardiographic fluctuations between the states. Serial observations of these parameters and enlarged cardiac silhouette to the left on plain chest film provided diagnostic evidence for development to the decompensated state. Pulmonary artery pressure changes on exercise and during sleep at night has been considered to impair right heart function. Prognosis of chronic cor pulmonale largely depends on the concentrated therapy of the decompensated state. 85% of patients in the current study returned to the compensated state with active intensive therapy. Recent therapeutic progress has made control of this serious disease possible, despite the appearance of right heart failure. Laborious prolonged therapy appears to be essential in order to improve long-term prognosis.

PULMONARY heart disease (cor pulmonale) is cardiac dysfunction resulting from alterations in the structure and/or function of the lung. Such alterations derive from a variety of lung diseases, and the many classifications of cor pulmonale represent different pathological conditions. There are two quite separate mechanisms for right heart involvement following chronic lung disease. Chronic cor pulmonale may be classified into two main types: asphyxial cor pulmonale is mainly associated with disorders of blood gases; obliterative cor pulmonale is related to obstruction of the pulmonary vascular bed¹. Asphyxial cor pulmonale is also known as

dysventilation syndrome² and the most common manifestation of chronic cor pulmonale. The clinical aspect of chronic cor pulmonale has changed, reflecting the decreased incidence of pulmonary tuberculosis and recent technological progress in diagnosis and treatment. Here we analyzed chronic cor pulmonale due to dysventilation syndrome. This condition might be considered the most important pathophysiologically and therapeutically on clinical grounds.

MATERIALS AND METHODS

One hundred thirty three patients, 92 men and 41 women, with chronic cor pulmonale due to dysventilation syndrome admitted to our hospital during the past 10 years were employed for the current study. Ages ranged from 19 to 86 years and averaged 65 ± 12 years, 1SD. 72 patients had chronic obstructive pulmonary

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Fig.1. Schema of the developmental process of chronic cor pulmonale due to dys-ventilation syndrome. Cor pulmonale was a stage defined as the presence of right ventricular hypertrophy which was clinically divided into the compensated state and the decompensated state.

disease; 38 chronic pulmonary emphysema, 21 chronic bronchitic origin and 13 bronchial asthmatic origin. 34 patients had old pulmonary tuberculosis with or without thoracoplasty and/or pneumoresection; 13 with thoracoplasty, 4 with pneumoresection and 1 with both. The remaining 16 had pleural callosity. 20 patients were in diffuse pulmonary fibrosis; 15 with idiopathic interstitial fibrosis and 5 with secondary pulmonary fibrosis. 6 patients were in kyphoscoliosis and 1 patient had respiratory muscle disorder due to mitochondrial myopathy.

Regarding diagnosis of chronic cor pulmonale, although it was defined in 1961 by a WHO committee as right ventricular hypertrophy caused by chronic pulmonary disease³ we experienced difficulty in assessing the exact appearance of right ventricular hypertrophy clinically even using advanced technology. Therefore the patients in this study were diagnosed clinically with the evidence of right heart failure at time of admission to our hospital with signs of systemic venous congestion such as leg and/or facial edema, and liver enlargement accompanied by neck vein engorgement. Chronic cor pulmonale was considered to be a stage of pulmonary heart disorder which had ultimately developed right ventricular hypertrophy as shown in Fig. 1. The stage depicted below the dotted line in this figure was assessed

to have right ventricular hypertrophy and therefore to have chronic cor pulmonale. Chronic cor pulmonale was the stage defined above and was separated into two states, compensated and decompensated state (failure).

Arterial blood gas analysis, anteroposterior plain chest roentgenography and electrocardiography were performed sequentially from decompensated state at the time of admission to compensated state after appropriate therapy. Echocardiography was used to visualize the cyclic movement of the dilated right heart and/or compressed left ventricle and to pursue the dynamic consequences of right ventricular enlargement in some patients. The ventilatory function was studied using standard spirometry (Benedict Roth spirometer) in the compensated state. Right heart catheterization was performed in the compensated state. The effect of 25 watts mild exercise imposed by bicycle ergometer on pulmonary hemodynamics was studied in 11 patients. Hemodynamic study was also done at decompensated state in a limited number of patients. Hemodynamic alterations, transcutaneous oxygen tension and ventilatory tidal volume were simultaneously monitored for 8 hours at night from 10:00 pm to 6:00 am next day in 5 compensated patients with chronic cor pulmonale. A Swan Ganz flow directed right heart catheter inserted into main pulmonary

TABLE I CAUSES OF CHRONIC COR PULMONALE DUE TO DYSPVENTILATION SYNDROME

<i>Causative Disease</i>	<i>No. of patients</i>	<i>%</i>
<i>Chronic Obstructive Pulmonary Disease (COPD)</i>	72	54.1
<i>Pulmonary Emphysema</i>	38	28.5
<i>Chronic Bronchitis</i>	21	15.8
<i>Bronchial Asthma</i>	13	9.8
<i>Old Pulmonary Tuberculosis (TB-O)</i>	34	25.6
<i>Thoracoplasty and/or Pneumoresection</i>	18	13.6
<i>Pleural Callosity</i>	16	12.0
<i>Diffuse Pulmonary Fibrosis (PF-D)</i>	20	15.0
<i>Idiopathic Interstitial Fibrosis</i>	15	11.2
<i>Secondary Pulmonary Fibrosis</i>	5	3.8
<i>Kyphoscoliosis (KS)</i>	6	4.5
<i>Respiratory Muscle Disorder (RMD)</i>	1	0.8
<i>Total</i>	133	100.0

TABLE II ARTERIAL BLOOD GASES IN DECOMPENSATION (D) AND COMPENSATION (C) OF CHRONIC COR PULMONALE DUE TO DYSPVENTILATION SYNDROME

	<i>No. of patients</i>		<i>PaO₂</i>		<i>PaCO₂</i>	
	<i>D</i>	<i>C</i>	<i>D</i>	<i>C</i>	<i>D</i>	<i>C</i>
<i>COPD</i>	72	69	50 ± 11.1	→ 70 ± 9.0***	53 ± 15.7	→ 42 ± 6.5***
<i>TB-O</i>	34	27	45 ± 11.9	→ 72 ± 7.1***	59 ± 15.7	→ 49 ± 7.6**
<i>PF-D</i>	20	13	48 ± 9.1	→ 69 ± 9.3***	39 ± 10.7	→ 39 ± 3.7
<i>KS</i>	6	5	43 ± 13.2	→ 64 ± 13.7*	65 ± 18.5	→ 53 ± 8.3
<i>RMD</i>	1	1	41	→ 65	61	→ 57
<i>TOTAL</i>	133	115	48 ± 11.2	→ 70 ± 8.8***	53 ± 16.4	→ 44 ± 7.5***

mean ± 1SD (torr), ****p* < 0.001, ***p* < 0.005, **p* < 0.05

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

artery, Hellige Oxymonitor SM361 attached to precordial or abdominal skin and Impedance Pneumography OGR 5100 connected to the bilateral chest wall, were used respectively.

RESULTS

Causative diseases of chronic cor pulmonale due to dysventilation syndrome are listed in Table I. Chronic obstructive pulmonary disease (COPD) was a major cause of chronic cor pulmonale, involving 54.1% of patients with the condition. Old pulmonary tuberculosis (TB-O)

was the next most important cause involving 25.6% of patients. Diffuse pulmonary fibrosis (PF-D) involved 15.0% of patients and other causes included kyphoscoliosis (KS; 4.5%) and respiratory muscle disorder (RMD; 0.8%).

There were major differences in arterial blood gases between the decompensated state at a time of admission and the compensated state after the improvement of overt right ventricular failure in dysventilation syndrome with cor pulmonale. Arterial blood gases in both states are listed in Table II. Arterial O₂ tension (PaO₂) was markedly decreased to 48 torr ± 11.2 torr, 1SD

TABLE III VENTILATORY FUNCTION IN COMPENSATED CHRONIC COR PULMONALE DUE TO DYSPVENTILATION SYNDROME

	No. of patients	%VC (VC/predVC)	FEV1% (FEV1/FVC)
COPD	61	63 ± 15.7	49 ± 10.4
TB-O	28	43 ± 13.5	71 ± 18.7
PF-D	15	59 ± 18.8	83 ± 11.2
KS	5	26 ± 1.9	80 ± 5.9
RMD	1	25	77
TOTAL	110	55 ± 18.6	61 ± 19.1

mean ± 1SD (%)

Abbreviations: VC = vital capacity; predVD = predicted vital capacity; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity

TABLE IV FREQUENCY OF RESPIRATORY ENCEPHALOPATHY "CO₂ NARCOSIS" AND NARCOTIC CO₂ LEVEL

	No. of patients	CO ₂ Narcosis	
		No. of patients (%)	PaCO ₂ level
COPD	72	11 (15%)	85 ± 10.5 torr
TB-O	34	12 (35%)	88 ± 10.5 torr
PF-D	20	0 (0%)	
KS	6	1 (17%)	97 torr
RMD	1	1 (100%)	92 torr
TOTAL	133	25 (19%)	87 ± 10.2 torr

mean ± 1SD

TABLE V ELECTROCARDIOGRAPHIC ALTERATIONS ACCOMPANIED BY DECOMPENSATED STATE EXPRESSED AS FURTHER DEVIATION FROM COMPENSATED STATE OF CHRONIC COR PULMONALE (24 patients)

Further ECG fluctuations	No. of patients	(%)
Significant Increase in SV_s	17	(71%)
Presence of Inverted $TV_1 \sim V_3$	15	(63%)
Rightward Shift of Axis ($> 30^\circ$)	14	(58%)
Significant Increase in RV_1	9	(38%)
Increase in $P_{II, III}$ (> 1.5 mm)	7	(29%)
Presence of Arrhythmia	6	(25%)
Presence of RBBB (complete, incomplete)	4	(17%)

in the decompensated state (D), however it was significantly ($p < 0.001$) increased to 70 torr ± 8.8 torr, 1SD in the compensated state (C) with adequate treatment. Arterial CO₂ tension (PaCO₂) was also increased to 53 torr ± 16.4 torr, 1SD in the decompensated state and significantly ($p < 0.001$) decreased to 44 torr ± 7.5

torr, 1SD in the compensated state. PaO₂ in the decompensated state was significantly decreased in COPD ($p < 0.001$), TB-O ($p < 0.001$), PF-D ($p < 0.001$) and KS ($p < 0.001$) compared with the compensated state. The PaCO₂ in the decompensated state was markedly increased in COPD ($p < 0.001$) and TB-O ($p < 0.005$) com-

Fig.2. Chest roentgenogram and echocardiogram in the compensated state (1985.12.25 and 1987.2.20) and decompensated state (1987.1.20) in a 72 year old female patient with chronic cor pulmonale due to old pulmonary tuberculosis (TB-O) with right thoracoplasty. Enlarged cardiac silhouette and compressed left ventricle at end-diastolic phase were demonstrated. RV = right ventricle, LV = left ventricle, PA = pulmonary artery pressure (mean), CO = cardiac output (index).

pared with the compensated state, although there was no significant difference in PaCO₂ in PF-D and KS. We were able to study ventilatory function in the compensated stable state. As listed in Table III, COPD was characterized by decreased FEV1% of 49% ± 10.4%, 1SD, suggesting obstructive ventilatory impairment. Other diseases, however, were characterized by considerably decreased %VC with fairly well retained FEV1%,

suggesting restrictive ventilatory impairment. The presence of neurologic signs such as mental confusion, agitation, diurnal somnolence and semicoma produced by CO₂ retention indicated a diagnosis of respiratory encephalopathy ("CO₂ narcosis"). Respiratory encephalopathy was caused during the therapeutic process from the decompensated state to the compensated state by advanced gas exchange abnormality in 19% of

Fig.3. Comparison of cardiothoracic ratio (CTR) between decompensated state (D) and compensated state (C) of chronic cor pulmonale due to dysventilation syndrome. It was shown that decompensated cardiac enlargement permitted the cardiac silhouette to deviate more leftward than rightward. Left and right indicate right part and left part of CTR, respectively.

TABLE VI EFFECT OF 25 WATT MILD EXERCISE ON PULMONARY HEMODYNAMICS AND BLOOD GASES IN COMPENSATED STATE OF CHRONIC COR PULMONALE

	No. of patients	Rest		Exercise
PAm (mmHg)	11	24.9 ± 6.6	→	51.6 ± 9.9**
CI (l·min ⁻¹ ·m ⁻²)	10	2.70 ± 0.63	→	4.90 ± 1.86**
TPR (mmHg·l ⁻¹ ·min)	10	6.5 ± 3.04	→	7.7 ± 3.91**
SAm (mmHg)	9	100 ± 11.5	→	133 ± 26.6**
PaO ₂ (torr)	15	71.9 ± 7.6	→	53.7 ± 5.3**
PaCO ₂ (torr)	15	45.4 ± 5.9	→	50.1 ± 6.5*
PvO ₂ (torr)	10	37.0 ± 3.4	→	25.6 ± 2.2**

mean ± 1SD, paired t test; **p < 0.001, *p < 0.005

Abbreviations: PAm = pulmonary artery mean pressure; CI = cardiac index; TPR = total pulmonary vascular resistance; SAm = systemic artery mean pressure; PaO₂ = arterial O₂ tension; PaCO₂ = arterial CO₂ tension; PvO₂ = mixed venous O₂ tension

the patients (25/133) and its narcotic PaCO₂ was 87 torr ± 10.2 torr, 1SD (Table IV). This was most common in patients with TB-0 and appeared in one patient with RMD; there was no narcotic patients in PF-D. As seen in Table V the most common electrocardiographic fluctuation was further appreciable increase in S_v (appearance of deeper S) seen in 71% of the patients at decompensation, when right ventricular failure developed. Appearance of T wave inversion including biphasic or flattened T was the second most common finding (63%) in the decompensated state.

Rightward shift of electrical QRS axis greater than 30 degrees was seen in 58% of patients. Significant increase in R_{v1}, increase in height of P_{II,III} more than 1.5 mm, provoked arrhythmia, and the presence of complete or incomplete right bundle branch block were less common findings.

Chest roentgenographic and echocardiographic abnormalities in chronic cor pulmonale are shown in Fig. 2. The centre portions show the decompensated state and the sides show the compensated states of chronic cor pulmonale.

Fig.4. Repeated elevation of pulmonary artery pressure (PA) in accordance with the appearance of disturbed ventilation induced spontaneously during sleep at night in a 53 year old patient with chronic cor pulmonale due to old pulmonary tuberculosis with left thoracoplasty. A mirror image was observed between pulmonary artery mean pressure (PAm) and trans-cutaneous oxygen tension (P_{TCO_2}). V_T = tidal volume measured by impedance pneumography.

TABLE VII COMPARISON BETWEEN ELEVATION OF PULMONARY ARTERY MEAN PRESSURE INDUCED BY NOCTURNAL HYPOXEMIA AT NIGHT AND SUBMAXIMAL EXERCISE IN THE DAYTIME IN CHRONIC COR PULMONALE

	No. of patients	PAm (mmHg)	
Control (before sleep)	5	19.2 ± 2.7	
Nocturnal Hypoxemia	5	59.6 ± 6.8	**
Submaximal Exercise	5	49.6 ± 7.4	* **

mean $\pm$ 1SD, paired t test; ** $p < 0.001$, * $p < 0.05$

Abbreviation: PAm = pulmonary artery mean pressure

Echocardiography shown is the short axis view of the left ventricle at end-diastolic period. The left ventricle is markedly compressed by the enlarged right ventricle in the decompensated state. There is no sign of pericardial effusion. Compression of the left ventricle in the diastolic phase disappeared in the compensated state after successful therapy. Cardiothoracic ratio (CTR) was increased significantly ($p < 0.01$ by paired t test)

from $52\% \pm 7.5\%$, 1SD in the compensated state to $64\% \pm 12.3\%$, 1SD in the decompensated state because of further enlargement of the right ventricle. Cardiac silhouette, however, with right ventricular enlargement on posteroanterior view of chest roentgenogram was much more deviated to the left than to the right, being quite similar to that of left ventricular enlargement. The left part of CTR was significantly ($p < 0.001$ by

paired *t* test) increased in 9 decompensated patients with chronic cor pulmonale as shown in Fig. 3. It averaged $43\% \pm 6.8\%$, 1SD in the decompensated state and $35\% \pm 5.7\%$, 1SD in the compensated state, whereas the right part of CTR averaged $21\% \pm 7.4\%$, 1SD in the decompensated state and $17\% \pm 3.9\%$, 1SD in the compensated state.

The effect of mild exercise on pulmonary hemodynamics was studied in 15 compensated patients with chronic cor pulmonale. As seen in Table VI pulmonary artery mean pressure (PAm) was significantly ($p < 0.001$ by paired *t* test) increased from $24.9 \text{ mmHg} \pm 6.4 \text{ mmHg}$, 1SD at rest to $51.6 \text{ mmHg} \pm 9.9 \text{ mmHg}$, 1SD on exercise, while systemic arterial pressure (SAm) was increased from $100 \text{ mmHg} \pm 11.5 \text{ mmHg}$, 1SD to $133 \text{ mmHg} \pm 26.6 \text{ mmHg}$, 1SD. PAm increased to much greater extent than SAm, while oxygen tension of arterial blood and of mixed venous

blood was significantly decreased during pre-scheduled 25 watt exercise.

Some patients with chronic cor pulmonale developed increased pulmonary artery pressure accompanied by dysventilation induced spontaneously during sleep at night. Fig. 4 shows simultaneous recordings of pulmonary artery pressure (PA), pulmonary artery mean pressure (PAm), trans-cutaneous oxygen tension (P_{TCO_2}) and tidal volume (V_T) breathing room air during sleep in a 53 year old male patient with chronic cor pulmonale due to old pulmonary tuberculosis with left thoracoplasty. Pulmonary artery pressure showed the same pattern several times a night, a great peak following gradual increment of precedent peaks and then a gradual return to the previous level following repeated subsequent small peaks. Such silhouette of pulmonary artery pressor response reflecting a mirror image against P_{TCO_2} in the tracing looked like a mountain range. The peak pulmonary artery pressure at night was significantly ($p < 0.05$ by paired *t* test) higher than that of submaximal exercise in the daytime in 5 individuals, as seen in Table VII.

Therapeutic agents employed in 133 decompensated patients are listed in Table VIII. Bronchodilators including expectorants combined with antibiotics were the most common drug therapy used to reduce airway obstruction and alleviate the inflammatory process. Loop diuretics were widely used to remove fluid accumulation in the body in the decompensated state under fluid restriction. Fifty-one of 133 decompensated patients were treated with a respirator and 33 patients returned to the compensated state with complete withdrawal from respirator control. Sixteen patients, however, died despite active elaborate therapy. The

TABLE VIII THERAPY OF DECOMPENSATED CHRONIC CHRONIC COR PULMONALE DUE TO DYS-VENTILATION (133 PATIENTS)

Therapeutic Agent	No. of patients	(%)
Bronchodilator (expectorant)	130	(98)
Antibiotics (antibacterial agent)	125	(94)
Loop Diuretics	109	(82)
Digitalis	64	(48)
Diamox	48	(36)
Catecholamine	32	(24)
Corticoids	24	(18)
Antiulcerative Agent	98	(74)
Respirator	51	(38)

TABLE IX OUTCOME IN DECOMPENSATED PATIENTS TREATED WITH AND WITHOUT ARTIFICIAL RESPIRATOR

	No. of patients	Discharge with Recovery	Impossible Withdrawal	Death
COPD	72 (20)	68 (16)	1 (1)	3 (3)
TB-O	34 (17)	27 (11)	0 (0)	7 (6)
PF-D	20 (9)	13 (3)	0 (0)	7 (6)
KS	6 (4)	5 (3)	0 (0)	1 (1)
RMD	1 (1)	0 (0)	1 (1)	0 (0)
TOTAL	133 (51)	113 (33)	2 (2)	18 (16)

() indicates No. of patients treated with artificial respirator

Fig.5. Mortality of chronic cor pulmonale according to causative disease with and without the use of a respirator.

TABLE X CAUSATIVE FACTORS LEADING TO DECOMPENSATION OF CHRONIC COR PULMONALE AND THEIR FREQUENCY (133 PATIENTS)

Causative Factor	No. of patients	(%)
Respiratory Infection	98	(74)
Overwork	64	(48)
Overintake of Water	45	(34)
Fever	24	(18)
Sleep Disturbance	16	(12)
Loss of Appetite	8	(6)
Diarrhea · Vomiting	5	(4)
Unknown	13	(10)

patients treated without the use of artificial respiration were all under controlled oxygen therapy. Therapeutic intervention, with and without a respirator, permitted 113 of 133 decompensated patients (85%) to return to the compensated state and to be discharged from hospital with fair improvement (Table IX). Total mortality was 14% with 18 deaths among 133 decompensated patients. Mortality according to causative disease is shown in Fig. 5. The highest mortality was observed in PF-D with decompensated cor pulmonale. This was 35% with 7 deaths among 20 patients. The lowest mortality was 4%, seen in COPD. Causative factors leading to decompensation of chronic cor pulmonale were

analyzed and are listed in Table X. Respiratory infection was the most common basic cause of right ventricular decompensation, and overwork and increased fluid intake proved to be the second and the third most important triggering factors for progression to cardiac decompensation.

DISCUSSION

Epidemiologic studies of the frequency of causative diseases of chronic cor pulmonale in Japan have shown old pulmonary tuberculosis (TB-O) to be the most common cause^{4,5}. Clinical observation in our NCVC hospital established recently in 1977 for the study of cardiovascular diseases found chronic obstructive pulmonary disease (COPD) to be the most frequent etiological disease. It affected more than half the patients with chronic cor pulmonale (54.1%) (Table I) and our figures agree with reports from western countries over a number of years^{6,7}.

Chronic cor pulmonale was considered to be a "stage" of right ventricular hypertrophy such as defined by WHO in 1961³ as a final consequence of altered pulmonary circulation in respiratory disease. Right ventricular failure does not necessarily indicate right ventricular hypertrophy and the failure has been considered to lie in the stage of right ventricular enlargement which signifies dilatation and/or hypertrophy. Although right ventricular dilatation alone is known to disappear

after successful therapy of cor pulmonale, some thickened right ventricular wall must remain. Right ventricular hypertrophy includes the compensated and decompensated states (Fig. 1). Right ventricular enlargement was developed in decompensated cor pulmonale as seen in Fig. 2. The right ventricle once enlarged in the decompensated state possibly returns to the basal level but must have some thickness of right ventricular wall remaining in the compensated state. Decompensation of the right heart due to dysventilation syndrome has been reliable diagnostic evidence of chronic cor pulmonale.⁸ Chest roentgenographic findings of enlarged right heart on cardiac silhouette in patients with decompensated chronic cor pulmonale has not been well recognized. Cardiac enlargement on chest roentgenogram was apparently seen in decompensated chronic cor pulmonale, probably indicating right ventricular dilatation combined with right atrial enlargement. It has been reported for a number of years that a CTR increase to the left was a sign of enlargement of the left ventricle and was frequently seen in left-sided cardiac diseases with or without left ventricular dysfunction. Enlarged cardiac silhouette to the left of the midline of the spine on postero-anterior chest roentgenogram, however, was also seen in patients with chronic cor pulmonale, especially in the decompensated state. Combined echocardiographic and radiologic studies revealed that right ventricular enlargement in chronic cor pulmonale was responsible for CTR increased to the left without signs of pericardial effusion (Fig. 2, 3). Such findings are useful not only diagnostically but also therapeutically for the proper assessment of pathophysiologic abnormalities.

Blood gases were quite different between the compensated and decompensated states. PaO_2 greatly decreased and PaCO_2 significantly increased in the decompensated state (Table II). Arterial blood gases in chronic cor pulmonale were shown to vary depending on the cardiac functional state. Electrocardiographic fluctuations due to the presence of the decompensated state of cor pulmonale were studied and assessed from the alterations of serial standard 12 lead electrocardiography performed through decompensated to compensated states. Table V shows these variations dependent on cardiac states.⁹ Thus parameters relating to blood gas and electrocardiography alone are not particularly useful in the diagnosis of chronic cor pulmonale,

but sequential observations are useful in the estimation of progression to decompensated cor pulmonale. Ventilatory function in some patients with chronic cor pulmonale revealed characteristically decreased FEV1% in COPD and decreased %VC in TB-O, in PF-D and in KS which might be each responsible for development of chronic cor pulmonale (Table III). Respiratory encephalopathy was seen in diseases that produce alveolar hypoventilation such as COPD, TB-O, KS and RMD. Narcotic level in chronic stage of cor pulmonale was assessed around 87 torr in PaCO_2 on average (Table IV) and immediate ventilatory support must be administered in this situation.

Pulmonary hemodynamic response induced by exercise was used to analyze the developmental process of chronic cor pulmonale. 25 watt mild exercise produced doubled elevation of pulmonary artery pressure for approximately thirty percent increase in systemic artery pressure (Table VI). Even mild exercise must impose more load on pulmonary circulation than on systemic circulation.¹⁰ Right ventricular overload imposed by exercise in chronic compensated cor pulmonale might impair right ventricular function and therefore lead to the decompensated state. Further elevation of pulmonary artery pressure was observed during sleep at night (Fig. 4). The mechanism of this pressor response was considered to be hypoxic pulmonary vasoconstriction due to alveolar hypoxia induced by spontaneous dysventilation.¹¹ This is evidenced by a mirror image between tracings of pulmonary artery pressure and trans-cutaneous oxygen tension. Peak elevation of pulmonary artery mean pressure (PAm) during sleep exceeded significantly PAm elevation induced by experimental submaximal exercise (Table VII).

Prognosis of chronic cor pulmonale largely depends on treatment for the decompensated state. Prompt and adequate therapeutic response to decompensation is required. Principal treatment of decompensated chronic cor pulmonale due to dysventilation syndrome is to relieve pulmonary hypertension as soon as possible by improving gas exchange through active continuous therapy. Bronchodilators, antibiotics and loop diuretics are essential in cases of severe dysventilation syndrome with right ventricular failure (Table VIII). Digitalis was sometimes effective⁶ for congestive failure. Diamox was also effective for chronic renal overcompensation with disproportionate increase of plasma bicarbonate ion in acid base regulation. If blood

pressure is lowered, catecholamine must be administered to keep the main organ circulation from deteriorating. Antiulcerative agents, including H_2 -receptor blockers, are recommended to prevent gastroduodenal ulcers which are frequently caused by coexistent respiratory failure. Controlled or assisted ventilation using an artificial respirator is essential to some decompensated patients in order to improve disturbed gas exchange and reduce elevated pulmonary artery pressure. Mortality of chronic cor pulmonale according to causative disease is summarized in Table IX and Fig. 5. Some patients with chronic cor pulmonale died in decompensated state despite active therapy and their mortality was 14% (18 among 133 patients). Patients treated with a respirator, however, showed high mortality of 31% (16 among 51 patients), although mortality in decompensated patients treated without a respirator was only 2.4% (2 among 82 patients). It was shown that the patients treated with a respirator were all more serious than those without a respirator. 38% (51 among 133 patients) of the patients were treated with a respirator: 16 died and 2 were unable to be withdrawn from the respirator. PF-D showed high mortality of 35% (7 among 20 patients), while mortality in COPD was only 4% (3 among 72 patients). Chronic cor pulmonale with PF-D was characterized by decreased $PaCO_2$ (Table II), maintaining hyperventilated state by some centripetal nervous stimulants originating from low compliant lung tissue and lying all the time in dyspneic state. Extremely lowered PaO_2 , despite hyperventilation due to the compensatory mechanism in PF-D with decompensated cor pulmonale, must have greatly increased alveolar arterial O_2 tension difference which is an expression of grave gas exchange abnormality in the lung. Chronic cor pulmonale caused by PF-D was considered to be much more severe pathophysiologically than other dysventilation syndromes.

It must be emphasized that maintainable therapy for compensated as well as for decompensated chronic cor pulmonale is important. Controlled oxygen therapy, including prolonged home oxygen therapy, was recommended in selected patients.¹² Pulmonary artery pressure elevation with a profile silhouette looking like a mountain range during sleep (Fig. 4) must be looked for as an indicator of the deterioration of chronic cor pulmonale. Preventive strategies for the pressure increase in the pulmonary artery

are not currently available, although nocturnal oxygen therapy has been proposed.¹³

Chronic cor pulmonale was considered to be universally fatal in Japan 20 to 30 years ago. However, since that time, a number of investigative endeavors have been directed towards its early detection. Recent therapeutic progress has made possible to control this serious disease and to cure it even though right ventricular failure may be present. So it is not too late for definitive diagnosis to be made by the appearance of right heart failure. Indeterminate diagnosis which stems from difficulties in the clinical estimation of right ventricular hypertrophy is useless and rather dangerous in that it delays appropriate therapeutic measures. Eighty-five percent of patients may now return from the decompensated state to the previous compensated state, as seen in Fig. 2 and listed in Table II, IX. Although the prognosis of chronic cor pulmonale has been greatly improved, the long-term prognosis must still be considered to be poor. Energetic and prolonged therapy is essential to improve that poor long-term prognosis, once chronic cor pulmonale is diagnosed.

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