Symposium* on
Treatment of Heart Failure

(Chairman: Prof. Dr. Kenzo Kusui)

1. Some Hemodynamic and Clinico-pathological Consideration of Congestive Heart Failure with Special Reference to Therapeutic Effect
2. The Pathogenesis and Treatment of Right Heart Failure with Special References to Cor Pulmonale
3. Clinical Aspect of Digitalis Treatment in Congestive Heart Failure Due to Acquired Heart Disease
4. Treatment of Congestive Heart Failure Infancy and Childhood
5. Discussion

1. Some Hemodynamic and Clinico-pathological Consideration of Congestive Heart Failure with Special Reference to Therapeutic Effect

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In this symposium on congestive heart failure (CHF) in particular to its therapeutic problems the authors were engaged in the two matters, both receiving hitherto relatively few attentions. The one was the left ventricular performance in various diseased states particularly under influences of some cardiovascular drugs, the investigation with the aid of transeptal left heart catheterization combined with radioisotope indicator-dilution method. The other was a clinico-pathological one with a special intention to reveal some factors related to the therapeutic responsibility or rather "refractoriness", besides an appropriate classification of various types of CHF.

I. Hemodynamic Studies Particularly Concerned with Left Ventricular Performance

Materials and Methods

A total of twenty-six patients with various cardiovascular diseases were selected: including 8 cases of mitral valve disease of which 3 had atrial fibrillations, 8 combined valvular disease of which 2 had atrial fibrillation, 1 thyrotoxic heart disease with atrial fibrillation, and 4 cases of hypertensive, and 5 of miscellaneous heart diseases, the latters without any fibrillation. These patients were considered in various degrees of CHF, that is, of latent or manifest ones, and as regards the left ventricular end-diastolic pressure (LVEDP) 7 cases had the values above 12 mm. Hg regarded as the upper normal limit at rest.\(^1\)

In these patients both right and left heart
catheterizations, the latter via transseptal route as described in detail elsewhere, were simultaneously carried out, thus obtaining pressure curves and blood samples from both sides of heart at the same time. Cardiac output was measured during steady state by the direct Fick method, and left ventricular external work per min was calculated as the product of ventricular output and brachial arterial mean pressure determined directly from the pressure curve through intra-arterial Courand needle. These values per beat of left ventricle were estimated as referred to the mean heart rates during measurements. Values of the actually developed pressure during left ventricular ejection periods per min., i.e., the so-called tension-time-index (TTI, mm. Hg sec./min.) after Sarnoff et al. one reliable measure of the myocardial oxygen consumed per min. by that ventricle on the one hand, were determined according to their original paper. Consequently the ratio of external work value to TTI may be considered as an index of the external work efficiency. Similarly the mean stroke volume per ejection period of left ventricle, namely the mean systolic ejection rate (MSER, ml./sec./M²) by Levine et al. regarded as one indicator of left ventricular contractility, was calculated in use of the original method. Measurements of the left ventricular volume, i.e., the end-diastolic and end-systolic (residual) volumes (EDV & ESV), were succeeded in twenty cases of this series utilizing the radioisotope indicator-dilution technic through left ventricular Brockenbrough catheter with the aid of precordial scintillation detector that was described originally by Folse et al. and recently somewhat modified at the authors' department. Thus determined values of EDV and ESV, however, may be regarded as functional or effective ones rather than anatomical or actual ventricular volumes, since both were primarily derived from the fraction of isotope discharged from left ventricular chamber per beat, that seemed equivalent to the ratio of forward stroke volume to end-diastolic volume (FSV/EDV) in this case irrespective of the aortic and/or mitral regurgitant flow, if present. All the values as obtained above, if corrected per square meters of body surface areas of the individual patients suitably for comparison.

The drugs used in this investigation were all infused through right heart catheter, then the second measurements were repeated as followed: (1) 0.4 mg. of lanatoside C was injected at first and then at the 30th minute the more 0.2 mg. was added, 30 minutes thereafter the re-measurement was performed, i.e., at the 60th minute from the onset of first injection, (2) similarly 30 minutes after the onset of an injection of 250 mg. of aminophylline, (3) a noradrenaline solution of 5 μg per ml. was slowly infused till the brachial arterial systolic pressure leveled off at about 170–200 mm. Hg, during which the second measurement was carried out, (4) also a 0.5 μg/ml. solution of angiotensin was administered in the same way as noradrenaline. No significant complications were noticed in any case.

**RESULTS**

**Left ventricular flow, pressure, and work.** These values before and after drug administrations were illustrated in Figs. 1 and 2, compa-

\[\text{Fig. 1. There were illustrated the variations of values of cardiac index (upper left), mean heart rate (upper right), stroke index (lower left) and left ventricular systolic pressure (lower right), each before (B.) and after (A.) the administrations of various cardiovascular drugs, namely aminophylline, lanatoside C, noradrenalin and angiotensin. In the control cases there were examined the spontaneous variations of individual values during two successive measurements (I & II) without any medications, thereby for assessment of the net effects of drugs administered.}\]
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values, i.e., ESV, EDV as well as FSV/EDV, were indicated in Figs. 3 and 4, especially in the latter related with other hemodynamic parameters, both before and after various drug administrations. There it was observed at first that the fraction of left ventricular volume ejected

Fig. 2. Similarly to the former figure here illustrated were the variation of left ventricular stroke work (upper left), tension-time index (upper right), ratio of left ventricular external work to tension-time index, that is, left ventricular external work efficiency (lower left) and mean systolic ejection rate, individually before and after drug administrations.

ing to the not medicated control ones. There it was observed that the left ventricular forward flow was more or less increased in almost all cases after drug administration, also associated with the elevated left ventricular pressure except in the case of aminophylline medication, so that the external work of left ventricle was augmented in almost all but aminophylline-injected cases. Values of actually developed tension, i.e., TTI per min. fairly comparable to the oxygen consumption of left ventricle, were observed markedly increased during course in the cases of induced hypertension such as after noradrenaline or angiotensin infusion, but seemingly in the other cases they were not so evidently differed or sometimes rather decreased as compared with control ones. In consequence the external work efficiency, i.e., the ratio of forward stroke work to TTI (FSW/TTI), of left ventricle after various medications was seen fairly divergent, excepting after acute digitalization where many cases seemed to show more improved efficiency than the others especially as compared with the controls. Similar situations were more evidently noticed with respect to the values of MSER, which were most apparently increased in the digitalized cases and somewhat so after aminophylline injection among others.

Left ventricular functional volume. These

Fig. 3. Similarly the variations of fraction of left ventricular volume ejected per beat, i.e., ratio of left ventricular forward stroke volume to end-diastolic volume of that ventricle (upper left), left ventricular end-systolic (residual) volume (upper right), left ventricular end-diastolic volume (lower left) and left ventricular end-diastolic pressure (lower right) induced individually by the drug used were illustrated.

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Fig. 4. There were illustrated the relations of varying left ventricular end-diastolic volumes through various medications to those of corresponding left ventricular end-diastolic pressure (upper left), left ventricular forward stroke work (upper right), left ventricular stroke index (lower left). Finally there were illustrated rather schematically the characteristic hemodynamic effects of aminophyllin and cedilanid comparatively to each other, there also suggested the probable case indication the intermediate response of these two drugs (lower right).
per beat, i.e., FSV/EDV, after medication was elevated in almost all cases of aminophylline and also probably in two cases of lanatoside C, though these in the remaining cases were somewhat lowered or likely comparable with the control ones, which seemingly well corresponded to the following observation that the calculated values of EDV and ESV after medication were apparently augmented in almost all but the aminophylline-injected cases where the variations of these values not so differed from the controls or showed something declines. From the other point of view the increased forward volume from left ventricle after various medications as aforementioned was associated with the not increasing but rather decreasing EDV and ESV after aminophylline injection, indicating an excellent contrast to the most cases after other drugs associated with the apparently increasing EDV and ESV of left ventricle. As for the variations of forward stroke work (FSW) as well as end-diastolic pressure of left ventricle (LVEDP) after drug administration both relating to those of EDV there seemed to be some parallel relationships, that is, the more the EDV were augmented, the more the FSW and the LVEDP were elevated, and vice versa in general but few exceptions as later discussed.

COMMENTS

Since the era of Frank and Starling there has been much interest in the functional ventricular volume as a fundamental regulatory factor of ventricular performance, though such investigations about actual ventricular volume particularly of left ventricle in various diseased states have been exceedingly scanty largely owing to many difficulties encountered in the practical execution. The authors’ method in the present investigation originally according to Folse et al.5) may also be not complete one for the present purpose, so far as radioisotope indicator-dilution method based upon many assumptions was employed,7,6) though in the near future more improved method will clear away much details still debatable. However, under such limitations involved in the present available procedures it may be most likely concluded from the observations as aforementioned that aminophylline among other cardiovascular drugs studied can augment FSV not depending upon the increasing left ventricular volume but rather with the decreasing ones, which seems to be at first sight not compatible with the traditional Starling’s law of heart, but rather to some extent in accord with the recent observations in the intact dogs under various stresses6,10) and probably with those in the normal human during exercise.11,12) This may be not surprising from the other point of view, that is, with reference to the fact that the left ventricular fraction ejected per beat, i.e., FSV/EDV of left ventricle, is apparently augmented after aminophylline injection, which would reflect a direct stimulant effect of this drug upon left ventricular myocardium. Fairly in contrast with the case of aminophylline the augmented FSV after an acute digitalization as above described seems to be well according to the original Starling’s law, as there have been almost always accompanied with the apparently increased left ventricular volume, which on the other hand may account for the elevated FSW in nearly proportion to the increasing EDV of left ventricle. The applicability of Starling’s law to the human left ventricle in variously ill states has been recently exemplified especially by Braunwald et al. and others,13-15) in particular in the same individuals with pulsus alternance.10) Though the circumstances may be so at the first glance, it seems questionable whether the myocardial efficiency or more strictly contractility of that ventricle functioning at the more increased EDV may be actually improved or strengthened, since on the one hand according to the law of Laplace17) the ventricle contracting with the more increased volume (that is nearly proportional to its radius) must need the more wall tension to develope the same pressure (P = T/R) so that the utilization of tension energy to effective ventricular work may be the more reduced. This seems, however, not always true for the case of acute digitalization just investigated, as there the calculated efficiency of left ventricular work, i.e., the ratio of external work value to tension-time-index, may be observed rather improved after digitalization in all but one case. And again as viewed from the variations of MSER, which are signigicantly
elevated in most cases after acute digitalization, though the mere elevation of MSER might be expected from the ventricle of increasing functional volume without any increase of myocardial contractile power per se, this probability may be properly precluded in most present cases after digitalization, since in these cases studied the ejection period was rather mostly decreased (not tabulated) in the face of the markedly increased stroke volume thereof. Lastly, as for the LVEDP there seems some direct relationship between the variations of EDV of left ventricle, which may suggest some constancy of the left ventricular distensibility in each individual cases throughout before and after various medications, though in few cases seemingly not so most probably due to the fact that the EDV here estimated as rather functional ones may sometimes considerably differ from the actual or in other words net end-diastolic volume in reality referable to the LVEDP, e.g., such as in the presence of significant regurgitation through mitral valve, particularly under various drug effects. However, the definite conclusion about these much disputable details should await further penetrating investigations.

Summary

A sum of twenty-six cases of various degrees of CHF were studied through right and left heart catheterizations simultaneously, of which twenty cases were abled to be determined the left ventricular functional volume, utilizing the radioisotope indicator-dilution method. In this paper special attention were directed to some hemodynamic factors regulating left ventricular performance in various diseased states in particular under acute effects of some choiced drugs such as aminophylline, lanatoside C, noradrenaline and angiotensin. It was observed at first that various hemodynamic parameters such as left ventricular forward flow, pressure, and work were more or less increased after individual medication in almost all cases. Subsequently, the left ventricular volume as one fundamental factor regulatory to cardiac performance was investigated with special reference to other hemodynamic parameters as cited above. Thus there was seemingly observed that after aminophylline injection the left ventricular stroke volume was augmented not depending upon the increasing end-diastolic volume of left ventricle, or in other words there the left ventricular fraction ejected per beat, i.e., FSV/EDV, was characteristically elevated, fairly in contrast with the other cases such as after acute digitalization among others, where the augmented forward volume was associated with the apparently increasing EDV of that ventricle. From these observations in the present investigation it may be most probably concluded that the left ventricular performance of various ill states seems to be augmented not always according to Starling’s law under some stimulant effects such as induced by aminophylline, though on the other hand such as after an acute digitalization the situations may be rather in accord with the original law of heart ascribed to Starling and his associates. Further arguments were elaborated with reference to myocardial efficiency or rather contractility of left ventricle particularly under the effects of acute digitalization.

II. Clinico-pathological Studies Concerned with Various Types of CHF

Materials and Methods

A total of forty-eight patients of various cardiovascular diseases as indicated for details in Table I were collected, who died following individually short or long admission into the authors’ clinic and were all autopsied thereafter. For these patients detailed clinical data as well as full course in particular concerned with their therapeutic results were thoroughly reviewed comparing with the minute pathological findings especially of various important organs such as lung, liver, kidney, and adrenal gland besides themselves of heart. Tissue stainings employed were such as hematoxylin-eosin, Mallory’s azan, and PAS methods.

Results

There seemed to be observed about four characteristic categories in the relations between clinical details and pathological findings, arbitrarily named in this paper such as A+, B+,...
<table>
<thead>
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<th>Original Cardiovascular Diseases</th>
<th>Types of Congestive Heart Failure</th>
<th>Total</th>
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<tbody>
<tr>
<td>Rheumatic Heart Disease</td>
<td>Group-A 6</td>
<td>Group-B 12</td>
</tr>
<tr>
<td>Subacute Bacterial Endocarditis</td>
<td>3</td>
<td>1</td>
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<td>1</td>
</tr>
<tr>
<td>Primary Myo-or Endomyo-pathies</td>
<td>2</td>
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<tr>
<td>Congenital Heart Disease</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td><strong>12</strong></td>
<td><strong>18</strong></td>
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</table>

C- and D-groups individually as followed, of which alone the cases involved in D-group died accidentally under the states considered at least free of usual CHF and accordingly were to be rather regarded as the controls of other three groups all with evident CHF. The numbers of these individual group-cases belonging to the various original cardiovascular diseases were illustrated in Table I. Microscopic photographs of various pathological changes observed rather typically in the individual group-cases were indicated in Fig. 5.

1. A-group: Clinical features were characterized as following, (1) frequent attacks of paroxysmal dyspnea with marked tachycardia were prominent sometimes associated with significant sweating and some mental disturbances, though the clinical signs suggesting pulmonary as well as systemic congestion were relatively mild, (2) relatively frequent complications of various types' inflammations such as rheumatic fever with carditis, subacute bacterial endocarditis and/or bronchopulmonary infections, (3) full course from the onset of symptoms about CHF till the lethal end seemed relatively short, that is, only seven months on the average, as compared with the other B- and C-groups, not indicating significant therapeutic effects throughout the course despite forcible treatments, therefore rather regarded as therapy-resistant or so-called "refractory" cases of CHF in the strict sense. 29, 35.

From the pathological view the characteristic findings were as followed, (1) relatively mild congestion and edema of all visera including liver, lung etc., (2) liver cells in general free of necrosis and/or bleedings anywhere showed, however, marked centrolubular fatty metamorphosis consisted of large fat-droplets, extending more than half of all the acini observed, (3) some atrophic and degenerative changes in the tubular epithelia of kidney particularly on the distal convoluted portions, (4) rather atrophic adrenal cortex having moderate lipid-contents in the deeper layers, i.e., zona reticularis, (5) most significantly the heart of this group indicated

Fig. 5. Illustration of various microscopic findings observed rather typically in the individual group-cases as followed: A-group (first rank), rheumatic myocarditis (A-1), primary myocardopathy (idiopathic cardiomegaly) (A-2), centrolubular fatty metamorphosis of the liver (A-3), emphysematous lung with slight congestion (A-4), degeneration and desquamation of the tubular epithelia of distal convoluted and Henle's portion (A-5), atrophic adrenal cortex with lipid in the deeper layer (A-6); B-group (second rank), not hypertrophic muscle fibers of the left ventricle with moderate interstitial edema (B-1), hypertrophic muscle fibers of the right ventricle in the same case of B-1 (B-2), centrolubular bleeding and necrosis of the liver (B-3), marked chronic congestion with infarction of the lung (B-4), congestion of kidney (B-5), hypertrophy and increased lipid content in both superficial and deep layers of the adrenal cortex (B-6); C-group (third rank), marked endocardial fibrosis as a significant mechanical factor (C-1), marked interstitial edema of the myocardium (C-2), marked centrolubular and periportal fibrosis fairly resulting in cardiac liver cirrhosis (C-3), moderate chronic congestion with vascular sclerosis of the lung (C-4), congestion and noticeable increase of juxtaglomerular cells of kidney (C-5), hypertrophy and increased lipid content in the superficial layer of the adrenal cortex (C-6); D-group (fourth rank), stenosis of the coronary artery due to localized atheromatous change (D-1), myocardial scar (D-2), simple congestion of the liver acutely induced by a sudden death (D-3), similarly acute congestion of the lung (D-4), acute congestion and vascular sclerosis of kidney (D-5), also acute congestion of the essentially normal adrenal cortex.

All specimens illustrated above were stained by hematoxylin-eosin except C-1 of van Gieson's stain of elastic fibers. Magnification 100×.
various active myocardial changes which were most likely considered responsible for the "refractory" CHF thereof, that is, acute or subacute rheumatic myocarditis, progressive metabolic and/or idiopathic myocardial degenerations with fibrosis, interstitial edema by subacute bacterial endocarditis, and so on.

2. B-group: Clinically there were observed, (1) severe dyspnea, not infrequently associated with pulmonary infarction and/or infection, though peripheral edema seemed moderate, (2) frequent positive reactions suggesting some inflammation, namely C-reactive protein (CRP) or Wassermann reaction, and/or leukocytosis, (3) most cases responded to some extent to therapeutic measures consequently with the relatively longer full course than that observed in the former group, lasting about two years on the average, that is, not considered as absolutely "refractory" one.25

Pathological findings observed were as follows, (1) rather moderate congestion and edema of all viscera but lung where marked congestion with many hemosiderin-laden macrophages, interstitial fibrosis and vascular sclerosis were rather characteristic, in most cases also associated with marked pulmonary bleeding, infarction and/or infection, (2) liver indicating moderate or sometimes marked centrolobular bleeding with liver cell necrosis and mild fibrosis,24 25 (3) rather hypertrophic adrenal gland showing in many cases moderate lipid-contents in both the superficial and the deeper layers, i.e., zona glomerulosa et reticularis, (4) heart in general with mild or moderate myocardial factors indicating rather deleterious mechanical factors such as valvular fibrosis resulted in stenosis and/or insufficiency, mostly associated with hypertrophic muscle fibers especially of right ventricle.

3. C-group: Clinically this group seemed fairly in striking contrast to the A-group in the following points such as, (1) remarkable peripheral edema not always associated with significant dyspnea but relatively with mild one, (2) rather rare positive reactions suggestive of inflammatory changes, i.e., CRP etc., (3) the most long-standing full course of CHF lasting about six years on an average, during which more than one remissions from evident CHF were experienced in most cases, thus seeming essentially "non-refractory" but rather so to speak "full-survived" CHF through relatively well therapeutic responses in the course, though fatal at last.

Again pathologically, this group seemed well contrasted with the A-group as followed, (1) in general most marked congestion and edema of all viscera, though pulmonary congestion similar to that observed in B-group may be somewhat mild in the degree as compared with the latter, (2) liver with extensive and marked centrolobular fibrosis sometimes resulting in apparent cardiac liver cirrhosis,26 (3) significantly congested kidney indicating sometimes increased juxtaglomerular cells characteristically, (4) hypertrophied and/or lipid-containing superficial layers of adrenal cortex, i.e., zona glomerulosa, though whole cortex rather atrophied, (5) heart characterized by the most remarkable mechanical factors such as severe valvular deformities, pericardial adhesion and endocardial sclerosis with moderate myocardial fibrosis, associated also with hypertrophied muscle fibers almost equally of both right and left ventricles.

4. D-group: The cases in this group essentially without any symptoms of CHF in their courses died suddenly most probably of coronary insufficiency or in some occasions directly after cerebral stroke, and so from the pathological view-point there were no characteristic changes ascribed to chronic CHF, though noticed mere congestion of viscera acutely induced by sudden death. However, cardiac changes responsible for sudden death were prominent, that is, consisted of extreme myocardial fibrosis and/or scars which seemed mostly due to myocardial ischemia conditioned by severe coronary sclerosis as well as marked myocardial hypertrophy there-of.27

COMMENTS

From the above observation there may be revealed some constant relations between clinical features and pathological findings in general, though some intermediate cases may be present in practice. Thus at first it may be almost self-evident that the systemic edema seen clinically
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may be fairly paralleled with the congestion of viscera at autopsies, where some definite changes in adrenal cortex, that is, hypertrophied and lipid-containing zona glomerulosa, sometimes associated also with increased juxtaglomerular cells especially observed in C-group, may suggest some hormonal disturbances or at least participation to the edema formation, in particular of aldosterone. Such characteristic reactions in adrenal gland seem not evident in the A-group of the present classification. Also as for the dyspnea as an important sign of CHF, there may be some relations to the pulmonary congestion, bleeding and/or infarction as especially seen in B-group, and somewhat so in C-group, though such pulmonary changes seem relatively mild in the A-group, where the frequent paroxysmal dyspnea sometimes with marked general sweating and/or pale appearance with some mental disturbances were rather characteristic indicating prominent tachycardia at the same time. Such a dyspnea characteristically seen in A-group seems due to marked decrease of forward stroke volume rather than backward congestion as typically seen in B- and C-groups, in other words there seems a sort of chronic or protracted shock state due to significant forward circulatory failure which may be paroxysmally more evident under various stresses probably corresponding to the rather atrophic adrenal gland at autopsy. Such a view of protracted shock-like states particularly in the A-group may be likely supported anatomically also by some characteristic liver damages consisted of remarkable centriobular fatty metamorphosis but without any necrosis or bleeding, the findings observed almost exclusively in this group, which seem to represent some chronic effects of hypoxia upon the liver without any significant congestion. Again from the other point of view, the above-mentioned situations may somewhat intimately correspond to the pathological natures of heart, mainly characterized by predominantly either mechanical or rather myocardial factors as commonly so called. Thus the predominant myocardial factors such as rheumatic or bacterial endocarditis, metabolic and/or idiopathic myocardial degeneration which were particularly prominent in the A-group among others and were considered as yet active or progressive from the various clinical findings as well as the minute pathological examinations in this group may be most likely responsible for the protracted shock-like states here conjectured and further for the so-called "refractory" CHF despite forcible treatments as usually partaken, though the mechanical factors such as valvular impairments seemed rather mild. On the other hand, rather pure mechanical factors such as marked valvular deformities resulting in significant stenosis and/or insufficiency as observed in B- and C-groups may be fairly paralleled with the predominant backward congestion of various grades, which themselves seemed to not so strongly or absolutely resist to usual therapeutic measures for CHF as in the case of above-cited A-group, but rather relatively well respond to the treatments, so far as the compensatory mechanisms such as ventricular hypertrophy to some degrees might be favorably acting and on the one hand any "active" myocardial damages were not progressing as really seen in C-group in particular.

In conclusion it may be re-emphasized that the active or progressive myocardial degenerations of either some inflammatory or idiopathic natures though clinically sometimes obscure may play an important role for the so-called "refractory" CHF in the strict sense as defined in this paper, rather than marked mechanical factors per se not associated with such "active" myocardial damages.

Summary

A total of forty-eight cases of various cardiovascular diseases were throughly examined clinicopathologically, classifying according to the types and degrees of CHF into four groups, namely A-, B-, C-, and D-groups, of which, however, D-group alone was essentially free of apparent CHF and thus to be considered as the control to the others. Thus from these studies there may be revealed to some extent the characteristic correlations between the clinical features and the pathological findings, especially concerned with the therapeutic responsibilities thereof. In conclusion it may be emphasized in

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this paper that the active or progressive myocardial degeneration not infrequently leading to some protracted shock-like states without evident backward congestion as typically demonstrated in the present A-group may be mainly responsible for the so-called "refractory" CHF in the strict sense, though there the mechanical factors such as valvular deformities per se seem rather mild, and in general vice versa as verified somewhat in the other groups.

Acknowledgment

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2. The Pathogenesis and Treatment of Right Heart Failure with Special Reference to Cor Pulmonale

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The term cor pulmonale is generally used to define the right heart enlargement secondary to lung disease with or without failure. The mechanism of cor pulmonale, however, is not completely understood, except for the important role played by the pulmonary hypertension.

The present study is conducted to examine the anatomical and functional vascular factors, which are responsible for the development of pulmonary hypertension. The management of cor pulmonale is also discussed, based on these findings.

I. Structural alterations of pulmonary vascular bed in cor pulmonale

1. Incidence of cor pulmonale among the aged

Out of 300 autopsy cases in Yokufuen during the last 3 years, 26 cases (9%) were diagnosed pathologically as cor pulmonale. The primary lung diseases consisted of pulmonary emphysema in 20 cases and pulmonary tuberculosis with marked pleural scal in 6 cases.

The pulmonary arterial system of these 26 cases and other 3 cases of cor pulmonale due to pulmonary embolism, primary pulmonary hypertension and pulmonary scleroderma were studied morphologically.

2. Anatomical changes of the pulmonary arterial wall in cor pulmonale

The thickness of intima and media of the arterioles, muscular arteries and elastic arteries of the pulmonary vessels were measured in addition to detailed histological observations.

Marked thickening of the intima and media of the pulmonary arterial walls were found in all cases of cor pulmonale, with a uniform distribution throughout the pulmonary vessels. Intimal fibrosis and the increase of elastica in media were also fairly common in the muscular pulmonary arteries in these cases.

These changes in the pulmonary arterial walls are considered to represent the results rather than the cause of the persistence of the pulmonary arterial hypertension.

3. Anatomical factors in response to the pathogenesis of pulmonary hypertension in several pulmonary diseases

Cor pulmonale is generally divided into two major categories: (1) diseases of the pulmonary vascular bed, (2) disorders of the lung parenchyma. The anatomical factors which might be directly responsible for the production of pulmonary hypertension are sought by standard histological methods and by post-mortem pulmonary arteriography on several lung diseases.

1) Diseases of the pulmonary vascular bed

1 Embolism of pulmonary tumor cells