

very slight.

In pulmonary infarction, we made measurements of BAF on 3rd, 7th, 21st and 35th day after inducement, and average BAF% were 4.55, 7.49, 16.11 and 10.73% respectively. In this case, increase of BAF was observed from early state, and after 21st day it was conspicuous.

In bronchiectasis, we determined BAF on 30th and 60th day after removal of obstructing sponge from bronchus. Their average BAF% were 7.17 and 14.04% respectively. Remarkable increase of BAF was observed on 60th day.

In pleurisy, we determined BAF on 7th and 21st day after terebene oil injection, and average BAF% were 2.98 and 5.54% respectively. In this case, increase of BAF was not remarkable.

Conclusion: Average BAF% of normal dogs was 1.56%, and in diseased dogs, BAF was increased with the progress of disease.

In diseases arising from circulatory impediment such as pulmonary embolism and infarction, increase of BAF occurred earlier than in inflammatory diseases such as pulmonary suppuration, bronchiectasis and pleurisy.

Clinical Studies on the Pulmonary Circulation in Heart Diseases Investigated with ^{131}I Macroaggregated Albumin (MAA) and RI(H)SA

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Pulmonary circulation in heart diseases has recently been a problem of increasing clinical interest. Since Taplin and Ueda et al. the measurement of regional pulmonary blood flow has been feasible through the use of MAA.

Some of our research results on the regional pulmonary blood flow in heart diseases have been reported at the 30th annual meeting of the Japanese Circulation Society. In addition to the findings obtained by MAA technique, here described are some results of analysis on the isotope (RISA) dilution curve in congenital heart diseases, particularly left to right shunt and rheumatic heart diseases.

Methods:

Cardiac dilution curve was obtained by means of a scintillation counter with a detector of NaI crystal 3×2 inches, which was located in a lead collimator, (with an aperture of 5 cm in diameter). The counter was placed on the 4th intercostal space at the left sternal border. Under sterile condition, RI(H)SA was diluted so that 10 to 20 microcuries were

contained in 0.5 ml of the solution. The RI (H)SA solution thus diluted was injected into the antecubital vein and rapidly solution flushed with 10 ml of saline solution. A cardiac output was calculated from the dilution curve according to Stewart-Hamilton principle, while "pulmonary blood volume" was derived from the cardiac index times R-L time. As we had previously reported, the regional pulmonary blood flow was measured in sitting position. In all of the cases, a dose of 100 to 200 microcuries of ^{131}I -MAA was injected slowly into the vein. Two or three minutes after injection a scintillation probe was positioned over the anterior chest wall to obtain the radioactivity at each of the intercostal spaces along the midclavicular line. After that, scanning was performed by a 3 inch crystal scintiscanner (Shimadzu Co. Ltd.). The data obtained in the case of the focal filling defects were omitted. A radioactivity was counted at the first and second intercostal spaces for the upper lung region, and the four and five intercostal spaces for

the lower lung region. In order to obtain blood flow per unit lung volume, the activity at the lower region was corrected by the thickness of thoracic wall.

Subjects:

The subjects investigated in this study were 127 in- and out-patients with heart diseases including; 15 mitral stenosis, 23 atrial septal defect (ASD), 28 ventricular septal defect (VSD), 6 patent ductus arteriosus Bottali (PDA) and 2 primary pulmonary hypertension. As a normal control group, in-patients without cardiovascular diseases, ranging from 18 to 40 in age, and healthy adults were also investigated.

Results:

A normal pulmonary upper-flow from ratio in sitting position was 0.51 ± 0.12 for the right lung, and 0.62 ± 0.12 for the left. It means that a normal right-to-left lung flow ratio was 0.82 ± 0.10 . In the normal lung, the blood flow in the upper pulmonary region was smaller than in the lower region, owing to the gravity, when subjects were sitting. Furthermore, more blood flow was noted in the right lung than the left. This finding was consistent with the left to right ratio of weight and oxygen uptake of the lung being 8:7. Next, a cardiac dilution curve had a peak which corresponded to left side of the heart. The ratio of C_2/C_1 (R-L) was $44.8 \pm 5.4\%$ for the normal person, where C_1 is the peak activity and C_2 the activity at the moment of R-L after the peak was noted. "The pulmonary blood volume" was 419 ± 58 ml per square meter for the normal one. The ratio of peak activity C_1 to the activity C_2 after the interval of built-up time (BT) was $38.1 \pm 9.0\%$. The index EXBT for the normal was $(10.5 \pm 2.4) \times 10^{-1}$, where K represents the slope of descending part of the pulmonary dilution curve as assumed exponential (e^{-Kt}). The blood flow ratio of upper to lower lung in ASD, VSD, PDA, averaged 0.6-0.7, without significant differences being noted from the normal one. The finding was in marked contrast with the increased upper to lower ratio on the mitral failure group. Marked decrease in the left pulmonary blood flow was frequently noted in ASD, 9 out of 11, and in VSD, 9 out of 19. An inverse correlation was observed between the L-R pulmonary flow

ratio and the pulmonary-systemic flow ratio, if the latter is below 3. (ratio of pulmonary flow to cardiac output. (Q_p/Q_s)) The value of K.BT showed a marked difference between the L-R shunt group and the normal one. Four cases with L-R shunt demonstrated K.BT within the normal range, two of which were diagnosed as VSD on the basis of phonocardiogram and amyl nitrite test but were free of complaints and chest X-ray and electrocardiographic findings. Small degree of VSD was revealed in the other two cases by cardiac catheterization, with Q_p/Q_s being 1.2. There were seven cases of L-R shunt of which the C_2/C_1 ratio on the pulmonary dilution curve ranged within the normal value. It follows that K.BT index is more sensitive means for the diagnosis of L-R shunt, while C_2/C_1 ratio is closely correlated to Q_p/Q_s , thus making an estimation of shunt volume possible. In regard to the C_2/C_1 (R-L) on the cardiac dilution curve, significant difference was found between ASD (82.9) and the other groups such as VSD (53.3) PDA (62.6) and the normal (44.8). The pulmonary dilution curve for ASD is characterized by the short period of R-L and the gentle slope of downward curve, while that for VSD made a clear appearance at the moment of recirculation through L-R shunt, which occurred halfway down the slope. While L to R ratio of C_2/C_1 was 1.03 in the normal, 1.09 in ASD, and 1.03 in VSD, it was 1.42 in PDA, which would indicate the opening of Ductus Bottali to be near the 1-pulmonary artery. An upper-lower flow ratio in various acquired heart diseases showed a mean of 1.45 in MS groups, 1.26 in MSI, 1.31 in MSI and AI, and 0.73 in AI. In other words, an inverse relation of upper-lower flow ratio was revealed in MS. In MS group, a significant correlation was found between the upper-lower pulmonary flow ratio and the wedge pressure (PC), with the correlation coefficient being 0.78 for the right lung, 0.68 for the left. However, the correlation of the upper-lower pulmonary flow ratio to the pulmonary artery pressure was rather low, significant only at 10% level. According to the value (high or low) of PA and PC, the flow ratio may be classified into four groups. The first group with high PA and high PC showed a high value of the upper-lower ratio, 1.52 in an average, while in the second group with normal PA and high PC the ratio was

1.19, high next to the first group. The ratio was 0.70 in the 3rd group with high PA and normal PC and 0.75 in the 4th group with normal PA and PC. On the basis of the above findings it was concluded that an abnormal increase of the upper-lower pulmonary flow ratio on mitral failure could be attributed primarily to the pulmonary vein. Histological examination of the lung was made on five patients with mitral failure on whom the upper-lower pulmonary flow ratio was also measured. Two were made in autopsy and the other three in the course of commissurotomy. In a mild case of MS, 17 year-old-girl with the upper-lower ratio of 1.14, the arterioles 300 micron in caliber in the left upper lobe showed no proliferation of the intima and the normal muscular layer, but lower lobe demonstrated intimal proliferation and normal muscular layer. In a severe case, 67 year old female, whose upper-lower ratio for the left lung is 2.73, histological examination revealed a moderate degree of hyperplasia of the intima, degeneration and atrophy of the media in the 300 micron arterioles. As those cases demonstrated, pathologic findings of the vessels are more marked in the lower lung lobe than that in the upper lung. Regional blood flow variation was measured when hypoxia of the unilateral lung was induced by inhalation of 7.9% oxygen for 5 minutes. In the normal cases the upper and lower lung showed an almost uniform and marked reduction in blood flow. In mitral failure on the hypoxic side, there occurred a less marked decrease in flow than the lower lung. This finding is considered to show that in mitral failure the pulmonary vessels hardly responded to hypoxia of the lung esp. in the lower lung fields. A decrease in the upper-lower flow ratio occurred after the commissurotomy or digitalisation, but the flow ratio showed rather higher value than normal. The functional capacity of patients was divided into 4 classes by the New York Heart Association. The upper-lower pulmonary flow ratio increased in class II and III, decreased in class IV. The decrease of the ratio in class IV was considered to indicate the decrease in the reserve capacity of the pulmonary vessels in the upper lung and marked pathologic alterations of the vessels in both the upper and lower lung region. Briefly, the pulmonary vein was assumed to be primarily responsible

for the abnormal distribution of the pulmonary blood flow in mitral failures. Although this view appeared to be consistent with that by J. B. West and Braunwald, it was further assumed that not only the pulmonary venous pressure or the left atrial pressure but also the consequent and irreversible changes in the wall of vessels, would also be associated with the above abnormal distribution. The pulmonary blood volume increased in class I, increased or decreased in class II, and decreased in class III. These evidences indicated that the pulmonary vascular beds were more or less injured in class II and severely injured with reduced pulmonary blood volume in class III. For obtaining information about the compliance of pulmonary vessels, the variation of pulmonary blood volume was measured before and after physical exercise. The pulmonary blood volume increased after exercise in the normal and class I but rather decreased in class II. Class III showed no changes in the pulmonary blood volume after exercise, maintaining a low value of the volume at rest. This finding was interpreted as indicated that the pulmonary vascular compliance decreases as the pulmonary vascular alteration becomes more marked. No significant differences in the pulmonary blood volume were noted among various heart diseases. A significant correlation between the pulmonary blood volume and the stroke volume indicated that the stroke volume was limiting factor for the pulmonary blood volume. Measurement of the pulmonary blood volume with the use of isotope requires further research, in spite of a great contribution by Lammerant (1957) and others. The normal value we obtained for the pulmonary blood volume was higher than that attained by Dock and others (1959) with the use of dye dilution method, suggesting that our method might measure not only the true pulmonary blood volume but also a part of the left and right heart volume together.

Summary:

1. We measured the distribution of pulmonary blood flow with ^{131}I -MAA, and the cardiac and pulmonary dilution curves with RISA.
2. There was no difference between ASD, VSD, PDA, and the normal controls in regard to the upper-lower ratio. Many

patients with ASD showed a reduced left-right lung flow ratio.

3. The K.BT index of the pulmonary dilution curve was most sensitive to the diagnosis of left to right shunt. The C_2/C_1 of the pulmonary dilution curve showed a close correlation to Q_p/Q_s . (K: the slope of descending part of the pulmonary curve. BT: build-up time)
4. The dilution curves make differential diagnosis feasible among ASD, VSD, and PDA.
5. Though the upper-lower flow ratio showed a close correlation to the pulmonary wedge

pressure, the former was not only dependent upon the latter, but also on the irreversible organic changes in the pulmonary blood vessels.

6. The pulmonary blood vessels in mitral failure demonstrated a reduced response to hypoxia, especially in the lower lung region.
7. The pulmonary blood volume in mitral failure decreased in class III of New York Heart Association, which indicated the reduced pulmonary vascular beds, accompanied by decreased pulmonary vascular compliance.

The Detecting Device for Determination of the Corrected R-L Time

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Since Prinzmetal and co-workers using ^{24}Na were able to demonstrate the double peaked curve, radiocardiogram has been utilized to measure pulmonary circulation time, lung blood volume, cardiac output and cardiac volumes. Although pulmonary circulation time is easily obtained from precordial isotope dilution curve, this simplest measurement which may be made of the distance between the peaks of right heart and left heart includes potential hazards. Because the descending limb of right heart dilution curve make the peak of the pure left heart curve shift to some extent. It is the fact that double peaked radiocardiograms are composed of the interference of two peaks. The uncorrected R-L time (peak to peak time) obtained from original radiocardiogram should be corrected by producing a derived curve which represents the pure left heart component.

In 1953, Shipley and his associates tried to correct the R-L time and designated corrected R-L time. The extended limb of right heart being derived by the extrapolation of the recorded portion of its downslope on semilogarithmic paper and the pure left ventricular component being obtained by subtraction of it from the original curve, time is here measured between the peak of right heart and

that of the derived left heart curve.

Our previous method using pure dilution curve of right heart of ^{131}I -MAA has been available. There are some cases with cardiac failure in which the pure left heart component can not be derived. Our present work is how to assess more accurately and easily the corrected R-L time as routine technique. The detecting device using 2 channel RI apparatus was tried. When one counter is positioned vertically in contact with the chest at the 4 interspace on the left sternal line, and another counter is collimated towards cardiac apex with 30° of angle from vertical line, the peak transit time from right heart to left heart, corresponding to the R-L time corrected by MAA time concentration curve, can be obtained without complicated analysis of semilogarithmic extrapolation and subtraction. That is, the curve recorded by the counter on the left sternal line has the right heart peak of no shift and the left heart curve shifted, however the left heart peak recorded by apical counter is not affected. The time between the right peak by sternal counter and the left peak by apical counter coincides with the corrected peak to peak time. This technique seems to be available for all cardiopulmonary disorders, if the single bolus of injection is carried out.