Detection of Pulmonic and Tricuspid Valvular Regurgitation by Means of Indicator Solutions

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The presence of pulmonic and tricuspid valvular regurgitation may often be suspected from careful clinical examination. However, the validity of the generally accepted clinical criteria remain to be established by technics that permit the direct demonstration of reverse flow across these valves during life. This has been made possible by the detection of cardiogreen and of radioactive krypton (Kr85) in the right atrium or right ventricle after injection of these substances into a distal chamber.

Although the presence of valvular regurgitation may be suspected from clinical studies, the actual demonstration of blood traversing a valve in reverse direction is necessary for a definitive diagnosis. Indicator-dilution curves recorded from a systemic artery following injections into the right side of the heart are often modified by the presence of a regurgitant valve between the sites of injection and of sampling.1-3 Decreased cardiac output or a left-to-right shunt may, however, obscure the changes produced in such curves by valvular regurgitation.

Mitr al regurgitation has been demonstrated by the prompt appearance in the left atrium of either an indicator dye4,5 or of a radiopaque medium6 following injection into the left ventricle. In the presence of aortic regurgitation, indicator dye injected into the descending thoracic aorta regurgitates to the ascending aorta and may be detected in the right ear.7 This lesion may also be demonstrated by thoracic aortography.8 The reflux of radiopaque dye into the right ventricle following its injection into the pulmonary artery has recently been observed in the presence of pulmonic regurgitation.9

It is the purpose of this report to describe 2 technics for the detection of pulmonic and tricuspid valvular regurgitation that may be applied conveniently at the time of right heart catheterization, and to present the results obtained in 29 patients studied at the National Heart Institute. A similar approach to diagnosis has also been described recently by Bajee, Birkhead, Carter, and Wood.10

Methods

Right heart catheterization was performed with a no.9 double-lumen Courand catheter, modified so that the openings of the 2 lumina were 5 mm apart. When the competency of the pulmonic valve was studied, the catheter was positioned so that the distal opening was in the pulmonary artery and the proximal one in the right ventricle. When tricuspid valve function was examined, the distal lumen opened into the right ventricle, while the proximal opened into the right atrium. Simultaneous pressures were recorded from each chamber immediately prior to and following injection of the indicator in order to confirm the position of the catheter.

Cardiogreen (triacarbocyanine) dye11 was injected through the distal opening of the catheter as blood was sampled continuously from the proximal opening (fig. 1). The concentration of the indicator was determined by withdrawal through a cuvette densitometer12 by means of a constant-rate motor-driven syringe. Time-concentration curves were recorded either with a photographic cathode-ray instrument or a direct-writing recorder.

The order of magnitude of the relationship between regurgitant and forward flows was estimated by the "forward triangle" method described by Hetzel and collaborators.13,14 The "regurgitant fraction" was calculated as the ratio of the product of the build-up time and peak-concentration of the "regurgitant curve" to that of the "recirculation curve" (fig. 2). It is realized that this ratio does not provide precise quantification.

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*Manufactured by Nuclear Corporation of America, Brooklyn, N. Y.
In 12 of the 29 patients valvular competency was studied in a similar manner with injections of 30 to 50 μe. of radioactive krypton (Kr85) solution into the distal opening of the catheter. Immediately after injection blood was sampled at a constant rate for 10 seconds from the proximal lumen and for 15 seconds from a systemic artery. The radioactivity in these samples was then measured by inserting them into a continuous gas-flow Geiger-Muller tube.

RESULTS

In the presence of a competent valve, either no dye or only a minimal quantity appeared in the proximal chamber immediately after injection. Fifteen to 20 seconds after injection, dye that had recirculated through the systemic circuit appeared (figs. 3 and 4). When valvular regurgitation was present, a substantial amount of dye appeared in the proximal chamber within 2 seconds of the onset of the injection, well before the appearance of the recirculation curve (figs. 2 and 5). In the presence of valvular regurgitation combined with a left-to-right shunt entering upstream to the proximal catheter opening, the curve produced by the regurgitant valvular flow was inscribed significantly earlier than the curve produced by the shunted blood; the latter, while delayed in its path through the pulmonary circulation and to the right side of the heart, nevertheless appeared earlier than the systemic recirculation curve (fig. 6).

The competency of the pulmonic valve was examined in 28 patients, and in 7 of these significant regurgitation was considered to be present with "regurgitant f. actions" ranging from 17 to 72 per cent. Three of these 7 patients (W.J., J.B., J.S.) had previously had portions of their pulmonic valves excised at the time of pulmonary valvulotomy, but only 2 (J.B., J.S.) had murmurs considered typical of pulmonic regurgitation. Another patient (M.B.) had previously undergone pulmonic valvulotomy and closure of a small ventricular septal defect in which no valvular tissue was removed. A murmur typical of pulmonic regurgitation developed. One patient (C.C.) had mitral regurgitation, pulmonary hypertension, and a typical Graham Steell murmur.
Patient J.K., who had not been operated upon, had the murmurs considered typical of pulmonic stenosis and regurgitation. At right heart catheterization, there was a gradient of 26 mm. Hg across the pulmonary valve, and the diastolic pressures in the pulmonary artery and right ventricle were identical. The seventh patient (S.C.) had an atrial septal defect, pulmonary hypertension, and a typical Graham Steell murmur; the presence of pulmonic regurgitation was confirmed at the time of operative closure of the defect when a distinct jet of blood was felt in the right ventricle during diastole. In only 3 (W.J., J.K., M.B.) of these 7 patients was the end-diastolic pressure in the pulmonary artery identical to that in the right ventricle. Pulmonary regurgitation was not suspected in 5 other patients who had "regurgitant fractions" ranging from 2 to 6 per cent. It is believed that such minute amounts of reflux do not necessarily indicate organic valvular dysfunction, but are presumably artifacts produced by the presence of the catheter. There was no relation between the presence of this small degree of regurgitation and the pulmonary artery pressure.

The competency of the tricuspid valve was tested in 17 patients and in 8 of these significant regurgitant flow was demonstrated. The "regurgitant fractions" ranged from 11 to 65 per cent in 7 of the patients and could not be calculated in the eighth, a patient with a very prolonged circulation time in whom no recirculation curve had appeared after 55 seconds of sampling. In all 8 of these patients there was clinical evidence of tricuspid regurgitation and the right ventricular pressure was elevated (table 1); in 5 of these, the mean right atrial pressure and the right atrial "v" wave pressures were elevated. In 2 of the patients with significant tricuspid regurgitation the diagnosis was confirmed at subsequent postmortem examination. In one of these patients, J.O., the tricuspid ring was widely dilated and the valve leaflets were held in a position of partial inversion into the right ventricle. In the other patient, A.R., the tricuspid valve was both stenotic and regurgi-
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FIG. 5 Top. Dye-dilution curve obtained from the right ventricle following pulmonary artery injection in a patient with pulmonary regurgitation. The dye that appears immediately (P.R.) indicates pulmonary reflux and precedes the recirculation curve (RECIRC.).

FIG. 6 Bottom. Dilution curve resulting from pulmonary artery injection and right ventricular sampling in a patient who had a portion of his pulmonary valve excised at the time of pulmonary valvotomy for pulmonic stenosis. A left-to-right shunt due to an atrial septal defect persisted. The first component of the curve (P.R.) is indicative of pulmonic regurgitation; the second (L.R.) is related to blood that has been shunted across the atrial septal defect, and the third component (RECIRC.) is due to systemic recirculation.

Discussion

The technics for the detection of pulmonic and tricuspid valvular regurgitation described herein have been found simple and convenient to apply at the time of right heart catheterization and should prove of considerable clinical value. The diagnosis of pulmonic regurgitation is usually made when a patient with evidence of pulmonary hypertension presents with a high-pitched, decrescendo, blowing diastolic murmur along the left sternal border, unaccompanied by the peripheral dynamics of aortic regurgitation. Seven such patients were studied with an indicator-dilution method for the detection and estimation of aortic regurgitant flow. It was with considerable surprise that mild aortic

It has been demonstrated previously that approximately 95 per cent of Kr\(^{85}\) injected into the venous system or right side of the heart is eliminated into the expired air during its passage through the pulmonary circulation.\(^{15-18}\) The small remaining fraction that reaches the systemic arterial bed does not behave in a fashion similar to a simple intravascular indicator such as cardiogreen. A portion leaves the intravascular compartment and diffuses into the interstitial fluid as well as into the cells,\(^{19}\) further diminishing the quantity of Kr\(^{85}\) in the systemic venous blood immediately after injection into the right side of the heart or pulmonary artery. The presence of Kr\(^{85}\) in the blood sampled from the right atrium or right ventricle immediately after injection into the right ventricle or pulmonary artery could therefore result only from valvular regurgitation.

Twelve patients had both Kr\(^{85}\) and cardiogreen dye tests for pulmonic regurgitation while 5 had both tests for tricuspid regurgitation. The results were in general agreement. In 8 tests the cardiogreen "regurgitant fraction" exceeded 15 per cent and the right heart Kr\(^{85}\) count per minute (c.p.m.) exceeded background by more than 100 c.p.m. Similarly, in 7 tests the cardiogreen regurgitant fraction ranged between 0 and 3 per cent while the right heart Kr\(^{85}\) activity ranged between 0 and 54 c.p.m. above background. However, the results in the other 2 patients indicated a discrepancy between the 2 tests. In patient J.B., significant pulmonic regurgitation was revealed only by cardiogreen dye while in patient M.E., it was demonstrated only with Kr\(^{85}\).
DYE DETECTION OF REGURGITATION

J. P. 27/11 28/1 4 6 — 0 ASD
R. J. 22/7 22/4 3 6 — 0 ASD
M. S. 42/20 42/8 7 10 — 0 MS, MI
A. L. 29/10 33/1 2 3 — 0 PDA
D. D. 54/12 54/0 1 3 0 0 VSD
M. B. 34/14 35/4 5 8 — 0 MS, AI
P. D. 47/34 48/4 5 7 — 0 VSD
A. R. 80/40 80/10 10 14 37 0 MS, MI, TS, TI
M. P. 72/34 73/7 8 18 50 0 MS, MI, TI
T. L. 25/9 28/5 5 6 — 0 AS
L. M. 40/20 43/4 4 7 65 3 MS, MI, TI
R. P. 41/23 42/0 5 6 0 2 MS, AI, TS
W. J. 20/3 45/3 4 6 0 53 PS, PI, ASD (postop.)
J. B. 64/30 66/10 6 7 — 29 PI, Tet. of Fallot (postop.)
C. C. 50/20 50/3 2 4 0 17 MI, PI
H. E. 56/14 58/5 10 16 22 2 MS, MI, TI
S. C. 78/30 80/4 4 3 11 23 ASD, PI, TI
J. S. 15/5 35/0 1 3 3 18 PS, PI (postop.)
C. M. 15/7 16/0 2 3 0 — MI
C. H. 23/7 23/6 7 8 0 2 AI, MS
J. O. 68/38 70/7 7 11 0 0 MS, MI, AS, AI, TI
R. J. 18/6 16/3 2 3 0 6 ASD
L. R. 50/30 54/4 4 5 — 0 MS, AI
D. M. 22/10 22/10 3 4 — 0 MS, AI
M. E. 40/20 40/6 10 15 12 0 MS, MI, TI
D. W. 78/34 75/7 5 6 59 0 MS, TI
J. K. 22/8 48/8 4 5 — 72 PS, PI
B. S. 43/22 43/5 4 4 0 0 AI, MI
M. B. 28/2 28/2 — — — 55 VSD, PS, PI (postop.)

TABLE 1.—Results of Dye-Dilution Tests for Valvular Regurgitation

All pressures expressed in mm. Hg; S/D, systolic/diastolic pressures; *large regurgitant curve but no recirculation curve recorded; ASD, atrial septal defect; MS, mitral stenosis; MI, mitral insufficiency; PDA, patent ductus arteriosus; AI, aortic insufficiency; VSD, ventricular septal defect; TI, tricuspid insufficiency; TS, tricuspid stenosis; AS, aortic stenosis; PS, pulmonic stenosis; PI, pulmonic insufficiency.

Regurgitation was discovered in 6 of these 7 patients believed on clinical grounds to have pulmonary regurgitation. If the indicator-dilution methods are applied to the study of both the aortic and pulmonic valves, the origin of any diastolic murmur due to regurgitation may be determined. A patient recently studied illustrates the clinical application of these technics.

L.R. (Clinical Center #00-24-61), an 18-year-old girl, was admitted for diagnostic study and the treatment of rheumatic heart disease. She had had acute rheumatic fever at 8 years of age and was told shortly thereafter that she had a heart murmur. No symptoms ensued until 1 year prior to admission when exertional dyspnea, easy fatigability, occasional paroxysmal nocturnal dyspnea, and hemoptysis began. On physical examination the blood pressure was 106/70; the pulse was 94 and regular. The point of maximal impulse was in the left midclavicular line in the fifth left intercostal space and there was only a slight right ventricular lift. At the apex the first heart sound was accentuated. The second heart sound in the pulmonic area was loud and showed normal respiratory splitting. In the pulmonic area and along the left sternal border there was a grade-II high-pitched, decrescendo, blowing diastolic murmur, and
a grade-II rumbling diastolic murmur with presystolic accentuation was heard at the apex. The electrocardiogram showed right ventricular hypertrophy and right axis deviation. X-rays revealed the heart to be slightly enlarged in its transverse diameter and there was prominence of the main pulmonary artery segment and enlargement of the left atrium. Right heart catheterization revealed the pulmonary artery pressure to be 50/30, the cardiac index was 1.98 L./min./M.², and no shunts were present. Transbronchial left heart catheterization revealed a mean left atrial pressure of 22 mm. Hg and the end-diastolic gradient across the mitral valve was 20 mm. Hg. It was considered that this patient had mitral stenosis and that the diastolic murmur along the left sternal border represented pulmonic regurgitation. However, no regurgitation was demonstrated either by the dye-dilution method (table 1, fig. 3) or by the Kr¹³¹ tecnic (table 2). Retrograde aortic catheterization and quantification of aortic regurgitation was then carried out and revealed regurgitation of dye from the thoracic aorta at the level of the eighth thoracic vertebra to the origin of the innominate artery.

The final diagnosis was severe mitral stenosis and moderate aortic regurgitation.

In the past, the definitive diagnosis of tricuspid regurgitation has rested primarily on clinico-pathologic correlations. It was suggested by the contour of the right atrial pressure pulse in 60 patients studied by Sepulveda and Lueas.²⁰ However, tricuspid regurgitation had been suspected clinically in only 23 per cent of this group. On the other hand, in the present investigation, substantial tricuspid regurgitation was demonstrated in patients L.M., S.C., and D.W. in whom the right atrial pressure pulse was normal. In this connection it is also of interest that the right atrial pressure pulse was not modified in the 4 patients with congenital left ventriculo-right atrial communications whom we have recently studied.²¹ In this malformation, blood is ejected into the right atrium during ventricular systole in a manner similar to tricuspid regurgitation.

It is anticipated that the methods described herein will provide a more precise approach to the diagnosis of tricuspid regurgitation and make clinico-hemodynamic-pathologic correlations more meaningful than heretofore. The recognition of tricuspid regurgitation may be of considerable clinical importance. It has been pointed out by Schilder and Harvey²² that patients with mitral stenosis and tricuspid regurgitation have been denied commissurotomy because the presence of a loud systolic murmur led to the erroneous diagnosis of mitral regurgitation. Such diagnostic errors should be obviated by the recognition of tricuspid regurgitation with the indicator-dilution or radioactive gas technics.

**Summary**

Technics for the demonstration of pulmonic and tricuspid regurgitation and the estimation of the magnitude of regurgitant flow are described. The pulmonic valve was studied by positioning a modified double-lumen catheter so that the distal lumen opened into the pulmonary artery and the proximal lumen opened into the right ventricle. When tricuspid function was examined, the distal lumen...
opened into the right ventricle and the proximal one into the right atrium. Cardiogreen dye and radioactive krypton (Kr\textsuperscript{85}) were injected through the distal opening of the catheter and sampled from the proximal opening. With a competent valve, either no dye or Kr\textsuperscript{85} or only a minimal quantity could be detected in the proximal chamber immediately after injection. In the presence of valvular regurgitation, substantial amounts appeared in the proximal chamber immediately after injection. Regurgitation was present in 7 of the 28 patients in whom the pulmonic valve was examined, with regurgitant fractions ranging from 17 to 72 per cent. Tricuspid regurgitation was proved in 8 of the 17 patients studied; the regurgitant fractions were 11 to 65 per cent. The methods described appear reliable, simple to apply in the course of right heart catheterization, and of clinical value in the study of patients with known or suspected valvular heart disease or with heart murmurs of uncertain etiology.

**Summario in Interlingua**

Es describite technicas pro le demonstration de regurgitation pulmonic e tricuspid e pro le estimation del magnitude del fluxo regurgitante. Le valvula pulmonic eseva studiata per positionar un modificato catheter a lumine duple de maniera que le lumine distal comunicava con le arteria pulmonar e le lumine proximal con le ventriculo dextere. In le examine del function tricuspid, le catheter eseva positionate de maniera que le lumine distal communicava con le ventriculo dextere e le lumine proximal con le atrio dextere. Un colorante cardio-verde e krypton radioactive (Kr\textsuperscript{85}) eseva injiecte via le lumine distal del catheter e specimens eseva obtenite ab le lumine proximal. Quando le valvula es competente, nulle colorante e nulle Kr\textsuperscript{85} — o al minus solmente un quantitate minimal de illos — poteva esser detegite in le camera proximal immediatamente post le injection. In le presentia de regurgitation valvular, quantitates substantial del indicatores appareva in le camera proximal immediatamente post le injection. Regurgitation eseva presente in 7 del 28 patientes in qui le valvula pulmonic eseva examinate. Le fractiones regurgitante variava inter 17 e 72 pro cento. Regurgitation tricuspid eseva constatate in 8 del 17 patientes studiata. Le fractiones regurgitante variava inter 11 e 65 pro cento. Le methodos describite es apparentemente digne de confidentia, simple a applicar in le curso de catheterismo dextero-cardiac, e de valor clinic in le studio de pacientes con establite o suspicite morbo de valvula cardiac o con murmures cardiac de etiologia incerte.

**REFERENCES**


With the invention of the microscope we can mark the first positive step towards the goal to-day. A Jesuit priest, Kircher, in 1671, was the first to investigate putrefying meat, milk, and cheese with the crude microscope of his day, and left us indefinite remarks concerning ‘very minute living worms’ found therein. Four years after Kircher a Dutch linen merchant, Antonius von Leeuwenhoek, by improving the lenses of the microscope saw in rain-water, putrefying fluids, intestinal contents, and saliva, minute, moving, living particles, which he called ‘animalculae.’ In medical circles of his day these observations aroused the keenest interest, and the theory that these ‘animalculae’ might be the cause of all disease was eagerly discussed. Pleneiz, of Vienna, after much observation of various fluids, putrefying and otherwise, wrote, in 1762, that it was his firm belief that the phenomena of diseases and the decomposition of animal fluids were wholly caused by minute living things.—William Osler. Aequanimitas and Other Addresses. Blakiston & Co., Philadelphia, and T. K. Lewis, London, 1904.
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