Comparison of Blood Oximetry and the Ascorbate Dilution Technique in the Diagnosis of Left-to-right Shunts

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Clark and Barger (1959a) described a new method for the detection and localization of cardiovascular shunts. The method is based on the measurable change of electrical potential (potentiometry) which an exploring platinum electrode, introduced into the blood-stream, develops with respect to a reference electrode, when the hydrogen concentration of the medium varies (Clark, 1960). Hydrogen was first used as an indicator (Clark and Barger, 1959a, b); later, because of easier handling, sodium ascorbate was introduced (Frommer, Pfaff, and Braunwald, 1961; Nixon *et al.*, 1963).

The practical advantages of an intravascular exploring unit, and some of the technical problems connected with the new method have been discussed (Clark, 1960; Frommer *et al.*, 1961; Samet, Bernstein, and Medow, 1965). Its higher sensitivity with respect to blood oximetry and the dye dilution technique has been demonstrated in one selected case (Nixon *et al.*, 1963).

The present report is concerned with a comparison of the results of the ascorbate dilution technique with those of blood oximetry, in a large series of patients undergoing cardiac catheterization.

THEORY

When sodium ascorbate is employed as an indicator, a constant baseline potential must be created between the intravascular platinum electrode and the reference skin electrode by connecting the former to the anode, and the latter to the cathode of a battery. A current thus flows between them through the body tissues, which can be measured as voltage across a resistance applied in series (polarography), and displayed on an oscilloscope (Clark, 1960). If the platinum electrode has a potential of at least +0.85 volts (the electro-oxidation potential of ascorbate), it will be able to oxidize ascorbic acid, injected in its vicinity, to dehydro-ascorbic acid. Hydrogen ions are thus liberated, which ionize immediately, and the released electrons are captured by the anode. The current is thereby increased, producing on the oscilloscope a deflection from the baseline current proportional to the increased flow of electrons. The reactions are illustrated below:

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PATIENTS AND METHODS

In 176 patients, ranging in age from 25 days to 49 years, 185 serial ascorbate dilution and blood oximetry studies were performed during right heart catheterization. Cardiac diagnosis had to be established in 164 patients, and the results of previous operations evaluated in the remaining 12.

Right heart catheterization was performed in the standard fashion, generally in the following order: after advancing, when possible, the tip of the platinum electrode catheter all the way into the wedge position, the catheter was pulled back during pressure recording into the main pulmonary artery, and expired air (in patients not under general anaesthesia), and blood samples from the pulmonary artery (usually two) and a systemic artery were collected for the calculation of pulmonary blood flow by the direct Fick principle. In anaesthetized patients, the O_2 uptake was obtained from prediction tables (Rudolph and Cayler, 1958, up to the age of 5 years; Boothby, Berkson, and Dunn, 1936, for older age). An ascorbate dilution procedure was performed with the catheter in this position, and the arterial systemic pressure was recorded. The catheter was then withdrawn in a step-wise fashion into the superior vena cava during pressure recording, serial blood sampling, and the ascorbate dilution procedures. These were carried out with injection into and detection from the outflow tract of the right ventricle, the lower portion of the right atrium and the superior vena cava. Frequently, additional curves were recorded from one or more locations for added evidence. Three blood samples for oximetry were obtained from the upper, middle, and lower portion of both right ventricle and atrium, and one sample each from superior vena cava and axillary vein. Samples of 1 ml. were taken from infants, and of 2 ml. from children and adults. Expired air was collected in a Tissot gasometer, and the oxygen tension was determined in a model C Pauling-Beckman O_2 analyser. Blood haemoglobin concentration and O_2 saturation were measured in a Model D-U Beckman spectrophotometer. Cardiovascular pressures were measured by Statham P23Db transducers, and recorded on an Electronics for Medicine DR-8 polyoscillograph.

Ascorbate Dilution Technique. The equipment used for the performance of the ascorbate dilution curves consisted of the following.

- (1) No. 5-6-7 F catheters with platinum ring electrode 1-2 mm. from the tip*. It was found advantageous to coat the platinum electrode with platinum black by electrolysis of a 5 per cent solution of platinum chloride† for 3-5 minutes before each catheterization (Clark and Barger, 1959a).
- (2) A large silver reference electrode, strapped tightly to the skin of the chest with the interposition of abundant electro-conductive paste.
- (3) The control unit, built in our laboratory from the diagram of Frommer *et al.* (1961). It consists

essentially of a battery-energized circuit applying +1 volt to the platinum electrode, and allowing a flow of current never exceeding 0.6 mA; a variable series resistor; and a zero offset circuit.

- (4) The amplification was provided by an Electronics for Medicine ECG/EEG/Phono Amplifier, and the curve was displayed and recorded on a DR-8 polyoscillograph at a paper speed of 2.5 mm./sec. and time line interval of 1 sec.

The control unit was connected to the exploring and reference electrodes, grounded to the common ground represented by the catheterization table, and turned on. Its output was fed into the amplifier for display and recording. The polarographic electrode is flow-sensitive (Müller, 1947). Before each injection of ascorbate into a cardiovascular compartment, a resistor was selected which allowed the flow pulse and/or electrocardiogram to become clearly visible on the oscilloscope baseline. This provision usually allowed the inscription of good amplitude ascorbate dilution curves for the dose of sodium ascorbate* injected (50-125 mg. at concentrations of 100-250 mg./ml.). The forceful manual injection of ascorbate was followed immediately by flushing of the catheter with 10 ml. 5 per cent glucose in water.

Curve Interpretation. In normal people the ascorbate curves from the pulmonary artery, right heart, and superior vena cava are similar in contour and consist of a sharp initial deflection of variable amplitude with rapid return to baseline (coincident with the injection of ascorbate and its short contact with the anode) followed, after an interval equal to the circulation time, by a rounded wave representing the reappearance of the diluted ascorbate after a full systemic circulation (Fig. 1A).

When the electrode lies within the superior vena cava and right atrium, slow oscillations synchronous with respiration are usually superimposed (Fig. 1B). Curves from the pulmonary artery and superior vena cava performed during certain phases of the cardiac cycle in inspiration may not show the initial spike, due to the velocity of blood flow past the catheter tip, preventing retrograde diffusion of the injected ascorbate (Fig. 2A). The duration of the initial spike is a function of injection time. It is important to keep this in mind in order to avoid diagnostic uncertainties when, especially with No. 5F catheters, the injection is slow. When relatively small ascorbate doses are used in large people, the re-circulation wave may be absent (Fig. 2B). In a number of cases individual curves may be unsatisfactory, either because of low sensitivity which necessitates repeating the injection at higher gain, or because of an extremely slow return of the initial spike to the baseline. This latter phenomenon occurs almost exclusively when the catheter tip is within the right ventricle and it is most likely due to permanent contact being made by part of the electrode with the ventricular wall with trapping of ascorbate between them (Clark, 1960), and is overcome by repeating the injection after changing the position of the catheter.

* Model 353-Pt. U.S.C.I., Glens Falls, N.Y., U.S.A.

† Fisher Scientific Co., Fair Lawn, N.J., U.S.A.

* Parke, Davis and Co., Detroit, Michigan, U.S.A.

FIG. 1A.—Normal standard ascorbate dilution curve. The initial spike with rapid return to the baseline is followed by a rounded wave representing recirculation of the diluted ascorbate past the platinum electrode. In this and the following figures the paper speed is 2.5 mm./sec., and the time line interval 1 sec.; the arrow indicates the time of injection.

FIG. 1B.—Normal ascorbate dilution curve recorded from the right atrium. Note the regular oscillations, synchronous with respiration, superimposed on the ascorbate dilution curve.

In the presence of a left-to-right shunt the curve is distorted. Large shunts are indicated by a break in the downstroke of the first spike by a gentle slope slowly returning to baseline and masking the recirculation wave (Fig. 3A). Small shunts are represented by one or more discrete secondary spikes preceding the systemic recirculation wave, and having a period corresponding to the circulation time of the short circuit (Fig. 3B).

The most proximal compartment where early recirculation can still be detected is the site of the left-to-right shunt. Thus, in atrial septal defects the abnormality is limited to the curves from pulmonary artery, right ventricle, and right atrium; in ventricular septal defects, to the curves from the pulmonary artery and right ventricle; and in patent ductus arteriosus, to the curve from the pulmonary artery (Fig. 4). If left-to-

FIG. 2A.—Normal ascorbate dilution curve recorded from the pulmonary artery. Because of the high velocity of blood past the electrode, retrograde contact of the injected ascorbate with the electrode by diffusion is prevented and the initial spike is absent.

FIG. 2B.—Normal ascorbate curve in an adult. The recirculation wave is minimal due to marked dilution of the indicator.

FIG. 3A.—Ascorbate dilution curve recorded after injection of the indicator into the right ventricle and detection from the same chamber in a patient with a large ventricular septal defect. The down-stroke is gentle and smooth almost from the beginning because of the continuous arrival through the shunt of large slowly decreasing concentrations of ascorbate.

FIG. 3B.—Ascorbate dilution curve recorded from the right ventricle in a patient with a small ventricular defect, after injection into the same chamber. The down-stroke of the initial spike, sharp down almost to the baseline, is broken by secondary spikes of decreasing height, representing the periodic arrival through the defect of small decreasing concentrations of ascorbate.

right shunting occurs at more than one site, only the one more upstream can be detected with certainty.

Blood Oximetry. Shunt Detection. Criteria for the detection and localization of the left-to-right shunts at the atrial, ventricular, and pulmonary arterial level by oximetry were respectively:

- (1) An increase of O_2 content in the averaged right atrial samples over the sample from the superior vena cava of 2 volumes per cent or more.
- (2) An increase of O_2 content in the averaged right ventricle samples over the averaged right atrial samples of 1 volume per cent or more.
- (3) An increase of O_2 content in the pulmonary arterial sample(s) over the averaged right ventricle samples of 0.6 volume percent or more.

RESULTS

The ascorbate dilution curves were technically unsatisfactory in 17 of the 176 cases, or approximately 10 per cent. In 12 of them, all infants and children in whom 5F catheters were used, injection was slow, probably because of partial occlusion of the lumen. In the remaining 5, despite repeated adjustments of the control unit sensitivity, the flow pulsations and the deflections following the injection of ascorbate were barely perceptible, possibly due to inadequate blackening of the electrode, or to undetected short circuits.

Adequate data for comparison of the ascorbate dilution and the blood oximetry technique were

FIG. 4.—Ascorbate dilution curve patterns from four representative compartments in a subject with no shunts (NHD) and in patients respectively with patent ductus arteriosus (PDA), ventricular septal defect (VSD), and atrial septal defect (ASD). The curves have been drawn from actual tracings. The arrows indicate injection of the indicator.

available in 159 patients, nine of whom were catheterized both pre- and post-operatively, a total of 168 studies. The two techniques were in agreement in 144 studies (85.7%) and in disagreement in 24 studies (14.3%) (Table I).

TABLE I
ASCORBATE DILUTION AND BLOOD OXIMETRY DATA

	Agreement	Disagreement
Studies followed by operation	40	6
Studies preceded by operation*	19	2
Studies not followed by operation	85	16
	144	24

* Seven of these studies had a pre-operative control, included in the figures above.

I: *Ascorbate and Blood Oximetry Results in Agreement.* The "agreement" refers both to presence or absence of the left-to-right shunt and to its location, when present. In 40 patients the studies preceded operation and in 19 they followed it (seven had both pre- and post-operative studies), while in 85 patients no operation followed the studies. More detailed information on this group is presented in Table II. When the results of the ascorbate dilution and blood oximetry techniques were in agreement, operation confirmed the pre-operative diagnosis. There were no false positive diagnoses.

The agreement in 18 out of 19 patients, between what was believed to have been accomplished surgically and the results of the post-operative studies (together with the concurring post-operative clinical findings), supports the validity of the ascor-

bate and blood oximetry results in this subgroup and measures the success of operation. In the patient in whom disagreement existed between the supposedly successful closure of an atrial septal defect of the primum type and the post-operative finding of a persistent left-to-right shunt, the evidence provided by the two independent methods for shunt detection would be hard to discard.

In 85 patients surgical confirmation is lacking. In view of the extreme rarity of false positive diagnosis of left-to-right shunts by blood oximetry, the ascorbate dilution curves can be considered valid in the 31 patients of this subgroup who had evidence of left-to-right shunt by both methods. In the 54 patients in whom no left-to-right shunts were detected, the clinical, electrocardiographic, and radiological findings concurring suggested their absence.

II: *Ascorbate and Blood Oximetry Results in Disagreement.* The disagreement in one patient was limited to the location of left-to-right shunting, while in 23 patients it centred in the existence of the shunt (Table I).

IIa: *Disagreement limited to the location of left-to-right shunt.* The clinical findings were highly suggestive of ventricular septal defect. Blood oximetry supported this diagnosis: 1.1 vol. per cent O₂ rise from the averaged right atrial to the right ventricle samples, and 1.5 vol. per cent from right atrium to pulmonary artery. The ascorbate technique, however, revealed abnormality also of the right atrial curve. It is suggested that this patient had a ventricular septal defect with a slight degree of tricuspid

TABLE
ASCORBATE DILUTION AND BLOOD

	No.	Studies before operation		
		Blood oximetry (difference in vol. %)	Ascorbate technique	Surgical diagnosis
Ventricular septal defect (acyanotic)	1	Not diagnostic RA→RV: + 0.7 RA→PA: + 0.8	Ventricular septal defect	Ventricular septal defect 0.4 cm. diameter
Ventricular septal defect (cyanotic)				
Atrial septal defect, partial anom. pulm. ven. drainage				
Patent ductus arteriosus	1	Not diagnostic RA→RV: - 0.5 RV→PA: + 0.4	Patent ductus arteriosus	Patent ductus arteriosus 0.7 cm. diameter
Pulmonary stenosis and ventricular septal defect	1	Not diagnostic RA→RV: + 0.6 RA→PA: + 0.2	Pulmonary stenosis and patent ductus arteriosus	Pulmonary stenosis and ventricular septal defect 0.3 cm. diameter
Pulmonary stenosis and ventricular septal defect (cyanotic)	2	Not diagnostic No difference	Pulmonary stenosis and ventricular septal defect	Pulmonary stenosis and ventricular septal defect 3 cm. diameter
Mitral stenosis and patent foramen ovale (stretched)	1	SVC→RA: + 3.3 MS + ASD	Not diagnostic mitral stenosis	Mitral stenosis and patent foramen ovale
Total	6			

* The + sign indicates higher O₂ content in the downstream compartment. RA→RV=right atrium to right ventricle. RA→PA=right atrium

insufficiency. In such a situation, the ascorbate technique will detect indicator in the chamber immediately upstream from the site of shunting, while the less sensitive blood oximetry will not.

IIb: Disagreement involving the existence of left-to-

right shunt. The studies preceded operation in 6 patients, and followed operation in 2 patients (both with studies in agreement before operation), while in 15 there was no operation (Table III).

TABLE II
ASCORBATE DILUTION AND BLOOD OXIMETRY DATA IN AGREEMENT

	Studies before operation			Studies after operation			Studies not followed by operation		Total No. of studies
	No left-to-right shunt detected	Left-to-right shunt detected	Surgical diagnosis	Surgical procedure	No left-to-right shunt detected	Left-to-right shunt detected	No left-to-right shunt detected	Left-to-right shunt detected	
No heart disease							30		30
Idiopathic dilatation of pulmonary artery							7		7
Pulmonary stenosis	7		Same	Relief of stenosis	2		11		20
Aortic stenosis (congenital)	1		Same				2		1
Hypertrophic subaortic stenosis							1		2
Aortic insufficiency (congenital)							1		1
Coarctation of aorta	1		Same						1
Undiagnosed							1		1
Ventricular septal defect		4	Same	Closure of defect	3			14	21
Atrial septal defect (secundum or primum) with or without PAPVD*		12	Same	Closure of defect	9	1		12	34
Patent ductus arteriosus		6	Same						6
Pulmonary stenosis + ventricular septal defect (acyanotic)		7	Same	Closure of defect and relief of stenosis	2				9
Pulmonary stenosis + ventricular septal defect (cyanotic)				1 Brock procedure 1 Potts procedure					
Ventricular septal defect + patent ductus arteriosus		2	Same			2	2		4
Persistent truncus arteriosus								1	3
Ventricular septal defect + coarctation of aorta								2	2
Aneurysm of sinus Valsalva ruptured into right atrium								1	1
								1	1
Total	40				19		85		144

* Partial anomalous pulmonary venous drainage.

III

OXIMETRY DATA IN DISAGREEMENT

No.	Studies after operation			No.	Studies not followed by operation		
	Surgical procedure	Blood oximetry (difference in vol. %)	Ascorbate technique		Clinical findings	Ascorbate technique	Blood oximetry* (difference in vol. %)
1	Complete repair of partial anom. pulm. ven. drainage	SVC→RA + 0.4 SVC→RA + 0.5	Persistent atrial septal defect	9	Loud pansystolic murmur; normal to 1 + heart; normal electrocardiogram	Ventricular septal defect	Not diagnostic RA→RV + 0.1 to + 0.8 RA→PA + 0.2 to + 0.8
				1		Ventricular septal defect	Not diagnostic no increase
1	Complete correction of ventricular septal defect + pulmonary stenosis	SVC→RA + 0.4 SVC→RV + 0.5	Persistent ventricular septal defect	3	Physiological splitting of 2nd sound; pulmonary ejection murmurs in 2	Atrial septal defect and/or partial anom. pulm. ven. drainage	Not diagnostic
				1	Loud pansystolic murmur; slightly enlarged heart; normal electrocardiogram	Ventricular septal defect	Not diagnostic RA→RV + 0.3 RA→PA + 0.4 Not diagnostic no rise
2				1		Ventricular septal defect	
				15			

to pulmonary artery, etc.

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FIG. 5.—In this 13-year-old girl with ventricular septal defect and mild pulmonary stenosis, no shunt is detected by blood oximetry, while the ascorbate dilution curve from the right ventricle (tracing on the right) is clearly abnormal. The normal curve from the right atrium (on the left) indicates that shunting is at ventricular level. Operation confirmed the presence of a ventricular septal defect. Oximetry figures are in volumes per cent.

Pre-operative studies: 6 patients. A 9-year-old boy had a grade 4/6 harsh pansystolic murmur best heard along the lower left sternal border, a normal electrocardiogram, and radiological evidence of slight pulmonary vascular prominence, all consistent with a small ventricular septal defect. Blood oximetry during heart catheterization was inconclusive: 0.7 vol. per cent O_2 rise from right atrium to right ventricle and 0.8 vol. per cent rise from right atrium to pulmonary artery, while the ascorbate curves detected a small ventricular septal defect. At operation the VSD, measuring 4 mm. in diameter, was located beneath the septal leaflet of the tricuspid valve.

A 13-year-old girl with a grade 3/6 ejection murmur at the second left intercostal space and a grade 3/6 pansystolic murmur along the lower left sternal border had pressure tracings of valvular pulmonary stenosis. Blood oximetry was not diagnostic: 0.6 vol. per cent O_2 rise between the averaged right atrium and right ventricle and 0.2 vol. per cent increase between the averaged right atrium and pulmonary artery samples. Ascorbate dilution curves were indicative of a small ventricular septal defect (Fig. 5). Operation, in addition to pulmonary stenosis, confirmed this finding: septal defect lay beneath the septal leaflet of the tricuspid valve and measured 3 mm. in diameter.

An 11-year-old girl had an intermittent machinery-like murmur in the second left intercostal space, normal electrocardiogram, and radiographs suggestive of slight cardiac and pulmonary artery enlargement, with a slight increase of the pulmonary vascular markings. There was no significant increase of O_2 content at any level within

the right heart and pulmonary artery above that of the superior vena cava. The ascorbate dilution curves indicated the presence of a left-to-right shunt within the pulmonary artery, and the catheter tip entered the descending aorta from the origin of the left pulmonary artery. At operation a patent ductus arteriosus 7 mm. in diameter, 6 mm. long, was discovered.

In two cases with cyanotic tetralogy of Fallot the existence of a small left-to-right shunt was detected by the ascorbate dilution technique and not by blood oximetry.

A 47-year-old woman with clinical findings of mitral stenosis, a huge heart, pulmonary hypertension, functional tricuspid insufficiency, and long-standing massive congestive heart failure, was suspected to have an associated atrial septal defect because of fixed splitting of the second heart sound. A large transmittal gradient was discovered at catheterization. Blood oximetry indicated a 3.3 vol. per cent O_2 increase between the superior vena cava and the averaged right atrial samples, while the ascorbate dilution curves were not diagnostic. Operative findings were those of mitral stenosis, large left atrium, and stretched patent foramen ovale, 1.0 cm. in diameter.

In five cases, then, the existence of a left-to-right shunt was detected by the ascorbate technique and not by oximetry: and in one oximetry proved superior. The ascorbate dilution technique seems to be far better, but its failure in one case is disturbing. The likely explanation lies in the large

FIG. 6.—In this patient, not operated upon, the presence and location of a small shunt at the ventricular level is clearly indicated by the discrete spike between injection spike and recirculation wave in the curve from the right ventricle (right of heart diagram), absent in the curve from the right atrium (left of the heart diagram). Blood oximetry (vol. %), again, is not diagnostic.

central blood volume of this patient and the consequent extreme dilution of the indicator.

The detection and location by the ascorbate technique of left-to-right shunts which blood oximetry has failed to reveal in patients with cyanotic heart disease, eliminates the need for more elaborate diagnostic investigation for the localization of the shunt in these patients.

Post-operative studies. A 6-year-old boy with pulmonary stenosis and ventricular septal defect who was acyanotic, underwent corrective surgery, and the ascorbate and blood oximetry results after operation were in disagreement. The former indicated a persistent left-to-right shunt at ventricular level, and the results from oximetry were borderline: 0.9 vol. per cent O_2 increase between the averaged right atrium, and right ventricle and pulmonary artery samples.

A 6-year-old boy with a pre-operative diagnosis of atrial septal defect (secundum type) had complete repair of a large defect, and of partial anomalous pulmonary venous drainage. After operation, a grade 2/6 ejection murmur persisted in the second left intercostal space, and the persistence of a small left-to-right shunt was detected by the ascorbate dilution technique, but not by blood oximetry: 0.4 vol. per cent O_2 increase between the superior vena cava and right atrium.

The evidence of persistent left-to-right shunt by the ascorbate technique in the first case was at least in part supported by the borderline results of blood oximetry. In the second case the two techniques were more clearly discrepant, but the clinical findings suggested persistence of a left-to-right shunt.

Studies not followed by operation. Ten patients, with few or no symptoms, grade 3-4/6 pansystolic murmurs

best heard along the lower left sternal border (one had also a thrill), normal or slightly enlarged hearts and pulmonary arteries, and normal cardiograms had no evidence of left-to-right shunt by blood oximetry: 0.1 to 0.8 vol. per cent O_2 rise from right atrium to right ventricle and 0.3 to 0.8 vol. per cent rise from right atrium to pulmonary artery. The ascorbate technique indicated the presence of small ventricular septal defects in all (Fig. 6). One had mild pulmonary stenosis as well.

In a cyanotic patient with a large ventricular septal defect and pulmonary hypertension, and a second with Fallot's tetralogy, blood oximetry failed to reveal the presence of a left-to-right shunt, which was clearly indicated and located by the ascorbate curves.

Finally, in three patients, one adult and two children, the diagnosis of atrial septal defect or partial anomalous pulmonary venous drainage was made from the ascorbate dilution curves, while the results of blood oximetry were not diagnostic. All had normal splitting of the second sound. The adult had no symptoms or positive physical signs and was catheterized (with negative blood oximetry results) because of the radiological suggestion of a "scimitar syndrome" and slight pulmonary artery enlargement. On a repeat catheterization, the blood oximetry data were significant: the rise of O_2 content was 1.7 vol. per cent from superior vena cava to right atrium and 2.1 vol per cent from superior vena cava to right ventricle and pulmonary artery. The two children had grade 2/6 and 4/6 ejection murmurs respectively, in the second left intercostal space, slight prominence of the pulmonary artery on x-ray examination, and electrocardiographic evidence of right bundle-branch block and slight right ventricular hypertrophy, respectively. In one, the catheter passed repeatedly from the right to the left atrium and an angiogram showed passage of contrast material from left to right atrium during the left heart phase. In the second child, with slight right

ventricular hypertrophy on the electrocardiogram, bilateral coarctation of the pulmonary artery was discovered, with slight right ventricular hypertension. In this patient abnormality of the curves persisted as far as the superior vena cava, and an insignificant rise of O₂ content occurred also within this vessel. It is concluded that this patient had slight bilateral coarctation of the pulmonary artery, and partial anomalous pulmonary venous drainage into the superior vena cava.

In 12 patients the discovery of small atrial and ventricular defects by the ascorbate technique is supported by one or more of the following: clinical and angiographic data, course of the catheter, and repeated catheterization. In the patient with a partial anomalous pulmonary venous drainage by the ascorbate technique, indirect evidence supports this diagnosis. In the two patients with cyanotic heart disease, the ascorbate curves indicated shunting at ventricular level, thus eliminating the need for additional investigation.

DISCUSSION

Since its introduction into the routine of right heart catheterization (Dexter *et al.*, 1946), blood oximetry has been the standard method for the detection and location of left-to-right shunts in most laboratories. The limits of confidence are well established and its reliability has been demonstrated many times by confirmation at operation, but its diagnostic inadequacy in the presence of small left-to-right shunts is recognized (Selzer, 1954).

Of the various methods used in conjunction with catheterization for the purpose, at least in part, of overcoming this limitation and using indicators other than oxygen, the ascorbate dilution technique is the most recent and least tested.

To gain wide acceptance a new method must be safe, simple, reliable, and sensitive. The safety and simplicity of the ascorbate dilution technique have been stressed in previous reports (Frommer *et al.*, 1961; Nixon *et al.*, 1963). This discussion is concerned essentially with the aspects of reliability and sensitivity.

The extent of the agreement between ascorbate dilution and oximetry techniques involved 144 out of 168 studies (85.7%) from 137 out of 159 patients. In 42 of these patients operation confirmed the absence, or presence and location of the left-to-right shunts. In view of much concurring indirect evidence, it appears safe to conclude that the diagnosis was correct also in the remaining 95 patients in whom surgical control was lacking. The ascorbate technique appears to be as reliable as blood

oximetry in the detection and location of left-to-right shunts.

The critical test of validity for a new method, however, is represented by situations in which its results are in disagreement with those of the older method, i.e. in this series 24 out of 168 studies, or 14 per cent. In one of these cases, proved at operation, the ascorbate technique yielded a false negative result where blood oximetry was clearly diagnostic of a left-to-right shunt. The most likely explanation for this sole failure of the ascorbate technique lies in the very large central blood volume of this adult patient and consequent extreme dilution of indicator. The use of larger doses in such cases should overcome this problem. In the other 23 patients the ascorbate technique detected and located small left-to-right shunts which oximetry failed to reveal. In five of these patients operation confirmed the ascorbate findings. The possibility of the other 18 representing false positive results cannot be categorically excluded, but is made unlikely by one or more of the clinical, electrocardiographic, radiological, and catheterization (course of catheter, angiography) findings, suggesting or indicating the presence and location of small left-to-right shunts. The ascorbate dilution method, therefore, appears to be more sensitive than blood oximetry for the detection and location of small left-to-right shunts.

The need for a diagnostic procedure at catheterization to yield the highest possible degree of accuracy is self-evident. Oximetry in conjunction with intracardiac pressure measurements supplied a diagnosis in 125 (85%) of the 147 patients who underwent catheterization for diagnostic purposes (12 of the 159 had only post-operative studies). For the ascorbate technique the figures were 145 out of 147, or 99 per cent. By combining ascorbate and oximetry techniques, only one patient remained undiagnosed: a young girl with angina, in whom no shunt and no congenital or acquired causes for this symptom were detected.

The case for combining oximetry and the ascorbate dilution technique during right heart catheterization appears strong. A common catheter is shared and the performance of even a large number of ascorbate dilution procedures should not add more than 15 minutes to the procedure. After an initial period of adjustment to the new method, the chance of false positives is eliminated, the sources of poor technical results (partial clotting in the catheter, short circuits) should be well recognized, and the percentage of technical failures should be less than 10 per cent. The returns, far outweighing the above difficulties, are a greater confidence in the haemodynamic diagnosis and a significantly higher diagnostic yield.

SUMMARY

The results of blood oximetry and the ascorbate technique during heart catheterization have been compared in 168 consecutive studies from 159 patients. The findings indicate that the ascorbate technique is as reliable as oximetry, and more sensitive in the detection of small left-to-right shunts. A specific diagnosis was reached by oximetry and intracardiac pressure recording in 85 per cent of the patients and by the ascorbate technique plus intracardiac manometry in 99 per cent. By combining the two methods, only one patient could not be diagnosed. The combined use of oximetry and the ascorbate dilution techniques during catheterization is recommended in order to increase diagnostic accuracy, especially in cases with small left-to-right shunts.

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