Abnormal Indicator Dilution Patterns in Dogs Produced by Flowmeter Probes on the Pulmonary Artery

By Irwin J. Fox, M.D., Ph.D., Aldo R. Castaneda, M.D., and Kenneth C. Weber, B.S.E.E.

Indicator dilution technics have been employed by Malooly and co-workers for the in vivo calibration of electromagnetic flowmeter probes. In attempting to apply this calibration procedure to the measurement of pulmonary arterial flow in anesthetized dogs, we noted that the presence of the flowmeter probe on the pulmonary artery was frequently associated with abnormal indicator dilution curves. In 16 out of 32 experiments the indicator dilution curves were so abnormal that they could not be used to calculate flow as required for calibration of the flowmeter probes. The abnormal curves resembled those observed in the presence of left-to-right shunts; typical examples are shown in figure 1.

The possibility that slight constriction or immobilization of the pulmonary artery could interfere so drastically with normal distribution of dye seemed to warrant further investigation. The following experiments show clearly that mechanical interference with the pulmonary artery, incident to placement of electromagnetic flow probes around the artery, can indeed produce striking abnormalities in indicator dilution curves recorded at the femoral artery.

Methods

A left thoracotomy was performed in dogs under sodium pentobarbital anesthesia (30 mg/kg) and they were studied in the right lateral recumbent position. The pulmonary artery was carefully freed by dissection. Under fluoroscopic control a no. 6F Courmand cardiac catheter connected to a strain gauge manometer was first advanced from the right jugular vein until its tip lay in the pulmonary artery and then withdrawn under continuous monitoring of the pressure until the first pressure pulses appeared indicating that the tip was in the right ventricle. Pulmonary and left femoral artery pressures were recorded via indwelling 19-gauge thin-wall needles while right ventricular pressure was recorded via the catheter, all pressures being recorded by Statham P23De strain gauges. Next a flowmeter probe,* deemed suitable in size by inspection, was placed on the proximal pulmonary artery. Usually a 10 or 12 mm probe was used in dogs weighing 10 to 14 kg. Suitability of a particular flowmeter probe in an animal was evaluated by pressures monitored visually and also recorded at the three sites (right ventricle, pulmonary, and femoral arteries). In most instances a systolic pressure gradient of less than 20 mm Hg (mean, 19; range, 0 to 58 mm Hg in 32 dogs) between the right ventricle and distal pulmonary artery persisted after a suitable probe was in place on the pulmonary artery. Animals having femoral arterial systolic pressures below 100 mm Hg were excluded from this study. Indocyanine green dye was injected into the right ventricular outflow tract, the dye-blood mixture being sampled from the right femoral artery through a densitometer* via an indwelling 19-gauge thin-wall needle, using technics described previously.2 The dynamic response characteristics of this densitometer-needle sampling system have been reported.3,4 A sampling rate of 15 ml/min was used for recording the dilution curves.

After the cause of the abnormalities was suspected, abnormal femoral arterial curves could often (but not invariably) be produced by pulling on a thread attached to the electrical leads.
Abnormal dilution curves recorded at femoral artery following injections of indocyanine green dye into right ventricular outflow tract in two open chest dogs having electromagnetic flowmeter probes on the pulmonary artery. Note abnormal secondary peak on disappearance slope of the curve (left panel) and the abnormal prolongation of the disappearance slope of the curve (right panel).

Comparison of dilution curves recorded at approximately five-minute intervals at the femoral artery in an 11.4 kg open chest dog following injections of dye into right ventricular outflow tract. Abnormal curves (left and right panels) were recorded with a 12 mm flowmeter probe on the pulmonary artery while the normal dilution curve (middle panel) was recorded with probe off the pulmonary artery.

On the normal curve (middle panel) the measurements (in cm) made to calculate the empirical ratios used to quantitate degree of dispersion of indicator particles in the circulation are shown. BT = build-up time; PC = peak concentration; CL = least concentration; CR = recirculation concentration; PHPC = period at half peak concentration (measurement is converted to seconds). Concentrations are assumed to be proportional to oscillograph deflections thus obviating the need to convert the cm measurements obtainable directly from the curve to mg/liter.

See table 1 for definitions of ratios used.

To establish if delayed clearing of dye from the region of the pulmonary artery upstream from the probe occurs, a fiberoptic densitometer catheter (O.D. 1.4 mm) was advanced into the proximal pulmonary artery inside a no. 7F thin-wall Courand catheter, whereupon the fiberoptic catheter tip was protruded until it lay near the wall of the artery just upstream from the probe. By visually monitoring the degree and direction of the transillumination of the pulmonary artery wall by the fiberoptic densitometer, its tip was maintained in approximately the same relation to the probe, thus distorting the pulmonary artery. In addition to the femoral artery sampling site, dilution curves were also recorded from the proximal pulmonary artery (upstream from the probe) by means of a standard densitometer* and also by means of a fiberoptic densitometer.15 16

*Model XC100A, Waters Corporation, Rochester, Minnesota.
1Kindly loaned to us for this study by Dr. M. Polanyi, American Optical Company, Southbridge, Massachusetts.

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the wall with the flowmeter probe on and off the artery.

Results

Figure 2 shows dilution curves recorded in the same dog at five-minute intervals at the femoral artery following dye injections into the right ventricular outflow tract alternately with the flowmeter probe on and off the pulmonary artery. The abnormal curve recorded initially with the flowmeter probe on the pulmonary artery is shown in the left panel. Removal of the probe from the pulmonary artery resulted in the normal curve seen in the middle panel and replacement of the probe again produced an abnormal dilution pattern as seen in the right panel. Findings similar to those shown in figure 2 were obtained in 38 such experiments in 12 dogs. Some of the measurements made for the empirical ratios used in quantitating the dispersion of indicator particles in the circulation are also shown in figure 2, middle panel.

That a disturbance in the normal flow pattern at or near the flowmeter probe was responsible for the abnormality of the dilution curves is evident from figure 3 in which the abnormal curve shown in the left panel was recorded at the femoral artery following injection of dye into the proximal pulmonary artery, upstream from the probe, while a fairly normal curve was recorded at the femoral artery four minutes later when the injection was made into the distal main pulmonary artery, downstream to the probe. The findings in figure 3 are representative of those in 12 experiments in 6 dogs.

The flowmeter probes were selected to fit snugly around the pulmonary artery in order to obtain good electrical contact with the outer wall of the vessel. Doubtless this caused some narrowing of the vessel lumen and the weight of the probe may have caused some kinking of the vessel. Pressure differences of the order of 5 to 20 mm Hg were commonly recorded between a point proximal to the probe and a point distal to the probe. However, there was no obvious relation between the magnitude of this pressure difference and the appearance of the abnormal curves, both normal and abnormal curves having been recorded in animals when the pressure difference across the probe was zero and when it was very high, e.g., greater than 50 mm Hg. The mean pressure difference across the probe in animals in whom abnormal curves were recorded was 21 mm Hg (range, 0 to 56)

![Comparison of dilution curves recorded at femoral artery following successive injections into proximal pulmonary artery (upstream to probe) and into distal main pulmonary artery (downstream to probe) in a 9.8 kg open chest dog. Note markedly abnormal dilution curve recorded following injection of dye upstream from the probe (left panel) as compared to the relatively normal appearing curve recorded following injection of dye just downstream to the probe four minutes later (right panel).](http://circres.ahajournals.org/content/15/10/303)

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TABLE 1

Comparison of Contours and Areas (cardiac output values) of Dilution Curves Recorded at Femoral Artery and at Proximal Pulmonary Artery With and Without Flowmeter Probe on Pulmonary Artery Following Successive Injections of Indocyanine Dye into Right Ventricle

<table>
<thead>
<tr>
<th></th>
<th>Femoral artery (means of 23 pairs of curves, 12 dogs)</th>
<th>Proximal pulmonary artery (means of 21 pairs of curves, 7 dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Probe off</td>
<td>Probe on pulmonary artery</td>
</tr>
<tr>
<td></td>
<td>BT</td>
<td>2BT</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>0.497</td>
<td>0.172</td>
</tr>
<tr>
<td>Probe off</td>
<td>(±0.101)*</td>
<td>(±0.055)</td>
</tr>
<tr>
<td></td>
<td>0.583</td>
<td>0.267</td>
</tr>
<tr>
<td>Probe on pulmonary artery</td>
<td>(±0.086)</td>
<td>(±0.086)</td>
</tr>
<tr>
<td>Difference</td>
<td>−0.066</td>
<td>−0.095</td>
</tr>
<tr>
<td></td>
<td>(±0.075)</td>
<td>(±0.080)</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Proximal pulmonary artery (means of 21 pairs of curves, 7 dogs)

<table>
<thead>
<tr>
<th></th>
<th>Probe off</th>
<th>Probe on pulmonary artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT</td>
<td>2BT</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>0.823</td>
<td>0.549</td>
</tr>
<tr>
<td>Probe off</td>
<td>(±0.108)</td>
<td>(±0.181)</td>
</tr>
<tr>
<td></td>
<td>0.843</td>
<td>0.817</td>
</tr>
<tr>
<td>Probe on pulmonary artery</td>
<td>(±0.065)</td>
<td>(±0.137)</td>
</tr>
<tr>
<td>Difference</td>
<td>−0.020</td>
<td>−0.068</td>
</tr>
<tr>
<td></td>
<td>(±0.120)</td>
<td>(±0.383)</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

\[ \frac{BT}{PC}, \frac{2BT}{PC} = \text{ratio of the deflection occurring \( 1BT \) \text{ (build-up time) or } 2BT \text{ after the peak deflection}} \]

\[ \frac{CL}{CR} = \text{ratio of the deflection at least concentration to that at systemic recirculation} \]

\[ \text{PHPC} = \text{period at half peak concentration in seconds; see figure 2 for illustration of actual measurements.} \]

Numbers in parentheses are standard deviations.

which did not differ greatly from a mean pressure difference of 18 mm Hg (range, 0 to 58) across the probe in animals in whom only normal curves were recorded. However, for identical pressure differences across the probe, dogs in whom abnormal curves were recorded tended to have lower values for cardiac output and systemic arterial systolic pressure than those in whom the recorded dilution curves were normal. Curves were considered abnormal if they differed in any two of the empirical ratios given in table 1 by more than two standard deviations from the mean values for femoral artery curves recorded without flowmeter probe on the pulmonary artery (table 1).

Because of this rise in pressure upstream from the probe, pulmonary and/or tricuspid valvular insufficiency had to be considered as possible causes of the abnormal curves. Following injection of dye into the low right ventricle, blood was sampled simultaneously from the right atrium at the tricuspid valve and from the femoral artery in 10 experiments on 3 dogs. In the presence of an abnormal curve recorded at the femoral artery, the absence of any detectable early-appearing dye at the right atrial sampling site was considered to be strong evidence that tricuspid regurgitation was not the cause of the abnormal femoral arterial dilution patterns. A typical experiment is illustrated in figure 4. In a similar manner dye was injected into the pulmonary artery just above the pulmonary valve while blood was sampled through densitometers from the right ventricular outflow tract and from the femoral artery as shown in figure 5. Again, the absence of any detectable early-appearing dye at the upstream sampling site, i.e., at the right ventricle, in the pres-
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FIGURE 4

Dilution curves recorded simultaneously at right atrium near tricuspid valve and at femoral artery following injection of indocyanine green dye into the low right ventricle. Note absence of early-appearing dye at right atrial sampling site (stable right atrial densitometer base line just after injection) in the presence of an abnormal curve recorded from femoral artery. This provides evidence against tricuspid regurgitation as cause of abnormal femoral arterial dilution curves.

FIGURE 5

Dilution curves recorded simultaneously at right ventricular outflow tract just below pulmonary valve and at femoral artery following injection of indocyanine green dye into pulmonary artery just above valve, in a 10.6 kg open chest dog, with a 12 mm probe on the pulmonary artery. Note absence of early-appearing dye at right ventricular sampling site (stable right ventricular densitometer base line just after injection) in the presence of an abnormal curve recorded from femoral artery. This provides evidence against pulmonary regurgitation as the cause of abnormal femoral arterial dilution curves.

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ence of an abnormal femoral artery curve, a result which was obtained in 10 satisfactory experiments in 3 dogs, was considered to be strong evidence against pulmonary regurgitation as the cause of the abnormal femoral curves. When, as occurred on several occasions, the upstream catheter tip was malpositioned as, for example, by being entangled in the chordae tendineae of the tricuspid valve, probably rendering the valve insufficient, early-appearing dye was detected at the upstream sampling site, attesting to the sensitivity of this application of the two-catheter sampling technic. In each of three instances in a total of 23 experiments in which early-appearing dye was detected at the upstream sampling site, definite malpositioning of the catheter tip was noted at autopsy.

That the abnormalities in the dilution curve under discussion may be quite subtle is apparent from figure 6 in which dilution curves recorded at the femoral artery of a dog following successive injections of dye upstream and downstream to the probe on the pulmonary artery are shown. At first glance both curves appear normal, but the CL/CR ratio (the ratio of the deflection at least concentration to that at systemic recirculation) of the curve on the left is 0.68 while that of the curve on the right is 0.45. This difference is statistically significant (table 1). On closer scrutiny it becomes apparent, however, that there are other subtle differences in contour between the two dilution curves shown in figure 6 and it is likely that the abnormal curves form a continuous spectrum with the normal ones.

Because of the nature of the abnormalities in the dilution curves, i.e., the presence of a secondary peak on the disappearance slope or prolongation of the disappearance slope, and especially since other causes of such abnormalities had been for all practical purposes ruled out (see above), it appeared that some of the dye particles (sometimes a large fraction of the total) were being held up at some point in their course through the circulation, most likely at a site at or near the flowmeter probe. To corroborate this, the contours and areas of dilution curves recorded at two different sites in the circulation following successive injections of dye into the right ventricular outflow tract with and without a flowmeter probe on the pulmonary artery were compared as shown in table 1. The position of the probe on the pulmonary artery was, of course, not deliberately distorted in any way for this study.

In table 1, lower half, the contours and areas, the latter expressed as cardiac output values, are compared in 21 pairs of curves recorded successively at the proximal pulmonary artery in seven dogs with and without a flowmeter probe on the pulmonary artery fol-

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**FIGURE 6**

Comparison of dilution curves recorded at femoral artery following successive injections of indocyanine green dye into right ventricular outflow tract and into main pulmonary artery distal to the probe in a 14.8 kg open chest dog. Note subtle abnormalities in dilution curve recorded upstream from probe (left panel) as compared to the normal curve recorded following injection of dye just downstream to probe one minute later (right panel).

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Comparison of dilution curves recorded simultaneously at femoral artery with a standard densitometer and at proximal pulmonary artery with a fiberoptic densitometer in an 11.0 kg open chest dog following injections of dye into right ventricular outflow tract with and without a flowmeter probe on the pulmonary artery. Note delayed clearance of dye from proximal pulmonary artery, upstream from probe, detected by the fiberoptic densitometer as compared to the rapid clearance of dye from this same region when the probe was removed. Note also abnormal contour of femoral arterial curve recorded with probe on the pulmonary artery as compared to the fairly normal femoral artery curve recorded eight minutes later, after the probe had been removed. (Note: Change in base line of fiberoptic densitometer is due to electronic repositioning of galvanometer.)

Following injection of dye into the right ventricular outflow tract. The sampling site was upstream from the probe. The mean time interval between successive curves was 7.8 minutes (range, 2 to 17 min). It is seen that the contours of the curves recorded with and without a probe are significantly different as judged by the CL/CR ratio and the PHPC (period at half-peak concentration in seconds) values. Similarly, the cardiac output values (areas) of the curves recorded successively at the pulmonary artery with and without a probe are significantly different, the areas of the curves sampled upstream from the probe being larger (cardiac output value smaller) than the areas recorded at the same site with the probe off.

In a second series of 12 dogs the contours and areas of 23 pairs of curves recorded at the femoral artery following successive injections of dye into the right ventricular outflow tract with and without a flowmeter probe on the pulmonary artery were compared as shown in table 1, upper half. The mean time interval between successive curves was 6.5 minutes (range, 1 to 16 min). Only curves whose degree of distortion was mild enough so as not to preclude calculation of cardiac output by the Stewart-Hamilton technic were included. Thus all curves with secondary peaks on the downslope were excluded. Despite the fact that the contours of the curves recorded successively at the femoral artery sampling site with and without a flowmeter probe on the pulmonary artery were significantly different, the areas of these same curves, again expressed as cardiac output values, were not significantly different.

Discussion

The abnormalities in the dilution curves described above, which represent an altered distribution of traversal times of the dye particles, we believe to be due to turbulence and eddy formation in the pulmonary artery near the flowmeter probe. Thus, turbulence and eddies due to kinking and constriction of the pulmonary artery by the probe delay some dye particles, particularly near the boundary layers.

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Turbulence cannot be the sole cause of the abnormalities since turbulence is present normally in the great vessels; moreover, normal dilution curves are recorded in cases of pulmonary or aortic valvular stenosis where turbulence is exaggerated. The evidence indicates that the abnormal curves are caused by "backwaters" upstream from the immobilized, asymmetrically kinked and constricted pulmonary artery. These "backwaters," probably not formed symmetrically around the circumference of the pulmonary artery at its deformation by the probe, permit a considerable fraction of the injected fluid to be trapped in eddies causing it to spend more than the average length of time in the vessel, while most of the flow takes place through a restricted channel, as noted by Danckwerts.12 The development of eddies downstream to constrictions has been described in textbooks of hydrodynamics.13,14 Also, recent studies have shown pulsatile flow to be more unstable in tubes of elliptic cross section such as might be expected at the site of the pulmonary artery deformation than in circular tubes.15

Turbulence and eddies downstream to severe pathologic narrowing in the circulatory system have been demonstrated by the so-called "jet lesions" in these regions.10 As already stated, these conditions (e.g., pulmonary and aortic valvular stenosis, etc.) are not associated with abnormal dilution patterns. Marked eddy formation and turbulence downstream to severe obstructions have also been reported in circulation models.17,18 In direct contrast, in this study the major site of turbulence and eddy formation, responsible for sequestration of dye, was located upstream from the deforming flowmeter probe. The recording of relatively normal curves at the femoral artery following dye injections just downstream to the probe, in contrast to abnormal curves recorded at this same site following injections made just upstream from the probe, is evidence for location of the turbulence upstream from the probe (figs. 3 and 6). This difference in location of the "backwaters" may be due to the fact that, in contrast to the clinical conditions and models cited, the flowmeter probe produces relatively mild obstruction, while at the same time deforming the pulmonary artery and immobilizing a large segment of it as a rigid tube. The presence of some eddies in the pulmonary artery downstream to the probe could explain residual abnormalities occasionally seen in curves recorded following injections of dye just downstream to the probe (e.g., curve of fig. 3, right panel failing to return sufficiently close to the base line [increased CL]). Nonuniform clearance of indicator will affect the dilution curve more when the cause of the nonuniformity is near the injection site, as in the present study, than when clearance is nonuniform at points downstream, since the former would lead to the greatest temporal separation of the two components of the indicator distribution.10,16

Further evidence for sequestration was obtained from the differences in dilution curves recorded from the proximal pulmonary artery and the femoral artery in the presence and absence of a probe. The effect of the probe was to increase the area under curves recorded from the pulmonary artery proximal to the probe. In contrast, the areas under curves recorded from the femoral artery were unaffected by the probe despite marked alterations of contour. The underestimation of flow from curves recorded proximal to the probe (i.e., increased area under dilution curve) is evidently due to the dye-blood mixture being sampled directly from the region in which dye was sequestered. Abnormalities in arterial dilution curves due to sequestration of indicator have also been reported following massive pulmonary embolism.21

A comparison of dilution curves recorded simultaneously at the femoral artery with a regular densitometer and at the proximal pulmonary artery with the fiberoptic densitometer following injection of dye into the right ventricular outflow tract with and without a flowmeter probe on the pulmonary artery is shown in figure 7. Note the delayed clearance of dye from the proximal pulmonary artery upstream from the probe detected by the
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fiberoptic densitometer as compared to the rapid clearance of dye from this same segment detected similarly when the probe was removed. The curves shown in figure 7 were very reproducible in the same animal. When the fiberoptic tip was positioned near the pulmonary artery wall downstream to the probe, no delay in clearance of dye was observed as compared to its clearance with the probe off.

Summary

In acute experiments on open chested dogs, indicator dilution curves were recorded before and after placing electromagnetic flow probes on the pulmonary artery. The flow probes caused severe abnormalities in the dilution curves. The abnormalities resembled those seen in cases with left-to-right shunts.

The following facts suggest that the abnormalities are caused by turbulence and eddy formation near the flowmeter probe: (a) Direct measurements with a fiberoptic densitometer showed that clearance of dye just proximal to the probe was delayed. (b) The abnormalities disappeared immediately after removal of the probe or when the dye was injected just downstream to the probe. (c) The areas under curves recorded from the pulmonary artery upstream from the probe were greater than the areas under curves recorded at this same site without the probe.

Cardiac output and systemic arterial pressure were lower in animals with abnormal dilution curves than in those with normal femoral curves.

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References

2. Fox, I. J., and Wood, E. H.: Circulatory sys-

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