Hyperventilation test for diagnosis of left-to-right circulatory shunts

S. R. Reuben and J. Butler¹

From the Cardiac Department, Radcliffe Infirmary, Oxford

Pulmonary and systemic arterial carbon dioxide tensions (PCO_2) were measured at cardiac catheterization in 15 patients with left-to-right circulatory shunts and in 15 patients with valvular heart disease. The measurements were performed under resting conditions and at 5-sec intervals during a 30-sec period of hyperventilation. In both groups the systemic arterial PCO_2 fell significantly during hyperventilation. In patients with left-to-right shunts the pulmonary arterial PCO_2 fell significantly ($P < 0.01$) 10 sec after the onset of hyperventilation, but in the patients without shunts, hyperventilation produced no change in the pulmonary arterial PCO_2 .

There are now several acceptable procedures to confirm the presence of a left-to-right shunt in patients with septal defects or a persistent ductus arteriosus. The standard practice is to demonstrate a 'step-up' in the blood oxygen saturation at the site of the shunt and distal to it (Dexter *et al.*, 1947). Additional procedures to confirm a circulatory shunt include the description of indicator dye dilution time-concentration curves (Swan, Zapata-Diaz, and Wood, 1953). The use of a catheter-tip platinum electrode with either inhalation of hydrogen (Clark and Barger, 1959; Vogel, Grover, and Blount, 1962) or the injection of ascorbic acid (Kaplan *et al.*, 1961) are based on the same principle as indicator dye dilution curves, as is the nitrous oxide test (Sanders and Morrow, 1958). More recently, Gamble and his colleagues introduced a fiberoptic catheter for intracardiac oximetry (Gamble *et al.*, 1965).

This paper presents data on a further simple test for the detection of moderate left-to-right circulatory shunts and is based on the appearance, in the pulmonary artery, of hypocarbic blood after a short period of hyperventilation.

Patients and methods

A total of 30 patients was studied at routine cardiac catheterization. Fifteen patients had circulatory shunts with pulmonary/systemic blood flow ratios ranging from 1.5:1 to 4.7:1 (Table 1). Nine patients had atrial septal defects, 4 had ventricular

septal defects, and 2 had persistent ductus arteriosus. The control group consisted of 15 patients undergoing investigation for valvular heart disease (Table 2).

Conventional right heart catheterization was performed from either a right antecubital vein or the right saphenous vein. In the adolescent and adult patients the right femoral artery was catheterized with a microcatheter by a modified Seldinger technique. In the infants, femoral arterial blood samples were taken by direct arterial puncture. Heparinized blood samples were removed from the right heart and femoral artery and analysed for oxygen and carbon dioxide tension using Standard Radiometer electrodes. Analysis of paired samples usually agreed within 2 per cent of each other. Pulmonary and systemic blood flows were determined by the Fick principle (Dexter *et al.*, 1947) after a 5-minute expired air collection.

On completion of the routine measurements, blood samples were withdrawn from the pulmonary and femoral arteries and analysed for carbon dioxide tension (PCO_2). The patients were then instructed to hyperventilate for a period of 30 seconds. Further blood samples were withdrawn from both sites at 5-second intervals over the following 25 seconds and likewise analysed for PCO_2 .

The patients in the control group, who had mitral or aortic valve disease, underwent retrograde catheterization of the aorta and left heart chambers, with appropriate angiocardiology where indicated.

Results

The diagnostic and blood gas data for the patients with proven shunts are shown in Table 1 and for the control group (no shunt) in Table 2. The resting femoral arterial PCO_2

Received 18 March 1971.

¹ Present address: Department of Medicine, Division of Pulmonary Diseases, University of Washington, Seattle, U.S.A.

of both groups is lower than the normal value of 40 mmHg, indicating that all the patients were hyperventilating, to some extent, under resting conditions. Hyperventilation produced femoral arterial hypocarbia in both groups of patients; all the PCO_2 values were significantly reduced from the resting value ($P < 0.001$). The patients with proven left-to-right shunts showed reductions in the pulmonary arterial PCO_2 from the resting value, though it was

only after hyperventilating for 10 seconds that the reduced values showed statistically significant differences from the initial value ($P < 0.005$). The largest and most significant fall in both femoral and pulmonary arterial PCO_2 occurred 20 to 25 seconds after the start of hyperventilation ($P < 0.001$). Table 2 shows that hyperventilation produced no significant change in the pulmonary arterial PCO_2 values of the control group of patients

TABLE 1 Systemic and pulmonary arterial PCO_2 in patients with proven shunts

Case No.	Sex	Diagnosis	Body surface area (m^2)	Cardiac index ($l./min/m^2$)	Pulm./systemic flow ratio	Pulmonary artery sampling period (sec)				
						Rest	5-10	10-15	15-20	20-25
1	F	Atrial septal defect	1.6	2.8	4.0:1	29	28	27	23	22
2	M	Atrial septal defect	2.0	2.6	3.6:1	37	33	28	24	22
3	F	Atrial septal defect	1.5	2.5	2.1:1	32	27	22	21	20
4	F	Ventricular septal defect	1.7	3.5	1.9:1	37	37	32	30	29
5	M	Atrial septal defect	1.7	2.6	3.0:1	31	30	30	28	28
6	M	Persistent ductus arteriosus	1.8	3.4	2.3:1	34	33	29	28	23
7	F	Atrial septal defect	1.0	2.4	3.4:1	25	27	27	26	20
8	F	Atrial septal defect	1.4	6.3	4.7:1	28	27	25	23	27
9	M	Ventricular septal defect	1.7	2.4	2.0:1	36	35	32	29	24
10*	F	Persistent ductus arteriosus	1.5	2.1	1.6:1	34	31	26	25	
11*	M	Ventricular septal defect	0.7	3.0	1.5:1	33	24	22		
12*	F	Atrial septal defect	0.9	4.5	3.4:1	36	27			
13*	M	Ventricular septal defect	1.8	2.6	2.0:1	48	42	40		
14*	F	Atrial septal defect	1.6	1.4	2.4:1	31	20	16		
15*	M	Atrial septal defect	1.5	3.4	2.9:1	42	34			
Mean						34.2	30.3	27.4	25.7	23.9
SD						5.7	5.5	5.8	3.0	3.4
t							1.89	3.13	4.34	4.93

* Infants in whom systemic arterial samples were obtained by direct needle puncture.

TABLE 2 Systemic and pulmonary arterial PCO_2 in patients without shunts

Case No.	Sex	Diagnosis	Body surface area (m^2)	Cardiac index ($l./min/m^2$)	Pulm./systemic flow ratio	Pulmonary artery sampling period (sec)				
						Rest	5-10	10-15	15-20	20-25
16	F	Mitral stenosis	1.5	1.7	1.0	31	34	35	35	37
17	F	Mitral stenosis; pulmonary hypertension	1.7	2.4	1.0	32	32	34	33	34
18	M	Pulmonary stenosis	2.2	2.7	1.0	35	35	37	36	36
19	F	Mitral stenosis	1.6	2.7	1.0	32	31	31	33	36
20	F	Normal	1.6	4.5	1.0	27	32	29	28	33
21	F	Mitral stenosis; pulmonary hypertension	1.6	1.6	1.0	42	43	44	46	45
22	M	Normal	2.1	2.7	1.0	40	38	38	42	42
23	F	Mitral incompetence	1.6	2.0	1.0	34	37	37	39	38
24	M	Ebstein's anomaly	1.9	1.9	0.6	31	33	36	36	36
25	F	Mitral stenosis	1.5	3.6	1.0	32	32	32	31	32
26	F	Mitral incompetence; pulmonary hypertension	1.5	4.0	1.0	37	34	36	34	33
27	F	Mitral stenosis; aortic incompetence	1.9	1.9	1.0	43	41	44	42	46
28	F	Aortic stenosis; tricuspid incompetence								
28	F	Pulmonary stenosis	1.4	3.2	1.0	35	35	35	35	34
29	F	Pulmonary stenosis	1.8	2.7	1.0	32	31	32	32	31
30	M	Mitral stenosis; mitral incompetence	1.6			38	37	36	35	35
30	M	Aortic incompetence								
Mean						34.7	35.0	35.7	35.8	36.5
SD						4.5	3.6	4.2	4.7	4.5
t							0.18	0.63	0.63	1.09

($P < 0.30$). The Fig. shows in graphical form the changes that occurred in femoral and pulmonary arterial PCO_2 during hyperventilation for both groups of patients.

Discussion

The majority of procedures for the diagnosis of circulatory left-to-right shunts depend on the early appearance, in the right heart chambers or vessels distal to the shunt, of

Systemic artery
sampling period (sec)

Rest	5-10	10-15	15-20	20-25
25	26	23	18	17
33	30	22	19	18
30	20	17	15	14
23	23	17	16	16
31	33	28	24	23
34	25	25	25	24
27	27	23	19	17
31	31	21	16	15
35	23	18	18	17
23				
44	35			
34	22			
41	30			
32.5	27.1	21.6	18.9	17.9
5.8	4.7	3.8	3.5	3.4
	2.52	4.94	6.25	6.73

Systemic artery
sampling period (sec)

Rest	5-10	10-15	15-20	20-25
32				
30	27	23	21	19
35	20	16	15	14
28	19	15	13	13
22	23	23	21	21
37	34	29	26	25
41	26	21	21	19
33	31	28	27	26
33	27	25	24	24
30	30	25	24	23
30	30	28	25	24
35	34	33	23	22
27	25	22	22	21
26	23	21	20	20
31.3	26.9	23.8	21.7	20.6
5.1	4.9	5.1	4.0	4.0
	2.29	3.79	5.35	6.39

FIG. 1 Pulmonary arterial (PA PCO_2) and systemic arterial (SA PCO_2) carbon dioxide tensions during hyperventilation in patients with left-to-right shunts (---●--- and ---○---) and no shunts (—▲— and —×—). The data points represent the average values for the group at each sampling point.

either a physiological substance in higher concentration than normal, or a foreign material that has been introduced into the circulation by injection or inhalation. The standard procedure for confirming a left-to-right shunt of blood is to demonstrate an increase in the oxygen saturation of blood at and distal to the point of entry of the suspected shunt. This is simply the result of mixing of venous blood with low oxygen saturation with shunted fully-saturated blood from the left heart chambers or aorta (Dexter *et al.*, 1947).

The indicator dye dilution method is an example of the use of the early appearance of a foreign material to confirm the presence of either left-to-right or right-to-left circulatory shunts. Characteristic distortions of the normal time-concentration curve are produced (Swan *et al.*, 1953). The use of a catheter-tip platinum electrode with either inhalation of hydrogen (Clark and Barger, 1959; Vogel *et al.*, 1962) or the injection of ascorbic acid (Kaplan *et al.*, 1961) is based on the same principle as indicator dye dilution curves, as is the N_2O test (Sanders and Morrow, 1958). Catheterization of the right heart chambers with a fiberoptic catheter allows instantaneous measurement of blood oxygen saturation and this provides a sophisticated procedure for the detection of small circulatory shunts (Gamble *et al.*, 1965).

Reversal of a small left-to-right shunt at atrial level can be shown by performing

Valsalva's manoeuvre while monitoring systemic arterial blood oxygen saturation with an earpiece oximeter (Lee and Gimlette, 1957; McIlroy, 1959). After release of the strain there is a large inflow to the right atrium sufficient to reverse the shunt and produce a transient reduction in oxygen saturation.

The principle underlying the procedure described here is similar to those already described. Hyperventilation produces a decrease in alveolar carbon dioxide tension, which leads to a fall in the PCO_2 of the pulmonary venous and left heart blood (Comroe *et al.*, 1962). In the presence of a left-to-right shunt, the hypocarbic left heart blood will be shunted into the right heart chambers, lowering the PCO_2 of blood distal to the defect. It is unlikely that hyperventilation lowers the mixed venous blood PCO_2 by perfusion of the tissues with hypocarbic systemic arterial blood, because the venous sump for carbon dioxide is so great. Moreover, the muscular work involved in hyperventilation might be expected to increase the mixed venous PCO_2 . Table 2 does in fact show that there was no fall in pulmonary arterial PCO_2 during hyperventilation in the control group of patients.

This procedure is simple to perform and requires only a standard blood gas analyser. It could be utilized as a screening test for left-to-right shunts without the need for formal catheterization, since the use of pulmonary artery 'float' catheters has become popular (Thomas, Malmcrona, and Shillingford, 1965). Reliable information could be obtained from analysis of a resting pulmonary artery blood sample and one withdrawn 10–15 seconds after the start of hyperventilation.

References

- Clark, L. C., Jr., and Barger, L. M., Jr. (1959). Left-to-right shunt detection by an intravascular electrode with hydrogen as an indicator. *Science*, **130**, 709.
- Comroe, J. H., Jr., Forster, R. E., II, DuBois, A. B., Briscoe, W. A., and Carlsen, E. (1962). *The Lung*, 2nd ed. Year Book Medical Publishers, Chicago.
- Dexter, L., Haynes, F. W., Burwell, C. S., Eppinger, E. C., Sosman, M. C., and Evans, J. M. (1947). Studies of congenital heart disease. III. Venous catheterization as a diagnostic aid in patent ductus arteriosus, tetralogy of Fallot, ventricular septal defect and atrial septal defect. *Journal of Clinical Investigation*, **26**, 561.
- Gamble, W. J., Hugenholtz, P. G., Monroe, R. G., Polanyi, M., and Nadas, A. S. (1965). The use of fiberoptics in clinical cardiac catheterization. I. Intracardiac oximetry. *Circulation*, **31**, 328.
- Kaplan, S., Clark, L. C., Edwards, F. K., Gallaher, M. E., and Fox, R. P. (1961). Localization of right to left shunts with an intravascular polarographic anode sensitive to ascorbic acid. *American Journal of Cardiology*, **8**, 659.
- Lee, G. de J., and Gimlette, T. M. D. (1957). A simple test for interatrial communication. *British Medical Journal*, **1**, 1278.
- McIlroy, M. B. (1959). The clinical uses of oximetry. *British Heart Journal*, **21**, 293.
- Sanders, R. J., and Morrow, A. G. (1958). The diagnosis of circulatory shunts by the nitrous oxide test; improvements in technic and methods for quantification of the shunt. *Circulation*, **18**, 856.
- Swan, H. J. C., Zapata-Diaz, J., and Wood, E. H. (1953). Dye dilution curves in cyanotic congenital heart disease. *Circulation*, **8**, 70.
- Thomas, M., Malmcrona, R., and Shillingford, J. (1965). Hemodynamic changes in patients with acute myocardial infarction. *Circulation*, **31**, 811.
- Vogel, J. H. K., Grover, R. F., and Blount, S. G., Jr. (1962). Detection of the small intracardiac shunt with the hydrogen electrode. A highly sensitive and simple technique. *American Heart Journal*, **64**, 13.

Requests for reprints to Dr. S. R. Reuben, Cardiac Department, Radcliffe Infirmary, Oxford.