Hæmodynamic Changes on Exercise in Patients with Left-to-right Shunts

HYWEL DAVIES AND NIKOS GAZETOPOULOS*

From the Cardiac Department, Guy's Hospital, London S.E.1

There have been several studies of the effect of exercise on the hæmodynamics in patients with cardiac septal defects and left-to-right shunts (Jönsson, Linderholm, and Pinardi, 1957; Scébat *et al.*, 1957; Bruce and John, 1957; Swan, Marshall, and Wood, 1958; Stephens, Shafter, and Bliss, 1964), but some uncertainty remains about the conclusions. Since any attempt to understand the disability of such patients depends on these, we have attempted a further investigation into the changes occurring during exercise. This paper deals with the hæmodynamics, and a following communication is concerned with ventilatory and metabolic aspects (Gazetopoulos and Davies, 1966).

SUBJECTS AND METHODS

Studies were carried out on 34 patients, 18 with atrial septal defect (ASD), 12 with ventricular septal defect (VSD), and 4 with patent ductus arteriosus (PDA).

The hæmodynamic studies were performed during cardiac catheterization in the supine position. Routine data having been first obtained, a catheter was left in the pulmonary artery and an indwelling needle in a brachial artery. Spirometry was carried out and blood samples were taken; the catheter was then withdrawn to the lateral wall of the right atrium and further blood samples were obtained. In patients with ASD a second catheter, placed in the inferior vena cava, was withdrawn to the superior vena cava for further sampling. Paired samples were thus obtained from brachial artery, pulmonary artery, right atrium, or cavæ for flow determinations by the Fick principle. Dye-dilution curves were also inscribed, as described below.

The catheters were then replaced in their original sites and the patient exercised with either a spring-loaded leg exerciser (earlier studies) or a bicycle ergometer (Elema-Schönander—later studies). Pulmonary and brachial arterial pressures were continuously monitored and, after the fifth minute of exercise,

spirometry was repeated with the same sampling sequence as described above. Dye-dilution curves were also recorded during exercise. The spirometer was of the closed-circuit type (Donald and Christie, 1949) and oxygen consumption was corrected to STPD. Blood oxygen saturations were measured spectrophotometrically (Unicam model 600).

As representative of mixed venous saturation we have used the mean of right atrial samples where the shunt was distal to this level, while in ASD the mean of two inferior caval and one superior caval value was taken. Dye-dilution curves were recorded on a Mark II Cambridge dye recorder with a high-resistance input circuit giving a linear response to concentration of dye (Gabe and Shillingford, 1961), Coomassie blue being used as indicator. Special attention was paid to injecting the same quantity of dye at the same site just above the pulmonary valve at rest and on exercise. The curves were replotted and extrapolated on semi-logarithmic paper, and the shunt calculated as a percentage of the pulmonary flow by planimetry. In cases with large left-to-right shunts, where the primary and secondary circulations could not be separated, the appropriate empirical formula of Carter *et al.* (1960) was used:

$$\frac{Q_p - Q_s}{Q_p} \times 100 = 135 \left[\frac{C_{(P+2BT)}}{C_p} \right] - 14, \text{ where } Q_p \text{ represents}$$

pulmonary flow, Q_s systemic flow, C_p peak concentration, and $C_{(P+2BT)}$ the concentration at a point twice the build-up time after peak concentration.

RESULTS

These are shown in the Table. For the purpose of analysis VSD and PDA have been considered together and the two resulting groups (ASD on the one hand, VSD and PDA on the other) have been subdivided into those cases with low, moderately raised, and high pulmonary vascular resistance. The findings will be described in relation to the major groups concerned. In all the subsequent diagrams (Fig. 1-9) the results of Fick analysis have been used.

Received July 21, 1965.

* Present address: Alex. Soutson 8, Athens 134, Greece.

TABLE

CLINICAL AND HÆMODYNAMIC DATA IN 18 PATIENTS WITH ATRIAL SEPTAL DEFECT, 12 WITH VENTRICULAR SEPTAL DEFECT, AND 4 WITH PATENT DUCTUS ARTERIOSUS

Case No., sex, and age	Diagn.	BSA m. ²	O ₂ Con- sump- tion ml./min. STPD	Heart rate	Flows (l./min.)			Shunts (l./min.)		Qp - Qe %		Pressures (mm. Hg)			
					Sys- temic	Pul- mon- ary	Effec- tive	Left- to- right	Right- to- left	Qp		PCV m.	PA s.d.m.	RV s.d.	Systemic s.d.m.
										Fick	Dye curves				
AN 1 M 14	ASD	1.65	R 240 E 520	100 130	9.2 14.3	14.0 17.2	9.2 14.3	4.8 2.9	0	34 17	33 35	12	25/12/17 35/20/25	25/7 35/7	125/80/95 160/80/105
AN 2 F 38	ASD	1.60	R 200 E 370	132 132	4.2 —	9.9 13.5	4.2 —	5.7 —	0	58 —	— —	11 11	26/16/20 28/15/20	26/5 —	— —
AN 3 F 30	ASD	1.70	R 170 E 420	70 90	3.8 6.2	10.0 15.0	3.8 6.2	6.2 8.8	0	62 59	68 84	5	33/10/17 —	36/10 39/6	125/65/82 135/72/90
AN 4 F 16	ASD	1.50	R 160 E 470	80 115	5.5 10.3	14.5 12.2	5.5 10.3	9.0 1.9	0	62 16	66 47	6	25/6/11 20/8/10	28/6 20/0	— —
AN 5 F 24	ASD	1.50	R 190 E 450	80 120	4.0 8.6	13.6 20.3	4.0 8.6	9.6 11.7	0	70 58	77 74	7	20/6/13 25/10/15	45/6 50/6	90/55/60 130/80/100
AN 6 F 28	ASD	1.60	R 250 E 390	68 94	6.4 6.1	23.6 23.2	6.4 6.1	17.2 17.1	0	73 74	81 115	10	34/12/20 36/20/25	32/6 33/8	125/75/90 125/75/80
AN 7 F 34	ASD	1.60	R 140 E 330	75 90	5.1 —	20.4 27.4	5.1 —	15.3 —	0	75 —	78 92	12	36/14/23 40/17/26	39/5 —	118/68/85 —
AH 38 M 52	ASD	2.10	R 190 E 790	50 85	3.6 —	8.0 15.0	3.6 —	4.4 —	0	55 —	40 35	6	40/15/22 50/15/28	40/10 —	100/55/75 100/55/75
AH 39 F 59	ASD (AF)	1.90	R 270 E 410	94 104	5.8 6.3	12.8 13.0	5.8 6.3	7.0 6.7	0	55 52	54 65	—	45/25/35 —	40/10 50/10	125/80/100 125/80/100
AH 40 F 59	ASD	1.50	R 180 E 450	70 94	3.8 6.0	10.9 18.8	3.8 6.0	7.1 12.8	0	65 68	67 90	5	40/15/26 50/15/28	40/10 —	95/55/65 —
AH 41 M 54	ASD (AF)	1.90	R 180 E 760	75 110	2.7 —	6.4 16.9	2.7 —	3.7 —	0	58 —	70 38	12	50/28/35 75/25/40	50/14 —	135/80/100 150/80/100
AH 42 M 48	ASD	1.80	R 200 E 870	90 110	5.0 12.4	9.8 18.9	5.0 12.4	4.8 6.5	0	46 34	74 —	6	90/35/50 100/45/55	90/4 —	150/100/120 —
AH 43 F 31	ASD	1.35	R 210 E 600	90 140	6.0 8.9	21.0 23.0	6.0 8.0	15.0 15.0	0 0.9	72 65	— —	7 10	72/28/43 105/43/100	75/10 —	120/70/90 170/85/112
AH 44 F 39	ASD	1.60	R 200 E 370	68 136	4.1 —	9.9 16.8	3.2 —	6.7 —	0.9 0	68 —	— —	—	72/15/20 75/24/39	74/0 —	99/70/84 114/85/99
AH 45 F 49	ASD (AF)	1.70	R 180 E 400	70 130	2.6 5.7	11.8 22.0	2.6 5.7	9.2 16.3	0	78 74	78 80	20	80/40/50 100/45/60	80/15 100/15	110/60/80 140/65/90
AE 61 M 35	ASD Eisen.	1.90	R 180 E 680	72 110	4.5 9.4	2.7 7.9	2.4 6.3	0.3 1.7	2.1 3.1	11 22	— —	—	80/30/45 110/40/65	80/3 —	80/45/60 110/55/75
AS 82 M 22	ASD + PS	1.90	R 280 E 590	84 106	6.5 —	25.4 24.3	6.5 —	19.0 —	0	75 —	70 75	12	30/14/17 48/15/28	40/10 85/10	138/85/90 165/90/105
AS 83 F 9	ASD + PS	0.90	R 130 E 230	100 120	2.9 —	6.8 7.7	2.9 —	3.9 —	0	57 —	— —	9	29/12/18 33/12/18	70/8 80/10	96/52/74 90/60/75
VN 1 M 14	VSD	1.60	R 250 E 800	68 100	6.0 10.2	9.0 13.8	6.0 10.2	3.0 3.6	0	33 26	40 54	11	23/13/16 28/19/22	36/10 41/8	105/70/85 120/72/85
VN 2 M 16	VSD	1.50	R 180 E 780	72 107	4.9 14.0	5.6 16.0	4.9 14.0	0.7 2.0	0	12 12	17 14	6	21/10/16 28/10/18	26/6 28/0	150/90/105 165/100/115
VN 3 M 37	VSD	1.80	R 240 E 620	92 88	5.7 8.9	9.6 12.9	5.7 8.9	3.9 4.0	0	40 31	45 25	11	25/12/17 28/18/22	30/8 34/8	160/100/110 160/90/110
VN 4 F 15	VSD	1.50	R 170 E 610	80 120	5.7 10.5	11.5 13.0	5.7 10.5	5.8 2.5	0	50 19	53 59	9	28/10/14 48/25/31	32/4 —	100/72/82 —
VN 5 M 15	VSD	1.40	R 230 E 440	72 —	6.2 7.5	19.0 —	6.2 7.5	12.8 —	0	67.5 —	30 23	13	32/15/24 —	52/7 —	140/80/100 160/95/112
VH 31 M 26	VSD	1.80	R 280 E 670	84 115	6.6 11.2	15.4 17.9	6.6 11.2	8.8 6.7	0	57 37	46 22	9	45/20/32 65/40/52	55/2 —	105/65/85 125/80/95
VH 32 M 17	VSD	1.50	R 200 E 530	60 130	3.8 5.3	11.3 18.0	3.8 5.3	7.5 12.7	0	66 70	68 64	9	100/25/60 135/50/90	100/10 —	130/70/95 145/85/105

TABLE (contd.)

Case No., sex, and age	Diagn.	BSA m. ²	O ₂ Con- sump- tion ml./min. STPD	Heart rate	Flows (l./min.)			Shunts (l./min.)		Qp - Qe %		Pressures (mm. Hg)			
					Sys- temic	Pul- mon- ary	Effec- tive	Left- to- right	Right- to- left	Qp		PCV m.	PA s.d.m.	RV s.d.	Systemic s.d.m.
										Fick	Dye curves				
VH 33 M 18	VSD	1.60	R 230 E 470	72 94	5.6 7.0	15.6 8.2	5.6 6.1	10.0 2.1	0	64 26	50 26	17 —	115/50/65 150/60/80	115/7 150/8	115/62/80 150/75/90
VE 62 F 19	VSD Eisen.	1.60	R 210 E 550	72 100	4.6 10.0	7.3 11.0	4.2 7.5	3.1 3.5	0.4 2.5	42 32	48 22	5 —	125/50/80 160/75/105	125/8 160/8	125/75/90 165/75/105
VE 63 M 25	VSD Eisen.	1.70	R 220 E 630	68 94	3.6 12.1	4.5 5.9	3.1 5.7	1.4 0.2	0.5 6.4	31 35	28 —	7 —	95/50/65 125/65/85	95/4 125/6	95/60/57 125/80/95
VS 81 M 23	VSD + PS	1.90	R 250 E 560	68 100	6.0 8.2	11.9 21.0	6.0 8.2	5.9 12.8	0	50 61	39 51	15 —	35/15/25 40/14/28	60/8 60/9	115/70/90 150/90/105
VS 82 M 19	VSD + PS	1.70	R 250 E 660	75 108	6.2 11.5	9.1 13.1	6.2 10.1	2.9 3.0	0	32 23	15 37	6 —	18/6/11 20/5/9	100/8 110/5	130/60/80 130/70/85
PN 1 M 10	PDA	1.20	R 160 E 450	88 115	4.0 7.0	5.1 —	4.0 7.0	1.1 —	0	22 —	12 28	— —	28/15/20 —	32/5 32/5	105/65/80 —
PH 30 F 21	PDA	1.30	R 180 E 320	85 105	2.7 3.6	13.9 9.0	2.7 3.6	11.3 5.4	0	80 60	95 58	17 15	100/55/70 105/60/78	100/7 100/7	165/65/95 —
PE 64 F 27	PDA Eisen.	1.50	R 200 E 460	75 107	5.3 —	3.3 4.2	2.9 —	0.4 —	2.4 —	12 —	— —	6 6	110/63/82 143/74/110	110/5 —	103/57/85 137/71/110
PE 65 F 34	PDA Eisen.	1.60	R 160 E 610	80 125	4.3 9.1	6.5 —	3.7 7.7	2.8 —	0.4 1.4	43 —	— —	8 —	110/70/85 150/80/110	110/8 —	110/70/85 —

ASD, atrial septal defect; AF, atrial fibrillation; MS, mitral stenosis; PS, pulmonary stenosis; VSD, ventricular septal defect; PDA, patent ductus arteriosus; STPD, standard temperature and pressure dry; PCV, pulmonary capillary venous (wedge); PA, pulmonary artery; RV, right ventricle; s.d.m., systolic, diastolic, mean.

Atrial Septal Defect. All cases had a large left-to-right shunt. Seven had a pulmonary arterial systolic pressure of 40 mm. Hg or less on exercise, while in the other 8 the pressure was higher than this. Fig. 1A and B illustrate the effects of exercise on the pulmonary and systemic flows in these patients. The shaded areas represent the limits of

normality of cardiac output during exercise (Gazetopoulos *et al.*, 1966). It is seen that in uncomplicated ASD the systemic flow varies widely at rest and has a more or less normal slope of increase with exercise, so that cases with the lower resting values show correspondingly low values on exercise. In the majority the pulmonary flow increased in parallel

FIG. 1.—Systemic (heavy line) and pulmonary (broken line) flows at rest and on exercise in patients with ASD. (A) refers to cases with low pulmonary arterial pressure and (B) to those with pulmonary hypertension. The shaded areas signify the normal range of systemic flow. (See text.)

FIG. 2.—Results in VSD and PDA: designations as in Fig. 1. (A) refers to patients with low pulmonary arterial pressure, and (B) to those with hyperkinetic pulmonary hypertension.

fashion to the systemic so that the magnitude of the left-to-right shunt remained much the same. Only in one case (AN 4) was a significant diminution of the pulmonary flow observed as a result of exercise.

In patients with ASD and pulmonary hypertension, still with a large left-to-right shunt, the systemic flow was usually in the low-normal or low range at rest and on exercise, the slope of increase with exercise being normal. The pulmonary flow increased in all cases in this group, conspicuously in some. There was a considerable increase in the left-to-right shunt in two patients (AH 40 and AH 45), the latter having associated moderate mitral stenosis.

Ventricular Septal Defect and Patent Ductus Arteriosus. Of the 16 cases studied, 6 had low pulmonary arterial pressure and 4 had hyperkinetic pulmonary hypertension. The changes of systemic and pulmonary flow in these 10 patients are illustrated in Fig. 2A and B, the limits of normality of systemic flow again being shown. In the group without pulmonary hypertension the systemic flow, as in atrial septal defect, responded normally to exercise. The pulmonary flow increased in a parallel fashion to the systemic, and the magnitude of the shunt usually remained unchanged. In the patients with hyperkinetic pulmonary hypertension, on the other hand, the resting and exercising systemic outputs were low in 3 of the 4 patients. The pulmonary flow increased in 2, while in the other 2 there was a sharp decrease in pulmonary flow on effort (VH 33 and PH 30). These 2 were the only patients in whom the indirect left atrial pressure was raised and in whom a gross reduction in the magnitude of the left-to-right shunt was seen, the findings being confirmed by dye curves. In con-

trast, Case VH 32 showed a considerable increase of the left-to-right shunt. Patients with the Eisenmenger syndrome or coexisting pulmonary stenosis have not been included in Fig. 1 and 2. Patients with pulmonary stenosis have been excluded also from all the other figures, for simplicity of presentation.

It is seen in Fig. 1 and 2 that the systemic output, though having a normal slope of increase during exercise, was impaired in a number of cases, particularly if there was pulmonary hypertension. In an attempt to understand the factors determining the impairment of cardiac output we have examined its relationship to age (Fig. 3), to PA systolic pressure (Fig. 4), and to the magnitude of the left-to-right shunt (Fig. 5). On the ordinate of each of these figures is plotted the effective systemic flow in litres/min. above or below the mean normal value for the particular exercise oxygen consumption (Gazetopoulos *et al.*, 1966). It is seen that the older the patient, the larger the left-to-right shunt, or the higher the pulmonary artery pressure, the greater the tendency for the effective flow to be impaired. In Fig. 6 we have plotted the changes with exercise in the pulmonary flow against those in systemic flow. The increase in systemic flow is in most cases associated with an increase in pulmonary flow (the two patients who showed a marked decrease in pulmonary flow, Cases VH 33 and PH 30, have already been discussed). The magnitude of the left-to-right shunt shows a variable pattern of change, but it is clear that there is a significant number of patients in each group in whom the shunt actually increases.

Fig. 7 relates the resting pulmonary flow to the change that occurs on effort. Patients in the Eisenmenger category have a low pulmonary flow which rises little with effort. Case AN 6, on the right of

FIG. 3.—Impairment of effective flow on exercise, expressed as deviation from the mean predicted for the particular oxygen uptake, in relation to age. ○ ASD; △ VSD; □ PDA.

FIG. 4.—Impairment of effective flow, in relation to pulmonary arterial systolic pressure, on exercise. Symbols as in Fig. 3.

FIG. 5.—Impairment of effective flow, in relation to magnitude of left-to-right shunts, on exercise. Symbols as in Fig. 3.

the figure, had a very large left-to-right shunt due to ASD, and had relatively fixed hæmodynamics at rest and on effort: otherwise it is seen that changes are variable, but the presence of a large resting pulmonary flow does not preclude a further increase with exercise. Fig. 8A relates the magnitude of the change in pulmonary flow to the resting pulmonary artery pressure in ASD: it is seen that

FIG. 6.—Changes in pulmonary flow (ordinate) and effective systemic flow (abscissa) on effort. Cases lying above the diagonal line have an increase in left-to-right shunt, and those below a decrease. ○ ASD; △ VSD; □ PDA. Open symbols represent cases with low pulmonary arterial pressure, semi-solid symbols those with hyperkinetic pulmonary hypertension, solid symbols those with the Eisenmenger state.

FIG. 7.—Change in pulmonary flow on exercise per 100 ml. increase of oxygen uptake in relation to magnitude of resting pulmonary flow. Symbols as in Fig. 6. It is seen that a high resting pulmonary flow by no means precludes a considerable increase on exercise in some cases.

a raised pressure was often associated with a rise in pulmonary flow on effort, a tendency which if anything increased at higher pressures (it is to be noted that this applies to the group of patients with hyperkinetic pulmonary hypertension and not to the Eisenmenger state). Fig. 8B shows the same information applied to VSD and PDA. Here the findings are more variable, and in contradistinction

FIG. 8.—Change in pulmonary flow on exercise per 100 ml. increase in oxygen uptake in relation to resting pulmonary arterial systolic pressure. (A) represents ASD and (B) VSD and PDA. Note that a considerable increase in pulmonary flow occurs in some patients with ASD whose resting pressure is considerably raised. In VSD and PDA the response is variable. Both patients who showed a decrease in flow in the latter group had raised left atrial pressures.

to ASD there is an over-all tendency for the pulmonary flow to increase less or even to decrease at higher pressures.

The effect of exercise on the pulmonary arterial pressure is also of some interest. It changed little in those cases where it was low, but the higher the

resting pressure the greater on the whole was the tendency to rise with effort. This applies to ASD (Fig. 9A) and to VSD and PDA (Fig. 9B).

Dye Dilution Studies. The Table shows the left-to-right shunt expressed as a percentage of the

FIG. 9.—Changes in pulmonary arterial systolic pressure on exercise. It is seen that in ASD (left), and in VSD and PDA (right) a high resting pressure tends to be associated with a considerable rise with effort.

FIG. 10.—Comparison between Fick and dye-dilution determinations of the ratio of left-to-right shunt to pulmonary flow, at rest and on exercise. The dye-dilution calculations give on the whole higher results than the Fick estimation, especially in ASD on exercise. This is likely to be due to an overestimation of exercising systemic flow in that group, the arterio-venous oxygen difference being probably greater than that calculated from the mean of 1 SVC and 2 IVC values.

pulmonary flow by both Fick and dye curve calculations, and in Fig. 10 the relation between the results by the two methods, at rest and on exercise, is expressed. As expected, the correlation is only a rough one, but in general the same pattern of change is observed. The purpose of using the dye curves was to confirm or to refute the conclusions from the Fick determinations. In Cases AH 40, AH 45, and VH 32, where we observed a marked increase in pulmonary flow and left-to-right shunt, the dye curves were confirmatory. In Cases AH 4, VH 33, and PH 30, where a marked decrease in those parameters was seen, the dye curves were also confirmatory of the pattern of change. In two cases, Fick and dye estimations were clearly contradictory (Cases AN 1 and VN 4). In the former the unusually high systemic flow on exercise suggests that the error lay there.

DISCUSSION

The difficulties of obtaining accurate measurements of flows and resistances in patients with left-to-right shunts are well known. When the pulmonary arterial oxygen saturation is high and the pulmonary arterio-venous difference is low, small errors in measurement lead to large errors in calculated flow by the Fick principle. To obtain a truly mixed venous sample in atrial septal defect is

virtually impossible, since the inferior vena caval blood itself is far from well mixed at any site near the heart, and the proportions of inferior and superior caval flows can only be guessed at. In this study, $1/3$ (2 IVC + 1 SVC) has been taken as a rough approximation. Furthermore, early recirculation on the dye curves often makes it impossible to separate the secondary curve from the primary systemic circulation. For these reasons the data must be interpreted according to the merits or demerits of the methodology, and we hoped that the measurement of outputs by both techniques would yield more representative results.

Current opinion appears to be that where there is a left-to-right shunt, exercise diminishes its degree. However, there are certain *a priori* reasons why this should not always be so, and particularly why the effect may not be the same in different types of lesions.

In trying to anticipate the results of exercise, the following line of reasoning may be followed. The factors that might be expected to influence the degree of shunting are:

- (a) The pressures in the chambers of the heart and in the great vessels.
- (b) The resistances of the pulmonary and systemic circuits.

- (c) The rate of the heart, and the stroke output of the ventricles.
- (d) The filling resistances of the two ventricles.
- (e) Whether the shunt is systolic, diastolic, or both.

If these variables are known, it should be possible to predict broadly the effect of exercise on the shunts.

Ventricular Septal Defect. Here several possibilities exist, each presenting its own problem. First, the small defect, which carries inevitably a left-to-right shunt since the RV pressure is always low. Second, the medium-sized defect with a left-to-right shunt and moderate increase in the pulmonary arterial pressure. Third, the large defect with systemic pressure in the right ventricle but a dominantly left-to-right shunt, the pulmonary vascular resistance being well below the systemic. Fourth, the large defect with a balanced shunt, the pulmonary vascular resistance being of the same order as the systemic resistance. Fifth, the VSD associated with pulmonary stenosis.

In the first and second groups, the main resistance to left-to-right shunting is at the site of the defect, in the third and fourth it is in the vessels of the lung, and in the fifth it is at the site of the RV outflow obstruction. In the first, second, fourth, and fifth groups this resistance is virtually fixed in magnitude, while in the third a change of resistance in pulmonary vessels lends a potential for variation.

By making an abstraction, it is possible to ascribe a resistance in units to the smaller defects, which enables us to compare it with the systemic resistance. The flow from LV, assuming this to be entirely systolic, would pass through the defect or through the aortic valve in inverse ratio to the respective resistances. A simple example serves to illustrate the changes expected. If the systolic flow is 6 l./min. and the pulmonary flow 9 l./min., the left-to-right shunt is 3 l./min. The left ventricular output is thus distributed in the ratio 2:1 between aorta and VSD, the resistance of the defect being then 32 units. If on effort the systemic blood pressure remains the same but the flow doubles, the systemic vascular resistance will halve to 8 units, and since the VSD resistance remains constant at 32 units, the shunt will be one-quarter of the systemic flow—again 3 l./min. So long as the systemic pressure remains the same, therefore, the shunt will be constant. Any increase in systemic pressure associated with exercise will thus lead to an increase in the absolute volume of shunt and, as is seen to be so in Fig. 1A, this is what happens. In symbolic terms, Q_s is the systemic flow, R_s systemic resistance, S the shunt, r the defect resistance,

and P_s the mean systemic pressure,

$$S = Q_s \frac{R_s}{r}.$$

$$\text{Since } Q_s = \frac{P_s}{R_s}, \quad S = \frac{P_s}{r}.$$

Since r is fixed, S will be constant for constant P_s and will increase with rising P_s .

This reasoning may be expected to apply to the first and second groups, and to the fourth and fifth groups when the right-sided resistance is high and constant. Effort will then increase the absolute amount of left-to-right shunt, while diminishing its proportion to systemic flow.

It will of course not apply if the size of the defect diminishes with contraction of the heart or if the right ventricular outflow obstruction is variable.

If the right-sided resistance is low but the defect large, as in hyperkinetic pulmonary hypertension, the bulk of the right-sided resistance lies at pulmonary vascular level and is often of the order of 5 to 8 units. Increase of left ventricular output, again distributed in inverse ratio to the respective circuit resistances, will pass preferentially through the defect, since at all times the right-sided resistance is lower than the systemic. Furthermore, the ratio of shunt to systemic flow will increase in this group. That this can in fact happen is seen from the response of Case VH 32.

We appreciate that this over-simplified line of reasoning cannot be expected accurately to fit all the facts, but at least gives ground for the feeling that an increase in left-to-right shunt might occur with exercise in VSD. Any increase in pulmonary vascular resistance with exercise will, however, minimize this tendency, and it is of some interest that the only two patients in this group who showed a decrease in left-to-right shunt had also a raised left atrial pressure. One of these two (Case VH 33) had clinical signs suggestive of coexistent mitral stenosis. Whether or not in these two cases there was an element of reactive pulmonary hypertension secondary to a raised left atrial pressure we do not know, but it remains a possibility to account for their anomalous behaviour. The same would apply to any other situation where there is impairment of filling of the left ventricle. Similar principles must apply in PDA.

Atrial Septal Defect. The situation is essentially different from that of VSD since the communication is between the two low pressure chambers. It is likely that much of the shunt occurs in diastole, as evidenced by the diastolic flow murmur which is a constant feature of those cases with a large shunt. It seems probable, therefore, that one of the main

factors promoting a shunt is the sucking effect of the right ventricle in diastole rather than the positive driving force of the left atrial pressure. The diastolic volume of the right ventricle, when there is a shunt, may be very large indeed, and this suction must exist if the ventricle is to expand in diastole. Its place in the hæmodynamic control in ASD cannot well be denied if nature is to continue to abhor a vacuum.

The bulk of the flow through the tricuspid valve takes place in early diastole (Wiggers, 1949; Rushmer, 1961), and it is possible that tachycardia, by increasing the total diastolic time of rapid filling, could augment the total minute volume of the shunt rather than diminish it. The lowering of left atrial pressure in response to a fall in systemic vascular resistance has been documented by Berglund (1955). This effect would be unlikely, we think, to play a major part in reducing the shunt on exercise in ASD, and a case can thus be made for expecting the shunt to increase rather than decrease with effort, particularly if there is coexisting mitral stenosis (Case AH 45) or increased resistance to left ventricular filling: dysfunction of the left ventricle in ASD has been discussed by Dexter (1956) and Davidsen (1960).

Several studies have been reported on the hæmodynamics at rest and on exercise in patients with left-to-right shunts. Brotmacher and Deuchar (1956) and Weidman *et al.* (1957) have shown, usually in young patients, a normal resting systemic output in the absence of cardiac failure. However, impairment of cardiac output is seen in older patients with large shunts (Kjellberg *et al.*, 1959). Scébat *et al.* (1957) confirmed these findings in 63 cases of ASD, 27 of VSD, and 52 of PDA, and presented exercise data in 14 of ASD, 3 of VSD, and 4 of PDA, all with low pulmonary vascular resistance. In ASD, the mean systemic index increased from 3.72 to 9.42 l./min./sq.m., while the left-to-right shunt decreased in all cases, the mean values at rest and on exercise being 8.6 and 3.8 l./min./sq.m. In 3 cases of VSD the mean systemic index increased from 4.69 to 6.52 l./min./sq.m., and the left-to-right shunt decreased in 2 cases and was unchanged in the third. In 3 cases of PDA, the systemic index increased from 5.24 to 7.95 l./min./sq.m.; the left-to-right shunt increased in 2 cases and decreased in the other 2. These authors concluded that the rise of systemic flow on effort was normal, and suggested that the important factor determining the magnitude of shunts between the two circulations was the lateral pressure at right angles to the main direction of the blood stream; since the increase in speed of flow of the systemic circuit is greater than that of the pulmonary cir-

cuit, the tendency to left-to-right shunting will be less. This appears to be a rather dubious concept, particularly where the communication is at atrial level and the shunt does not depend primarily on the pressure gradient between the atria: this is the case also where it is at ventricular level and anatomical considerations seem to dominate over such factors as speed of flow. The total abolition of large shunts on exercise in two of the patients with ASD in the series described by Scébat *et al.*, and the findings of a higher-than-normal systemic output in this condition, make the conclusions acceptable with some difficulty.

Jönsson *et al.* (1957), studying patients with ASD, concluded that the pulmonary flow increased with stepwise increase of exercise load in such a fashion that the shunt remained unchanged or decreased somewhat. Plotting their data as in our Fig. 2 and supposing with them a normal slope of increase of systemic flow, a small over-all increase in left-to-right shunt would be apparent rather than a decrease, though we have no comparable data at maximal exercise levels.

Swan *et al.* (1958) studied the hæmodynamics during supine exercise in 30 patients with septal defects. Their data show that there were 9 patients in the Eisenmenger category: in these the pulmonary flow remained essentially unchanged, while the increase in systemic flow was less than normal. Where the pulmonary artery pressure was low, the pulmonary flow behaved in a manner similar to that of our cases, i.e. some over-all increase, while there was a small rise in the magnitude of the left-to-right shunt with exercise in the 6 cases where this could be calculated. In 8 patients with hyperkinetic pulmonary hypertension, the pulmonary flow increased little in 6 patients with VSD and PDA, while in 2 with ASD there was a greater increase. The left-to-right shunt in 3 with PDA and 2 with VSD showed some decrease. These authors conclude that patients with large left-to-right shunts may show little change in pulmonary vascular dynamics with effort, no further stress thus being thrown on the overburdened pulmonary circulation. We cannot agree with this conclusion when applied to the group of cases with ASD and hyperkinetic pulmonary hypertension.

Bruce and John (1957) studied patients with ASD, VSD, and PDA at rest and on exercise in the upright position, measuring only the pulmonary flow. They found a larger increase in this than the anticipated rise of systemic flow, indicating an increased left-to-right shunt with effort. These authors concluded that the upright posture explained their differences from Swan *et al.* (1958).

Stephens *et al.* (1964) described the effects of

exercise in the upright position in patients with left-to-right shunts. Eight had VSD and one had PDA. Five (Cases 1-5) had normal pulmonary artery pressures and pulmonary vascular resistance: in 3 of these the systemic flow increased normally, the pulmonary flow increased to a lesser degree, and the absolute volume of the left-to-right shunt diminished. In one other (Case 4) the increase of systemic flow was less, while the pulmonary flow and left-to-right shunt increased very much; in Case 5 there was a small increase in left-to-right shunt, both pulmonary and systemic flow increasing together. Case 6 had moderate pulmonary hypertension but a small shunt which increased a little on exercise. Case 7 was the only one with truly hyperkinetic pulmonary hypertension, and here the pulmonary flow diminished in the face of a normal increase of systemic flow with virtual abolition of the left-to-right shunt (this patient had the highest wedge pressure). In the last two cases with the Eisenmenger complex there was a small increase in systemic flow, a small increase in pulmonary flow, and there was little change in the left-to-right shunt. In the last 4 cases a significant right-to-left shunt appeared. Again the increase in pulmonary artery pressure was greater in those cases where it was already raised.

The lack of uniformity of data reflects in large part the difficulties of accurate measurement of flow and pressure. The previous impressions that the economy of the pulmonary circulation was protected in the presence of large shunts by lack of further change on exercise has not been borne out by our studies, especially where atrial septal defect is associated with hyperkinetic pulmonary hypertension. This situation is most commonly found in older patients, and we have been impressed with the considerable rise that can occur in the pulmonary flow with effort in such patients, associated with a significant increase in the pulmonary artery pressure. Whether or not this is linked to their increased dyspnoea on effort is not clear, since other factors such as lung damage and impairment of systemic flow also operate in this group, but it remains a possibility.

In VSD and PDA, with the exception of Case VH 32 who showed a rise in left-to-right shunt and pulmonary blood flow on exercise, our impression has been that the same tendency has not been present. It is possible that the raised left atrial pressure in this situation, of which we have seen evidence in Cases VH 33 and PH 30, may increase the reactive element of the pulmonary vascular resistance, and hence diminish the tendency to increase the left-to-right shunt. The presence of mitral stenosis or filling difficulty of the left ven-

tricle in such patients would also operate to diminish this tendency, in contradistinction to the situation in ASD.

SUMMARY

Studies were carried out on 34 patients with cardiac septal defects, and the changes in haemodynamics on exercise were assessed. In ASD and VSD with low pulmonary vascular resistance parallel increase in systemic and pulmonary flow was observed, with little change in the magnitude of the left-to-right shunt. In ASD with high flow and raised pressure in the pulmonary circuit, marked increases in both these parameters and in the left-to-right shunt were observed. In VSD and PDA with hyperkinetic pulmonary hypertension, the changes were variable. In one such patient both pulmonary flow and left-to-right shunt increased considerably; in two others, both with raised left atrial pressures, these diminished.

The effective systemic flow tended to decrease with increasing age, pulmonary arterial pressure, and magnitude of left-to-right shunt.

The earlier published data have been briefly discussed. The previous impression that exercise does not lead to marked changes in the pulmonary vascular dynamics have not been supported by this study, especially in patients with atrial septal defect and pulmonary hypertension associated with high pulmonary flow.

The factors governing the haemodynamics in such patients have been discussed.

We wish to thank Drs. C. G. Baker, R. Kauntze, and D. C. Deuchar for permission to study patients under their care; the technicians of the Cardiac Department, Guy's Hospital; and Mrs. Gillian Brewer for secretarial assistance.

REFERENCES

- Berglund, E. (1955). The function of the ventricles of the heart. *Acta physiol. scand.*, **33**, Suppl. 119.
- Brotmacher, L., and Deuchar, D. C. (1956). The systemic blood flow in congenital heart disease, with an examination of the validity of the cardiac index. *Clin. Sci.*, **15**, 441.
- Bruce, R. A., and John, G. G. (1957). Effects of upright posture and exercise on pulmonary hemodynamics in patients with central cardiovascular shunts. *Circulation*, **16**, 776.
- Carter, S. A., Bajec, D. F., Yannicelli, E., and Wood, E. H. (1960). Estimation of left-to-right shunt from arterial dilution curves. *J. Lab. clin. Med.*, **55**, 77.
- Davidson, H. G. (1960). *Atrial Septal Defect*. Munksgaard, Copenhagen.
- Dexter, L. (1956). Atrial septal defect. *Brit. Heart J.*, **18**, 209.
- Donald, K. W., and Christie, R. V. (1949). A new method of clinical spirometry. *Clin. Sci.*, **8**, 21.

- Gabe, I., and Shillingford, J. (1961). The photo-electric earpiece technique for recording dye dilution curves. *Brit. Heart J.*, **23**, 271.
- Gazetopoulos, N., and Davies, H. (1966). The ventilatory response to exercise in patients with left-to-right shunts. *Brit. Heart J.*, **28**, 590.
- , —, Oliver, C., and Deuchar, D. (1966). Ventilation and hæmodynamics in heart disease. *Brit. Heart J.*, **28**, 1.
- Jönsson, B., Linderholm, H., and Pinardi, G. (1957). Atrial septal defect: A study of physical working capacity and hemodynamics during exercise. *Acta med. scand.*, **159**, 275.
- Kjellberg, S. R., Mannheimer, E., Rudhe, U., and Jönsson, B. (1959). *Diagnosis of Congenital Heart Disease*, 2nd ed. Year Book Publishers, Chicago.
- Rushmer, R. F. (1961). *Cardiovascular Dynamics*, 2nd ed. Saunders, Philadelphia.
- Scébat, L., Voridis, E., Renais, J., and Lenègre, J. (1957). Étude du mécanisme des shunts dans les communications interauriculaires, interventriculaires et aortopulmonaires. *Arch. Mal. Cœur*, **50**, 818.
- Stephens, N. L., Shafter, H. A., and Bliss, H. A. (1964). Hemodynamic and ventilatory effects of exercise in the upright position in patients with left-to-right shunts. *Circulation*, **29**, 99.
- Swan, H. J. C., Marshall, H. W., and Wood, E. H. (1958). The effect of exercise in the supine position on pulmonary vascular dynamics in patients with left-to-right shunts. *J. clin. Invest.*, **37**, 202.
- Weidman, W. H., Swan, H. J. C., DuShane, J. W., and Wood, E. H. (1957). A hemodynamic study of atrial septal defect and associated anomalies involving the atrial septum. *J. Lab. clin. Med.*, **50**, 165.
- Wiggers, C. J. (1949). *Physiology in Health and Disease*, 5th ed. Lea and Febiger, Philadelphia.