

Respiratory changes after open-heart surgery

J. B. McCLENAHAN¹, W. E. YOUNG², AND M. K. SYKES

From the Departments of Medicine and Anaesthesia, Postgraduate Medical School and Hammersmith Hospital, London, W.12

Patients who have undergone cardiac surgery with the aid of extracorporeal circulation (E.C.C.) often exhibit varying degrees of respiratory embarrassment in the post-operative period. When severe, this pulmonary dysfunction is a prominent cause of morbidity and mortality. The general clinical picture and pathological changes in those who die have been well described (Muller, Littlefield, and Dammann, 1958; Dodrill, 1958; Baer and Osborn, 1960). The patient leaves the operating room in reasonably good condition, but within the first few hours dyspnoea, cyanosis, fever, and hypotension develop. If death ensues, it usually occurs within the first two days. No specific therapy is known. At necropsy the lungs are congested with focal zones of collapse and haemorrhage. The alveoli and bronchi are filled with red blood cells and proteinaceous oedema fluid.

Specific alterations in lung function result from these changes. Schramel, Cameron, Ziskind, Adam, and Creech (1959) found a reduction in diffusing capacity for carbon monoxide, but similar findings were noted in patients and experimental animals who had undergone thoracotomy without total body perfusion. Preliminary studies in this Unit (Sykes, McCormick, Sandison, and Harrison, 1961) revealed that the arterial CO₂ tension (Paco₂) was seldom raised above 50 mm. Hg, but that arterial desaturation occurred almost invariably. The desaturation was usually present for three or four days after surgery, but in some cases it persisted for longer. In a few cases the desaturation was not completely relieved by the inhalation of 100% oxygen. In 1961, Beer, Loeschcke, Schaudig, Pasini, Auberger, Ranz, and Borst reported that there was a reduction in diffusing capacity and an increase in right-to-left intrapulmonary shunting in both patients and animals who had been subjected to thoracotomy and total body perfusion. Howatt, Talner, Sloan, and DeMuth (1962) and Ellison, Yeh, Moretz, and Ellison (1963) noted a similar reduction in diffusing capacity, and Osborn, Popper, Kerth, and Gerbode

(1962) reported increased arterial-alveolar carbon dioxide tension differences and arterial desaturation; they attributed this to patchy atelectasis.

This paper describes studies which were made on two groups of patients in an attempt to assess the effects of extracorporeal circulation on post-operative lung function.

METHODS

This series consists of 14 patients who were studied in Hammersmith Hospital in 1962 (Table I). The patients have been divided into two groups.

In group I were eight patients who underwent cardiac surgery with the aid of extracorporeal circulation. All but one included in this group appeared to have a normal post-operative course without any cardiological complication. The exception (A.C.) was progressing satisfactorily but died suddenly on the evening of the first post-operative day from a coronary artery occlusion.

In group II were six patients subjected to intrathoracic surgery without extracorporeal circulation. In this group one patient (M.H.) was operated upon with the aid of surface hypothermia, but all patients had normal lung function pre-operatively with the exception of M.D., a patient who had clinical evidence of chronic bronchitis and emphysema of moderate severity.

No patient in either group had any evidence of right-to-left intracardiac shunt on pre-operative examination or cardiac catheterization. Two patients in group I and three patients in group II had significant left-to-right intracardiac shunts before operation. There was no clinical evidence of a residual cardiac shunt in any patient after operation.

ANAESTHESIA AND PERFUSION Premedication consisted of a quinalbarbitone suppository, 3 to 4 mg./kg., two hours before operation followed by a subcutaneous injection of pethidine, 2 to 3 mg./kg., and promethazine, 1.0 to 1.5 mg./kg., one hour before operation. Anaesthesia was induced with thiopentone, 50 to 250 mg., and muscular relaxation was obtained with D-tubocurarine, 15 to 30 mg. Respirations were controlled using a mixture of nitrous oxide 70% and oxygen 30% from a non-rebreathing system on a mechanical ventilator, except during the period of total cardiopulmonary bypass, when the lungs were held inflated with a mixture of helium, or nitrogen, and oxygen. Small doses of pethidine, 10 to

¹Supported by Fellowship, U.S. Public Health Service. Now Research Associate, Palo Alto Medical Research Foundation—Stanford University Health Service.

²R. S. McLaughlan Travelling Fellow. Now at St. Michael's Hospital, Toronto, Canada

TABLE I
GROUP I. PATIENTS STUDIED

Patient	Sex	Age	Weight (kg.)	Height (cm.)	Surface Area (m. ²)	Diagnosis	Operation	Perfusion Time (min.)	Total Bypass (min.)	Lowest Temp. Recorded (°C. oesophageal)	Pulmonary Complications
V.P.	F	29	42.5	153	1.37	Atrial septal defect	Closure	48	44	30	? Pulmonary artery thrombosis on second post-op. day
E.W.	M	32	64.0	168	1.75	Aortic incompetence	Aortic valve replacement	—	—	—	Patchy collapse and consolidation—right middle and lower zones
H.A.	M	25	56.5	178	1.70	Aortic incompetence	Aortic valve replacement	207	220	22	Some left lower lobe collapse
T.C.	M	19	51.8	159	1.51	Obstructive cardiomyopathy	Infundibular resection	69	59	24	Some left lower lobe collapse
S.R.	F	25	64.5	157	1.67	Obstructive cardiomyopathy	Infundibular resection	67	50	24	Slight left lower lobe collapse
J.B.	F	36	45.0	156	1.42	Obstructive cardiomyopathy	Infundibular resection	76	60	26	Some collapse both bases
A.C.	M	33	58.5	171	1.62	Aortic incompetence	Aortic valve replacement	240	222	23	Nil
P.H.-R.	M	16	56.0	173	1.68	Ventricular septal defect	Closure	83	63	24	Nil

GROUP II. CONTROLS

Patient	Sex	Age	Weight (kg.)	Height (cm.)	Surface Area (m. ²)	Diagnosis	Operation	Pulmonary Complications
R.P.	M	24	66.8	184	1.86	Coarctation of aorta	Resection and graft	Nil
R.McN.	M	16	61.0	—	—	Patent ductus arteriosus	Ligation	Left haemothorax with some left lower lobe collapse
M.H.	M	15	68	178	1.85	Atrial septal defect	Closure	Slight collapse left base
J.L.	M	22	74.2	—	—	Coarctation of aorta	Resection	Small left pneumothorax
P.H.-R.	M	16	56.0	173	1.68	Patent ductus arteriosus and ventricular septal defect	Closure of patent ductus arteriosus	Nil
M.D.	M	40	58.2	—	—	Granuloma of lung	Total resection of granuloma of lung	No clinical or radiological change

Incisions—Group I, median sternotomy
Group II, transverse thoracotomy

20 mg., were used to supplement the anaesthesia and additional doses of pethidine and D-tubocurarine were given to maintain anaesthesia during the period of perfusion. A Melrose-N.E.P. pump-oxygenator was used for bypass, and blood flow rates were maintained at 2.4 l./min./m.² body surface area. Flow rates were reduced slightly when hypothermia was utilized as an adjunct to the perfusion technique (El Sayed and Melrose, 1962). The lowest temperatures recorded (Table I) were used to achieve hypothermic arrest of the heart. During the rest of the perfusion the body temperature was maintained at 30° C. or above. Rheomacrodex, a low-molecular-weight dextran, 1,100 ml., was added to 4,000 ml. of priming blood. At the end of bypass the lungs were inflated for a short period with positive pressures of up to 30 cm. H₂O in an attempt to re-expand any atelectatic areas. At the conclusion of operation residual curarization was reversed with atropine, 1.2 mg., and neostigmine, 2.5 mg., in divided doses. Artificial ventilation was maintained until spontaneous ventilation was adequate. A similar anaesthetic technique was used for patients not subjected to total body perfusion. Oxygen was administered during transfer to the recovery ward. Patients in group I were then nursed in an oxygen tent for three days and patients in group II for 24 hours.

Patients were studied one or two days before operation,

two to three hours after return to the recovery ward, on the first and second post-operative days, and, in a few cases, several weeks after the operation. All measurements were made with the patient in the supine position with the head resting on one pillow. The patients breathed through a mouthpiece connected to a low-resistance non-rebreathing valve. The dead space of the valve and mouthpiece was 80 ml. Expired gas was collected in a Douglas bag, the volume being subsequently measured on a calibrated dry test gas meter.¹ Studies were made with the subjects breathing air, 100% oxygen, and, in some cases, 35% oxygen. After the desired gas mixture had been respired for eight to 10 minutes, the bag was washed out twice with expired gas and emptied again. Expired gas was then collected for a period of five to six minutes. At the same time an arterial blood sample, from a needle or catheter in the brachial or radial artery, was slowly withdrawn into an oiled, heparinized syringe which was capped and stored in iced water. Immediately after the period of collection, four samples of mixed expired gas from the Douglas bag were flushed through a 100-ml. oiled syringe, the fifth sample being retained for analysis. Finally, the barometric pressure, room temperature, and patient's temperature were recorded.

¹ Type C.D.1, Parkinson-Cowan Ltd., London

BLOOD-GAS ANALYSIS The oxygen and carbon dioxide tensions of both expired gas and arterial blood were determined on the combined electrode system described by Severinghaus and Bradley (1958).² The oxygen electrode was calibrated using pure nitrogen, air, and a 95% O₂:5% CO₂ mixture. The carbon dioxide electrode was standardized using 3% CO₂ and 6% CO₂ in oxygen. All CO₂ mixtures were analysed on a standard Haldane gas analysis apparatus, calibrated by mercury displacement and checked by the analysis of total absorbable gas in air. The electrodes were maintained at a constant temperature of 37° C. ± 0.1° C.

SOURCES OF ERROR

(a) *Expired gas volume* The gas meter was calibrated against a spirometer which was in turn calibrated by water displacement. Suitable temperature corrections were made. When random volumes of gas were passed through the spirometer at rates approximating to those used in the studies, the mean error of the gas meter was -32.6 ml./litre. The S.D. of the difference between the known and observed was 6.45 ml. and the S.E. of the mean difference equalled 1.42. Since this error was small no correction was applied to the volumes measured.

(b) *Oxygen* The accuracy of the oxygen tension determinations on gases was assessed initially and checked throughout the period of study by measuring the oxygen tension of gases of known oxygen concentration. Gases were analysed on a standard Haldane gas analysis apparatus and the Po₂ was calculated directly from the oxygen percentage, or, in the case of the 5% CO₂:95% O₂ mixtures, by subtracting the % CO₂ from 100%. In 109 determinations on 8.8 to 21.0% O₂ in N₂ the mean error of the electrode was +0.024 mm. Hg (S.D. = 1.04 mm. Hg; S.E. of mean = 0.11).

Three factors reduced the degree of accuracy obtained in these studies. First, blood samples from a tonometer gave lower readings on the electrode than did the gas with which they were equilibrated. This 'blood-gas' ratio varied from day to day and was determined at the time of each study using the patient's blood in the majority of instances. Correction factors varying from 100 to 112% were applied to the readings obtained. Second, the electrode was frequently alinear over the 300 to 700 mm. Hg range of oxygen tensions. The electrode was checked daily by measuring the Po₂ of a range of known gas mixtures, and appropriate corrections were applied to the readings obtained. The third source of error was the rapid fall of Po₂ in blood having a high initial oxygen tension. The rate of fall varied widely and was dependent on the initial O₂ tension and the duration and temperature of storage. A number of experiments were performed to determine this rate of fall, and a correction factor was applied to all measurements made at high oxygen tensions. Although arterial oxygen tensions were always determined within 10 minutes of sampling, the errors introduced by the determination and application of these correction factors probably reduced the

accuracy of the electrode to ±30 mm. Hg at O₂ tensions above 400 mm. Hg. Such an error would limit the accuracy of shunt determination to approximately ±3% at high oxygen tensions.

(c) *Carbon dioxide* PCO₂ was determined on a standard Severinghaus electrode using a 1/1,000-in. teflon membrane and 0.01 M NaHCO₃ and 0.10 M KCl buffer. The output was read on a Vibron electrometer, model 33B,³ as a difference in millivolts from a standard CO₂-O₂ mixture. The % CO₂ was then read from a semi-logarithmic plot of concentration versus millivolts. The accuracy of this system was assessed initially and throughout the course of the studies with known CO₂-O₂ gas mixtures and with blood equilibrated in a tonometer with gas of a known PCO₂. In 32 determinations on mixtures containing 2.64 to 9.59% CO₂ in O₂, the mean difference between the electrode reading and the known concentration of the standard gas was +0.044 mm. Hg (S.D. 0.45 mm. Hg). With 28 samples of equilibrated blood the mean error was +0.28 mm. Hg (S.D. 0.65 mm. Hg). Eighteen duplicate determinations were carried out during the course of the studies: these all agreed within 0.5 mm. Hg.

The PCO₂ of blood samples stored in iced water was found to be stable within the limits of the method for up to two hours. Blood gas tensions were corrected to body temperature using the nomograms of Bradley, Stupfel, and Severinghaus (1956).

Blood pH measurements were made using an Astrup macro-electrode system (Astrup and Schröder, 1956), and a Radiometer PHM4 pH meter.⁴

CALCULATIONS Physiological dead space (\dot{V}_D) and alveolar oxygen tension (PAO₂) were calculated from the standard equations (Comroe, Forster, Dubois, Briscoe, and Carlsen, 1962a). The physiological right-to-left shunt or venous admixture effect was calculated from the values obtained when breathing air using the formula

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{Ca_{O_2} - Cc'_{O_2}}{C\bar{V}_{O_2} - Cc'_{O_2}}$$

where \dot{Q}_s/\dot{Q}_t = shunt expressed as % of cardiac output, CaO₂ = arterial oxygen content (vol.%), Cc'O₂ = end-pulmonary capillary oxygen content (vol.%), and C \bar{V} O₂ = mixed venous oxygen content (vol.%).

Blood with an oxygen tension of 170 mm. Hg was considered fully saturated (Haab, Piiper, and Rahn, 1960). The solubility coefficient for dissolved oxygen was taken as 0.003 vol.% mm. Hg (Finley, Lenfant, Haab, Piiper, and Rahn, 1960). Oxygen capacity was assumed to be 20 vol.% unless the packed cell volume was below 40% or above 50%. In these circumstances the capacity (vol.%) was taken as Hb (g.) × 1.34 (Comroe, Forster, Dubois, Briscoe, and Carlsen, 1962b).

When calculating CaO₂ the arterial oxygen tension (PaO₂) and pH were used to read the percentage oxygen saturation (SaO₂) from the dissociation curve.

Then CaO₂ = (capacity × [SaO₂/100]) + (PaO₂ × 0.003).

² Yellow Springs Instrument Company, Yellow Springs, Ohio, U.S.A.

³ Electronic Instruments Ltd., Richmond, Surrey, England

⁴ Radiometer Ltd., Copenhagen, Denmark

TABLE II

	Frequency (breaths min.)				Minute Volume (l. min. B.T.P.S.)				Vd Vr (%)				Paco ₂ (mm. Hg body temp.)				O ₂ Consumption (ml. min. S.T.P.D.)								
	Pre-op.	P.O. 3 hr.	P.O.D. 1	P.O.D. 2	P.O.D. 8+	Pre-op.	P.O. 3 hr.	P.O.D. 1	P.O.D. 2	P.O.D. 8+	Pre-op.	P.O. 3 hr.	P.O.D. 1	P.O.D. 2	P.O.D. 8+	Pre-op.	P.O. 3 hr.	P.O.D. 1	P.O.D. 2	P.O.D. 8+					
Group I	Air	Mean	14.2	27.9	28.8	32.8	7.01	9.36	0.51	8.78	23.1	26.6	31.3	30.3	26.9	35	47	40	39	39	177	213	248	221	
		Range	12.5-16.5	27.7-33.7	22.3-35.0	22.8-30.0	13.8-27.4	6.51-16.12	6.81-14.56	8.55-13.5	6.05-11.10	12.8-31.8	18.3-32.8	21.9-42.1	23.2-42.5	35.5-31.7	23-41	43-56	36-46	29-44	34-42	124-219	140-298	188-287	174-270
		Mean	18.9	27.2	30.6	—	—	9.72	8.11	—	—	30.0	27.3	24.8	—	—	37	43	42	—	—	—	—	—	—
35% O ₂	Air	Mean	15.3-23.0	25.7-30.8	25.5-37.3	—	7.75-10.80	7.08-7.10	5.53-7.10	—	—	7.9-10.5	24.0-25.2	—	—	—	37	42	37	—	—	—	—	—	—
		Range	19.6-25.0	28.2-36.7	28.2-32.0	33.4-48.0	19.0-22.8	9.02-11.62	8.17-13.39	11.2-13.74	9.43-12.34	26.1-38.8	28.8-30.5	22.2-42.8	29.5-44.1	27.8-39.6	34	42	41	36	38	—	—	—	—
		Mean	19.6	29.8	28.2	33.4	19.0	9.02	8.17	11.2	9.43	26.1	28.8	22.2	29.5	27.8	34	42	41	36	38	—	—	—	—
Group II	Air	Mean	15.9	24.0	21.5	25.6	9.45	9.68	10.22	8.70	—	26.1	30.9	34.2	29.3	—	39	46	41	41	—	267	263	264	208
		Range	11.5-23.8	14.0-32.3	17.5-26.3	22.3-30.7	16.3-16.8	7.16-11.29	7.11-13.4	8.74-11.77	8.70-12.52	8.70-12.52	16.3-39.7	28.7-40.3	20.8-40.3	36.4-42.2	35-41	41-49	35-42	39-43	35-43	219-299	252-289	261-281	251-259
		Mean	19.0	19.8	23.2	24.8	11.6	8.08	9.13	10.22	8.75	8.25	22.8	34.9	33.3	33.4	41	45	42	42	41	—	—	—	—
35% O ₂	Air	Mean	15.0-23.8	13.7-24.5	21.3-25.0	20.3-29.3	6.76-9.90	5.69-9.50	8.94-11.49	8.94-11.49	8.38-11.49	20.9-49.9	26.5-45.4	35.4-43.0	22.5-40.1	30.6-40.1	36-44	36-47	36-47	38-44	38-44	—	—	—	—
		Range	23.8-33.7	24.5-33.7	25.0-33.7	29.3-35.0	15.5-15.5	9.90-11.35	9.13-11.10	10.22-13.30	8.75-10.49	8.25-10.49	22.8-29.4	34.9-43.1	33.3-43.1	33.4-50.8	41-42	42-47	42-47	42-47	42-47	39-42	39-42	39-41	35-41
		Mean	17.1	23.6	23.2	26.2	12.1	8.88	9.57	10.98	9.51	8.74	27.2	30.5	40.1	30.6	37.9	44	42	42	39	39	—	—	—
100% O ₂	Air	Mean	17.1	23.6	23.2	26.2	12.1	8.88	9.57	10.98	9.51	8.74	27.2	30.5	40.1	30.6	37.9	44	42	42	39	39	—	—	—
		Range	17.1-21.5	23.6-33.7	23.2-24.3	26.2-35.0	9.3-15.0	7.95-10.26	7.54-11.10	7.48-13.30	8.74-10.49	8.74-10.49	27.2-29.4	30.5-43.1	30.6-50.8	37.9-43.6	33-42	33-42	33-42	33-41	33-41	41-42	41-42	41-42	41-42
		Mean	17.1	23.6	23.2	26.2	12.1	8.88	9.57	10.98	9.51	8.74	27.2	30.5	40.1	30.6	37.9	44	42	42	39	39	—	—	—

¹ Full details on which this table is based are available from the authors on request.
 Pre-op. = before operation; P.O. 3 hr. = three hours after termination of anaesthesia; P.O.D. 1 = first post-operative day; P.O.D. 2 = second post-operative day; P.O.D. 8+ = two to five weeks after operation.

When calculating $Cc'o_2$ the same formula was applied, but it was assumed that the end-pulmonary capillary blood had the same PO_2 as the calculated mean PAO_2 . Thus any A-c' oxygen tension gradient was included in the calculated venous admixture effect.

$C\bar{V}O_2$ was assumed to equal $CaO_2 - 5$ vol.% unless otherwise stated. In those patients in whom intracardiac left-to-right shunts were demonstrated at pre-operative cardiac catheterization, the A-V difference found at that time was utilized when calculating the pre-operative value for \dot{Q}_s/\dot{Q}_t .

For calculation of true (anatomical) shunt the values obtained when breathing 100% oxygen were substituted in the shunt equation quoted above. Since arterial blood is fully saturated at these levels the difference in content must be calculated from the oxygen dissolved in plasma. If (A-a PO_2) represents the alveolar-arterial oxygen tension difference, the shunt equation then simplifies to:

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{(A-a PO_2) \times 0.003}{[(A-a PO_2) \times 0.003] + 5}$$

RESULTS

VENTILATION (TABLE II; FIG. 1)

Frequency of respiration In group I, the frequency of respiration (f) increased immediately after operation and reached a peak on the second post-operative day. In a number of cases the respiratory rate was still raised one week after operation. In group II, similar changes were seen but the increase in frequency was less marked. The respiratory rate was normal after one week.

Tidal volume In group I, the tidal volume (\dot{V}_T) fell dramatically immediately after operation and was still reduced several weeks after operation. In group II, the fall in tidal volume was much less marked.

Minute volume In group I, there was a reduction in minute volume (\dot{V}_E) three hours after operation, but this then increased to reach a maximum on the second post-operative day. In group II, similar findings were noted.

Physiological dead space In group I, the physiological dead space (\dot{V}_D) fell to half the pre-operative value immediately after operation and then gradually returned to normal values. The dead space/tidal volume (\dot{V}_D/\dot{V}_T) ratio increased slightly after operation and remained at the upper limits of normal for several weeks.

In group II, the reduction in physiological dead space was less marked and the \dot{V}_D/\dot{V}_T ratio was

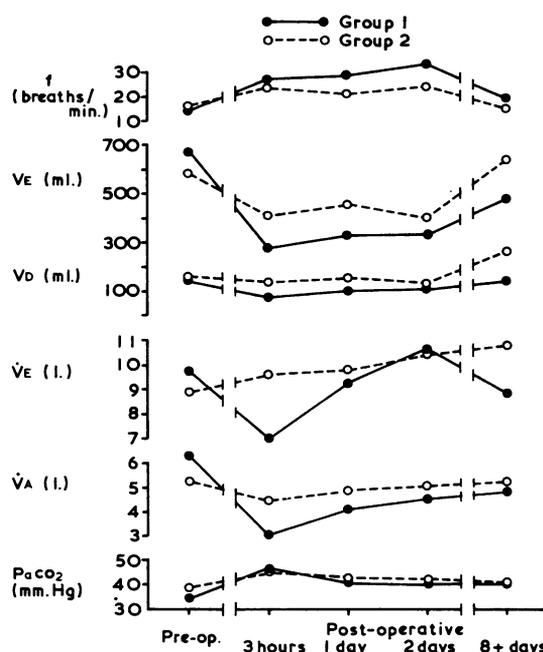


FIG. 1. Ventilatory changes. Abscissa: measurements taken before operation ('Pre-op'), 3 hours after the end of anaesthesia ('3 hours post-op'), on the first and second post-operative days, and one to three weeks after operation ('8+ days').

slightly increased after operation. Patient M.D. had a raised \dot{V}_D/\dot{V}_T ratio before operation which remained unaltered during the post-operative period.

Alveolar ventilation In group I, the alveolar ventilation was reduced immediately after operation and did not return to normal until the second post-operative day. In group II, there was a reduction in alveolar ventilation for several hours after operation, but values were normal by the first or second post-operative day.

OXYGEN TRANSFER (TABLES III AND IV)

Pre-operative studies Pre-operatively, the alveolar-arterial oxygen tension difference (A-a PO_2) while breathing air was less than 10 mm. Hg in all but two patients. Patient J.B. (group I), a woman with obstructive cardiomyopathy, had an A-a PO_2 of 17 mm. Hg. Patient M.D. (group II), an older man with known chronic lung disease, had an A-a PO_2 of 40 mm. Hg. For this reason all values for patient M.D. were excluded from the group means. When breathing 100% oxygen the A-a PO_2 in group I ranged from 42 to 136 mm. Hg with a mean of

TABLE III
SUMMARY OF RESULTS: A-a Po₂ (mm. Hg)

	Sample Time														
	Pre-operative			3 Hours Post-op.			P.O.D. 1			P.O.D. 2			Weeks Post-op.		
	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂
Group I: Extracorporeal circulation															
Mean ¹	8	34	79	33	—	236	36	101	326	40	—	357	7	—	—
Range	4-17	31-36	42-136	12-51	76-128	66-442	8-46	83-115	121-465	7-77	—	207-611	0-22	—	76-153
Group II: No extracorporeal circulation															
Mean ¹	0	11	45	14	24	111	11	—	118	18	—	138	—	—	—
Range	(40)	(115)	(—)	(41)	(100)	(149)	(52)	(126)	(255)	(40)	(128)	(247)	(45)	(85)	(161)
	0	9-17	17-65	6-23	16-32	33-211	10-12	33-44	62-157	12-25	32	65-212	11	29	64

¹ Values for patient M.D. given in brackets. These figures are excluded from the group means.
3 hours post-op. = 3 hours after termination of anaesthesia; P.O.D. 1 = first post-operative day; P.O.D. 2 = second post-operative day.

TABLE IV
SUMMARY OF RESULTS: VENOUS ADMIXTURE AND TRUE SHUNTS

	Sample Time														
	Pre-operative			3 Hours Post-op.			P.O.D. 1			P.O.D. 2			Weeks Post-op.		
	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂	Air	35% O ₂	100% O ₂
Group I: Extracorporeal circulation															
Mean	2.8	1.9	4.4	21.4	—	12.0	21.1	16.6	16.2	23.8	—	19.3	3.6	—	—
Range	1.8-4.4	1.8-2.0	2.2-7.5	8.9-33.0	10.0-26.0	3.8-21.0	3.1-31.0	10.0-23.0	6.7-22.0	3.8-46.0	—	11.0-39.0	0-12.0	—	4.3-8.4
Group II: No extracorporeal circulation															
Mean ¹	0	1.0	3.6	8.0	1.6	6.0	5.5	—	6.5	9.7	—	—	—	—	—
Range	(24.0)	(19.0)	(—)	(29.0)	(14.0)	(8.0)	(27.0)	(20.0)	(13.0)	(24.0)	(20.0)	(13.0)	(23.0)	(21.0)	(8.8)
	0	0.8-1.3	1.0-8.9	5.8-15.0	0.9-2.0	1.0-11.0	5.0-5.9	2.0-2.6	3.6-7.4	6.3-13.0	1.9	3.7-11.0	—	—	—

¹ Values for patient M.D. given in brackets. These figures are excluded from the group means.
3 hours post-op. = 3 hours after termination of anaesthesia; P.O.D. 1 = first post-operative day; P.O.D. 2 = second post-operative day.

79 mm. Hg, whereas the A-a Po₂ in group II ranged from 17 to 65 mm. Hg with a mean of 45 mm. Hg. On a 35% oxygen mixture the A-a Po₂ was 31 to 36 mm. Hg and 9 to 17 mm. Hg for groups I and II respectively.

The mean calculated physiological shunts for the two groups breathing air were 2.8% for group I and 0% for group II.

Post-operative studies All patients but one who were operated upon under extracorporeal circulation developed large alveolar-arterial oxygen tension differences during the 48 hours after surgery. These were usually evident within three hours after return to the recovery ward. The abnormal A-a Po₂ was most marked on the morning after operation and of similar magnitude on the next day. In group I, the A-a Po₂ varied from 8 to 77 mm. Hg when breathing air, and on 100% oxygen differences ranged from 66 to 611 mm. Hg. On three occasions it was deemed unwise to evaluate the patient on air.

In group II, the maximum A-a Po₂ on air was

52 mm. Hg in patient M.D. who had an abnormal value (40 mm. Hg) in his pre-operative study. In the other five patients the A-a Po₂ ranged from 6 to 25 mm. Hg. Breathing 100% oxygen, the maximum A-a Po₂ in the non-perfusion group was 212 mm. Hg (excluding M.D.). This was lower than the minimum A-a Po₂ found in all but one of the perfusion cases. The A-a Po₂ breathing 35% O₂ was also of lesser degree in the patients in group II. These results are illustrated in Figs 2 and 3. When the total venous admixture was calculated from this data there was again a striking difference between the two groups (Fig. 4). Breathing air, five out of the eight patients in group I had a venous admixture effect equivalent to more than 25% of the cardiac output. In group II, only one patient developed a venous admixture effect of more than 7%. The values for patient M.D. were almost unchanged after operation.

When breathing 100% O₂ (Fig. 5), the differences were equally marked. In group I, every patient except P.H.-R. developed a true shunt of more than 16% of the cardiac output at some stage of the post-

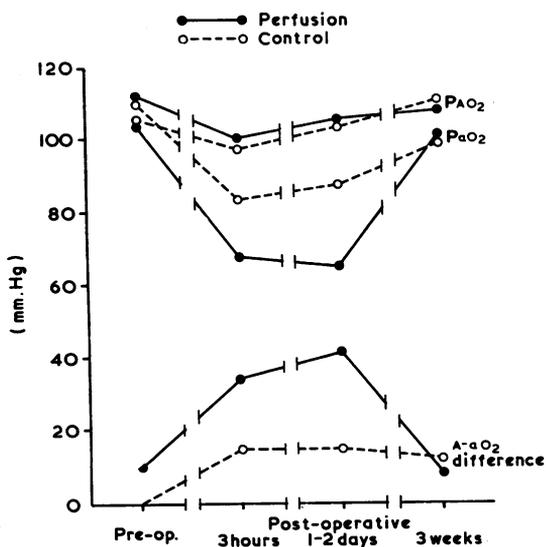


FIG. 2. PAO₂, PaO₂, and A-a PO₂ breathing air.

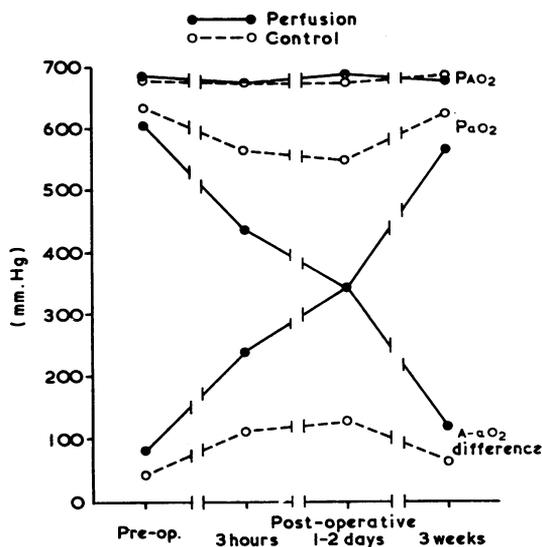


FIG. 3. PAO₂, PaO₂, and A-a PO₂ breathing 100% O₂.

operative period, whereas in group II only patient M.D. had a true shunt greater than 11%.

In those cases in which measurements were made when breathing 35% O₂, lower values for calculated venous admixture were obtained than on air. In a

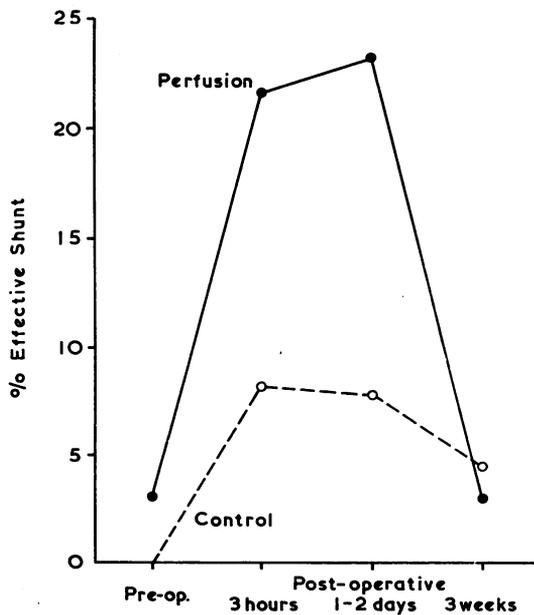


FIG. 4. Percentage shunt breathing air.

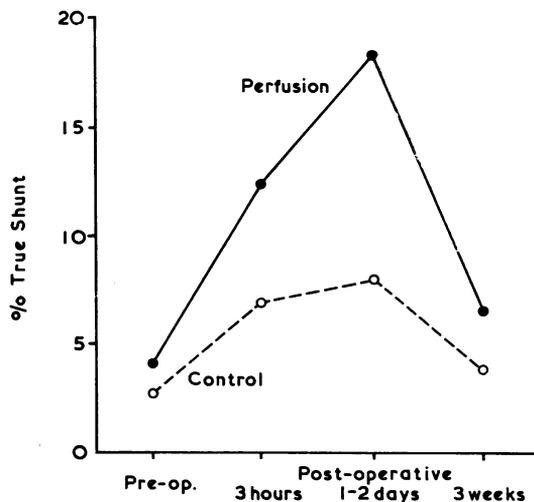


FIG. 5. Percentage shunt breathing 100% O₂.

number of cases the venous admixture was less on 35% O₂ than it was on 100% O₂, but there are too few results to draw any conclusions.

DISCUSSION

The data show that the majority of patients who undergo cardiac surgery with extracorporeal circulation develop abnormal alveolar-arterial oxygen

tension differences in the post-operative period. Seven of the eight patients in this group developed an abnormal A-a P_{O_2} when breathing air. Only one of the five patients who had thoracic or cardiac surgery without cardiopulmonary bypass, however, developed an A-a P_{O_2} of more than 15 mm. Hg. The sixth patient (M.D.) showed little increase on the pre-operative A-a P_{O_2} . Another way of expressing this difference between the two groups is to calculate the percentage of venous admixture which would account for the A-a P_{O_2} using the equation

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{Ca_{O_2} - Cc'_{O_2}}{C\bar{v}O_2 - Cc'_{O_2}}$$

When using this equation, two assumptions are involved: (1) all sources of venous admixture have the same oxygen tension as the blood in the pulmonary artery, and (2) the volume of the pulmonary artery inflow is equal to the volume of the outflow from the pulmonary veins (Finley *et al.*, 1960). The former would be strictly true only for anatomic shunts through the lungs involving the pulmonary circulation; the latter may be invalidated if blood is added to the pulmonary vein flow from the systemic circulation, *e.g.*, bronchopulmonary flow. Under most conditions these sources of error are small and do not significantly impair the validity of the calculation.

Unless pulmonary artery blood can be sampled directly, the $C\bar{v}O_2$ can only be estimated. For the shunt calculations quoted in this paper a normal A-V difference of 5 vol.% was used (*i.e.*, $C\bar{v}O_2 = Ca_{O_2} - 5$ vol.%). The oxygen consumption measurements recorded in this study were within the normal ranges; similar findings have been reported after open-heart surgery by Boyd, Tremblay, Spencer, and Bahnson (1959). These authors also measured cardiac output, using the Fick principle. From their data on a group of patients who underwent open-heart surgery it can be calculated that, in 19 patients who had a cardiac index greater than 2 litres per minute and a pulmonary arterial saturation of more than 50% during the post-operative period, the average A-V difference on the day of operation and for the two days thereafter was 5.3 vol.% (45 determinations), 5.0 vol.% (23 determinations), and 5.0 vol.% (six determinations). The cardiac index in this group ranged from 2.3 to 7.4 litres per minute. All these patients survived the immediate post-operative period. In a second group of 15 patients whose post-operative cardiac indices were less than 2 litres per minute and whose pulmonary arterial saturation fell below 50% on one or more occasions, the average A-V difference was approximately 8 vol.%; only five of these patients survived the first

few days following operation. Clowes, Sabga, Konitaxis, Tomin, Hughes, and Simeone (1961) have also made measurements of cardiac output after open-heart surgery. Using the dye technique, they showed that, if no significant metabolic acidosis was present, cardiac output was generally increased after operation. These authors comment that if the output did not rise after operation the prognosis was usually poor.

Since all cases with a doubtful or poor post-operative cardiovascular status were excluded from the data presented, it appears that the assumption of an A-V difference of 5 vol.% for the calculation of shunt was reasonable. Indeed, if the A-V difference had been 8 vol.% in group I cases and 5 vol.% in group II cases, the average % shunt would still have been greater in group I than in group II cases.

By equating the end-capillary oxygen tension with the mean alveolar P_{O_2} all three sources of arterial desaturation, anatomical shunt, distribution, and diffusion are included in the A-a P_{O_2} and percentage venous admixture calculated when breathing air. The latter two components are eliminated by breathing 100% O_2 ; even 35 to 50% O_2 is effective in this regard (Finley *et al.*, 1960; Riley and Courmand, 1951; Riley, Courmand, and Donald, 1951; Asmussen and Nielsen, 1960; Piiper 1961). This

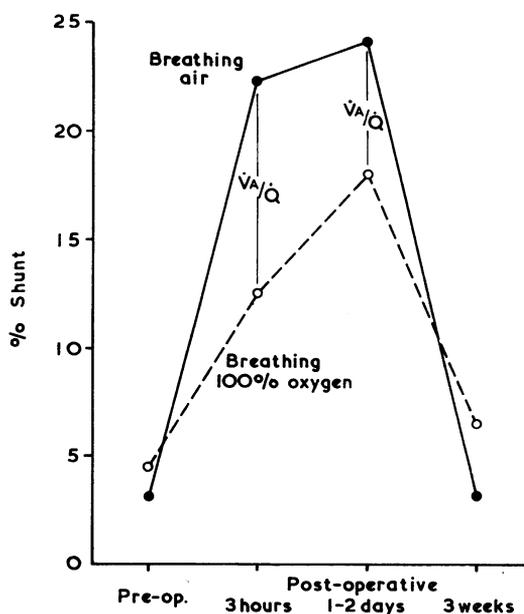


FIG. 6. Anatomical shunt and total venous admixture after total body perfusion.

is illustrated in Table IV. It may be seen from Tables III and IV and from Figs 4, 5, and 6 that the calculated shunt was reduced in each instance when the patient breathed 100% O₂: in several cases the percentage venous admixture was reduced by approximately half. This demonstrates clearly the importance of true shunt in the causation of the arterial desaturation noted in this study. The remainder of the desaturation was presumably due to areas of lung where ventilation and perfusion were unequal. Although a number of authors (Schramel *et al.*, 1959; Howatt *et al.*, 1962; Ellison *et al.*, 1963) have demonstrated reductions in diffusing capacity after open-heart surgery, it is likely that the changes noted could be accounted for by the ventilation-perfusion inequalities present.

Although PaCO₂ is usually not greatly influenced by uneven ventilation and perfusion (Riley *et al.*, 1951), it should be pointed out that with distribution (\dot{V}_A/\dot{Q}) abnormalities of the magnitude encountered in these studies arterial-alveolar gradients for CO₂ may be present (Williams and Rayford, 1956). In these circumstances, the measured PaCO₂ would be higher than the PACO₂: by equating PaCO₂ with PACO₂ in the alveolar air equation, a falsely low PAO₂ would be calculated. This in turn would lead to an underestimation of the A-a Po₂ and the magnitude of right to left shunt.

The changes in lung function were observed within a few hours of the conclusion of surgery. Indeed, in a proportion of cases they may be detected within an hour of perfusion (Young, McClenahan, and Sykes, 1965). The changes appear to reach a maximum on the first or second post-operative day and, although measurements were not made from the third post-operative day onward, the clinical condition usually improved rapidly after this time. Three of the four patients in group I tested several weeks after operation showed almost complete resolution of their abnormality. One, who had to be re-operated upon for sternal wound infection, still showed some impairment three weeks after the second procedure, but to a lesser degree. Patient V.P. showed the most striking changes, developing a 46% shunt on air and a 611 mm. Hg gradient on 100% oxygen on the second post-operative day; three weeks after operation there was no measurable abnormality.

In attempting to explain pulmonary complications which follow open-heart surgery with extracorporeal circulation, multiple factors require consideration. Arterial desaturation may be due to hypoventilation or to an increase in the alveolar-arterial oxygen tension difference. Hood and Eeall (1958) have stressed the importance of hypoventilation as a

cause of desaturation after thoracic surgery. This cause was excluded in the present series by the normal range of carbon dioxide tensions encountered. Kolff, Effer, Groves, Fughes, and McCormack (1958) suggested that the complications resulted from pulmonary capillary damage initiated by the temporary overloading of the lesser circulation with blood. Eaer and Osborn (1960) pointed out, however, that the syndrome had occurred even when the left atrium was carefully drained. Decreased oxygen saturation has been noted following massive pulmonary embolus in dogs (Stein, Forkner, Robin, and Wessler, 1961). After total unilateral pulmonary artery occlusion shunting was detected when blood flow was restored; this shunting was thought to be secondary to atelectasis which resulted from reflex bronchoconstriction and small airway closure (Severinghaus, Swenson, Finley, Lategola, and Williams, 1961).

In patients with the tetralogy of Fallot, flow through the enlarged bronchial system, if this persists after complete correction, could account for arterial blood desaturation. If intracardiac defects were not closed or a patent ductus arteriosus remained patent, a shunting of blood right to left through these communications might occur. Differences in the operative technique, such as placement of the incision, the nature of the repair, and the duration of the procedure, may contribute to the genesis of the post-operative abnormalities encountered. An attractive hypothesis is that the desaturation is a consequence of a significant amount of blood shunting through multiple areas of patchy atelectasis which has resulted from an alteration in the surface tension properties of the fluid lining the alveoli. The stability of the alveolar structure depends upon the surface tension of the lining fluid and the modification of these forces by a lipo-protein 'surface-active material'. This latter substance tends to lower the surface tension as the alveolus becomes smaller and so prevents its collapse (Pattle, 1958; Clements, 1962). Tooley, Gardner, Thung, and Finley (1961) found that, in dogs which had undergone extracorporeal circulation for one hour, the surface tension of extracts of their lungs was raised within five hours after perfusion. It has also been found that sometimes following bypass a rapid decrease in 'surface-active material' occurs (Clements, 1962). Eaer and Osborn (1960) circulated blood from the carotid to the femoral artery of dogs using a DeBakey pump and a constriction to the outflow tubing to increase turbulence. Several, but not all, of the sacrificed animals showed evidence of congestion, focal collapse, and pulmonary haemorrhage despite the fact that the chest had not been opened.

Gardner, Finley, and Tooley (1962) added blood which had been pumped through a bubble oxygenator for several hours and normal blood to extracts of dog lung. The surface tension was markedly increased in the pumped blood mixture, whereas that of the non-perfused blood mixture remained normal. This evidence and the findings in this study suggest that the pumping process *per se* may destroy a blood component or somehow alter its production, which in turn affects the stability of the pulmonary alveolar structure and leads to atelectasis and shunting through the lungs. Further support for this hypothesis has recently been provided by Nahas, Melrose, Sykes, and Robinson (1965a, b).

SUMMARY

Patients who undergo cardiac surgery with extracorporeal circulation develop significant alveolar-arterial oxygen tension differences and venous admixture in the early post-operative period. Up to 50% of this abnormality is due to anatomical right to left shunting through the lungs; the remainder is most likely to be due to ventilation-perfusion inequality. The changes appear to be completely reversible. The cardiopulmonary bypass procedure may be responsible for initiating the underlying pathology, since changes of this magnitude were not found in cardiothoracic surgery patients in whom this technique was not required.

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ADDENDUM

Since this paper was submitted for publication Hedley-Whyte, Corning, Laver, Austen, and Bendixen (1965) have published similar findings.

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