Respiratory changes after open-heart surgery

J. B. McClenahan, W. E. Young, 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 resulting 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, Loescheke, Schaudig, Pasini, Auburger, 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 pathological 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. Respiration 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

1 Supported by Fellowship, U.S. Public Health Service. Now Research Associate, Palo Alto Medical Research Foundation - Stanford University Health Service
2 R. S. McLaughlan Travelling Fellow. Now at St. Michael's Hospital, Toronto, Canada
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 were 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. 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 ten 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, the blood was washed, centrifuged, and the plasma was analyzed for blood gases.

TABLE I
GROUP I. PATIENTS STUDIED

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Weight (kg.)</th>
<th>Height (cm.)</th>
<th>Surface Area (m.²)</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Perfusion Time (min.)</th>
<th>Total Bypass (min.)</th>
<th>Lowest Temp. Recorded (°C. oesophageal)</th>
<th>Pulmonary Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>V.P.</td>
<td>F</td>
<td>29</td>
<td>42-5</td>
<td>153</td>
<td>1-37</td>
<td>Atrial septal defect</td>
<td>Closure</td>
<td>48</td>
<td>44</td>
<td>30</td>
<td>? Pulmonary artery thrombosis on second post-op. day</td>
</tr>
<tr>
<td>E.W.</td>
<td>M</td>
<td>32</td>
<td>64-0</td>
<td>168</td>
<td>1-75</td>
<td>Aortic incompetence</td>
<td>Aortic valve replacement</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Patchy collapse and consolidation — right middle and lower zones</td>
</tr>
<tr>
<td>H.A.</td>
<td>M</td>
<td>25</td>
<td>56-5</td>
<td>178</td>
<td>1-70</td>
<td>Aortic incompetence</td>
<td>Aortic valve replacement</td>
<td>207</td>
<td>220</td>
<td>22</td>
<td>Some left lower lobe collapse</td>
</tr>
<tr>
<td>T.C.</td>
<td>M</td>
<td>19</td>
<td>51-8</td>
<td>159</td>
<td>1-51</td>
<td>Obstructive cardiomyopathy</td>
<td>Infundibular resection</td>
<td>69</td>
<td>59</td>
<td>24</td>
<td>Some left lower lobe collapse</td>
</tr>
<tr>
<td>S.R.</td>
<td>F</td>
<td>25</td>
<td>64-5</td>
<td>157</td>
<td>1-67</td>
<td>Obstructive cardiomyopathy</td>
<td>Infundibular resection</td>
<td>67</td>
<td>50</td>
<td>24</td>
<td>Some left lower lobe collapse</td>
</tr>
<tr>
<td>J.B.</td>
<td>F</td>
<td>36</td>
<td>45-0</td>
<td>156</td>
<td>1-42</td>
<td>Obstructive cardiomyopathy</td>
<td>Infundibular resection</td>
<td>76</td>
<td>60</td>
<td>26</td>
<td>Some collapse both bases</td>
</tr>
<tr>
<td>A.C.</td>
<td>M</td>
<td>33</td>
<td>58-5</td>
<td>171</td>
<td>1-62</td>
<td>Aortic incompetence</td>
<td>Aortic valve replacement</td>
<td>240</td>
<td>222</td>
<td>23</td>
<td>Nil</td>
</tr>
<tr>
<td>P.H. R.</td>
<td>M</td>
<td>16</td>
<td>56-0</td>
<td>173</td>
<td>1-68</td>
<td>Ventricular septal defect</td>
<td>Closure</td>
<td>83</td>
<td>63</td>
<td>24</td>
<td>Nil</td>
</tr>
</tbody>
</table>

GROUP II. CONTROLS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Weight (kg.)</th>
<th>Height (cm.)</th>
<th>Surface Area (m.²)</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Perfusion Time (min.)</th>
<th>Total Bypass (min.)</th>
<th>Pulmonary Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.P.</td>
<td>M</td>
<td>24</td>
<td>66-8</td>
<td>184</td>
<td>1-86</td>
<td>Coarctation of aorta</td>
<td>Resection and graft</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>R.McN.</td>
<td>M</td>
<td>16</td>
<td>61-0</td>
<td>—</td>
<td>—</td>
<td>Patent ductus arteriosus</td>
<td>Ligation</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M.H.</td>
<td>M</td>
<td>15</td>
<td>68</td>
<td>178</td>
<td>1-85</td>
<td>Atrial septal defect</td>
<td>Closure</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>J.L.</td>
<td>M</td>
<td>22</td>
<td>74-2</td>
<td>178</td>
<td>—</td>
<td>Coarctation of aorta</td>
<td>Resection</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>P.H.-R.</td>
<td>M</td>
<td>16</td>
<td>56-0</td>
<td>173</td>
<td>1-68</td>
<td>Patent ductus arteriosus and ventricular septal defect</td>
<td>Closure</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M.D.</td>
<td>M</td>
<td>40</td>
<td>58-2</td>
<td>—</td>
<td>—</td>
<td>Granuloma of lung</td>
<td>Total resection of granuloma of lung</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

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

J. B. McClanahan, W. E. Young, and M. K. Sykes

1 Type C.D.I, 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). 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 +0-004 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, 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.

CALCULATIONS Physiological dead space (Vₚ) 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

\[
\frac{Q_b}{Q_t} = \frac{CaO_2 - CcO_2}{CVO_2 - CC'O_2}
\]

where Q_b/Q_t = shunt expressed as % of cardiac output, CAO₂ = arterial oxygen content (vol.%), CC'O₂ = end-pulmonary capillary oxygen content (vol.%), and CVO₂ = 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

\[
CAO_2 = (capacity \times [SAO_2/100]) + (PAO_2 \times 0-003).
\]
### Table II

<table>
<thead>
<tr>
<th></th>
<th>Frequency (breaths min.)</th>
<th>Minute Volume (l. min. B.T.P.S.)</th>
<th>Vo Vr (%)</th>
<th>Paco₂ (mm. Hg body temp.)</th>
<th>O₂ Consumption (ml. min. S.T.P.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-op.</td>
<td>P.O. 3 hr.</td>
<td>P.O. D. 1</td>
<td>P.O. D. 2</td>
<td>Pre-op.</td>
</tr>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air</td>
<td>Mean</td>
<td>14.2</td>
<td>27.9</td>
<td>28.8</td>
<td>32.8</td>
</tr>
<tr>
<td>35% O₂</td>
<td>Mean</td>
<td>18.9</td>
<td>27.2</td>
<td>30.6</td>
<td>33.0</td>
</tr>
<tr>
<td>100% O₂</td>
<td>Mean</td>
<td>19.6</td>
<td>29.8</td>
<td>32.8</td>
<td>33.4</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air</td>
<td>Mean</td>
<td>15.9</td>
<td>24.0</td>
<td>25.6</td>
<td>25.2</td>
</tr>
<tr>
<td>35% O₂</td>
<td>Mean</td>
<td>19.0</td>
<td>25.1</td>
<td>28.7</td>
<td>25.0</td>
</tr>
<tr>
<td>100% O₂</td>
<td>Mean</td>
<td>17.1</td>
<td>23.6</td>
<td>29.2</td>
<td>24.3</td>
</tr>
</tbody>
</table>

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 Ce'02 the same formula was applied, but it was assumed that the end-pulmonary capillary blood had the same Po2 as the calculated mean PAO2. Thus any A-c' oxygen tension gradient was included in the calculated venous admixture effect.

CV02 was assumed to equal Ca02 - 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 Qs/Qt.

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 Po2) represents the alveolar-arterial oxygen tension difference, the shunt equation then simplifies to:

\[
\text{Qs} = \frac{(A-a \text{ Po}_2) \times 0.003}{(A-a \text{ Po}_2) \times 0.003 + 5}
\]

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 (Vt) 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 (Ve) 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 (VD) fell to half the pre-operative value immediately after operation and then gradually returned to normal values. The dead space/tidal volume (VD/Vt) 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 VD/Vt ratio was slightly increased after operation. Patient M.D. had a raised VD/Vt 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 Po2) 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 Po2 of 17 mm. Hg. Patient M.D. (group II), an older man with known chronic lung disease, had an A-a Po2 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 Po2 in group I ranged from 42 to 136 mm. Hg with a mean of
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 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-
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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% \( O_2 \), lower values for calculated venous admixture were obtained than on air. In a number of cases the venous admixture was less on 35% \( O_2 \) than it was on 100% \( O_2 \), but there are too few results to draw any conclusions.

**FIG. 2.** \( P_{A\text{o}_2}, P_{A\text{o}_3}, \) and A-a \( P_{O_2} \) breathing air.

**FIG. 3.** \( P_{A\text{o}_2}, P_{A\text{o}_3}, \) and A-a \( P_{O_2} \) breathing 100% \( O_2 \).

**FIG. 4.** Percentage shunt breathing air.

**FIG. 5.** Percentage shunt breathing 100% \( O_2 \).

**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 Po₂ when breathing air. Only one of the five patients who had thoracic or cardiac surgery without cardiopulmonary bypass, however, developed an A-a Po₂ of more than 15 mm. Hg. The sixth patient (M.D.) showed little increase on the pre-operative A-a Po₂. 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 Po₂ using the equation

\[ \frac{Q_1}{Q_t} = \frac{Cao_2 - Cc' o_2}{Cvo_2 - Cc' o_2} \]

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 Cvo₂ can only be estimated. For the shunt calculations quoted in this paper a normal A-V difference of 5 vol.% was used (i.e., Cvo₂ = Cao₂ - 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 Po₂ all three sources of arterial desaturation, anatomic shunt, distribution, and diffusion are included in the A-a Po₂ and percentage venous admixture calculated when breathing air. The latter two components are eliminated by breathing 100% O₂; even 35 to 50% O₂ is effective in this regard (Finley et al., 1960; Riley and Cournand, 1951; Riley, Cournand, and Donald, 1951; Asmussen and Nielsen, 1960; Piiper 1961).
Respiratory changes after open-heart surgery

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 (VA/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 during surgery, by equating Paco2 with Paco2 in the alveolar air equation, a falsely low Paco2 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 a hour of perfusion (Young, McClanahan, 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 Beall (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, Effler, Groves, Hughes, and McCormack (1958) suggested that the complications resulted from pulmonary capillary damage initiated by the temporary overloading of the lesser circulation with blood. Eater 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 alveoli becomes smaller and so prevents its collapse (Pattie, 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). Eater 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 surface 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-Whitte, Corning, Laver, Austen, and Bendixen (1965) have published similar findings.

**REFERENCES**


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