Instruments and techniques

Oxygen method for calculation of right to left shunt: new application in presence of right to left shunting through the ductus arteriosus

WELTON M. GERSONY, GABRIEL V. DUC, RALPH B. DELL, and JOHN C. SINCLAIR

From the Department of Pediatrics, College of Physicians and Surgeons of Columbia University, New York, N.Y., U.S.A.

AUTHORS’ SYNOPSIS The usual shunt equation has been misapplied to the calculation of shunts when a right to left ductal shunt may be present – for example, respiratory distress syndrome. New equations are derived and discussed which correctly estimate the percentage of the total cardiac output which is shunted, even in the presence of a right to left ductal shunt.

Pulmonary disease in the newborn infant is usually associated with hypoxaemia. Hypoventilation, pulmonary diffusion defects, ventilation-perfusion inequalities, and true intrapulmonary right to left shunts account for part of the oxygenation defect. In addition, when pulmonary vascular resistance is greater than systemic, the transitional circulation of the neonate allows right to left shunting of blood through the ductus arteriosus and foramen ovale (Strang, 1961).

The idiopathic respiratory distress syndrome (RDS) is the pulmonary disorder that has been most thoroughly studied with respect to the genesis of the oxygenation defect. It is recognized that right to left shunting is a major cause of the hypoxaemia in these babies (Prod’hom, Heyman, Battey, and Ferguson, 1955; Strang and MacLeish, 1961; Chu, Clements, Cotton, Klaus, Sweet, and Tooley, 1967). Right to left shunts have been described as occurring in the lung (Stahlman, Shepard, Young, Gray, and Blankenship, 1966; Wallgren, Hanson, Tabakin, Räihä, and Vapaavuori, 1967; Murdock, Kidd, Llewellyn, Reid, and Swyer, 1969), through a patent foramen ovale (Stahlman et al., 1966; Wallgren et al., 1967), and through a patent ductus arteriosus (Stahlman et al., 1966; Murdock, and Swyer, 1968; Robertson, and Dahlenburg, 1969).

The principal method which has been employed for quantitation of these shunts has been the ‘oxygen method’ which is based upon the application of the Fick principle to the uptake and release of oxygen (Berggren, 1942; Strang and MacLeish, 1961; Gorlin, 1966). It is the purpose of this paper to point out a conceptual error in the usual application of this method to the calculation of right to left shunts in the presence of a right to left ductal shunt, and to present a quantitative analysis of errors which have resulted from this misapplication. Modified equations are derived and nomograms presented which allow the valid application of the oxygen method to the determination of right to left shunting in the presence of a right to left ductal shunt.
Theoretical considerations

The usual shunt equation:

$$\frac{Q_h}{Q_T} = \frac{C_v - C_a}{C_o - C_v}$$  \hspace{1cm} (1)

assumes a single value for arterial oxygen content, but in the presence of a right to left ductal shunt (see Fig. 10) no such single value exists (for explanation of symbols see Appendix). This consideration leads to the derivation of two new equations (for derivation see appendix):

$$\frac{Q_h}{Q_T} = \frac{C_v - kC_{au} - (1-k)C_{al}}{C_o - kC_{au} - (1-k)C_{al} + av}$$ \hspace{1cm} (2)

and

$$\frac{Q_{DA}}{Q_T} = \frac{(1-k)(C_{au} - C_{al})}{(1-k)(C_{au} - C_{al}) + av}$$ \hspace{1cm} (3)

Both of these equations require the same assumptions that have always been made when using the oxygen method of estimating shunts, plus knowledge of the oxygen content of samples of pre- and postductal blood. In addition to these facts, a new variable, \(k\), is introduced which represents the proportion of the total blood flow perfusing the upper portion of the body – that is, blood leaving by all arterial branches of the preductal portion of the aorta. Presumably blood flow to the brain accounts for most of the blood going to the upper portion of the body in infants. Exact information regarding cerebral blood flow has not been obtained in this age group but is approximately 14% of the cardiac output in adult man (Scheinberg and Stead, 1949). It is likely to be a larger fraction in infants due to their relatively larger brain and higher blood flow per gram of tissue (Kennedy and Sokoloff, 1957). Therefore, even if \(k\) is not measured, it can be estimated within limits. It is unlikely that \(k\) will ever be lower than 0-2, or greater than 0-7, even in premature infants. The effects of variations in the magnitude of \(k\) are explored in the result section. Note that if right to left ductal shunt is not present (\(C_{al}\) and \(C_{al}\) identical), estimation of the value of \(k\) becomes unnecessary to solve the equation.

Results

The characteristics of the modified shunt equation for total shunt (equation 2) are examined in Fig. 1. For the purpose of displaying the shunt data, in this and subsequent figures \(C_o\) will be assumed to be 22 vol% and the arteriovenous \(O_2\) difference 3 vol%. These assumptions are not intrinsic to the model, but are made for illustrative purposes only. The effect of \(C_{au}\) and \(k\) upon the magnitude of the total shunt is plotted for \(C_{al}\) values of 20, 18 and 13 vol%. Increasing \(C_{au}\) is associated with a fall in total shunt – that is, a larger portion of the cardiac output is being oxygenated, since the intrapulmonary and intra-cardiac shunts must decrease if \(C_{au}\) is to rise. As \(C_{au}\) rises the low \(C_{al}\) is increasingly produced by right to left shunting through the ductus until at a \(C_{au}\) of 22 vol% (equal to total \(O_2\) capacity of the blood in this example) the total shunt is all ductal. Increasing the ductal proportion of the total shunt means that less desaturated blood need enter the arterial side in order to produce the observed desaturation of postductal (umbilical artery) blood. As \(k\) increases, a larger proportion of the cardiac output is going to the upper portion of the body so that less right to left ductal shunting is required to produce the observed \(C_{al}\). Hence with increasing \(k\) the total shunt falls even more sharply as \(C_{al}\) rises. It is also apparent from a comparison of Figs. 1a, b, and c that both \(k\) and \(C_{al}\) are less important in determining total shunt as \(C_{al}\) becomes lower, since only large shunts can reduce \(C_{al}\) to markedly low levels regardless of the site. The dotted lines in Fig. 1 indicate the total shunt which would be calculated from the usual application of the shunt equation – that is, assuming that \(C_{al}\) represents the oxygen content of the entire arterial tree. Note that this way of exploring the effect of variation of each of the variables on calculated total shunt and ductal shunt. The per cent error of the usual way of calculating these shunts was computed by dividing the difference between the usual and correct way of estimating the shunts by the correct way. Finally, the magnitude of the errors which would be made in estimating total and ductal shunt by the new equations, if the assumption of a systemic arteriovenous \(O_2\) content difference of 3 vol% were incorrect, is presented.

Methods

The new shunt equations, equations 2 and 3, together with the usual shunt equation, equation 1, were programmed in Fortran IV on the IBM model 360-75/91 computer for purposes of systematically
New equation for right to left shunt

FIG. 1 Relationship between \( \frac{Q_s}{Q_T} \) and \( C_{au} \) for \( k = 0.2, 0.5, \) and 0.7 at \( C_{al} = 20, 18, \) and 13 vol\%.

Note that in Fig. 1c the relationship between \( \frac{Q_s}{Q_T} \) and \( C_{au} \) for \( k = 0.5 \) and 0.7 does not extend the full length of the graph. This is due to the assumption that there is no retrograde flow up the aorta from the ductus. This then means that the sum of the proportion of the cardiac output going to the upper portion of the body, \( k \), and the proportion of the cardiac output going through the ductus, \( \frac{Q_{da} + Q_s}{Q_T} \), cannot be greater than one—that is, \( k + \frac{Q_{da} + Q_s}{Q_T} < 1 \). Therefore any combination of variables which yielded values for \( k + \frac{Q_{da} + Q_s}{Q_T} > 1 \) were considered to be biologically impossible combinations and hence no values for \( \frac{Q_s}{Q_T}, \frac{Q_{da} + Q_s}{Q_T}, \) etc., were computed in Fig. 1c and subsequent Figures. If retrograde aortic flow does occur then extrapolation of the curves is necessary.

calculating total shunt yields a value which is always an overestimation when \( C_{au} \) is higher than \( C_{al} \)—that is, where there is appreciable ductal shunting.

Figure 2 shows the per cent error made in calculating the total shunt if the usual shunt equation is used (with \( C_a \) assumed to be \( C_{al} \)) as a function of preductal oxygen content for three different values of \( k \) at three different values of \( C_{al} \). The error is always positive—that is, using the usual shunt equation always results in an overestimate of total shunt. The per cent error increases with increasing \( k \) and with increasing \( C_{au} \) at any given \( C_{al} \). Note that if \( C_{au} \) and \( C_{al} \) are identical the per cent error is zero. Comparison of Figs. 2a, b, and c shows that for any given value of \( k \) and \( C_{au} \) the per cent error falls as \( C_{al} \) falls, but, since total shunt is increasing, this smaller percentage error of a larger number results in absolute errors in calculated total shunt that are virtually identical for all three values of \( C_{al} \). Thus, if there is a right to left shunt through the ductus, the usual shunt equation overestimates total shunt, an overestimation which increases as the ductal portion of the total shunt increases or as the fraction of the cardiac output perfusing the upper portion of the body increases.

An analysis of the ductal equation (equation 3) is illustrated in Fig. 3. Examination of equation 2 shows that the ductal shunt is dependent upon two factors, \( C_{au} - C_{al} \) and hereafter called \( d \) and \( k \). An increasing \( d \) indicates that more venous blood is passing through the patent ductus arteriosus and hence the calculated ductal flow increases. However, the greater the proportion of the cardiac output which is perfusing the upper body (\( k \) increasing), the lesser the ductal shunt which is necessary to lower \( C_{al} \). In other
words, for any given $d$, as $k$ increases, $\frac{Q_{DA}}{Q_T}$ falls.

The magnitude of the ductal shunt is usually estimated by calculating total shunt by the usual shunt equation using the oxygen content of postductal blood ($C_{aL}$), and then subtracting from this the estimated intracardiac and intrapulmonary right to left shunt which is calculated by the usual shunt equation using the oxygen content of preductal blood ($C_{aU}$) (Murdock and

**Figure 2** Relationship between the percent error in calculating total shunt via the standard shunt equation ($E_{ST}$) and $C_{aU}$ for $k = 0.2, 0.5$, and $0.7$ at $C_{aL} = 20, 18$, and $13$ vol%. $E_{ST} = (\text{old value} - \text{new value})/\text{new value}$. See Note Fig. 1.

**Figure 3** Relationship between $\frac{Q_{DA}}{Q_T}$ and $C_{aU} - C_{aL}$ for $k = 0.2, 0.5$ and $0.7$. See Note, Fig. 1.
FIG. 4 Relationship between the percent error in calculating ductal shunt via the usual procedure ($E_{SD}$) and $C_{au}$ for $k=0.2$, 0.5, and 0.7 at $C_{al}=20$, 18, and 13 vol%. $E_{SD}=\frac{\text{old value} - \text{new value}}{\text{new value}}$. See Note, Fig. 1.

Swyer, 1968; Robertson and Dahlenburg, 1969). However, this latter procedure for estimating the intrapulmonary and intracardiac shunts calculates only the proportion of the left ventricular output which is shunted rather than the proportion of the total cardiac output which is shunted; that is, $(Q_{BP} + Q_{SPFO})/Q_{LH}$ is calculated instead of $(Q_{BP} + Q_{SPFO})/Q_T$ (see Fig. 10). Since $Q_T = Q_{LH} + Q_{DA}$ (Fig. 10), the denominator of the ratio $(Q_{BP} + Q_{SPFO})/Q_{LH}$ is too small by the amount of the ductal flow. Thus, the very factor which we are trying to estimate is ignored! This error results in an overestimate of intracardiac and intrapulmonary shunting. As discussed above, the total shunt is also overestimated when $C_a$ is taken to be $C_{al}$ in the usual shunt equation. However, this overestimate is not related in any constant way to the overestimate of the intrapulmonary and intracardiac shunts. Therefore subtracting these two erroneous estimates results in a calculated ductal shunt which may be too large, too small, or by chance, close to accurate.

The magnitude of these errors is illustrated in Fig. 4. Again the magnitude of the error is dependent upon three factors: postductal oxygen content ($C_{al}$); the proportion of blood flowing to the upper portion of the body ($k$); and the amount of intrapulmonary and intracardiac shunting (how far $C_{al}$ is from 22 vol%). If there is no shunting other than through the ductus ($C_{al}$ is 22 vol%), then the usual way of calculating the ductal shunt results in an overestimate. This overestimate increases with $k$ but decreases with decreasing $C_{al}$ (Figs. 4a, b, and c). However, if there is some intrapulmonary and/or intracardiac shunting, then the usual way of estimating ductal shunting will yield either values which may or may not overestimate the true ductal shunt depending upon $k$ (Fig. 4a) or values which almost always underestimate the true ductal shunt (Fig. 4c) regardless of $k$. In general, larger ductal shunts (low $C_{al}$, Fig. 4c) are markedly underestimated in the presence of large intrapulmonary and/or intracardiac shunting (low $C_{al}$), while smaller ductal shunts (high $C_{al}$, Fig. 4a) are overestimated.

Figure 5 shows the effect on the calculated shunts if the systemic arteriovenous difference for oxygen content is 1 vol% higher or lower than the assumed value of 3 vol%. Equal changes
in the systemic oxygen difference, \( \Delta V \), in either direction cause the same per cent error in the calculated shunt. Furthermore, the change is linear, so that if the change is twice as large or half as large as the 1 vol% change shown in Fig. 5, the percentage error in calculated shunt will be twice as large or half as large, respectively as that shown in the Figure. For the ductal shunt, the error decreases with increasing \( d \) but increases with increasing \( k \). For the total shunt, the

![Graph showing the effect of the actual systemic arteriovenous oxygen difference on calculated ductal shunt (\( \Delta S_D/S_D \)) and calculated total shunt (\( \Delta S_T/S_T \)).](image)

**Fig. 5** The effect of the actual systemic arteriovenous oxygen difference being 1 vol% higher than the assumed value of 3 vol% on calculated ductal shunt (\( \Delta S_D/S_D \)) and calculated total shunt (\( \Delta S_T/S_T \)). See Note, Fig. 1.
Models A and B based on the following assumptions:

1. $Q_T = 600$ ml.
2. Arterial-venous oxygen difference across the tissues = 3 vol%.
3. Infant breathing 100% $O_2$.
4. Blood total $O_2$ capacity = 22 vol%.

Model A. Upper body lower blood distribution ($k$) = 60/40. Measured umbilical arterial content = 19 vol%. Measured temporal arterial content = 21.5 vol%.

Model B. Upper body lower body blood distribution ($k$) = 40/60. Measured umbilical arterial content = 10 vol%. Measured right radial arterial content = 15 vol%.

Note: For the purpose of simplifying the diagram, only a pulmonary shunt is assumed. All or part of the 'pulmonary' shunt may include right to left shunt through the foramen ovale without affecting the calculations.

<table>
<thead>
<tr>
<th></th>
<th>Actual shunt ratios</th>
<th>Calculated shunt ratios: standard equation</th>
<th>Calculated shunt ratios: new equation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$Q_{m}/Q_T = 150 + 50/600 = 33%$</td>
<td>$22 - 19 = 25%$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$Q_T/QT = 50/600 = 8%$</td>
<td>$22 - 16 = 14%$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$Q_{DA}/QT = 150/600 = 25%$</td>
<td>$Q_{m}/Q_T - Q_{p}/Q_T = 36%$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$0.4 - 2.5% = 25%$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model B</td>
<td></td>
<td>$Q_{m}/Q_T = 300 + 160/600 = 77%$</td>
<td>$22 - 10 = 80%$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$Q_T/QT = 160/600 = 27%$</td>
<td>$22 - 7 = 70%$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$Q_{DA}/QT = 300/600 = 50%$</td>
<td>$0.6 - 5% = 50%$</td>
</tr>
</tbody>
</table>

1 Equation (1)  2 Equation (2)  3 Equation (3)
per cent error in calculated shunt, if the actual systemic arteriovenous oxygen difference is not that assumed, increases if either $k$ or $d$ increases, and falls if $C_{at}$ falls.

**RDS models**

Figure 6 presents hypothetical examples of right to left shunting in models of mild (A), and severe (B) respiratory distress syndrome where significant ductal shunting has been postulated. Numbers inside the vessels are flows in ml./min, while numbers outside the vessels indicate oxygen content in vol%. The actual values for the shunt as well as the values calculated by the original and new equations are shown in the legend. It is quite apparent from a comparison of the actual and calculated shunt values that the magnitude of the errors is dependent upon the severity of the disease. In model A (mild RDS) the total shunt is overestimated by approximately

![Nomogram for calculating ductal right to left shunt.](image-url)
New equation for right to left shunt

50%; whereas in model B (severe RDS) the total shunt is calculated nearly correctly, but the ductal shunt is markedly underestimated because the intrapulmonary and/or intracardiac shunts are markedly overestimated. In model B it is clear that the usual application of the shunt equation to calculate total and pulmonary shunt has significantly underestimated the importance of the ductal right to left shunt. Only a 10% ductal shunt is calculated when the actual ductal shunt is 50%! In each of the examples, the shunts are accurately calculated by use of the new equations.

Use of nomogram
The nomogram for calculation of the ductal shunt (Fig. 7) is a simple alignment nomogram. The value for k is found on the left hand scale, the value for the difference $C_{au} - C_{al}$ is found on the right hand scale and the ductal shunt is read off the middle scale as a percentage of cardiac output. This nomogram is independent of oxygen capacity and depends only upon $k$ and $C_{au} - C_{al}$.

The nomogram for calculation of the total shunt (Fig. 8) is somewhat more complicated because of the form of the total shunt equation (equation 1). Three separate steps are needed to arrive at the final answer. First the product of $k$ and the difference $C_{au} - C_{al}$ ($d$) is computed on the left or circular portion of the nomogram by finding the value for the difference, $d$, on the left portion of the circle and the value for $k$ on the right portion of the circle and then reading off the value of the product on the left hand member of the two vertical scales, scale A. One of the diagonal lines is followed to the right hand scale, scale B, and the ruler moved to that point. The ruler is now rotated to cross the extreme right hand scale, the $C_{al}$ scale, at the value for $C_{al}$. The total shunt is read off as a percentage on the scale in middle. In the example, $d = 2.5 \text{ vol} \%$.

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FIG. 8 Nomogram for calculating total right to left shunt — see text.
and $k=0.5$ and $CaL=17 \text{ vol}\%$. A dotted line drawn from $d=2.5$ to $k=0.5$ crosses scale A at the point indicated. Then a diagonal is followed down to the corresponding point on scale B and a line is drawn connecting that point on scale B with 17 on the $CaL$ scale. The value for the total shunt (52%) is then read off the $Q_{sl}/Q_T$ scale.

Alternatively, one can compute the product of $k$ and $d$ find that value on the B scale. Then connecting the value on the B scale with the appropriate value on the $CaL$ scale and noting where the line crosses the $Q_{sl}/Q_T$ scale gives the total shunt. Thus, in the example $d \times k = 2.5 \times 0.5 = 1.25$, 1.25 is located on the B scale and connected with 17 on the $CaL$ scale. The line crosses the $Q_{sl}/Q_T$ scale at 52%.

Unlike the ductal equation, the equation for total shunt is not independent of the oxygen content of end pulmonary capillary blood. The nomogram was constructed assuming $C_{e}=22 \text{ vol}\%$. $C_e$ is in fact unmeasurable and must be calculated. Haemoglobin oxygen carrying capacity is calculated as $1.34 \times \text{haemoglobin concentration in g./100 ml. (g. %)}$ and to this is added the oxygen dissolved in plasma ($0.003 \times PaO_2$). The $PaO_2$ of the end pulmonary capillary blood can be calculated from the alveolar air equation assuming no alveolar-arterial gradient for oxygen. For example, the figure of 22 vol% for $C_e$ is derived as follows:

\[
1.34 \times \text{Hb} + 0.003 \times PaO_2 = 1.34 \times 15 + 0.003 \times 670 = 22 \text{ vol}\% \quad (\text{the } PaO_2 \text{ of } 670 \text{ mm Hg was calculated previously, using the alveolar air equation). The value calculated for the subject under consideration may be different from 22 vol% because of changes in haemoglobin or because } F_{ao2} \text{ is not 1. The value calculated for the patient must be subtracted from 22 and added to the observed } CaL, \text{ (observing sign!). This adjusted } CaL \text{ is then used in the nomogram for total shunt. Thus if } F_{ao2} \text{ were 1 and haemoglobin } 18 \text{ g } \%\text{ then the calculated } C_e \text{ would be 26 vol}.\%
\]

This adjusted value is used in the nomogram for $CaL$ to find the total shunt. 52\%.

**Discussion**

Right to left shunts in babies with RDS have been assessed by several methods. Cardiac catheterization studies by Rudolph, Drorbaugh, Auld, Rudolph, Nadas, Smith, and Hubbell (1961) and Moss, Emmanouilides, Rettori, Higashino, and Adams (1963) indicate that small right to left shunts occasionally occur at the ductal level in severe RDS. On the other hand, Stahlman et al. (1966), utilizing indicator dilution methods, found large right to left shunts at the foramen ovale and/or ductal level in severely ill babies, although her investigations did not delineate which site was more important. All of the more recent studies have utilized the oxygen method (Nelson, Prod'hom, Cherry, Lipsitz, and Smith, 1963; Chu et al., 1967; Murdock and Swyer, 1968; Sinclair, Engel, and Silverman, 1968; Adamson, Hawker, Reynolds, and Shaw, 1969). In two of these studies (Murdock and Swyer, 1968; Roberton and Dahlenburg, 1969) it was concluded that the ductus arteriosus is not an important site of right to left shunting; but, as has been demonstrated in this paper, the usual shunt equation has been misapplied when calculating ductal right to left shunting. We have shown that findings suggesting a very small ductal right to left shunt cannot be accepted in those patients in whom oxygen contents in the ascending and descending aorta are significantly different.

Murdock and Swyer (1968) determined simultaneously the radial and descending aortic arterial blood oxygen content in babies with RDS. Table 1 compares the magnitude of the shunts calculated by the new equations with the magnitude of the shunts obtained by the usual application of the shunt equation for oxygen data in three of their cases. Since the distribution of blood flow to the upper and lower body ($k$) is not known, ranges of shunt flows calculated by the new equations are shown. The mean values represent the magnitude of shunting when 40% of the total cardiac output supplies the upper body ($k=0.4$).

In example A, a massive (78–80%) total right to left shunt is present. Ductal shunt is grossly underestimated via the old method (6 vs. 35–52%). Ductal shunt accounts for 45% to 65% of the total shunt rather than the 8% initially calculated. However, the total shunt calculated by the old method is close to accurate, as is always true with large right to left shunts.

In example B, when the disease results in
somewhat less total right to left shunting (63–66%) the ductal right to left flow underestimation is less striking, but still considerable (8% compared with 14–25%). In example C, when total shunt is under 50%, ductal right to left shunt is estimated nearly correctly but now the total shunt is substantially overestimated by the old method.

Using the standard shunt equation, Murdock and Swyer (1968) stated that the ductal shunt was less than 10% of the cardiac output in 30 of 33 patients; and in only one patient was the ductal shunt as high as 21%. Detailed information was given on 17 of the patients studied. Reanalysis of the data utilizing the new equations (assuming a minimum k of 0.2 and, as did the authors, an arteriovenous O₂ content difference of 3 vol%) indicates that at least 11 of the 17 had ductal

<table>
<thead>
<tr>
<th>Case</th>
<th>Oxygen saturation (%a)</th>
<th>Method of calculation</th>
<th>Q₁/Qₜ (%)</th>
<th>Q₀₄/Qₜ (%)</th>
<th>Q₀₄/Qₑ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radial a</td>
<td>Umbilical a</td>
<td>Standard equation:</td>
<td>New equation:</td>
<td>Range (k=0.2-0.6)</td>
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<tr>
<td>A</td>
<td>54</td>
<td>32</td>
<td>Standard equation:</td>
<td>New equation:</td>
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<tr>
<td>C</td>
<td>100</td>
<td>94.8</td>
<td>Standard equation:</td>
<td>New equation:</td>
<td>42</td>
</tr>
</tbody>
</table>

TABLE 2

Possible right to left total arteriovenous shunts calculable from a single umbilical arterial sample depending upon site of shunt and cerebral blood flow

<table>
<thead>
<tr>
<th>PO₂ (mm Hg)</th>
<th>O₂ content*</th>
<th>Q₁/Qₜ (%)</th>
<th>Q₀₄/Qₜ (%)</th>
<th>Site of shunt†</th>
<th>Cerebral blood flow</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(Standard equation)</td>
<td>(New equation)</td>
<td>Low</td>
<td>Mod.</td>
</tr>
<tr>
<td>55</td>
<td>19 vol%o</td>
<td>50</td>
<td>50</td>
<td>DA</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>½ DA + ½ lung and/or FO</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lung and/or FO</td>
<td>50</td>
</tr>
<tr>
<td>100</td>
<td>20 vol%o</td>
<td>40</td>
<td>40</td>
<td>DA</td>
<td>35</td>
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<td>½ DA + ½ lung and/or FO</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Lung and/or FO</td>
<td>40</td>
</tr>
</tbody>
</table>

* Based upon a total oxygen capacity of 22 vol% with infant breathing 100% oxygen.
† DA = ductus arteriosus.
FO = foramen ovale.
shunts greater than 10%; and in five, the minimum ductal right to left shunt was greater than 20%. The greatest ductal shunt calculated at \( k = 0.2 \) was 35% of the cardiac output (case A, Table 1). If \( k \) is higher than 0.2, as is likely, then ductal right to left shunting is larger (see Table 1).

Murdock and Swyer (1968) reported 50 paired measurements of pre- and postductal oxygen content in their patients. In seven pairs the postductal oxygen saturation was less than 82%; and in six of the seven, substantial (> 10%) ductal shunts are calculated using the new equation. In the remaining 43 paired samples, the postductal oxygen saturation was higher than 82%, and in only nine instances was the ductal shunt calculated by the new equation greater than 10%.

These data suggest that the ductus may be an important shunting channel in the babies with the most severe oxygenation defects. Animal and human studies showing both pulmonary hypertension and dilatation of the ductus in the presence of severe hypoxia in the neonatal period tend to support this thesis (Moss, Emanouilides, and Duffie, 1963; Rudolph and Yuan, 1966).

**Interpretation of umbilical artery \( \text{PO}_2 \) in presence of right to left ductal shunt**

\( \text{PO}_2 \) of postductal aortic blood reflects the oxygen content of blood flowing to the lower, but not necessarily the upper, portion of the body. Thus, when only postductal blood is sampled, the \( \text{PO}_2 \) of blood flowing to the brain and to the retina will be underestimated if a right to left shunt through the ductus arteriosus is present. It is generally recognized that exclusive reliance on this sample may lead to misrepresentation of both the status of cerebral oxygenation, and the risk of retinal oxygen toxicity.

A change in postductal aortic \( \text{PO}_2 \) is likewise subject to possible misinterpretation. For example, a rise in postductal aortic \( \text{PO}_2 \) after therapeutic intervention in babies with RDS breathing high oxygen concentrations is usually interpreted as evidence of a reduction in overall right to left shunting. However, Table 2 shows that a rise in \( \text{PO}_2 \) – for example, from 55 to 100 mm Hg – is subject to several interpretations. One interpretation would be that the overall right to left shunt has fallen from 50% to 40% of the cardiac output. A second possible interpretation is that the overall right to left shunt has stayed the same, or has even risen somewhat, but there has been a change in the site of right to left shunting. For example, a postductal \( \text{PO}_2 \) of 55 mm Hg in a baby shunting from right to left exclusively through the ductus arteriosus would indicate a right to left shunt of 33% of the cardiac output (at moderate cerebral blood flow). As shown in Table 2, a change in the site of shunting to include shunting through the ductus and the lung, or through the lung alone, with the overall right to left shunt remaining unchanged or in the latter case even rising, would be sufficient to account for the observed rise in postductal \( \text{PO}_2 \). Finally, the observed rise in postductal \( \text{PO}_2 \) could be due to a redistribution of cardiac output, the site of shunt remaining unchanged, and the overall right to left shunt staying the same or even rising. For example, in a baby shunting exclusively through the ductus, and whose cerebral blood flow was high, a postductal \( \text{PO}_2 \) of 55 mm Hg would indicate a 23% right to left shunt. With cerebral vasoconstriction, but no change in the site of shunt, a rise in postductal aortic \( \text{Po}_2 \) to 100 mm Hg would now indicate an increase in overall right to left shunt to 35% of the cardiac output. This rise in postductal aortic \( \text{Po}_2 \) results because relatively well-oxygenated blood, formerly perfusing the brain, is now diverted to the descending aorta. Thus, in the presence of a ductal right to left shunt, a rise in postductal aortic \( \text{PO}_2 \) may mean reduction in overall right to left shunt, change in site of shunt, or reduction in cerebral blood flow.

Cerebral blood flow is thought to depend on arterial blood pressure and on neurogenic and humoral factors which exert a certain degree of intrinsic control over the cerebral circulation. Among the intrinsic mechanisms, oxygen and especially carbon dioxide tensions appear to be predominant. In normal adults, inhalation of 5-7% \( \text{CO}_2 \) produces an increase in cerebral blood flow averaging 75% (Kety and Schmidt, 1948); although an increase in arterial \( \text{PCO}_2 \) of up to 4-5 mm Hg is without measurable effect on the cerebral vessels, further elevations in arterial \( \text{PCO}_2 \) produce substantial increases in cerebral blood flow. For example, an increase of 3 mm Hg above the threshold value for \( \text{PCO}_2 \) is associated with a 50% rise in cerebral blood flow.
Patterson, Heyman, Battey, and Ferguson, 1955). These effects of oxygen and carbon dioxide are due to a change in the vascular resistance of the brain without changes in systemic blood pressure. Adrenaline on the other hand, produces an increase in mean arterial blood pressure and cerebral blood flow without a significant change in cerebrovascular resistance, whereas noradrenaline produces a marked increase in cerebrovascular resistance and a decrease in cerebral blood flow despite a substantial increase in mean arterial blood pressure (King, Sokoloff, and Wechsler, 1952).

Therapy of babies with RDS usually includes one or more of the following: oxygen administration, correction of acidosis with sodium bicarbonate or THAM, assisted ventilation, and vasoactive drugs. Each of these therapeutic manoeuvres has been observed frequently to be accompanied by a rise in postductal aortic PO2, a rise which could be caused by a decrease in pulmonary vascular resistance with a decrease in extrapulmonary (ductal and foramen ovale) shunting, and/or improvement in lung inflation with a reduction in intrapulmonary shunting. Alternatively, each of these treatments might cause cerebral vasoconstriction, and thereby lead to a rise in the PO2 of postductal aortic blood, without necessary change in site or magnitude of right to left shunting. It is not possible to distinguish between these several explanations for the response to therapy in RDS by measuring only postductal PO2.

The present analysis indicates that the inappropriate application of the oxygen method to the quantitation of right to left shunting in the presence of any degree of right to left ductal shunting has resulted in underestimation of the magnitude of the ductal shunt in some cases. Indeed, it appears probable that, in some babies with RDS, or at some stages of the illness, right to left ductal or foramen ovale shunting may comprise the dominant sites of venous admixture, and that, on other occasions, an intrapulmonary shunt may predominate. Classification may be improved, interindividual variation lessened, risk categories better defined, and response to therapy more correctly evaluated in the future if the specific shunt sites and their relative importance are more accurately assessed.

Although this paper has stressed the application of the new equations to the study of right to left shunting in RDS, the equations are, of course, equally applicable to studies of other situations in which right to left ductal shunting occurs – for example, severe pulmonary vascular obstructive disease, preductal coarctation of the aorta, etc.

**Summary**

The magnitude of right to left shunts, regardless of site, is usually assessed by using the standard shunt equation \( Q_{S}/Q_T = (C_c - C_a)/(C_c - C_v) \), where \( Q_{S}/Q_T \) is the proportion of the cardiac output which is shunted, \( C_c \) the oxygen content of end pulmonary capillary blood, \( C_a \) the oxygen content of arterial blood, and \( C_v \) the oxygen content of mixed venous blood. When the oxygen content of postductal blood is used for \( C_c \), then \( Q_{S}/Q_T \) has been taken to mean total right to left shunt, and when the oxygen content of preductal blood is used, then \( Q_{S}/Q_T \) has been taken to mean intrapulmonary and intracardiac right to left shunts. However, the standard shunt equation is valid only if \( C_a \) represents the oxygen content of the entire arterial tree. With right to left shunting of blood through the ductus, pre ductal blood will have a higher oxygen content than postductal blood, and hence there is no single value for \( C_a \). These considerations have led to the derivation of two new equations:

\[
Q_{DA}/Q_T = (C_c - kC_{au} - (1 - k)C_{au})/(C_c - C_v)
\]

for total shunt and

\[
Q_{DA}/Q_T = (1 - k)(C_{au} - C_{au})/(C_{au} - C_v)
\]

for ductal shunt. \( C_{au} \) is the oxygen content of postductal blood, \( C_{au} \), the oxygen content of preductal blood and \( k \) represents the proportion of the cardiac output which exits through preductal arteries. The equations were programmed on the computer and the results obtained utilizing the new equations were compared with those using the standard equation. Use of the standard equation results in an overestimate of total shunt, while \( Q_{DA}/Q_T \) is either overestimated, underestimated, or correctly estimated depending upon \( k \) and upon the difference in oxygen content between pre- and postductal blood. Nomograms are presented which allow graphic solutions of the new equations.

Figures 1–5 were drawn by the Stromberg-Carlson 6040 using programmes written by Miss Lee Nussdorf. We also wish to express our thanks to Mrs. Clare Phillips for assistance in preparation of the manuscript.
References


Appendix

Recognizing that:

\[ O_2 = \dot{Q}C_{ao2} \]

where

\[ O_2 = \text{amount of oxygen in blood in mL/min} \]
\[ \dot{Q} = \text{blood flow in 100 mL blood/min} \]
\[ C_{ao2} = \text{concentration of oxygen in mL/100 mL blood} \]

allows calculation of the amount of \( O_2 \) in arterial blood (Fig. 9) as follows:

\[ \dot{Q}T_Ca = \dot{Q}pC_a + \dot{Q}bC_b \]

(4)

where \( C_a, C_c, \) and \( C_v \) are the \( O_2 \) content of arterial, end pulmonary capillary and mixed venous blood respectively and \( \dot{Q}_T, \dot{Q}_P, \) and \( \dot{Q}_A \) are total, effective pulmonary, and shunt blood flows.

Since:

\[ \dot{Q}_T = \dot{Q}_P + \dot{Q}_A \]

then

\[ \frac{\dot{Q}_B}{\dot{Q}_T} = \frac{C_c - Ca}{Ce - C_v} \]

(5)

Equation (5) is the usual shunt equation (equation 1 in text) and is usually evaluated by having the patient breathe 100% \( O_2 \) for 30 min to eliminate ventilation/perfusion inequalities and to overcome diffusion defects and by calculating \( C_c \) from the alveolar air equation (Rahn and Fenn, 1955) and \( C_v \) as \( C_a - 3 \) (Murdoch and Swyer 1969).
New equation for right to left shunt

In the presence of a right to left ductal shunt, $C_a$, representing $O_2$ content of arterial blood cannot be obtained directly, since $O_2$ content of pre- and postductal blood is not the same. Instead, analogous to the derivation of equation (1) (Fig. 10) a new equation is derived:

$$Q_L C_{al} = Q_{DA} C_C + Q_{LH} C_{au} - Q_U C_{au} \tag{6}$$

where

- $Q_L$ = blood flow through the lower portion of the body
- $Q_U$ = blood flow through the upper portion of the body
- $Q_{DA}$ = blood flow (right to left) through the ductus arteriosus
- $Q_{LH}$ = blood flow through the left heart
- $C_{al}$ = oxygen content of blood going to lower portion of the body
- $C_{au}$ = oxygen content of blood going to upper portion of the body

In the presence of right to left pulmonary and foramen ovale shunting, the amount of oxygen exiting from the left heart is given by (Fig. 10):

$$Q_{LH} C_{au} = Q_L C_C + (Q_{SP} + Q_{SFO}) C_C$$

where $Q_{SP}$ is the right to left pulmonary shunt and $Q_{SFO}$ is the right to left foramen ovale shunt.

Now letting $Q_s = Q_{DA} + Q_{SP} + Q_{SFO}$ and substituting into equation (6) yields:

$$Q_L C_{al} + Q_U C_{au} = Q_s C_C + Q_s C_C \tag{7}$$

From Fig. 10,

$$Q_T = Q_L + Q_U$$

and defining k as

$$k = Q_U / Q_T$$

then

$$Q_U = k Q_T$$

and

$$Q_L = (1 - k) Q_T$$

Also from Fig. 10,

$$Q_s = Q_T - Q_{SFO} - Q_{DA} - Q_{SP} = Q_T - Q_s$$
Substituting into equation (7) these expressions for \( Q_U, Q_L, \) and \( Q_T \) yields:

\[
\frac{Q_D}{Q_T} = \frac{C_o - kC_{au} - (1-k)C_{al}}{C_v - C_T}
\] (8)

If the systemic arteriovenous oxygen difference \( (av) \) is to be assumed rather than measured then \( C_T \) may be calculated from:

\[
Q_T C_T = kQ_T(C_{au} - av) + (1-k)Q_T(C_{al} - av)
\]

or

\[
C_T = kC_{au} + (1-k)C_{al} - av
\]

Substituting this expression for \( C_T \) into equation (8) yields:

\[
\frac{Q_D}{Q_T} = \frac{C_o - kC_{au} - (1-k)C_{al}}{C_T - kC_{au} - (1-k)C_{al} + av}
\] (9)

The ductal shunt equation can be derived from equation (6) as follows:

\[
Q_T = Q_{TH} + Q_{DA}
\]

Solving this expression for \( Q_{TH} \) and substituting into equation (6) the expression for \( Q_U \) and \( Q_L \) as above yields:

\[
\frac{Q_{DA}}{Q_T} = \frac{(1-k)(C_{au} - C_{al})}{C_{au} - C_T}
\] (10)

and if \( C_T \) is not measured but a value for \( av \) is assumed then:

\[
\frac{Q_{DA}}{Q_T} = \frac{(1-k)(C_{au} - C_{al})}{(1-k)(C_{au} - C_{al}) - av}
\] (11)