CIRCULATION-TIME MODELS OF THE UPTAKE OF INHALED ANAESTHETICS AND DATA FOR QUANTIFYING THEM

W. W. MAPLESON

SUMMARY

Conventional compartmental models of the uptake and distribution of inhaled anaesthetics assume that blood moves from lungs to tissues and from tissues back to lungs in zero time. Three new models which incorporate alternative representations of the finite time actually taken have been constructed in terms of Algol programs for a digital computer. It is shown that the conventional approach causes systematic errors in the computed uptake of low-solubility agents, in the arterial tension of high-solubility agents, and in the tissue tensions of all agents. The errors are important in the first minute or two of administration or recovery. The conventional distribution of blood volume between compartments is shown to be in error and to cause even greater systematic errors in computed results. Three different published distributions of tissue volume and cardiac output give different computed results and a “preferred” distribution is suggested.

In anaesthetics of very short duration, or in obstetric analgesia where inhalation of the agent is intermittent, the time taken for the blood to circulate round the body is not much shorter than the period for which the inspired gas contains an anaesthetic agent. Therefore, inaccurate representation of the circulation may cause appreciable errors in theoretical computations of the uptake and distribution of the agent. Several models of the uptake and distribution of inhaled agents have been described. In almost all of them, with the notable exception of those with which Perl was involved (Perl, 1963; Perl et al., 1965; Rackow et al., 1965), the body tissues are grouped into independent compartments on the basis of perfusion and tissue/blood partition coefficient, and the following assumptions are made (though often not explicitly). (1) Arterial blood leaving the lungs, alveolar gas, and lung tissue are all in equilibrium. (2) All tissues in a compartment are at the same tension and in equilibrium with the venous blood leaving the compartment.

In most of the models the circulation time from lungs to tissues and back is assumed to be zero. Then, by invoking the law of conservation of matter, the system is defined for any given set of volumes, flows, partition coefficients and inspired concentration.

Eger's (1963a) digital model includes a finite circulation time but this appears to be designed for economy of computation rather than verisimilitude. Mapleson (1963a) described how a passive-analogue model might be elaborated to incorporate circulation time realistically and discussed the likely effects of so doing. Waud and Waud (1970) used an active-analogue model in which the total circulation time was zero; then they delayed the computed brain tension by 7 sec.

The need for a more accurate representation of the circulation was appreciated, but not satisfied, in a theoretical study of obstetric analgesia (Mapleson, 1969) and the problem was finally studied in some detail for the purpose of matching experimental data on short-term nitrous-oxide uptake and elimination (Mapleson and Smith, 1972).

This paper compares four models, constructed in terms of Algol programs for a digital computer (ICL System 4). One is equivalent to most previous models in that it contains no direct representation of circulation time; the other three contain different direct representations.

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*Passive analogues are usually electric and comprise a network of components which obeys the same mathematical equations as those assumed to be obeyed by the real system to which it is analogous. The only power source is that corresponding to the input to the real system (inspired concentration of anaesthetic in the present case). An active analogue incorporates “active” components, such as electronic amplifiers, which require an additional power source.
The construction of these models drew attention to the importance of the disposition of the blood volume within any model. Yet some authors omit part of the blood volume altogether. Sluijter (1970) mentions only 1.4 l, Eger and Severinghaus (1964) only 1 l, and Waud and Waud (1970) less than 0.3 l. In all three cases the blood is put in the lung compartment. Eger's (1963a) circulation appears to contain only 3 l, or sometimes only 1.5 l, of blood which is alternately in the venous and arterial positions. These arrangements would clearly underestimate the total uptake of the body at equilibrium. Other authors (Mapleson, 1963a; Severinghaus, 1963; Munson and Bowers, 1967; Whelpton, 1969; Ashman, Blesser and Epstein, 1970; Cowles, Borgstedt and Gillies, 1971, 1972) include the whole blood volume, with the arterial blood in a pool in the lungs and the venous blood in pools in the tissue compartments; but they all share the total volume of venous blood between compartments in the same proportion as they share the cardiac output.

This distribution of blood between the compartments was found to lead to absurd conclusions so an attempt has been made (Appendix I) to assess the actual distribution of blood and to examine the effect of this on computed results.

The opportunity has been taken to compare the three main published distributions of tissue volume and cardiac output and to propose a preferred distribution (Appendix II).

Figure 1 shows a possible basic model of the ventilation and circulation of a "compartmentalized" man, together with the four actual models, O, F, M, and P, used in this study. These actual models are best described in terms of modifications of the basic model.

The basic model.

In the basic model each tissue compartment has its own "artery" and its own "vein". Three of each are shown but there can be any number. Each artery and vein is divided into segments, all of such a length as to contain the volume of blood which flows through the artery or vein in one heartbeat. Therefore, at a heart rate of 60 beats/min the number of segments in an artery (or vein) is equal to the transit time in seconds from lungs to tissues (or tissues to lungs)—although the number shown in figure 1 was chosen for clarity, not accuracy.

At each heartbeat a stroke volume of blood leaves the lungs and is divided into fractions in proportion to the blood flow to each compartment. These fractions enter the corresponding arteries as plugs or boluses and displace all the existing fractions by one segment without any longitudinal mixing. Therefore a fraction is ejected from the end of each artery and these fractions flow through their corresponding compartments, enter the corresponding veins, and displace all the fractions in the veins by one segment.

![Fig. 1. The basic model and four derived models of the uptake and distribution of an inhaled agent. The four derived models, of which only the arterial halves are shown, were constructed in terms of digital-computer programs and compared (figs. 2-4). SV=stroke volume, VI=inspired tidal volume, VE=expired tidal volume.](image-url)
The fractions ejected from the ends of the veins are combined to form a complete stroke volume which enters the lungs.

Thus, allowing for the simplification of grouping the body into a small number of compartments, this model of the circulation is thorough to the extent that it allows different circulation times for each compartment; it is less thorough to the extent that there is no longitudinal mixing in the arteries or veins.

If the uptake of an anaesthetic were to be calculated according to this model there would be one complete cycle of calculation for each heartbeat. The cycle would begin by taking from each vein the fraction of a stroke volume nearest the lungs, mixing these fractions to form a stroke volume at mixed-venous tension, and putting this into the lungs. If, during the particular heartbeat represented, there happened to be an inspiration, then the appropriate tidal volume (less deadspace) of inspired mixture would also be put into the lungs. Then the incoming gas and blood would be equilibrated with the gas and tissue already in the lungs. Then a stroke volume of blood at this (arterial) tension would be ejected into the arteries and, if there happened to be an expiration during the particular heartbeat, the appropriate volume of gas at the same tension would also be ejected. At each tissue compartment the appropriate fraction of a stroke volume of blood from the corresponding artery would be equilibrated with the tissue and ejected into the corresponding vein.

Model O—zero circulation time.
The first actual model, model O, has no direct representation of circulation time and is as nearly as possible an exact replica in digital terms of the Mapleson (1963a) analogue. Its derivation from the basic model is as follows. All the arterial blood is put in the lung compartment and the blood from each vein is put in the corresponding tissue compartment. Thus the stroke volumes of blood go directly from lungs to tissues or tissues to lungs, without delay; but this is compensated to some extent by the fact that, on arrival, the stroke volume has to equilibrate with the blood in the compartment as well as with the tissue, instead of with just the tissue.

Model F—finite circulation time.
Model F is intended to be as close to the basic model as possible without making excessive demands on computer storage. It is derived from the basic model by removing from each of the longer arteries and veins sufficient segments to leave only as many as are in the artery and vein of the shortest circulation. The blood so obtained is put into the corresponding tissue compartments. The three arteries are then fused into one, and the three veins into one, so that there is just a single circulation.

Thus, whereas in model O the circulation times of all compartments were reduced to zero and the blood volume was redistributed to compensate, in model F only the slower compartments (which receive together only a minor fraction of the cardiac output—table I) are modified, and in them the circulation times are reduced merely to that of the fastest compartment, again with compensating redistributions of the associated blood volumes. Thus, the changes made in the basic model to reach

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Volume of tissue (l.)</th>
<th>Per cent of cardiac output</th>
<th>Per cent of blood volume associated with compartment</th>
<th>Partition coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Traditional</td>
<td>New</td>
</tr>
<tr>
<td>Lung tissue</td>
<td>0.6</td>
<td>—</td>
<td>63.0</td>
<td>39.9</td>
</tr>
<tr>
<td>Viscera</td>
<td>6.2</td>
<td>63.0</td>
<td>13.1</td>
<td>36.4</td>
</tr>
<tr>
<td>Lean</td>
<td>39.2</td>
<td>13.1</td>
<td>4.0</td>
<td>11.1</td>
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<tr>
<td>Fat</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>0.0</td>
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<tr>
<td>Bone cortex</td>
<td>6.4</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Peripheral shunt</td>
<td>0.0</td>
<td>19.9</td>
<td>19.9</td>
<td>12.6</td>
</tr>
<tr>
<td>“Sample” tissue</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>White matter</td>
<td>0.0007</td>
<td>0.0022</td>
<td>0.0022</td>
<td>0.0014</td>
</tr>
<tr>
<td>Grey matter</td>
<td>0.0007</td>
<td>0.0086</td>
<td>0.0086</td>
<td>0.0055</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.0007</td>
<td>0.0432</td>
<td>0.0432</td>
<td>0.0274</td>
</tr>
<tr>
<td>Blood volume</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial</td>
<td>1.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous</td>
<td>4.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>70.00</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FRC = 2.5 l.; alveolar ventilation = 4 l./min BTPS; cardiac output = 6.48 l./min.
model F are the same in kind as those to reach model O, but much less in degree. Therefore if, as will be shown, the difference between the results for model O and model F is not great, the difference between those for model F and the basic model must be small.

**Model M—finite circulation time with longitudinal mixing.**

Model M is similar to model F, with a single circulation, but with longitudinal mixing of blood therein instead of plug flow. The blood volume is shared between the artery, the vein, and the slow tissue compartments exactly as in model F. The artery and the vein are assumed to be uniform cylindrical pipes through which blood flows with a perfect parabolic velocity profile with no slip at the wall. Thus, when a stroke volume of blood enters the artery it occupies the volume enclosed by the uppermost parabola drawn in the artery in figure 1. The previous stroke volume is driven forward into the volume between that parabola and the next, and so on. The stroke volume driven out of the end of the artery contains blood from all previous stroke volumes. These are mixed before being shared between the tissue compartments. A similar sequence of events occurs in the vein.

For both the artery and the vein, the assumption of a parabolic velocity profile causes the minimum transit time (at the centre of the pipe) to be half the mean transit time; the maximum transit time (at the wall of the pipe) is infinity. The true distribution of transit times in a real man will be different from this because, on the one hand, the velocity profile in the major arteries (Schultz et al., 1969; Reuben, Swadling and Lee, 1970) is more nearly flat than parabolic while, on the other hand, there are wide ranges of transit times through some tissues (Wheeler et al., 1955). However, in model F all transit times (across the diameter of the artery or vein) are the same, and therefore equal to the mean; consequently the magnitude of the difference between the results from model M and model F will show whether the nature of the distribution of transit times is important.

**Model P—separate pools for arterial and venous blood.**

Model P is a simplification of model F: the artery, instead of being a queue of non-communicating stroke volumes, is a well-mixed pool of blood; the same is true of the vein. The blood volume is shared between the artery, the vein, and the slow tissue compartments in exactly the same way as in model F. In each cycle of calculation a stroke volume is drawn from the venous pool, equilibrated with the lung compartment, and then handed on to the arterial pool where it is equilibrated with all the blood already there. Concurrently a stroke volume is similarly transferred from the arterial pool, through the tissue compartments, to the venous pool. The model requires less computer storage than model F and is much more easily adapted to the artificially slow heart rates necessary to compute results for long periods of real time within a small amount of computer time. The model is also suitable for active-analogue simulations.

All four models allowed for the "concentration effect" (Eger, 1963b). The particular case adopted (Mapleson, 1964) was that in which the FRC and the expired ventilation remain constant and the gas volume lost from the lungs by solution of the agent in the tissue and blood in the lungs is replaced by an increase in the inspired ventilation. The equations solved by the computer program are given in Appendix III.

**DATA FOR QUANTIFYING THE MODELS**

For most of the calculations reported in this paper, with all four models, a heart rate of 60 beats/min and a respiratory rate of 15 b.p.m. were assumed. It was also assumed that inspiration occurred entirely within the first of the 4 seconds or heartbeats in each respiratory cycle and that expiration occurred entirely within the third.

The numerical values used in most of the calculations are given in table I. The tissue volumes and blood flows, and the grouping of these into compartments, are those of Mapleson's (1963a) "standard" man. However, since Mapleson (1963a) showed that, to compute accurately the tension in a particular tissue it is necessary to give that tissue a separate compartment, three small "sample" tissue compartments have been included. Each is of negligible volume (0.7 ml) and the perfusions are 10, 80 and 400 ml/min per 100 ml of tissue, corresponding to white matter, to grey matter or heart, and to kidneys. The partition coefficients are approximate values, adequate for comparative purposes.

Traditionally (Mapleson, 1963a; Severinghaus, 1963; Munson and Bowers, 1967; Whelpton, 1969; Ashman, Blesser and Epstein, 1970; Cowles, Borgstedt and Gillies, 1971, 1972) the total blood volume
has been shared between compartments in the same proportions as the cardiac output is shared. This leads to the same total circulation time for all compartments. In terms of mean transit time (see Appendix I) this is equal to the total blood volume divided by the cardiac output (50 sec in the standard man). A new and more likely distribution is derived in Appendix I and listed in table I. This leads to different circulation times for different compartments, the shortest being that for the visceral compartment (32 sec).

In models F, M and P it is the total blood volume which is shared between compartments according to these distributions (new or traditional); in model O only the venous blood (less the circulating stroke volume) is so shared, all the arterial blood being placed in the lung compartment.

In addition to Mapleson's (1963a) "standard" man in table I, two other distributions of tissue volume and cardiac output have appeared in the anaesthetic literature (Eger, 1963a; Cowles, Borgstedt and Gillies, 1971). The three distributions are compared in table II and a new "preferred" distribution is derived in Appendix II and listed in table III.

RESULTS AND DISCUSSION

Comparison of models.

Figure 2 shows the computed results according to three of the models (O, F and M) for the case of a standard man (table I) inhaling 75% nitrous oxide for 2 min followed by

![Figure 2. Comparison of models for the case of a 1963 standard man (table I) inhaling 75% nitrous oxide for 2 min and recovering on air for 4 min. New" distribution of blood volume. Computed values, obtained from an Algol program run on an ICL 4-70 computer, and plotted by a graph plotter controlled by a second Algol program. "Uptake" refers to uptake by solution in the alveoli—and to elimination by dissolution during recovery.]

TABLE II. Comparison of distributions of tissue volume and cardiac output.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tissue volume (l.)</td>
<td>Cardiac output (%)</td>
<td>Perfusion (ml/100ml per min)</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------</td>
<td>-----------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Lung tissue</td>
<td>0.6</td>
<td>63.0</td>
<td>66</td>
</tr>
<tr>
<td>Viscera/vessel rich</td>
<td>6.2</td>
<td>63.0</td>
<td>66</td>
</tr>
<tr>
<td>Lean/muscle group</td>
<td>39.2</td>
<td>13.1</td>
<td>2.2</td>
</tr>
<tr>
<td>Fat</td>
<td>12.2</td>
<td>4.0</td>
<td>2.1</td>
</tr>
<tr>
<td>Bone cortex/—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Peripheral shunt/—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Blood volume</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Arterial</td>
<td>1.4</td>
<td>1.4</td>
<td>—</td>
</tr>
<tr>
<td>Venous</td>
<td>4.0</td>
<td>4.0</td>
<td>5.0</td>
</tr>
</tbody>
</table>

FRC=2.5 litres; alveolar ventilation = 4 l./min BTPS; cardiac output = 6.48 l./min (used for all distributions).

*Eger (1963a) used 3 or 1.5 l. of blood volume, alternately arterial and then venous; the blood volume figures here are those of Seuringhaus (1963) which have been adopted by subsequent users of Eger's distribution (Ashman, Blesser and Epstein, 1970; and probably Munson and Bowers, 1967, and Munson, Eger and Bowers, 1968).

† Cowles, Borgstedt and Gillies (1971) gave weights and perfusions for about 20 groups of tissues. These have been allocated to compartments on the basis of their perfusion in the same way that Mapleson (1963a) did, and a density of 1 kg/l. has been assumed for all tissues.
the first 4 min of recovery on air. The “new” distribution of blood volume has been used.

The effect of taking account of the circulation time (model F or M) is to delay the uptake and the initial release of the nitrous oxide. This is because the uptake in model O is artificially high initially, owing to the whole of the arterial blood volume being in the lung compartment and hence available to absorb nitrous oxide from the beginning.

The delay amounts to about 150 ml in terms of volume or 1,0 sec in terms of time. Whether or not there is any longitudinal mixing (compare model M with model F) makes little difference. The volume discrepancy is about 8% of the accumulated uptake after 2 min, or 40% of that after only 30 sec. Supplementary computations showed it to remain at about 150 ml for at least 24 min of continuous inhalation although it is then a very small percentage error and must eventually become zero even in absolute terms. Reverting to air after 1 or 4 min made no great difference to the discrepancy between the models in recovery.

In terms of alveolar or arterial tension at the lungs the effect of introducing the circulation time is barely detectable (always less than 10 mm Hg or 5%). In terms of mixed-venous tension the effect is more striking and even the difference between the two circulation-time models (F and M) becomes appreciable. In terms of tissue tensions the effect of circulation time is very marked in the best perfused tissues.

Computations for a doubled alveolar ventilation gave a somewhat greater discrepancy between models.

Figure 3 shows similar computed results for a standard man inhaling 1% methoxyflurane. With this

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### Table III. Preferred tissue volumes, blood flows and blood volumes for a standard man.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Mass (kg)</th>
<th>Volume (l)</th>
<th>Perfusion (ml/min per 100 g)</th>
<th>Perfusion (ml/min)</th>
<th>( % of cardiac output)</th>
<th>Blood volume (% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung compartment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung parenchymal tissue</td>
<td>0.50</td>
<td>0.50</td>
<td>508</td>
<td>102</td>
<td>1.6</td>
<td>61.9</td>
</tr>
<tr>
<td>Visceral compartment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.02</td>
<td>0.02</td>
<td>500</td>
<td>100</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.02</td>
<td>0.02</td>
<td>396</td>
<td>1188</td>
<td>18.3</td>
<td></td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.30</td>
<td>0.28</td>
<td>81</td>
<td>243</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>0.30</td>
<td>0.28</td>
<td>53</td>
<td>795</td>
<td>12.3</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>1.50</td>
<td>1.43</td>
<td>49</td>
<td>10</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>0.02</td>
<td>0.02</td>
<td>39</td>
<td>1529</td>
<td>23.6</td>
<td></td>
</tr>
<tr>
<td>Splanchnic tissue</td>
<td>3.92</td>
<td>3.73</td>
<td>30</td>
<td>27</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Salivary glands, eyes, thymus</td>
<td>0.09</td>
<td>0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testes</td>
<td>0.04</td>
<td>0.04</td>
<td>23</td>
<td>9</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Spinal cord</td>
<td>0.03</td>
<td>0.03</td>
<td>16</td>
<td>5</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>6.24</td>
<td>5.94</td>
<td></td>
<td></td>
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<tr>
<td><strong>Lean compartment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red marrow</td>
<td>1.40</td>
<td>1.33</td>
<td>10</td>
<td>140</td>
<td>2.2</td>
<td></td>
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<tr>
<td>Skin and non-fat subcutaneous tissue</td>
<td>6.10</td>
<td>5.81</td>
<td>5</td>
<td>305</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>Lymphoid tissue, blood vessels, cartilage, nerves</td>
<td>1.09</td>
<td>1.04</td>
<td>5</td>
<td>55</td>
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<tr>
<td>Non-parenchymal lung tissue</td>
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<td>0.50</td>
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<td>25</td>
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<td>Muscle and bladder</td>
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<td>28.71</td>
<td>2</td>
<td>603</td>
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<tr>
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<td>37.39</td>
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<tr>
<td><strong>Fat compartment</strong></td>
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<tr>
<td>Fatty marrow</td>
<td>2.20</td>
<td>2.32</td>
<td>2.8</td>
<td>62</td>
<td>1.0</td>
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<td>Fat tissue</td>
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<td>10.52</td>
<td>2.4</td>
<td>240</td>
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<tr>
<td><strong>Total</strong></td>
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<td>12.84</td>
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<tr>
<td><strong>Bone cortex</strong></td>
<td>6.40</td>
<td>3.42</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td></td>
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<tr>
<td>Teeth</td>
<td>0.02</td>
<td>0.01</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td></td>
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<tr>
<td>Arterial blood</td>
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<td>1.03</td>
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<td>Venous blood</td>
<td>4.32</td>
<td>4.11</td>
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<tr>
<td>Peripheral shunt</td>
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</tr>
<tr>
<td><strong>Grand total</strong></td>
<td>70.00</td>
<td>65.24</td>
<td></td>
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</table>
CIRCULATION-TIME MODELS OF UPTAKE OF INHALED ANAESTHETICS

Fig. 3. Comparison of models for a standard man inhaling 1% methoxyflurane. Otherwise as for fig. 2. Note that the graph-plotting program interrupts the lines for models F and M at fixed intervals in the horizontal (time) direction, not at fixed distances along the length of the plotted line. The arterial tension curve for model M is omitted to reduce confusion. It is identical to that for model F except that the kink at about 30 sec is smoothed out—in the same way that the corresponding abrupt start to the mixed-venous tension curve in model F is smoothed out in model M.

high-solubility anaesthetic, with all models, elimination is very much slower than uptake because the alveolar tension driving out anaesthetic in recovery (<0.2 mm Hg in this example) is much less than the inspired-to-alveolar tension difference driving it in during administration (nearly 7 mm Hg in this example).

Differences in uptake between the models are barely detectable. This is because the uptake of a high-solubility anaesthetic is almost entirely determined by the ventilation and hence negligibly affected by the details of the circulation.

Conversely, differences in arterial or alveolar tension are much more marked than with nitrous oxide. The pronounced oscillation in the arterial tension of the blood leaving the lungs arises because, out of the 4 sec in the respiratory cycle, inspiration is assumed to be confined to the first sec; during the other 3 sec, therefore, there is no input of methoxyflurane to the lungs and the mixed-venous blood entering the lungs absorbs a substantial fraction of the methoxyflurane already there. The oscillation is less marked in model O because it is damped by the large pool of arterial blood contained in the lung compartment. This pool also accounts for the considerably slower initial rise in the mean arterial tension with model O (for a time it is 50% lower than with model F) and the slower initial fall in recovery (for a time the tension with model O is 50% higher). However, these mean differences have largely disappeared within 2 min of the start of inhalation or of recovery.

Differences between models in mixed-venous tension are less marked than with nitrous oxide but in the tissues the differences are very similar.

It seems clear that model O causes appreciable systematic errors. On the other hand, model M is not, in general, sufficiently different from model F to justify the greater computing time (30%) and computer storage capacity required. Only in the case of mixed-venous tension in the first minute of induction or recovery is the difference appreciable. For the accurate computation of mixed-venous tensions, therefore, it would probably be necessary to use a more elaborate model than either F or M. Such a model would have to reproduce the true distribution of transit times rather than that of the particular longitudinal mixing scheme used in model M.

The curves for model P are omitted from figures 2 and 3 to reduce confusion: they almost coincided with those for model M for both nitrous oxide and methoxyflurane. The only exception was that the mixed-venous tensions according to model P were a little in advance of those according to model M in the first minute of administration and of recovery.

Therefore, model P seems as good as models F and M; it also has the advantage of suitability for active-analogue simulations and of convenience in long-term digital simulation. (Model F is used in later computations in this paper merely because they had been executed before model P was developed.) With a purely passive analogue even model P cannot be built and model O must be resorted to; but it can be improved.

Improvement of model O.

The reason why the tissue tensions computed by model O rise too slowly in the best perfused tissues
(figs. 2 and 3) is that these compartments are "loaded" with a relatively large volume of venous blood. If all venous blood is omitted from the model the uptake is seriously underestimated. However, if the venous blood is omitted only from the sample-tissue compartments, computation shows that the volume of these is so small that the effect on whole-body uptake is negligible. But the effect on computed tissue tension is to give a much closer approximation to that computed by model F. Indeed, with the low-solubility anaesthetic nitrous oxide, since the arterial tension is almost the same with model O as with model F (fig. 2) the tissue tensions computed according to the improved model O are almost identical (fig. 4) to those according to model F, except for being about 6 sec too early. With the high-solubility anaesthetic methoxyflurane, the arterial tension curve is a different shape according to model O from that according to model F (fig. 3). Therefore the tissue-tension curve according to the improved model O is not only 6 sec early but also a different shape from that according to model F. In the circumstances of these trials, these two differences happen nearly to cancel so that there is a fortuitously close agreement between the improved model O and model F in terms of sample-tissue tension (fig. 4).

**Simplification of model O.**

In the present models the peripheral shunt (table I) is directly represented by a compartment which contains zero volume of tissue. However, in model O this compartment does contain the appropriate volume of venous blood which therefore gradually equilibrates with arterial tension. In their analogue computations Mapleson (1962, 1963a,b,c, 1964) and Whelpton (1969) did not represent the shunt directly; instead they omitted the shunt part of the cardiac output completely and put the appropriate volume of venous blood in the lung compartment so that it was always at arterial tension. When this economy measure was tried in the present model O it was found that the direct "loading" of the lung compartment with this venous blood, as well as with all the arterial blood, exaggerates the differences in both uptake and arterial tension between model O and model F by about 20% of the differences shown in figures 2 and 3. Therefore, in circumstances where model O is acceptable, the additional error of not representing the peripheral shunt directly is probably also acceptable.

**Distribution of blood volume.**

The results so far (figs. 2–4) have been based on the "new" distribution of blood volume listed in table I and derived in Appendix I. To indicate the likely effect of the uncertainty in the "new" distribution, the computations on model F were repeated using the "traditional" distribution—in which blood volume is shared between compartments in the same proportions as is the cardiac output. The results are compared with those for the "new" distribution in figures 5 and 6.

The important difference between the two distributions is that, in the traditional one, the visceral and peripheral-shunt compartments have a greater blood volume associated with them than in the new distribution. This increases the total circulation time of these compartments (the fastest with the new distribution) from 32 to 50 sec. As a result, with both nitrous oxide and methoxyflurane the initial rise in mixed-venous tension is nearly 20 sec later with the traditional distribution (figs. 5 and 6) and the initial rise in tissue tension about 4 sec later. In the case of nitrous oxide this leads to a greater uptake once the mixed-venous tension begins to rise; with methoxyflurane it leads, after a similar delay, to lower arterial tensions. The differences persist for at least 24 min. With model O they are similar in kind but less in degree, at least for nitrous oxide.
CIRCULATION-TIME MODELS OF UPTAKE OF INHALED ANAESTHETICS

The differences are sufficient to justify abandoning the traditional distribution. As better data on the actual distribution of blood volume become available, computed values will differ from those obtained with the present “new” distribution; but it seems likely that the differences will be fairly small compared to those between the present “new” and the “traditional” distributions.

Distribution of tissue volume and cardiac output.

Most models of anaesthetic uptake and distribution have shared the tissue volume and cardiac output between compartments in much the same way as either that described by Eger (1963a) or that by Mapleson (1963a). Recently, Cowles, Borgstedt and Gillies (1971) have proposed a third distribution. The three distributions are compared in table II. For computation the Eger distribution of tissue volume was scaled to 70 l. and, for simplicity, the “traditional” distribution of blood volume between compartments (in proportion to the blood flows) has been assumed in all three cases. The resulting computed curves according to model F are shown in figures 7 and 8. It is clear that the differences between the three sets of curves are appreciable and it is interesting to see how they arise.

The large lung tissue volume in the Cowles, Borgstedt and Gillies distribution “loads” the lung compartment and thereby reduces the amplitude of the oscillation in the arterial tension of methoxyflurane. This “loading” of the lung compartment also accounts, in the first minute of administration, for the slower rise in mean arterial tension of methoxyflurane and the greater uptake of nitrous oxide. The Eger arterial curve is omitted from figure 8 to reduce confusion but, because of the slightly smaller lung tissue volume compared to the Mapleson distribution, the oscillation is slightly wider and the rise in mean arterial tension is slightly more rapid.

The presence of a large peripheral shunt in the Mapleson distribution causes a rapid rise in mixed-venous tension of both agents once recirculation commences. This accounts for the decreased uptake of nitrous oxide after the first minute while, with methoxyflurane, it accounts for the more rapid rise in mean arterial tension, and hence in tissue tension, after the first minute.
The greater perfusion of the visceral compartment in the Eger distribution causes (in comparison with the Cowles, Borgstedt and Gillies curves) a slightly more rapid rise in mixed-venous tension of both agents, and hence a lesser uptake of nitrous oxide and a slightly more rapid rise in arterial tension of methoxyflurane.

Eger's smaller fraction of arterial blood (one-sixth of the total instead of one-quarter) accounts for the earlier changes of tissue tension in the Eger curves.

The differences in lean and fat perfusion and the effect of the "vessel poor group" in Eger's distribution would become apparent only after much longer administration. However, it can readily be deduced that at least the perfusion differences would lead to differences in nitrous oxide uptake and methoxyflurane tensions of a magnitude comparable to the differences shown in figures 7 and 8.

It is evident that the various differences between the three distributions cause appreciable differences in computed uptake and tension. Mapleson (1963a) and Cowles, Borgstedt and Gillies (1971) give detailed support for their data, yet the discrepancies between their distributions are only partly attributable to the greater volume of literature available to Cowles, Borgstedt and Gillies; some of the more important discrepancies arise from differences of interpretation, particularly where measurements are lacking. Therefore the acquisition of better data on the true distribution, either by direct observation or by careful matching of computed and observed uptake data, is greatly to be desired. In the meantime a "preferred" distribution for a standard man is derived in Appendix II.

CONCLUSIONS

Failure to represent circulation time leads to systematic errors in the computation of the uptake and distribution of inhaled anaesthetics. The errors are
of importance only in the first few minutes of administration or recovery, or after any other changes of inspired concentration.

Differences between the three circulation-time models, F, M and P, are mostly small, so the simplest and most convenient, model P, may as well be used. The only exception concerns the calculation of mixed-venous tension in the first minute after a change of inspired concentration. This requires a knowledge of the true distribution of transit times in the circulation and the construction of a model to incorporate this distribution.

Model P can be used in active-analogue simulations but with passive analogues recourse must be had to model O. It is then very important, in computing a tissue tension, to have a separate compartment representing a small volume of that tissue and containing no blood.

In any model, inaccurate distribution of blood volume between compartments causes systematic errors which persist for many minutes after a change of inspired concentration. The traditional distribution of blood volume, in the same proportion as cardiac output, is sufficiently inaccurate to cause appreciable errors. Inaccuracies in the new distribution, derived here, probably lead to only minor errors; but more reliable information on the true distribution is desirable.

Inaccurate distribution of tissue volume and cardiac output between compartments causes errors which must persist throughout any computation. Again, more information is needed.

The errors demonstrated in this paper are probably of little consequence in purely theoretical studies, comparing different circumstances in hypothetical patients—except, perhaps, in modelling the intermittent inhalation of obstetric analgesia. However, in matching experimental observations it is clearly of importance to eliminate any avoidable sources of systematic error.

**ADDENDUM**

Since completing this study a further distribution of blood and tissue volumes and cardiac output has been published (Zwart, Smith and Beneken, 1972; Smith, Zwart and Beneken, 1972). This uses nine tissue compartments but seems to follow Mapleson (1963a) fairly closely for individual tissue volumes and blood flows except for a reduced shunt and reduced cardiac output. A relatively small part of the blood volume is put into arterial and venous pools as in model P and the remainder is shared between tissues, mostly in proportion to their perfusions but with some deviations.

**APPENDIX I**

**ESTIMATION OF CIRCULATION TIMES AND DISTRIBUTION OF BLOOD VOLUME IN THE MAPLESON (1963a) STANDARD MAN**

For the present purposes it is essential to use the term distribution time in the sense of mean transit time (MTT) where the MTT between two points in the circulation is given by the volume of blood between those points divided by the flow, which is assumed to be equal at the two points. Some authors, including Blumgart and Rowlands (1971), use the terms in the sense of appearance time (AT), the time at which an indicator, introduced at the first point, just becomes detectable at the second point. The AT is always less and sometimes much less than the MTT.

**Pulmonary circulation time.**

The blood in the pulmonary circulation and heart chambers is taken as 15.3% (Green, 1950) of the total (5.4 l. in the standard man)=0.83 l. Therefore circulation time=0.83 sec. divided by the cardiac output (6.48 l./min in the standard man)=7.5 sec. This time is common to all circulations.

**Circulation time from local artery to local vein.**

- Kidney: 2.5 sec in dogs (Wolgast, 1968; Pinter, 1969).

In man with hypertension (Takeuchi et al., 1970) the renal blood volume is 45 ml. Therefore, at the standard-man flow of 1240 ml/min, circulation time would be 2.2 sec. Say 2.5 sec.

- Heart: 6.5 to 11 sec in normal or near-normal man (Gorlin and Storaasli, 1956). Say 9 sec.

Splanchnic blood volume is 20% of the total in supine man (Bradley, 1955) =1.08 l. Therefore, at the standard-man flow of 1580 ml/min, splanchnic circulation time=41 sec. This is consistent with the MTT of >30 sec that can be calculated from the data of Wheeler and associates (1955) for dogs.

Adrenals and thyroid: assume 2.5 sec because of their similar perfusion to the kidneys.

Other small glands and organs: assume 8.5 sec because of their similar perfusion to the brain.

**“Highway” circulation time (from left ventricle to local artery and from local vein to right atrium).**

This can be estimated in two ways. Firstly, common carotid artery cross-sectional area=0.81 cm² (Bunce, 1971), length=say 20 cm; therefore volume ~16 ml.

The volume of the systemic veins is about four times that of the systemic arteries (Green, 1950). Therefore the jugular vein volume ~64 ml and the total volume ~80 ml.

Flow ~760 ml/min, therefore circulation time ~6.3 sec.

Secondly, the time from antecubital vein to carotid artery in man=12 sec (Oldendorf, 1962), less 7.5 sec for pulmonary circulation and heart chambers, leaves 4.5 sec.

Say 5.5 sec highway time (but zero for coronary circulation).

**Distribution of blood volume between compartments.**

**Viscera.** For each tissue in the compartment the associated blood volume was calculated from blood flow × total circulation time (pulmonary+local+highway). Mean total vascular circulation time came from total associated blood volume (2156 ml) divided by total flow (4080 ml/min)=31.7 sec.

**Peripheral shunt.** Assumed to have the same total circulation time as the visceral compartment: a shorter local time will tend to compensate for a longer highway time.
Lean and fat. The remaining blood volume was shared between the lean and fat compartments in proportion to their flows—as is argued in the text their exact circulation times are not critical.

Division of blood volume into arterial and venous fractions. For all the calculations in this paper, Mapleson (1963a) and Cowles, Borgstedt and Gillies (1971) have been followed in assuming, on the basis of Green’s (1950) data in dogs, that the volume of blood at arterial tension is one-quarter of the total. However, the more recent estimates of Iberall and associates (1971) suggest one-fifth.

APPENDIX II

Preferred distribution of tissue volume, cardiac output and blood volume in the 1973 standard man (Table III)

For tissue masses Cowles, Borgstedt and Gillies (1971) use the figures of the International Commission on Radiological Protection (ICRP) (1960) unamended. Here the documented modifications of Mapleson (1963a) are retained, but the parenchymal fraction of the lung tissue mass is reduced to 0.5 kg (Cander and Forster, 1959; Sackner, Feisal and Dubois, 1964; Puy et al., 1968), and the fraction of the total blood volume assumed to be at arterial tension is reduced from one-quarter (Green, 1950) to one-fifth (Iberall et al., 1971). The ICRP figures for total blood mass and fat-tissue mass are given in Table III although, for matching individuals, these are better estimated separately from height and weight (e.g. Brown, 1971; Allen et al., 1956).

The tissue masses must be converted to volumes because the solubilities of anaesthetics in tissues are related to volume. The assumption of Mapleson (1963a) and of Cowles (1970) of a density of 1 kg/l for all tissues is hardly adequate and the densities which Eger (1963a) apparently used are not documented. Data on tissue densities from Vierordt (1906), Nadeshin (1932), Documenta Geigy (1956, p.303), Allen, Krzywicki and Roberts (1959), Steward, Mapleson and Allott (1972), and P. N. T. Wells (1972, personal communication), suggest that, at least in man, a value of 1.05 kg/l would be near enough for all aqueous tissue, including blood, but excepting lung (1.00 kg/l; Evans, 1956). These figures are consistent with the widely accepted figure of about 1.10 kg/l of human body (Behnke, Feen and Welham, 1942; Keys and Brozek, 1955; Von Döbeln, 1956) for the mean density of all non-adipose tissue. The density of extracted human fat is clearly 0.90 kg/l at 37°C (Fidanza, Keys and Anderson, 1953; Yeh and Peterson, 1963; Hodgman, 1962) but, for fat tissue, there is less certainty. However, body density measurements during weight gain in ten subjects (Keys, Anderson and Brozek, 1955) indicate 0.95 kg/l, and this is quite well supported by similar measurements during weight loss in one subject (Behnke, Feen and Welham, 1942) and by an estimate (Von Döbeln, 1956) based on the chemical composition of human fat tissue and the densities of its components.

For blood flows the more recent perfusion estimates of Cowles, Borgstedt and Gillies (1971) are adopted except as follows. Small organs for which no measurements are available (salivary glands, eyes and thymus) are assumed to have the same perfusion as the mean of those for the prostate, testes and spinal cord. Because of the variation in the perfusion of skin and subcutaneous tissue (Whisham and Yalow, 1952; Seibert, 1966; Yipintsoi and Bassingthwaighte, 1971) and because of the extreme variability of muscle perfusion under anaesthesia (Slijjer and Sih, 1970) the estimates of Cowles, Borgstedt and Gillies (1971) are rounded to 5 and 2 ml/min per 100 g of tissue respectively.

For red marrow Mapleson (1963a) estimated a perfusion of 9 ml/min per 100 ml whereas Cowles, Borgstedt and Gillies (1971), mainly on the basis of rat and rabbit data, chose 40 ml/min per 100 g. However, table IV reveals a fairly clear tendency for all bone perfusions to decrease as body weight decreases so, in round figures, 10 ml/min per 100 g still seem a plausible figure for red marrow perfusion. Combined with the fatty marrow perfusion it is about adequate to explain the whole bone perfusion in man in Table IV.

Table IV. Means of published estimates of bone blood flow

<table>
<thead>
<tr>
<th></th>
<th>Marrow</th>
<th>Cortex</th>
<th>Whole bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Man</td>
<td>7 (1)</td>
<td>- (0)</td>
<td>2.5 (4)</td>
</tr>
<tr>
<td>Dogs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a)</td>
<td>6 (3)</td>
<td>1.5 (1)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>(b)</td>
<td>9 (4)</td>
<td>7 (2)</td>
<td>11 (14)</td>
</tr>
<tr>
<td>Rabbits</td>
<td>4 (4)</td>
<td>- (0)</td>
<td>1.6 (6)</td>
</tr>
<tr>
<td>Rats</td>
<td>25 (4)</td>
<td>14 (1)</td>
<td>32 (3)</td>
</tr>
</tbody>
</table>

Flows are in ml/min per 100 g or 100 ml wet tissue. The numbers in brackets are the numbers of investigations used for each mean. Line (b) for dogs includes data from investigations in immature animals. Equal weight was given to each investigation and estimates based on 42Ca and 82Sr clearance were corrected by dividing by 0.43 and 0.76 respectively, as suggested by Kane (1968). Where investigators reported only a range of values the geometric mean of the limits was used as the estimate for that investigation. Inconsistencies within the table arise from gross inconsistencies between investigators.

The investigations included are as follows: Eholm, Howarth and McMichael (1945); Petrakis et al. (1953); Laing and Ferguson (1958, 1959); Cuming (1962); Cuming and Nutt (1962); Breuer, Hirsch and Sachweh (1964); Shim, Copp and Patterson (1966, 1967); Semb (1966, 1971); Matumoto and Mizuno (1966); Michelsen (1968); Brookes (1968, 1970); Kane and Grim (1969); Sim and Kelly (1970); Kelly Yipintsoi and Bassingthwaighte (1971); and other quoted by Kane (1968).

For cardiac output the Cowles, Borgstedt and Gillies (1971) cardiac index of 3.5 (L/min)/m² is combined with the 1.85 m² body surface area of a 30-year-old, 70-kg man of medium build (Documenta Geigy, 1956, pp. 250, 255). Mapleson (1963a) is followed in attributing the unaccounted fraction of the cardiac output to peripheral shunt. This may be justified on two counts. Firstly, increases in skin blood flow above basal are mainly through arteriovenous anastomoses (Hyman, 1961). Secondly, many estimates of blood flow are based on the clearance of diffusible indicators and therefore are estimates of “effective” blood flow which may be less than the total (Hills, 1967)—although the difference is probably small (F. Gillespie, 1972, personal communication). However, it should be noted that the data in Table IV may be consistent with the unaccounted fraction of the cardiac output going largely to bone cortex.

Cowles, Borgstedt and Gillies (1971) attribute their unaccounted fraction of the cardiac output to a group of tissues which includes lymphoid tissue, blood vessels, cartilage and nerves, and which thereby acquires a perfusion of 40 ml/min per 100 g. This seems rather high since the nerves might be expected to match the spinal cord and, although blood vessels are in some degree muscular, 40 ml/min per 100 g is about the perfusion for non-specialized muscle (L. Cader and Dahn, 1965). Here a figure of 5 ml/min per 100 g is used for all three tissues and this is also applied to the non-parenchymal tissue of the lung.
The grouping of tissues into compartments in table III is that justified (within limits) by Maplestone (1963a).
The blood volumes were calculated in the same way as in Appendix I but using the blood flows in table III.
The cardiac index given by Cowles, Borgstedt and Gillies (1971) is based on 510 subjects whose mean age falls in the 30–39 decade of age. The cardiac index of Brandfonbrener, Landaworne and Shook (1955) for this decade agrees to within 1% so their data for other decades from 20 to 89 may be used with confidence.

**APPENDIX III**

**EQUATIONS SOLVED IN EACH CYCLE OF CALCULATION**

As the lungs.

\[
P'_A = (X_0 P_V + X_1 P_A) (1 - F_0) + V_A P_A + V_P I
\]

\[
W = (X_0 + X_1) P'_A - X_3 P_V - X_4 P_A
\]

\[
V'_A = V_A + V_I - V_T
\]

At the tissues.

\[
P'_I = \frac{X_0 P_I + X_2 P_V}{X_I + X_2} \quad \text{(for each tissue)}
\]

\[
P'_U = \frac{\Sigma P'_I Q_I}{Q}
\]

To transfer blood from lungs to tissues and from tissues back to lungs.

Model O: \(P'_T = P_A, P'_V = P_U\)

Model F: \(P'_T = P'_A, P'_V = P_U\)

Model P: \(P'_T = (P'_A + (N_A - 1) P_I) / N_A, P'_V = (P'_V + (N_V - 1) P_I) / N_V\)

Model M: the calculations made here are mostly clearly expressed by the Algol Procedure used for the purpose. A copy of the Procedure will be sent on request.

**Explanation of symbols.**

F = concentration of agent as volume fraction of dry part of gas.
N_A, N_V = number of stroke volumes of blood in the artery or vein (model F) or in the arterial or venous pool (model P).

P = partial pressure of agent as a fraction of an atmosphere.
Q = volume of blood.
Q = cardiac output.
Q_I = blood flow through i th compartment.
U = volume of tissue.
V = volume of gas (BTPS).
W = volume of agent dissolving (BTPD).
X_I = \(\lambda_A Q_I + \lambda_I U\).
X_V = \(\lambda_V Q_V + \lambda_I U\).
X_W = \(\lambda_W Q_V\).
A = in the alveoli or the arterial blood in the lungs.
B = in blood in general.
E = expired.
I = inspired.
L = in the lung compartment.
S = in the circulating stroke volume.
T = arterial blood at the tissues.
U = in mixed venous blood at the tissues.
V = in mixed venous blood at the lungs.
R = in the i th tissue compartment.

At 60 calculations/min and 15 respirations/min \(V_I\) and \(V_V\) are zero for three out of every four cycles of calculation.

Initial values: \(V_A = FRC, P_A = P_T \Rightarrow P_U = P_V = 0\).

**ACKNOWLEDGEMENTS**

The author is grateful to Professor William W. Mushin for his continual interest and encouragement over the years in the development, refinement and application of models of the uptake and distribution of inhaled anaesthetics; to Dr W. D. A. Smith and Dr M. Rosen for posing the problems which provided the incentive for this particular study; to Mrs D. Winterburn for assistance with literature searches; and to Mr E. K. Hillard for the draughtsmanship of figure 1.

**REFERENCES**


MODELES-TEMPS DE CIRCULATION DE LA RESORPTION D'ANESTHESIQUES INHALES ET DONNEES SERVANT A LEUR QUANTIFICATION SOMMAIRE

Des modèles compartimentés conventionnels de la résorption et distribution des anesthésiques inhalés s'assument que le sang se déplace des poumons aux tissus et retour en nul temps. Trois nouveaux modèles, qui incorporent des représentations alternatives du temps minime actuellement nécessaire, ont été construits en termes des programmes Algol pour computer digital. Il est prouvé que l'approche conventionnelle est la cause d'erreurs systématiques dans la résorption computerisée d'agents peu solubles, dans la pression artérielle d'agents très solubles et dans la pression tissulaire de tous les agents. Les erreurs sont importantes dans les une ou deux premières minutes de l'administration ou du rétablissement. Il est démontré que la distribution conventionnelle du volume sanguin entre les compartiments est fautive et cause des erreurs systématiques encore plus importantes des résultats computerisés. Trois différentes distributions publiées du volume tissulaire et du débit cardiaque donnent des résultats computerisés différents et une distribution "préférentielle" est suggérée.

ZIRKULATIONS-ZEIT-MODELLE FÜR DIE AUFNAHME VON INHALTIONS-NARKOTICA UND DATEN FÜR DENEN QUANTITATIVE MESSUNG

ZUSAMMENFASSUNG


**MODELOS DEL TIEMPO DE CIRCULACION EN LA ABSORCION DE LOS ANESTESICOS DE INHALACION Y DATOS PARA LA CUANTIFICACION DE LOS MISMOS**

**RESUMEN**

Los modelos compartimentados convencionales de la absorción y distribución de los anestésicos de inhalación suponen que la sangre se mueve desde los pulmones a los tejidos y desde los tejidos a los pulmones en un tiempo cero. Se han construido tres nuevos modelos que incorporan una representación alternativa del tiempo finito transcurrido en los términos de programas de Algol para una computadora digital. Se ha demostrado que el método convencional da lugar a errores sistemáticos en la absorción computada de agentes de baja solubilidad, en las tensiones arteriales de agentes de elevada solubilidad y en las tensiones tisulares de todos los agentes. Los errores son importantes durante el primer o segundo minutos que siguen a la administración o a la recuperación. La distribución convencional del volumen sanguíneo entre los diferentes compartimentos se demuestra que es errónea y que da lugar a errores sistemáticos todavía mayores en los resultados computados. Tres distribuciones diferentes publicadas del volumen tisular y del volumen de bombeo cardíaco dan resultados computados diferentes y se propone una distribución preferible.

**CORRESPONDENCE**

**THE SECOND THOUSAND EPIDURAL BLOCKS IN AN OBSTETRIC HOSPITAL PRACTICE**

Sir,—Dr Crawford mentions in his article (Brit. J. Anaesth. (1972), 44, 1277) a complication of a patchy numbness on the outer aspect of the thigh which persisted for 6 weeks following delivery.

In his large experience of over 2000 cases, he reports 3 similar events. Dr Crawford is of the opinion that this complication could well be entirely unrelated to the nerve. In our article (Birkhan and Heifetz, 1961) a similar complication was reported and we are still of the opinion that this is due to trauma produced by the needle and catheter.

The hooking and looping of the catheter has been convincingly demonstrated under X-ray control. Trauma and evulsion of a nerve root could neurologically explain this event.

H. J. BIRKHAN
M. HEIFETZ
Haifa, Israel

**REFERENCE**


Sir,—There can be no doubting that the explanation proffered by Drs Birkhan and Heifetz could well be correct, although the matter is unlikely ever to be finally settled.

I am unwilling unreservedly to accept the explanation for the following reasons. In each case (and we have now records of four patients with persistent numbness on the outer aspect of a thigh, and one with the outer aspect of a calf so affected, from a series of approximately 4,000 lumbar epidural blocks) the condition was self-limiting, persisting for approximately 6 weeks. Thus evulsion of the nerve is an unlikely explanation, and the trauma, if it had been sustained, must have been of a very selective nature.

Secondly, the extent of the "lesion" was well circumscribed, and in four of the cases to which I have just referred, lay in the middle of that area of skin which is supplied by the lateral cutaneous nerve of thigh (L1, L2). Yet there was no evidence of sensory deficit in other areas supplied by these roots, and the peripheral nerve itself arises as a discrete entity within the psoas major muscle, long after its composite fibres have traversed the epidural space.

It is the occurrence of oddities such as this (including the "missed segment story") which encourages me repeatedly to suggest to colleagues (trained and in training) that the successful practice of epidural block is composed of science plus art plus an unknown factor, and that revelation of the latter, it is not likely, will be at the hands of the anatomists.

J. SELWYN CRAWFORD
Birmingham

**AIRWAY FOR DIRECT COUPLING TO THE ANAESTHETIC CIRCUIT**

Sir,—If Dr Foster (Brit. J. Anaesth. (1972), 44, 1336) had looked deeper into the matter he would have realized that the thought behind the development of the airway came independently from Dr Mathias and myself. Portex Ltd produced the airway for both of us and Dr Mathias saw fit to publish his article in a different journal. This does not discredit the contribution of either as Dr Foster's ungracious note seems to imply.

R. V. A. CONSIGLIO
Preston