EFFECT OF ANAESTHESIA WITH CYCLOPROPANE, HALOTHANE OR
THIOPENTONE ON THE VASCULAR COMPARTMENT IN SHEEP

BY

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SUMMARY

Measurements of the volume and protein content of the plasma, and the red cell and haemoglobin content, haematocrit and gas tension of the blood were made on normal, adult sheep during three consecutive 2-hour periods: control, anaesthesia and recovery. During the period of anaesthesia, cyclopropane, halothane or thiopentone was administered. Red cells were removed from the circulation during the control periods and during anaesthesia with thiopentone or halothane, but returned during the recovery periods. The red cell concentration increased both during and after the administration of cyclopropane, and reached a value 30 per cent higher than the mean concentration present during the control period. Cyclopropane anaesthesia was not accompanied by a significant loss of fluid or protein from the circulation, but the rate of protein loss increased after the cyclopropane was withdrawn. No significant changes in either the volume of plasma or the total plasma protein occurred during the early stages of either halothane or thiopentone anaesthesia, but in each case the mean plasma protein concentration was significantly lower during anaesthesia than during the control period.

Changes in the volume and composition of the blood that occur during surgical manoeuvres performed under general anaesthesia may be important in determining both the efficiency of perfusion of vital areas and the subsequent clinical course of the patient. Some of these changes result from the exchange of fluids with the exterior, but important movements of blood constituents may occur between the different compartments of the body (Stewart and Rourke, 1938). There is some evidence that anaesthetic agents may affect these movements of fluid and cells (Hausner, Essex and Mann, 1938; Courtice and Gunton, 1949; Swingle and Swingle, 1963), and so modify the effects of blood and other fluid loss, and of replacement therapy on the effective intravascular volume (Courtice and Gunton, 1949). Some studies have been made on the effects of anaesthetic agents on the volume of plasma and whole blood (Stewart and Rourke, 1938; Price, Helrich and Conner, 1956; Payne, Gardiner and Verner, 1959; Grable et al., 1962; Morse et al., 1963), but marked differences exist between these studies in the analytical techniques and experimental design, previous history and medication of the patients and the duration and exact nature of the anaesthetic. For this reason, it is difficult to assess the significance of the results obtained with the different drugs.

This study was designed to provide comparative information concerning the effects of important anaesthetic agents on the vascular compartment. Observations were made before, during and after the administration of cyclopropane, halothane or thiopentone to sheep under controlled experimental conditions.

PROCEDURE

Measurements of the volume and protein content of the plasma, and the red cell and haemoglobin content and the haematocrit, $P_{\text{O}_2}$, $P_{\text{CO}_2}$ and pH of the blood of twenty-one sheep were made at intervals during three consecutive 2-hour
periods while the animals were lightly restrained in left lateral recumbency. The measurements were made on conscious, resting sheep during the first 2-hour (control) period, then during a 2-hour period of deep surgical anaesthesia, and were continued for a period of 2 hours after the administration of the anaesthetic had ceased.

**Animals.**

Healthy adult Merino or Merino-cross ewes or wethers that had not been used for any previous experiments were deprived of water for 10–12 hours but did not receive any form of preliminary medication. Immediately before the beginning of the control period, a p.v.c. cannula (i.d. 0.86 mm) was passed through a 14 s.w.g. needle into an external jugular vein and positioned so that the tip rested near the entrance to the right atrium. In six sheep a Riley arterial needle was inserted into a common carotid artery that had been exteriorized in a skin flap three months before the experiment. Approximately 100 ml blood was removed during sampling from each sheep, and this was not replaced.

**Anaesthesia.**

In each experiment, cyclopropane, halothane or thiopentone was used for both the induction and the maintenance of a state of deep surgical anaesthesia, and no other drugs were administered. The state of deep surgical anaesthesia was considered to be present when the corneal reflex was sluggish and the palpebral and cutaneous reflexes and the withdrawal reflex to interdigital pressure were no longer present.

Anaesthesia was induced with thiopentone by the intravenous infusion of a 5 per cent solution at a dose of 20–25 mg/kg. A tightly-fitting face mask and an otherwise closed circuit was used to administer oxygen and either cyclopropane, in a concentration of 30–50 per cent in oxygen, halothane, administered from a Stephens vaporizer adjusted to 4/4 open, or 5 per cent thiopentone, administered intravenously in volumes of 2–5 ml as required.

**Measurements.**

The volume of plasma was measured once during each control, anaesthetic and recovery period by the dilution of labelled albumin. A measured amount (10–20 \(\mu\)C) of \(^{131}\)I-labelled albumin (The Radiochemical Centre, Amersham, Bucks,) was injected into a jugular vein 30 minutes after the beginning of each period, and blood samples removed from the venous cannula into heparinized tubes 10, 30 and 60 minutes later. Duplicate samples of plasma were plated on to planchets, and the level of activity in the dried samples estimated with a thin end-window Geiger Müller tube and Philips PW4032 Universal Counter. Corrections were applied for background radiation and self-absorption and, where applicable, for the level of radioactivity present in the plasma from the preceding estimation. The regression coefficient (b) of the logarithm of the corrected counting rate against sample time was calculated and used to estimate both the level of radioactivity that would have been present in the plasma at the time of injection if mixing had been instantaneous, and the plasma volume (equation 1). The half-time of the labelled albumin in the circulation was calculated (equation 2) and was used to estimate the rate of net removal of the labelled albumin from the plasma (equation 3).
BLOOD CHANGES DURING ANAESTHESIA

Plasma volume (ml) = \( \frac{\text{Total counts/min injected}}{\text{Estimated counts/min/ml at To}} \) …………. (1)

Half-time = \( \frac{\log_{10} 2}{b} \) …………. (2)

\[
\text{Per cent net removal of labelled albumin per hour half-time (hours)} = \frac{0.692 \times 100}{\text{half-time (hours)}}
\] …………. (3)

At 30-minute intervals, measurements were made of the plasma protein concentration, by the biuret method (Gornall, Bardawil and David, 1949), and of the haematocrit, measured in microhaematocrit tubes with no correction applied for trapped plasma. At intervals of 1 hour, measurements were made of the concentration of haemoglobin by the cyanmethaemoglobin method, and of red cells by counting in a haemocytometer. Estimates were made of the red cell volume (in cubic microns), by dividing the volume of packed cells (ml/l.) by the red cell concentration (millions/mm\(^3\)), and of the total amount of circulating plasma protein, from the product of the volume and protein concentration of the plasma.

In two experiments with each anaesthetic agent, samples of arterial blood were removed at intervals of 30 minutes into glass syringes in which the deadspace had been filled with heparinized saline. The syringes were sealed immediately, then transferred to an ice bath and analyzed for Po\(_3\), Pco\(_2\), and pH within 15 minutes of collection. The Po\(_3\) was estimated with a Clarke polarographic oxygen electrode standardized against water equilibrated with air. Pco\(_2\) was estimated with a Severinghaus carbon dioxide electrode, standardized against two known mixtures of carbon dioxide and oxygen, and pH was estimated with a glass microelectrode, standardized against precision buffers. All electrodes were maintained at 38°C, and were connected to a Radiometer pH meter.

Statistical analyses.

Student’s t test was used to determine whether significant differences in the various parameters existed between the experimental periods. The values of t were estimated by substituting the mean values (\( \bar{X}_1, \bar{X}_2 \)), the error mean square (EMS), estimated by analysis of variance (table I), and the number of animals (N) in equation 4.

\[
t = \frac{(\bar{X}_1 - \bar{X}_2)}{[2 \cdot \text{EMS} (N^{-1})]^{1/2}}
\] …………. (4)

The standard error of the mean of a single time interval was estimated for the different parameters from the EMS and sample number, as indicated in equation 5 (Chalmers et al., 1965).

\[
\text{SEM} = [\text{EMS} (N^{-1})]^{1/2}
\] …………. (5)

RESULTS

During the experiments, the sheep lay quietly on the table, and induction and maintenance of anaesthesia proceeded without major incident in all cases. Some of the sheep anaesthetized with cyclopropane did have minor, spontaneous movements of skeletal muscles. All the sheep were well oxygenated during anaesthesia and had arterial Pco\(_3\) values lower than, and pH values higher than, conscious sheep (figs. 1–3). These parameters all returned rapidly to the control values when administration of the drug was discontinued.

Cyclopropane.

During the administration of cyclopropane, the plasma volume decreased a little and its

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Degrees of freedom</th>
<th>Sum of squares</th>
<th>Mean square</th>
<th>Variance ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between times (control, anaesthesia, recovery)</td>
<td>2</td>
<td>44,150</td>
<td>22,075</td>
<td>0.92 NS</td>
</tr>
<tr>
<td>Between drugs (cyclopropane, thiopentone, halothane)</td>
<td>2</td>
<td>784,460</td>
<td>392,230</td>
<td>16.3*</td>
</tr>
<tr>
<td>Between sheep</td>
<td>18</td>
<td>7,293,770</td>
<td>405,209</td>
<td>16.9*</td>
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<tr>
<td>Error</td>
<td>40</td>
<td>961,050</td>
<td>24,026</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>9,083,430</td>
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</table>

NS = not significant. * P<0.001.
TABLE II
Effect of anaesthesia with cyclopropane on blood components.

<table>
<thead>
<tr>
<th></th>
<th>Mean during</th>
<th>Tests of significance</th>
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<tr>
<td></td>
<td>Control</td>
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<tr>
<td>Plasma volume (ml)</td>
<td>1601</td>
<td>1511</td>
</tr>
<tr>
<td>Plasma protein conc. (g/100 ml)</td>
<td>6.83</td>
<td>7.07</td>
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<tr>
<td>Total protein (g)</td>
<td>107</td>
<td>107</td>
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<tr>
<td>Net removal of labelled albumin (% per hour)</td>
<td>8.0</td>
<td>3.7</td>
</tr>
<tr>
<td>Red cell concentration (millions/mm³)</td>
<td>9.03</td>
<td>9.20</td>
</tr>
<tr>
<td>Red cell volume (µ³)</td>
<td>36.2</td>
<td>33.8</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>30.4</td>
<td>29.6</td>
</tr>
<tr>
<td>Haemoglobin (g/100 ml)</td>
<td>10.8</td>
<td>10.9</td>
</tr>
</tbody>
</table>

NS = not significant.  *P<0.05.  †P<0.01.  ‡P<0.001.

![Diagram](image-url)

Fig. 1
Mean percentage changes in the plasma volume and large vein haematocrit, and in the concentration of red cells and of plasma protein in a group of seven sheep anaesthetized with cyclopropane. Vertical bars at left represent ±SE of mean for a single time interval. Absolute blood-gas values, obtained from a single, typical sheep in this group, are shown in lower three panels.
TABLE III
Effect of anaesthesia with halothane on blood components.

<table>
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<tr>
<th>Tests of significance</th>
<th>Mean during</th>
<th>Control</th>
<th>Anaesthesia</th>
<th>Recovery</th>
<th>Control-anaesthesia</th>
<th>Control-recovery</th>
<th>Anaesthesia recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>Anaesthesia</td>
<td>Recovery</td>
<td>Control-recovery</td>
<td>Control-recovery</td>
<td>Anaesthesia recovery</td>
</tr>
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<td>Plasma volume (ml)</td>
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<td>1583</td>
<td>1653</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>protein conc. (g/100 ml)</td>
<td></td>
<td>7.21</td>
<td>6.92</td>
<td>7.01</td>
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<td>NS</td>
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<td>total protein (g)</td>
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<td>118</td>
<td>117</td>
<td>122</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>net removal of labelled albumin (% per hour)</td>
<td></td>
<td>11.2</td>
<td>10.2</td>
<td>16.6</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Red cell concentration</td>
<td></td>
<td>7.80</td>
<td>6.72</td>
<td>8.17</td>
<td>7.71‡</td>
<td>2.64*</td>
<td>10.4‡</td>
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<td>(millions/mm³)</td>
<td></td>
<td>31.5</td>
<td>33.0</td>
<td>31.0</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>volume (µl)</td>
<td></td>
<td>28.1</td>
<td>23.1</td>
<td>27.1</td>
<td>4.55‡</td>
<td>NS</td>
<td>3.64‡</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td></td>
<td>28.1</td>
<td>23.1</td>
<td>27.1</td>
<td>4.55‡</td>
<td>NS</td>
<td>3.64‡</td>
</tr>
</tbody>
</table>

NS = not significant. *P < 0.05. ‡P < 0.001.

Mean percentage changes in the plasma volume and large vein haematocrit, and in the concentration of red cells and of plasma protein in a group of seven sheep anaesthetized with halothane. Vertical bars at left represent ± SE of mean for a single time interval. Absolute blood-gas values, obtained from a single, typical sheep in this group, are shown in the lower three panels.
protein concentration increased progressively but the total amount of protein in the plasma remained constant (table II, fig. 1). During the recovery period the plasma volume increased to slightly exceed the control value, but the protein concentration decreased rapidly, and by the end of the experiment was less than the mean value present during the control period (fig. 1). This decrease in plasma protein concentration during the recovery period was accompanied by a significant increase in the net movement of labelled albumin out of the plasma compartment.

The haematocrit decreased progressively during the control period and for the first 30 minutes of anaesthesia, and reached a value 16 per cent lower than that present at the beginning of the experiment (P<0.005). This decrease in haematocrit was associated with significant decreases in both the concentration (8.2 per cent; P<0.05; fig. 1) and the volume (10 per cent; P<0.001; fig. 4) of the red cells. The volume of the red cells remained constant from the beginning of anaesthesia until late in the recovery period, when a further significant decrease occurred (P<0.001; fig. 4). The red cell concentration and haematocrit increased progressively from 30 minutes after induction, and, by the end of the first 90 minutes of anaesthesia had exceeded the mean values present during the control period (fig. 1).

Halothane.

The values for plasma volume and total circulating protein obtained early in the period of halothane anaesthesia were almost identical to those obtained during the control period, but the mean of four estimates of protein concentration made at 30-minute intervals during anaesthesia was significantly less than the mean control value (P<0.05; table III). The administration of halothane was not accompanied by any significant changes in the total plasma protein or in the rate of net removal of labelled albumin from the plasma (fig. 2).

The haematocrit decreased during the control period, but a further significant decrease (P<0.01) to 83 per cent of the mean control value occurred during the first 30 minutes of anaesthesia (fig. 2). It was then relatively constant for the remainder of the anaesthetic period, but increased significantly during the first 30 minutes after halothane was withdrawn (P<0.001) and slowly approached the mean control value during the next hour. The red cell concentration and haematocrit were both significantly lower during halothane administration than during either the control or the recovery period (P<0.001 in each case; table III), but no significant differences occurred in the volume of the red cells.

Thiopentone.

The concentration of protein in the plasma decreased progressively during the control period and the first 30 minutes of anaesthesia, then remained constant at a value that was significantly less than the mean concentration present during the control period (P<0.01; table IV, fig. 3). During the recovery period, it increased again (P<0.01) and approached the control values. No significant changes occurred in the plasma volume, the total circulating protein or the rate of net removal of labelled albumin from the plasma.

Both the red cell concentration and the haematocrit decreased during the control period, but a further, precipitous fall in both parameters occurred immediately after the injection of thiopentone (P<0.001 in each case; fig. 3). The volume of the red cells also decreased progressively during the control and anaesthetic periods (fig. 4). During the last 90 minutes of thiopentone administration the red cell concentration and haematocrit remained relatively constant, but they increased significantly (P<0.05 and P<0.001 respectively) during the first 30 minutes of recovery and approached the mean control values.

DISCUSSION

The dramatic decrease in the concentration of red cells that occurred when either halothane or thiopentone entered the circulation was almost certainly due to the accumulation of red cells in the spleen, and possibly in other parts of the viscera (Hausner, Essex and Mann, 1938; Courtice and Gunton, 1949; Rieke and Everett, 1957; Sliwinski and Lilienfield, 1958; Hodgetts, 1961). A similar decrease in haematocrit was
## Table IV

*Effect of anaesthesia with thiopentone on blood components.*

<table>
<thead>
<tr>
<th>Tests of significance</th>
<th>Mean during</th>
<th>Control</th>
<th>Anaesthesia</th>
<th>Recovery</th>
<th>Control</th>
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<th>Recovery</th>
<th>Control</th>
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<th>Recovery</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td>Anaesthesia</td>
<td>Recovery</td>
<td>Control</td>
<td>Anaesthesia</td>
<td>Recovery</td>
<td>Control</td>
<td>Anaesthesia</td>
<td>Recovery</td>
</tr>
<tr>
<td>Plasma volume (ml)</td>
<td></td>
<td>1851</td>
<td>1804</td>
<td>1821</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>protein conc. (g/100 ml)</td>
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<td>7.05</td>
<td>7.39</td>
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<td>2.75†</td>
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<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>NS</td>
</tr>
<tr>
<td>net removal of labelled albumin (% per hour)</td>
<td>8.8</td>
<td>9.7</td>
<td>16.7</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Red cell concentration (millions/mm³)</td>
<td>10.2</td>
<td>8.6</td>
<td>10.2</td>
<td>3.81†</td>
<td>NS</td>
<td>3.74†</td>
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<td></td>
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<td>volume (µl)</td>
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<td>29.5</td>
<td>2.78*</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Haematocrit (%)</td>
<td>32.4</td>
<td>25.3</td>
<td>30.3</td>
<td>8.82‡</td>
<td>2.66†</td>
<td>6.16‡</td>
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<tr>
<td>Haemoglobin (g/100 ml)</td>
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<td>NS</td>
<td>4.88‡</td>
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</table>

NS = not significant. *P<0.05. †P<0.01. ‡P<0.001.

### Fig. 3

Mean percentage changes in the plasma volume and large vein haematocrit, and in the concentration of red cells and of plasma protein in a group of seven sheep anaesthetized with thiopentone. Vertical bars at left represent ±SE of mean for a single time interval. Absolute blood-gas values, obtained from a single, typical sheep in this group, are shown in the lower three panels.
noted by Hodgetts (1961) after the administration of pentobarbitone to sheep, but when she injected adrenaline the sequestered cells were mobilized immediately and the haematocrit increased by about 50 per cent.

The level of activity in the sympathoadrenal system would probably have been fairly high at the beginning of our experiments but as the sheep gradually became accustomed to the unfamiliar surroundings the sympathoadrenal activity and the degree of stimulation of the smooth muscle of the spleen would have been expected to decrease. This would have been followed by relaxation and expansion of the spleen and a decrease in the concentration of red cells, as was noted during the control periods.

The rate of decline in sympathoadrenal activity would have been increased by the introduction of either thiopentone or halothane into the circulation. Barbiturates have been shown to cause a decrease in transmission through sympathetic ganglia (Larrabee and Posternak, 1952), a decrease in the output of catecholamines from the adrenal medulla (Walker et al., 1959), and a decrease in the level of catecholamines in the peripheral blood (Montagu, 1955; Weil-Malherbe, 1955). Halothane may also impair transmission in the sympathetic nervous system (Raventos, 1956; Black, 1965), but does not appear to result in a decrease in the level of catecholamines in the blood (Price et al., 1959; Hamelberg et al., 1960). It may, however, decrease the contractile response of smooth muscle to the catecholamines that are present (Price and Price, 1962). These effects result in expansion of the spleen, as was shown by Raventos (1956) in chloralose-treated cats that received halothane, and by Hausner, Essex and Mann (1938) in dogs anaesthetized with barbiturate, and a decrease in the concentration of red cells in the circulation (figs. 2, 3).

Cyclopropane, on the other hand, causes an increase in the activity in the sympathoadrenal system, a marked increase in the plasma levels of catecholamines (Price et al., 1959; Hamelberg et al., 1960; Price et al., 1963) and an increase in the concentration of red cells in the circulation (fig. 1). During the administration of cyclopropane to our sheep the concentration of red cells increased to exceed that present in the conscious and probably frightened sheep at the beginning of the experiment and the elevated level was maintained for at least 2 hours after the drug was withdrawn (fig. 1). By this time only a vanishingly small concentration of cyclopropane would have remained in the blood (Orcutt and Seevers, 1937; Price and Dripps, 1965).

Although the spleen in man is relatively smaller than in sheep, it may be expected to
provide a dynamic reservoir of concentrated
ing blood (Sliwinski and Lilienfield, 1958; Hodgetts,
1961). The increase in sympathoadrenal activity
that occurs during anaesthesia with cyclopro-
pame would result in the release of much of
this blood into the general circulation and would
help in the maintenance of the stable blood
pressure that is characteristic of patients receiv-
ing this drug (Price et al., 1959).

An increase in venous pressure also occurs
during cyclopropane anaesthesia (Price, Helrich
and Conner, 1956) but no information is avail-
able concerning the pressure within the capil-
laries. We found that the administration of
cyclopropane was often associated with the
removal of fluid from the circulation and suggest
that this was probably due to increases in the
mean capillary hydrostatic pressure (Pappen-
heimer and Soto-Rivera, 1948).

An increase in plasma volume during the
administration of halothane either alone or with
nitrous oxide has been reported (Grable et al.,
1962; Payne, Gardiner and Verner, 1959). These
observations were made on premedicated surgi-
cal patients by injecting Evans Blue and
estimating the concentration in one or two blood
samples. Morse and associates (1963) believed
that it was difficult to assess the significance of
these observations from the limited information
presented. Morse and his colleagues found that
the plasma volume did not change significantly
during the administration of halothane, but they
made no observations during the recovery
period. In our experiments no changes occurred
in the plasma volume during the administration
of halothane but a slight increase in plasma
volume, and significant increases in haematocrit
and red cell concentration accompanied the
return of sympathoadrenal tone during the
recovery period.

When Price, Helrich and Conner (1956) ad-
ministered thiopentone with nitrous oxide to
premedicated surgical patients, they noted a
slight but significant increase in plasma volume,
especially during the first 30 minutes. Con-
versely, we found that the plasma volume
did not change significantly when thiopentone
alone was used to produce a state of deep sur-
gical anaesthesia (fig. 3, table IV). Page, Del
Greco and Corcoran (1954) also found no change
in plasma volume in dogs anaesthetized with
pentobarbitone sodium but other authors have
reported increases in plasma volume of up to
20 per cent during pentobarbitone anaesthesia
(Hamlin and Gregersen, 1939; Courtice and
Gunter, 1949; Rieke and Everett, 1957). Al-
though some of the differences between reports
may be due to variations between species and
between the effects of the different barbiturates,
differences in the duration and depth of anaes-
thesia may be of paramount importance. Korner,
Uther and White (1968) found that the arterial
pressure of the rabbit falls by about 20 per
cent shortly after the induction of anaesthesia
with pentobarbitone sodium but no significant
changes occur in either right atrial pressure or
total peripheral resistance. During this period
of early anaesthesia, the hydrostatic pressure
within the capillaries may be expected to
decrease and to promote the net movement of
fluid into the capillaries. These authors found
that as the rabbits attained a steady state of
moderate surgical anaesthesia, the arterial pres-
Sure increased towards the pre-anaesthetic level
and the peripheral resistance decreased a little,
but no significant changes occurred in the right
atrial pressure. This condition may be associated
with an increase in the hydrostatic pressure
within the capillaries and the net removal of
fluid from the vascular compartment.

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of Miss J. Garson.

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**EFFET DE L'ANESTHESIE AVEC CYCLOPROPANE, HALOTHANE OU THIOPENTONE SUR LE COMPARTIMENT VASCULAIRE DU MOUTON**

**SUMMAIRE**

Le volume et le taux protidique du plasma, le nombre de globules rouges et le taux d'hémoglobine, l'hématocrite et la pression gazeuse du sang ont été mesures chez des moutons adultes normaux durant 3 périodes consecutives de 2 heures: contrôle, anesthésie et rétablissement. Cyclopropane, halothane ou thiopentone a été administré durant la période d'anesthésie. Les globules rouges ont été prélevés durant la période de contrôle et durant l'anesthésie avec thiopentone ou halothane, mais réinjectés durant les périodes de rétablissement. La concentration érythrocytaire augmentait aussi bien durant qu'après l'administration de cyclopropane et était de 30 pour cent plus élevée que la concentration moyenne durant la période de contrôle. L'anesthésie au cyclopropane ne s'accompagnait pas d'une perte significative de liquide ou de protéines de la circulation, mais la perte de protéines augmentait après l'arrêt de l'administration de cyclopropane. Des modifications significatives du volume plasmocratique ou du taux total de protéines du plasma ne se manifestaient pas durant la phase précédente de l'anesthésie avec halothane ou thiopentone, mais dans chaque cas la concentration moyenne protidique du plasma était significativement plus petite durant l'anesthésie que durant la période de contrôle.
ZUSAMMENFASSUNG


CORRESPONDENCE

ANAPHYLACTIC REACTION TO DEXTRAN

Sir,—I should like to offer some additional comments to those made by Dr. J. R. Maltby in his case report of an anaphylactic reaction to dextran published in the July issue (Brit. J. Anaesth., 1968, 40, 552).

As Dr. Maltby states an increase in incidence and severity of side effects mentioned, namely antigenicity, interference with blood grouping and interference with blood coagulation are directly related to an increase in molecular weight and degree of branching of the dextran used.

Salsbury (1967) showed that while Macrodex (dextran of molecular weight 70,000) is unlikely to interfere with blood grouping by causing erythrocyte aggregation both dextrans of molecular weight 110,000 and 150,000 are likely to do so. This confirms previous studies by Arndt-Hanser (1956), Pettenkofer (1959) and others.

Nilsson and her co-workers have studied the effects of dextrins of varying molecular weight on the coagulation system. In 1964 they showed that dextran with an average molecular weight below 75,000 in recommended dosage did not significantly affect the various coagulation factors. Dextran with an average molecular weight of 130,000 in the same dosage produced a moderate coagulation defect.

Dr. Maltby discusses primary anaphylactoid reactions to dextrans which have been reported on rare occasions with no previous history of exposure to dextrans. It has not been possible to detect precipitating antibodies in the serum of these patients on the occasions when this has been done. There are a number of theories as to the cause of this type of reaction. One as is mentioned is a cross immunological reaction with a polysaccharide contaminant of sugar. It must be remembered that cane sugar contains more dextran with a polysaccharide contaminant of sugar. It must be remembered that cane sugar contains more dextran than beet sugar. This might possibly explain why the frequency of these primary reactions varies from country to country.

The fact that primary reactions to dextran have virtually never been reported when dextrin is being used clinically for shock and especially in anaesthetized patients may possibly correlate to the normal physiological response to stress. A theory has been advanced that trauma, e.g. surgical incision, etc., by causing an increase in the circulating glucocorticoid level affords protection against an anaphylactoid reaction in these circumstances.

As Dr. Maltby correctly states, earlier dextrans with a greater degree of branching were more markedly antigenic (Kabat et al., 1957) than the modern ones. Kabat and Bezer (1958) were able to cause an increase in circulating dextran precipitable antibodies by subcutaneous injections of small amounts of dextrans with an average molecular weight over 91,700, but they were unable to do this with an injection of a dextran with a molecular weight below 51,300. Grönwall (1959) was unable to cause a significant increase in precipitating antibodies with a dextran of average molecular weight 80,000. The dextran used in both these latter studies were of the linear type.

In summary, therefore, dextrans with an average molecular weight below about 80,000 are unlikely to be associated with the side effects mentioned, i.e. antigenicity, haemorrhage or interference with blood typing and crossmatching provided they are of the linear type and given in the recommended dosage. Primary anaphylactoid reactions apparently entirely unrelated to previous exposure to dextrans and resultant sensitization may occur on rare occasions. The frequency of such reactions is far less than when blood or blood products are used.

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