CIRCULATORY EFFECTS OF ATROPINE DURING HALOTHANE ANAESTHESIA

BY

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SUMMARY
The circulatory response to the injection of 0.6 mg atropine during nitrous oxide, oxygen and halothane anaesthesia was studied in fifteen patients. Cardiac output was measured by the dye-dilution method and blood pressure and heart rate by manual methods. There was an immediate mean increase in heart rate from 61 to 110 beats/min, accompanied by a 48 per cent increase in cardiac output and a 24 per cent increase in mean arterial pressure. Stroke volume fell by 17 per cent and peripheral resistance by 17 per cent. These changes were of shorter duration than the change in heart rate. No change was observed in left ventricular stroke work or "central" blood volume. Three patients developed transient arrhythmias after the injection of atropine.

METHODS
Cardiac output was measured by the indicator-dilution method, employing the technique described by Gabe and Shillingford (1961). The indicator was Coomassie Blue (ICI). Cartridges of 2 ml capacity were filled with a 2 per cent solution of the dye. 40-mg doses were injected via a three-way tap into a venous catheter, using a modified dental cartridge syringe. Each dose of dye was immediately flushed in with 20 ml of dextrose-saline solution. This washes the indicator rapidly into the central veins and ensures a well-defined curve (Bousvaros et al., 1963). The shape of the curves was in all cases satisfactory. After an injection had been made the cartridge syringe was removed from the tap and the drip tubing connected in its place. The quantity of dye actually used was calculated by weighing the cartridge before and after discharging it.

A Cambridge Mark II dye-dilution curve recorder with a lightweight photo-electric earpiece (Cambridge Instrument Co.) was used to record the passage of dye through the ear. It has been shown that when a high resistance is placed in the input from the photocells, the response of this recording system to changing concentrations of dye in the blood is linear within the range of clinically permitted doses (Gabe and Shillingford, 1961). The apparatus was therefore used in this manner so that the areas under the curves obtained from successive injections of dye were always inversely proportional to the cardiac output. By this means changes of output can be determined without the need to calibrate individual
cures. This has the advantage that the taking and analyzing of blood samples is unnecessary. Absolute figures for cardiac output were only obtained in four patients but the present investigation was mainly concerned with changes in output.

The height of each dilution curve was measured in mm at intervals of 1 sec. The downslope of the curve, which was always exponential, was replotted on semilogarithmic paper to give a straight line. The time-constant of the exponential was measured from the slope of this line. The area beneath the decaying part of the curve was obtained by multiplying the time-constant by the height of the curve at the start of the exponential decay. This value was then added to the sum of the heights (at 1-sec intervals) of the earlier part of the curve, to give the area beneath that part of the curve which related to the first passage of dye only. By this means the effect of recirculating indicator was eliminated. Cardiac output was expressed as the product of the dye dose and the reciprocal of the area beneath the dilution curve.

Heart rate was measured from the pulsations seen on the record, or if these were not visible, it was counted from a peripheral artery, immediately before or after the dye injection.

Blood pressure was measured at the same time with a sphygmomanometer. Mean arterial pressure was calculated conventionally by adding one-third of the pulse pressure to the diastolic pressure (Bell, Davidson and Scarborough, 1961).

Peripheral resistance was then derived by dividing the mean arterial pressure by the figure for cardiac output. Stroke volume was obtained by dividing the cardiac output by the heart rate. The work done by the heart was expressed as the left ventricular stroke work, employing the formula:

\[
\text{left ventricular stroke work (gm cm)} = \frac{\text{cardiac output}}{\text{heart rate}} \times (\text{mean arterial pressure} - 5 \text{ mm Hg})
\]

The left ventricular end-diastolic pressure has been assumed to remain constant at 5 mm Hg.

The "central" blood volume (Hamilton et al., 1928) was obtained by multiplying the cardiac output by the mean transit time of the indicator. This is the volume between the point of injection of the indicator and the sampling point and their temporal equivalents.* The major part of this volume is accounted for by the blood in the heart and lungs and should therefore give an indication of the pulmonary blood volume.

Circulation time was obtained from the recorder tracing by measuring the interval between the peaks of the primary and the recirculatory curves. In this case the time measured is that taken by the greatest concentration of dye to pass from the ear to the heart and back again to the ear. It represents the most rapidly circulating part of the blood volume.

The repeatability of the methods employed was assessed by making a series of eight observations in one patient (not in the series) while circulatory conditions were stable. The standard deviations of individual observations for the various parameters are given in table I.

**PROCEDURE**

The investigation was made on fifteen adult patients (eleven men and four women) undergoing operations which involved minimal blood loss. All the patients were normotensive and free from circulatory disease. Their average age was 43 years and their average weight 72 kg. Each patient was seen at the pre-operative visit when the nature of the investigation was explained and consent for the procedure obtained. Premedication consisted of an opiate with hyoscine (twelve patients) or atropine (two patients); one patient had no premedication.

* Temporal equivalents are all points which have the same circulation times as the injection and sampling sites.
Ages, weights and sexes of the patients studied, with doses of the drugs used.

<table>
<thead>
<tr>
<th>Operation</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Wt. (kg)</th>
<th>Premedication (mg)</th>
<th>Thiopentone (mg/kg)</th>
<th>Halothane conc. (%)</th>
<th>Atropine (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Stripping varicose veins</td>
<td>58</td>
<td>F</td>
<td>64</td>
<td>Papaveretum 15</td>
<td>6.3</td>
<td>0.5</td>
<td>0.0093</td>
</tr>
<tr>
<td>2 Inguinal hernia repair</td>
<td>58</td>
<td>M</td>
<td>61</td>
<td>Papaveretum 20</td>
<td>4.1</td>
<td>1</td>
<td>0.0098</td>
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<tr>
<td>3 Inguinal hernia repair</td>
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<td>M</td>
<td>71</td>
<td>None</td>
<td>7.0</td>
<td>1</td>
<td>0.0085</td>
</tr>
<tr>
<td>4 Oophorectomy</td>
<td>31</td>
<td>F</td>
<td>60</td>
<td>Papaveretum 20</td>
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<td>1</td>
<td>0.01</td>
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<tr>
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<td>42</td>
<td>F</td>
<td>52</td>
<td>Papaveretum 10</td>
<td>6.7</td>
<td>1</td>
<td>0.015</td>
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<tr>
<td>6 Inguinal hernia repair</td>
<td>56</td>
<td>M</td>
<td>56</td>
<td>Pethidine 100</td>
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<td>1</td>
<td>0.0079</td>
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<tr>
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<td>45</td>
<td>M</td>
<td>64</td>
<td>Papaveretum 20</td>
<td>5.8</td>
<td>1</td>
<td>0.0087</td>
</tr>
<tr>
<td>8 Removal of lump, breast</td>
<td>42</td>
<td>F</td>
<td>52</td>
<td>Morphine 10</td>
<td>3.8</td>
<td>1</td>
<td>0.015</td>
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<tr>
<td>9 Inguinal hernia repair</td>
<td>46</td>
<td>M</td>
<td>66</td>
<td>Papaveretum 20</td>
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<td>M</td>
<td>69</td>
<td>Papaveretum 20</td>
<td>5.8</td>
<td>2</td>
<td>0.0087</td>
</tr>
<tr>
<td>11 Inguinal hernia repair</td>
<td>24</td>
<td>M</td>
<td>76</td>
<td>Papaveretum 20</td>
<td>5.3</td>
<td>2</td>
<td>0.0079</td>
</tr>
<tr>
<td>12 Inguinal hernia repair</td>
<td>42</td>
<td>M</td>
<td>79</td>
<td>Papaveretum 20</td>
<td>6.3</td>
<td>2</td>
<td>0.0076</td>
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<tr>
<td>13 Inguinal hernia repair</td>
<td>30</td>
<td>M</td>
<td>86</td>
<td>Papaveretum 20</td>
<td>5.8</td>
<td>2</td>
<td>0.0098</td>
</tr>
<tr>
<td>14 Inguinal hernia repair</td>
<td>27</td>
<td>M</td>
<td>76</td>
<td>Papaveretum 20</td>
<td>4.0</td>
<td>2</td>
<td>0.0095</td>
</tr>
<tr>
<td>15 Stripping varicose veins</td>
<td>44</td>
<td>M</td>
<td>93</td>
<td>Papaveretum 20</td>
<td>4.3</td>
<td>2</td>
<td>0.0097</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Operation</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Wt. (kg)</th>
<th>Premedication (mg)</th>
<th>Thiopentone (mg/kg)</th>
<th>Halothane conc. (%)</th>
<th>Atropine (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Means</td>
<td>43</td>
<td>—</td>
<td>72</td>
<td>5.3</td>
<td>1.4</td>
<td>0.0098</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>10.6</td>
<td>—</td>
<td>12.6</td>
<td>1.2</td>
<td>—</td>
<td>0.0018</td>
<td></td>
</tr>
</tbody>
</table>

(see table II). The mean interval between premedication and the induction of anaesthesia was 88 minutes.

Anaesthesia was induced with thiopentone (mean 5.3 mg/kg) followed by suxamethonium 50 mg prior to endotracheal intubation. After the return of spontaneous respiration, anaesthesia was maintained with nitrous oxide (60 per cent), oxygen and 0.5–2 per cent halothane from a Fluotec vaporizer, using a Magill attachment. The patients lay supine with one arm extended on an armboard. An intravenous infusion of dextrose/saline solution was set, using a large-bore venous catheter ("Intracath", C. R. Bard, Inc.) or a cannula, inserted so that the tip lay in the upper arm. The operations performed, ages and weights of the patients and doses of premedicant drugs, thiopentone, halothane and atropine are given in table II. A period of at least half an hour elapsed between the start of anaesthesia and the recording of observations. This permitted the achievement of a steady circulatory state and allowed time for the apparatus to be prepared. A time was chosen when surgical procedures likely to induce circulatory changes were absent and when the arterial pressure and heart rate were steady. An initial set of observations, consisting of recording a dye-dilution curve and measuring arterial pressure and
heart rate, was then made. In six cases these readings were duplicated.

Atropine sulphate 0.6 mg was injected into the drip and immediately flushed in with dextrose/saline solution. This dose was chosen because it was considered sufficient to cause acceleration of the heart (Morton and Thomas, 1958). A second set of observations was made when the heart rate appeared to have reached a maximum, between 2 and 5 minutes from the time of injection. In eight patients further sets of observations followed.

RESULTS

For each patient the control values for each parameter, before giving atropine, are expressed as 100 and those obtained afterwards as percentages of the controls. The results are tabulated as changes occurring within 2-5 minutes of giving atropine. The mean changes occurring in this period were obtained and standard errors calculated. Differences in the response to atropine of patients breathing various halothane concentrations are also reported. The statistical significance of a change in any parameter was assessed by Student's t test. For certain parameters results are also plotted as percentage changes against time. Individual results are summarized in table III.

The effect of atropine on heart rate.

The mean heart rate before giving atropine was 61 beats/min (SE ± 2.0). The rate began to increase within an average of 19 seconds (SE ± 1.7) of the atropine injection, continued to accelerate during the next 10-30 seconds and then became steady. The maximum rate was achieved in 32 seconds (SE ± 2.8). The mean increase in rate was 49 beats/min (SE ± 2.8), giving a final rate of 110 beats/min (SE ± 3.2). There was no significant difference in initial heart rate or change of rate between those on different concentrations of halothane. Figure 1 shows how the heart rate, expressed as a percentage of the control value, increased in each patient. The mean increase was 84 per cent (P < 0.001).

![Figure 1](https://academic.oup.com/bja/article-abstract/39/3/226/239088)

**Fig. 1**

The effect of atropine on the heart rate.

The control values are expressed as 100 per cent. Patients having 0.5 per cent (---), 1 per cent (—) and 2 per cent (----) halothane.

<table>
<thead>
<tr>
<th>Table III</th>
<th>2-5 minutes after receiving atropine.</th>
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</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Heart rate</td>
</tr>
<tr>
<td>1</td>
<td>+79</td>
</tr>
<tr>
<td>2</td>
<td>+54</td>
</tr>
<tr>
<td>3</td>
<td>+74</td>
</tr>
<tr>
<td>4</td>
<td>+65</td>
</tr>
<tr>
<td>5</td>
<td>+52</td>
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<tr>
<td>6</td>
<td>+72</td>
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<td>7</td>
<td>+127</td>
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<td>8</td>
<td>+77</td>
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<td>9</td>
<td>+86</td>
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<td>+120</td>
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<td>11</td>
<td>+87</td>
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<td>12</td>
<td>+42</td>
</tr>
<tr>
<td>13</td>
<td>+74</td>
</tr>
<tr>
<td>14</td>
<td>+139</td>
</tr>
<tr>
<td>15</td>
<td>+99</td>
</tr>
</tbody>
</table>
**TABLE IV**

Circulatory changes 2-5 minutes after giving atropine. Results are expressed as percentages, ± standard errors, followed by the probability, P, that the changes observed were due to chance.

<table>
<thead>
<tr>
<th>Heart rate</th>
<th>Cardiac output</th>
<th>Stroke volume</th>
<th>Mean arterial pressure</th>
<th>L.V. stroke work</th>
<th>Peripheral resistance</th>
<th>Circulation time</th>
<th>&quot;Central&quot; blood volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 patient on 0.5% halothane</td>
<td>+79</td>
<td>+28</td>
<td>-28</td>
<td>+36</td>
<td>+1</td>
<td>+8</td>
<td>-35</td>
</tr>
<tr>
<td>7 patients on 1% halothane</td>
<td>+74±7</td>
<td>+42±6</td>
<td>-18±5</td>
<td>+28±5</td>
<td>+5.4±5</td>
<td>-13±4</td>
<td>-32±3</td>
</tr>
<tr>
<td>2% halothane</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.02</td>
<td>&lt;0.01</td>
<td>&gt;0.3</td>
<td>&lt;0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Percentage difference</td>
<td>18</td>
<td>16</td>
<td>3</td>
<td>11</td>
<td>3.4</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>All 15 patients</td>
<td>+84±7</td>
<td>+48±6</td>
<td>-17±4</td>
<td>+24±4</td>
<td>+3.5±6</td>
<td>-17±1</td>
<td>-34±2</td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
<td>&gt;0.5</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&gt;0.6</td>
</tr>
</tbody>
</table>

**Effect on cardiac output.**

Compared with the initial values, cardiac output increased by 48 per cent in the period following the injection of atropine. This change is highly significant (P<0.001). The mean cardiac output in the four patients whose control dye curves were calibrated (Nos. 7, 13, 14, 15) was 2.43 l/min (SE±0.097).

Patients breathing 2 per cent halothane showed a mean increase of 58 per cent, while those who had 1 per cent halothane showed a mean increase of 42 per cent. This difference is not significant (P>0.1). Individual percentage changes are shown in figure 2.

**Effect on stroke volume.**

As a result of giving atropine, stroke volume fell by 17 per cent. This change is significant (P<0.01) and emphasizes the disparity between the cardiac rate and output responses to atropine. Only two patients showed an increase in stroke volume. Individual percentage changes are shown in figure 3.

**Effect on blood pressure.**

Mean arterial pressure began to rise when the heart rate increased. The mean value before giving atropine was 76 mm Hg (SE±2.8) and it rose to 93 mm Hg (SE±3.1) afterwards. This represented a highly significant increase of 24 per cent (P<0.001). Patients on 2 per cent halothane showed a mean increase of 17 per cent, while those on 1 per cent halothane showed an increase of 28 per cent. This difference is not significant (P>0.1). Figure 4 shows the individual changes.
CIRCULATORY EFFECTS OF ATROPINE

in mean arterial pressure, again expressed as percentages of the control values.

![Graph showing the effect of atropine on mean arterial pressure.](https://academic.oup.com/bja/article-abstract/39/3/226/239088)

Fig. 4

The effect of atropine on the mean arterial pressure. The control values are expressed as 100 per cent. Patients having 0.5 per cent (...) and 2 per cent (---) halothane.

**Effect on cardiac work.**

The work done by the heart has for convenience been expressed as the work done during each beat by the left ventricle, the left ventricular end-diastolic pressure being assumed to remain constant at 5 mm Hg. Left ventricular stroke work increased after giving atropine in eleven patients but in the other four it fell moderately. The mean increase in stroke work was 3.5 per cent (P>0.5) which is not statistically significant. Figure 5 shows the percentage changes in each patient.

![Graph showing the effect of atropine on left ventricular stroke work.](https://academic.oup.com/bja/article-abstract/39/3/226/239088)

Fig. 5

The effect of atropine on left ventricular stroke work. The control values are expressed as 100 per cent. Patients having 0.5 per cent (...) and 2 per cent (---) halothane.

**Effect on peripheral resistance.**

Total peripheral resistance fell in all but two of the patients after they received atropine. The mean fall was 17 per cent (P<0.001). The seven patients given 2 per cent halothane showed a significantly greater fall in peripheral resistance of 25 per cent (P<0.05) than those on 1 per cent halothane (13 per cent). Individual changes are shown in figure 6.

![Graph showing the effect of atropine on peripheral resistance.](https://academic.oup.com/bja/article-abstract/39/3/226/239088)

Fig. 6

The effect of atropine on peripheral resistance. The control values are expressed as 100 per cent. Patients having 0.5 per cent (...) and 2 per cent (---) halothane.

**Effect on the rhythmicity of the heart.**

In three of the fifteen patients the intravenous injection of atropine 0.6 mg was followed by an irregular cardiac rhythm detectable on the recorder tracing. The arrhythmias lasted for 2, 3½, and over 8 minutes respectively. They consisted in all cases of multiple extrasystoles but as electrocardiograms were not recorded their origin could not be determined.

**Effect on circulation time.**

The peak-to-peak circulation time was 23 seconds (SE ± 3.6) before giving atropine and it fell to 15 seconds (SE ± 2.2) afterwards, a decrease of 34 per cent. This fall is highly significant (P<0.001) but there was no significant difference between patients on different concentrations of halothane.

**Effect on “central” blood volume.**

“Central” blood volume fell in seven patients and rose in eight. The mean change was an increase of 2.79, which was not statistically significant (P>0.6). Patients who received 2 per cent halothane showed a mean increase of 12 per cent, whereas those on 1 per cent showed a fall of 5.6 per cent but the difference between these groups is not significant (P>0.1).
DISCUSSION

The purpose of this investigation was to determine the extent to which clinical anaesthesia employing halothane modifies the circulatory response to atropine. It has been established that atropine injected intravenously in a dose of 0.4–0.6 mg or more will cause an increase in heart rate in conscious subjects (Morton and Thomas, 1958). This increase in rate is the result of blocking the vagal nerve endings in the heart. In supine conscious subjects the increase in rate is accompanied by a proportional increase in cardiac output, with little change in the output per beat (Weissler, Leonard and Warren, 1957; Gravenstein, Andersen and De Padua, 1964). Arterial pressure rises and peripheral resistance falls (Jones, Deutsch and Turndorf, 1961; Gravenstein, Andersen and De Padua, 1964). The effect of atropine on the pulmonary circulation is less certain; Weissler, Leonard and Warren (1957) reported a 25 per cent increase in “central” blood volume in twelve subjects given 2 mg of atropine, but Daly, Ross and Behnke (1963), using a radioactive indicator technique, found a reduction in pulmonary blood volume with this dose and suggested that atropine caused a shift of blood from the pulmonary to the systemic circulation.

The effect of halothane on the circulation is almost the opposite to that of atropine. In the dog heart-lung preparation increasing concentrations of halothane depress both the rate and force of contraction of the heart (Flacke and Alper, 1962) and strain gauge studies by Mahaffey and his co-workers (1961) confirmed this effect in man. Etsten and Li (1960), however, thought that myocardial depression only occurred with high concentrations and that the fall of blood pressure commonly observed under clinical conditions was due to vasodilatation resulting from sympathetic depression. This agreed with the observations of Payne, Gardiner and Verner (1959) who found that cardiac output in fact rose slightly after induction of halothane anaesthesia. A more recent study by Deutsch and his group (1962), in which unpremedicated volunteers were anaesthetized with halothane, showed that cardiac output fell at first but later returned to the control level as a result of increases in heart rate. They observed sustained falls in stroke volume, blood pressure and peripheral resistance. While a fall in stroke volume is consistent with a reduction in myocardial contractility it is more likely to result from a reduction in venous return to the heart in the presence of an increase in heart rate. There has been no agreement about the cause of the vasodilatation which occurs with halothane. The principle theories favour either a direct effect on the vessel walls or else a paralysis of sympathetic vasomotor function. Etsten and Shimosato (1965) have suggested that halothane causes an adrenergic block by preventing catecholamine release. Recently, however, Price and Price (1966) appear to have resolved these inconsistencies by showing that in dogs the circulatory effects of halothane can be attributed to a combination of central autonomic paresis, ganglion block and suppression of the peripheral actions of noradrenaline.

Mahaffey and his group (1961) and Flacke and Alper (1962) noted that atropine was capable of reversing the bradycardia seen during deep halothane anaesthesia and of restoring cardiac output and blood pressure to light anaesthesia levels. In the investigation reported here the mean initial heart rate was 61 beats/min. Observations were made at a time when secondary bradycardia following hyoscine administration might have been expected (List and Gravenstein, 1965). Atropine caused tachycardia in all the patients; the rate suddenly quickened 15 to 30 seconds after it was given and increased up to a final level around 110 beats/min just over half a minute from the time of injection. This increase is of the same order as in the conscious subjects studied by Weissler, Leonard and Warren (1957) who were given 2 mg atropine. This suggests that the patients reported here showed a maximal response to atropine.

Morton and Thomas (1958) reported that the increase in rate was complete 2–3 minutes after the intravenous injection, without flushing, of large doses of atropine, while Craig and Cummings (1965) observed cardiac acceleration on average 1.3 minutes after giving 0.5 mg slowly over a period of 1 minute. As expected, the onset of acceleration was earlier in the present series in which the atropine was injected into a fast-flowing drip. The duration of the phase of acceleration was presumably related to the speed of injection but the time of onset of the tachycardia seemed to depend on the initial rate of circulation. There was no period of slowing detectable before the increase in
rate, in contrast to the findings of Jones, Deutsch and Turndorf (1961). In eight of their patients given atropine 0.4 mg under halothane-oxygen anaesthesia, there was a 3–6 second period of bradycardia before the rate increased. Munchow and Denson (1965), on the other hand, found that atropine rarely caused deceleration of the heart under light halothane anaesthesia.

Unlike the conscious subjects studied in previous investigations the increases in cardiac output seen in this series were not proportional to the changes in the heart rate. The 48 per cent mean increase in output was little more than half the change in rate (84 per cent) and there was a 17 per cent (mean) fall in stroke volume. Halothane is known to reduce both myocardial contractility and heart rate in man (Mahaffey et al., 1961; Theye and Tuohy, 1964), but only the change in rate appears to be reversible by atropine. Indeed, in two cases (both anaesthetized with halothane) reported by Theye and Tuohy, atropine 0.4 mg caused tachycardia without any increase in cardiac output. By contrast, two patients in the present study (Nos. 12 and 13 in table III) showed small increases in stroke volume. Nevertheless, these findings tend to confirm that atropine causes an increase in cardiac output mainly by increasing the heart rate. Halothane anaesthesia reduces the output response to atropine, while the rate response is relatively unimpaired.

In the eight patients on whom further observations were made after the peak effect was reached, the cardiac output was seen to fall again about 5 minutes after the atropine was given. In one patient (No. 1 in table III) who was studied 25 minutes after the atropine injection, the heart rate was still 59 per cent above the control level, while cardiac output was only increased by 14 per cent. It is tempting to postulate that initially the venous filling pressure was high (cf. Theye and Tuohy, 1964) but that it soon fell when the output increased. Atropine 2 mg caused a mean fall of 3.3 cm H₂O in central venous pressure in the series of Gorten and associates (1961) and the same dose lowered right atrial pressure in the subjects studied by Daly, Ross and Behnke (1963). Such a reduction of filling pressure would account for the secondary fall in cardiac output seen even while the tachycardia persisted. This hypothesis implies that there is a net shift of blood to the periphery which would be consistent with the reduction in peripheral resistance observed after giving atropine.

The observation of Payne (personal communication) that the blood pressure rose after the injection of atropine before the heart rate increased, was not confirmed. The 24 per cent increase in blood pressure appears to be due to the increase in cardiac output. The increase in pressure is, however, proportionately less than the increase in output and the difference is accounted for by the 17 per cent fall in peripheral resistance. Such a fall could be entirely passive and there may be no need to invoke circulatory reflexes to account for it. In the conscious subjects studied by Gravenstein, Andersen and De Padua (1964) a comparable increase in cardiac output was accompanied by a fall of about 30 per cent in peripheral resistance, the blood pressure remaining unchanged. This difference may be related to the low initial pressure (m.a.p. 76 ± 2.8 mm Hg) in the present group rather than to an effect of halothane on peripheral vessels. Patients given 2 per cent halothane showed a greater fall in resistance than those on 1 per cent, but this difference was not statistically significant.

As a result of the increase in output and the consequent rise in arterial pressure, the external work done by the heart every minute increased after atropine was given. Changes in stroke work were related to changes in stroke volume, increasing in patients who showed the least fall (or even a rise) in stroke volume, and vice versa. The calculation of left ventricular stroke work depends on the assumption that left ventricular end-diastolic pressure remains constant at 5 mm Hg. This is probably true of normal subjects and even if this figure were doubled the calculated left ventricular stroke work would only differ by 7 per cent.

As the average heart rate after atropine was 110 beats/min and the maximum rate 130, the shortening of diastole was not marked. The work done per stroke showed no significant overall change. The use of atropine is therefore unlikely to have impaired the metabolism of the heart.

There was a mean increase of 2.7 per cent in "central" blood volume which was not statistically significant. The large standard deviation of a single observation (see table I) suggests that this measurement is unreliable. This is perhaps not surprising considering that the temporal equiva-
lents of the injection and sampling sites embrace a large proportion of the total blood volume. The calculated mean “central” volume in four patients in whom the control dye curves were calibrated was 0.79 l. (SE ± 0.12) a surprisingly low figure. The present investigation does not reveal any significant change in central blood volume following the use of atropine.

Peak-to-peak circulation time was reduced from 23 seconds to 15 seconds after atropine was given. This time is not directly related to any of the other parameters measured and its principal value is to give an immediate estimate of any changes in cardiac output, to which it is inversely proportional.

Three of the fifteen patients developed arrhythmias after atropine was given. This is a frequent observation (Eger, 1962) although less common than in patients receiving cyclopropane. In five of the twelve patients under halothane/oxygen anaesthesia studied by Jones, Deutsch and Turndorf (1961) electrocardiographic irregularities followed the injection of 0.4 mg atropine. On the other hand, atropine may convert pre-existing A-V nodal rhythm back into sinus rhythm and Payne (personal communication) has observed that the increase in rate is very large in these circumstances. It is difficult to say whether these transient arrhythmias are dangerous but they are certainly an indication for further checking of a patient’s circulatory state.

CONCLUSIONS
Atropine consistently increased heart rate, blood pressure and cardiac output during halothane anaesthesia. The increases in cardiac output and blood pressure were much less, both in degree and duration, than the increase in heart rate. Stroke volume fell and the work done by the heart at each beat increased slightly. Part of the increase in cardiac output was accommodated by a passive reduction in total peripheral resistance, although the increase in blood pressure was greater than that seen in conscious subjects. Atropine caused a considerable reduction in circulation time. No final conclusion could be made about the effect on the pulmonary circulation but no significant change in “central” blood volume was observed. Three patients developed transient arrhythmias after the atropine was injected.

ACKNOWLEDGMENTS
I wish to thank Professor W. W. Mushin, Dr. W. W. Mapleson and Mr. E. K. Hillard for their valuable help and encouragement in this work.

REFERENCES


CIRCULATORY EFFECTS OF ATROPINE


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