EFFECT OF MORPHINE AND ETHER UPON CARDIOVASCULAR FUNCTIONS IN THE DOG

ESTHER M. GRESHEIMER, PH.D., M.D., DOROTHY W. ELLIS, A.B.
GEORGE H. STEWART, B.S., LYDIA MAKARENKO

The cardiovascular effects of ether without preanesthetic agents have been reported (1).

The purpose of the present investigation was to determine the change in the above effects due to the subcutaneous administration of morphine sulfate (3 mg./kg.) about 50 minutes before the inhalation of ether was begun. This dose was selected on the basis of personal experience, as it tranquilizes the dogs without depressing respiratory functions. Although this dose seems exceedingly large when compared with the human sedative dose, it is smaller than that used by many investigators. Schmidt and Livingston (2) described a small dose up to 10 mg./kg. and a moderately large dose between 75 and 100 mg./kg. Doses of 20 to more than 100 mg./kg. have been used (3-6). Issekutz (7) used a dose identical with ours.

METHOD

Mongrel dogs were used. Morphine was injected subcutaneously. After the usual response (vomiting, defecation, or both) was completed a sample of blood was drawn to serve as a nitrogen blank for ether determinations. Then a tracheal cannula was inserted under local anesthesia (2 to 3 cc. of 2.0 per cent procaine hydrochloride, intradermally).

About fifty minutes after administration of morphine the inhalation of ether was begun. The bag of the anesthesia machine (Heidbrink, Kinet-O-Meter) was filled with oxygen and the ether gauge set between 6 and 8 before the tubes were connected with the tracheal cannula. As soon as the excitement stage was over and relaxation noted, the bag was flushed, refilled with oxygen and the ether gauge turned to 1 or 2. Only if the animal stirred was the gauge turned higher temporarily. The flow of oxygen varied from 100 to 200 cc./min., according to the size of the dog. Freshly opened anesthetic ether was used in each experiment, and the soda lime was changed frequently.

The left external jugular vein was catheterized for injection of dye (T-1824). The left femoral artery was connected with the cuvette oximeter and strain gauge by means of an indwelling needle. When

Accepted for publication August 20, 1936. The authors are in the Departments of Physiology and Medical Physics, Temple University School of Medicine, Philadelphia 40, Pennsylvania.
not recording, 0.9 per cent sodium chloride containing 0.1 mg. per cent of liquaemin (heparin) was permitted to drip slowly into the artery from a pressure bottle.

The method of recording, injecting dye, calibrating the cuvette, and measuring the dye curves for cardiac output has been described in detail by Nicholson and Wood (8). This method was used by the authors.

Details of the method used for determination of ether concentration in blood have been described (1).

Electrocardiographic tracings were recorded, using lead II.

Six successive determinations of cardiovascular functions were made on each animal within one-half to two hours after ether administration was begun.

RESULTS

Sixty determinations were made on 10 dogs. The range of cardiac index was 2.26–8.76, with a mean of $4.70 \pm 0.25$ l./m.$^2$/min. The standard deviation was 1.94.

The range of systolic blood pressure was 135–194, with a mean of 168 mm. of Hg. The range of diastolic blood pressure was 44–101, with a mean of 66 mm. of Hg. The range of mean blood pressure was 74–131, with a mean of $100 \pm 1.66$ mm. of Hg. The standard deviation was 13.08.

The range of total peripheral resistance was 1,265 to 7,425, with a mean of $3417 \pm 212$ dynes/sec./cm.$^{-2}$. The standard deviation was 1,641. By Bazett's formula the range was 28–174, with a mean of 77.

The range of heart rate was 87–207, with a mean of 138 beats per minute, counted on the electrocardiograms.

The range of stroke index was 14–62, with a mean of 33 cc./beat/m.$^2$.

The range of ether concentration in arterial blood was 0.68–2.29, with a mean of 1.53 cc./liter. In terms of milligrams per cent the range of concentration of ether was 47–159, with a mean of $106 \pm 13.7$, and a standard deviation of 35.1.

No cardiac irregularities were noted in any of the dogs.

In order to test the variability of cardiovascular functions a series of 6 successive determinations was made on each dog, at approximately 10-minute intervals. The means found for the 10 dogs on successive determinations are presented in table 1.

The following differences were found between the means of the first (after 43 minutes under ether) and of the sixth (after 92 minutes under ether) series of determinations. The cardiac index increased, the systolic blood pressure rose, the diastolic pressure fell, and the mean blood pressure fell. The peripheral resistance (absolute units) decreased, the heart rate increased, and the stroke index increased. During this interval the concentration of ether in arterial blood rose 2.1 per cent.
DISCUSSION

When the results of these 60 observations on 10 dogs under morphine sulfate and ether were compared with 72 observations on 12 dogs * under ether alone the following differences were noted.

The ranges of cardiac index, total peripheral resistance and stroke index were slightly greater in the present series than in the series with ether alone.

The ranges of systolic blood pressure, diastolic blood pressure, mean blood pressure and heart rate were smaller in the present series than with ether alone.

**TABLE 1**

RESULTS OF A SERIES OF 6 SUCCESSIVE DETERMINATIONS OF CARDIAC OUTPUT

<table>
<thead>
<tr>
<th>Dye Curve</th>
<th>Number of Dogs</th>
<th>Cardiac Index (l/min./m²)</th>
<th>Blood Pressure (mm. Hg)</th>
<th>Peripheral Resistance</th>
<th>Heart Rate (beats./ min.)</th>
<th>Stroke Index (cc./beat/m²)</th>
<th>Ether Concentration</th>
<th>Duration of Anesthesia (min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>4.00</td>
<td>167 70 102</td>
<td>4126</td>
<td>94</td>
<td>137</td>
<td>29</td>
<td>1.49 103.4</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>4.33</td>
<td>170 68 102</td>
<td>3717</td>
<td>84</td>
<td>139</td>
<td>31</td>
<td>1.56 108.7</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>4.63</td>
<td>168 66 100</td>
<td>3467</td>
<td>79</td>
<td>138</td>
<td>33</td>
<td>1.56 108.7</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>5.10</td>
<td>167 63 97</td>
<td>3049</td>
<td>69</td>
<td>138</td>
<td>36</td>
<td>1.52 105.6</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>4.94</td>
<td>169 64 99</td>
<td>3198</td>
<td>72</td>
<td>138</td>
<td>34</td>
<td>1.51 104.8</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>5.23</td>
<td>169 65 100</td>
<td>2943</td>
<td>66</td>
<td>139</td>
<td>37</td>
<td>1.52 105.6</td>
</tr>
</tbody>
</table>

Taking the results of the series with ether alone as the control, the addition of morphine led to the following differences in mean values.

Cardiac index was 1.1 per cent higher, the systolic blood pressure was 13.4 per cent lower, the diastolic blood pressure was 28.3 per cent lower, the mean blood pressure was 20.6 per cent lower, the total peripheral resistance was 1.0 per cent higher, the heart rate was 23.7 per cent lower, the stroke index was 26.9 per cent higher, and the concentration of ether was 25.3 per cent lower.

In the series with ether alone, the correlation coefficient between ether concentration in arterial blood and cardiac index was −0.015 ± .079. In the present series, the correlation coefficient between ether concentration in arterial blood and cardiac index was +0.49 ± .07, which indicates a slight relationship between the two. One cannot say, however, that the concentration of ether in the blood is a major factor in determining the cardiac output.

* There were 12 dogs in the earlier series (1) on each of which 6 satisfactory successive determinations were completed.
The change in each cardiovascular function under ether when morphine was used as a preanesthetic agent was less marked than when ether alone was used as shown in table 2.

The effects of ether and of morphine on the cardiac output were reviewed in references 1 and 9 respectively.

### TABLE 2

**Cardiovascular Functions with Ether and Morphine and Ether Alone**

<table>
<thead>
<tr>
<th>Function</th>
<th>Ether after Morphine (43-92 minutes after ether administration was begun)</th>
<th>Ether Alone (22-50 minutes after ether administration was begun)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac index</td>
<td>+30.7%</td>
<td>+70.1%</td>
</tr>
<tr>
<td>Systolic</td>
<td>+ 1.2%</td>
<td>+ 0.5%</td>
</tr>
<tr>
<td>Diastolic</td>
<td>- 7.1%</td>
<td>- 12.7%</td>
</tr>
<tr>
<td>Mean</td>
<td>- 2.9%</td>
<td>- 8.3%</td>
</tr>
<tr>
<td>Peripheral resistance</td>
<td>-28.7%</td>
<td>-41.1%</td>
</tr>
<tr>
<td>Heart rate</td>
<td>+ 1.4%</td>
<td>- 0.1%</td>
</tr>
<tr>
<td>Stroke index</td>
<td>+27.6%</td>
<td>+68.4%</td>
</tr>
</tbody>
</table>

### SUMMARY

Several cardiovascular functions were observed in dogs under morphine and ether. The results were compared with those observed in dogs under ether, without morphine as a preanesthetic agent.

The most striking differences were (1) the lower systolic and diastolic blood pressure, (2) the slower heart rate, and (3) the greater stroke index when morphine was administered before ether. The cardiovascular functions were steadier when morphine was used as a preanesthetic agent before ether.

### REFERENCES