The Adrenal Gland and the Cardiovascular Changes in Acute Anoxic Anoxia in Dogs

By C. W. BAUGH, M.D., R. W. CORNETT, M.D., AND J. D. HATCHER, M.D.

The hyperkinetic circulatory state observed in intact anesthetized dogs at the end of a 15 minute period of breathing 6 per cent oxygen in nitrogen was absent in a similar series of dogs acutely adrenalectomized by the ligation technic. Blood removed from intact animals at the end of the anoxic period and infused into normal assay dogs produced a rise in cardiac output in the latter which was not observed with comparable infusions of normal blood or blood removed from adrenalectomized anoxic dogs. The transferable agent demonstrated by this study is considered responsible for the rise in cardiac output in the anoxic donor. It is suggested that this agent arises from the adrenal medulla.

There is disagreement concerning the mechanism responsible for the elevated cardiac output in acute anoxic anoxia. Some investigators1-3 have suggested that the rise in cardiac output is secondary to a decrease in total peripheral resistance, which results in turn from a direct vasodilating action of anoxia on peripheral vessels. Nahas and colleagues4 have presented evidence that adrenaline, which is known to be released during acute periods of anoxia,5, 6 is responsible for the rise in cardiac output. However, this view is opposed to the previous findings of Harrison and co-workers.7

This communication deals with changes in cardiac output and related indexes in intact and adrenalectomized dogs breathing 6 per cent oxygen in nitrogen. In addition, assays comparable to those previously reported in a study of anemic anoxia8 were done in which the cardiovascular effects produced in normal dogs by infusions of blood removed from these anoxic donors were observed.

Method

All dogs were anesthetized with sodium pentobarbital. An initial dose of 30 mg./Kg. was given intravenously, followed by 60-120 mg. (total dose) intramuscularly every one to two hours as necessary. Measurements were begun two to two and one half hours after the initial dose of anesthetic. Six per cent oxygen in nitrogen was administered for 7 to 35 min. to 32 intact donor dogs, and for 5 to 22 min. to 15 adrenalectomized donor dogs. Measurements and calculations (described below) were made in the anoxic donors before and at the end of the period of anoxia, and in normal assay dogs before and immediately after the infusion of blood obtained from the anoxic donor.

The cardiac output was measured by the direct Fick technic. The oxygen content of mixed venous blood, obtained from the right ventricle, and of peripheral arterial blood, was measured by the Van Slyke-Neill manometric procedure. A Donald-Christie apparatus9 was used to administer the low oxygen mixture at atmospheric pressure and to measure the oxygen consumption of donor dogs while breathing 6 per cent oxygen. Other determinations of oxygen consumption were made with a Benedict-Roth spirometer containing pure oxygen. Right ventricular and systemic arterial pressures were recorded with a Sunborn electromanometer and a direct-writing recorder. The heart rate was counted from the pressure tracing. Calculations of stroke volume and total systemic resistance were made.

Ten control experiments were done in which intact dogs breathed room air instead of 6 per cent oxygen from the Donald-Christie apparatus for 30 min.

Adrenalectomy was performed in two stages. One or two days prior to the experiment the right adrenal gland was removed, and a loose ligature was placed about the vessels leading to and from the left adrenal gland. The free ends of the ligature were passed through the abdominal wall. Adrenalectomy was completed by tightening the ligature at the moment the animals started to breathe the low oxygen mixture. A necropsy was done in each case to check the adequacy of the ligation. In three instances an incomplete ligature was found, and these results are considered together...
TABLE 1.—Statistical Summary of Donor Data

<table>
<thead>
<tr>
<th>Per cent change in:</th>
<th>A-V O₂ diff.</th>
<th>O₂ cons.</th>
<th>Cardiac output</th>
<th>Stroke vol.</th>
<th>Satur. arterial blood</th>
<th>Satur. mixed ven. blood</th>
<th>Utilie. arter. O₂</th>
<th>Arterial pressure</th>
<th>Heart rate</th>
<th>Resp. rate</th>
<th>Arter. hematocrit</th>
<th>Change in r. ventr. pressure</th>
</tr>
</thead>
</table>

Cardiovascular changes in 10 normal dogs breathing room air from Donald-Christie apparatus for 30 min.

A. Cardiovascular changes in 6 anoxic dogs with ligation of mesenteric vessels and 3 anoxic dogs with unsuccessful ligation of adrenal vessels (average duration of anoxia, 16.1 min., range 12-25 min.).

B. Cardiovascular changes in 6 anoxic dogs with measurement of mesenteric vessels and 3 anoxic dogs with unsuccessful ligation of adrenal vessels (average duration of anoxia, 16.1 min., range 12-25 min.).

C. Cardiovascular changes in 27 intact anoxic dogs (average duration of anoxia, 14.2 min., range 7-22 min.).

D. Cardiovascular changes in 9 adrenalectomized anoxic dogs (average duration of anoxia, 14.0 min., range 7-22 min.).
with a control group of 6 dogs in which a ligature
previously placed about a branch of the superior
mesenteric artery near the posterior attachment of
the mesentery was tightened at the moment the
dogs began to breathe the anoxic mixture.

Blood for assay was collected within 60 to 90
seconds after the final measurements were made
in the anoxic donors, while these dogs were still
breathing the anoxic mixture. In a few instances
artificial respiration was required during the col-
lection of blood for assay. Infusion of this blood
at 0.5 ml./Kg./min. was begun within 10 min.
after collection. The total volume infused was
equal to 20 per cent of the calculated blood
volume (based on 90 ml. of blood/Kg.) of the as-
say dog. Only one assay was done with blood from
each donor.

Control experiments were carried out by infus-
ing normal dogs at 0.5 ml./Kg./min. with similar
volumes of blood obtained from normal dogs. The
significance of changes produced by infusion of
normal blood has been reported previously. 8

All infusions were given by syringe through a
cardiac catheter into the right atrial area. Heparin
was used as the anticoagulant. Neither microscopic
nor “clinical” evidence of blood group incompati-
bility was observed during any of the experiments
reported.

RESULTS

Donors. Among 32 intact dogs subjected
to anoxia for 7 to 38 minutes (average 20
min.) there were five deaths after 6 to 25
min. (average 17.2 min.) of anoxia. Among
15 adrenalectomized dogs subjected to anoxia
for 5 to 22 min. (average 14) six deaths oc-
curred after 5 to 22 min. of anoxia (average
11.5). Final measurements were not obtained
in the animals which died. Thus the death
rate in adrenalectomized dogs was 37.5 per
cent with an average duration of anoxia of
14 min., which is to be compared with the
death rate in intact dogs of 16.2 per cent
after an average of 20 min. of anoxia.

In 14 of the 27 surviving intact dogs the
duration of anoxia was comparable to that
in the 9 surviving adrenalectomized anoxic
dogs (7 to 22 min.). A statistical summary
is given in table 1 for this subgroup of 14
and for the total group of 27 intact anoxic
dogs.

The degree of anoxia produced in the 14
intact and 9 adrenalectomized anoxic dogs
was the same, since the percent saturations
of arterial and mixed venous blood samples
were comparable in both groups at the end
of the anoxic period.

Statistical comparisons have been made
between the intact group of 14 anoxic dogs
and the control group breathing room air
(p in table 1, D). In the group of 14
anoxic dogs there was a rise in cardiac out-
put which was associated with a fall in
arteriovenous oxygen difference and in total
systemic resistance. The oxygen consumption
remained unchanged. Significant increases
were also recorded in the per cent utilization
of arterial oxygen, hematocrit, systolic ar-
terial pressure and right ventricular systolic
and mean pressures. The increase in stroke
output and heart rate noted at the end of
the anoxic period lacked statistical signi-
ficance (p = 0.08 and 0.06 respectively).
However, a minute-to-minute analysis showed
a maximum and significant increase in heart
rate (p less than 0.01) from the fourth to the
twelfth minute of anoxia, after which the
heart rate began to decline.

A similar comparison has been made be-
tween the 9 adrenalectomized anoxic dogs
TABLE 2.—Statistical Summary of Assay Data

<table>
<thead>
<tr>
<th>Percent change in:</th>
<th>A-V O₂ diff.</th>
<th>O₂ cons.</th>
<th>Cardiac output</th>
<th>Stroke vol.</th>
<th>Mean arter. bl. pressure</th>
<th>Tot. periph. resist.</th>
<th>Heart rate</th>
<th>Change in r. vent. end diastol. pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Cardiovascular effects of infusion of normal blood at 0.5 ml./Kg./min. in 12 dogs</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mean</td>
<td>+13.8</td>
<td>+ 0.4</td>
<td>− 4.3</td>
<td>+ 3.7</td>
<td>+ 8.3</td>
<td>+24.0</td>
<td>− 8.0</td>
<td>+ 1.7</td>
</tr>
<tr>
<td>S.D.</td>
<td>±33.4</td>
<td>± 6.5</td>
<td>±27.0</td>
<td>±30.8</td>
<td>± 6.9</td>
<td>±42.3</td>
<td>± 7.9</td>
<td>± 1.9</td>
</tr>
<tr>
<td>S.E.M.</td>
<td>± 9.7</td>
<td>± 1.9</td>
<td>± 7.8</td>
<td>± 8.9</td>
<td>± 2.0</td>
<td>±12.2</td>
<td>± 2.3</td>
<td>± 0.5</td>
</tr>
<tr>
<td>B. Assays of blood obtained from 11 intact anoxic dogs (infusion rate 0.5 ml./Kg./min., duration of donor anoxia 7-22 min.)</td>
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<tr>
<td>(1) Ten assays showing type 1 response</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>−32.4</td>
<td>+ 2.1</td>
<td>−58.0</td>
<td>+71.5</td>
<td>+ 9.3</td>
<td>−27.2</td>
<td>−12.7</td>
<td>+ 0.4</td>
</tr>
<tr>
<td>S.D.</td>
<td>±16.0</td>
<td>± 9.5</td>
<td>±34.0</td>
<td>±29.6</td>
<td>±10.2</td>
<td>±21.2</td>
<td>± 9.7</td>
<td>± 3.3</td>
</tr>
<tr>
<td>S.E.M.</td>
<td>± 5.1</td>
<td>± 3.0</td>
<td>±10.8</td>
<td>± 9.4</td>
<td>± 3.2</td>
<td>± 6.7</td>
<td>± 3.1</td>
<td>± 1.1</td>
</tr>
<tr>
<td>( p_1 )</td>
<td>&lt; 0.01</td>
<td>&gt; 0.5</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&gt; 0.5</td>
<td>&lt; 0.01</td>
<td>0.21</td>
<td>0.27</td>
</tr>
<tr>
<td>(2) One assay showing type 2 response</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mean</td>
<td>+118.7</td>
<td>—</td>
<td>—</td>
<td>—43.3</td>
<td>—</td>
<td>−20.7</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>C. Assays of blood obtained from 19 intact anoxic dogs (infusion rate 0.5 ml./Kg./min., duration of donor anoxia 7-36 min.)</td>
<td></td>
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<tr>
<td>(1) 16 assays showing type 1 response</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Mean</td>
<td>−22.4</td>
<td>+ 5.0</td>
<td>+44.4</td>
<td>+61.4</td>
<td>+ 8.8</td>
<td>−19.5</td>
<td>−13.8</td>
<td>+ 0.6</td>
</tr>
<tr>
<td>S.D.</td>
<td>±23.7</td>
<td>± 9.0</td>
<td>±35.3</td>
<td>±31.8</td>
<td>± 8.7</td>
<td>±25.2</td>
<td>± 8.8</td>
<td>± 3.1</td>
</tr>
<tr>
<td>S.E.M.</td>
<td>± 5.9</td>
<td>± 2.2</td>
<td>± 8.8</td>
<td>± 8.0</td>
<td>± 2.2</td>
<td>± 6.3</td>
<td>± 2.2</td>
<td>± 0.8</td>
</tr>
<tr>
<td>( p_1 )</td>
<td>&lt; 0.01</td>
<td>&gt; 0.5</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&gt; 0.5</td>
<td>&lt; 0.01</td>
<td>0.09</td>
<td>0.29</td>
</tr>
<tr>
<td>(2) Three assays showing type 2 response</td>
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<tr>
<td>Mean</td>
<td>+90.2</td>
<td>−39.4</td>
<td>−56.9</td>
<td>−43.5</td>
<td>−47.0</td>
<td>+60.2</td>
<td>− 8.7</td>
<td>− 0.7</td>
</tr>
<tr>
<td>D. Assays of blood from 10 adrenalectomized anoxic dogs (infusion rate 0.5 ml./Kg./min., duration of donor anoxia 7-22 min.)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>+10.7</td>
<td>− 2.0</td>
<td>− 5.0</td>
<td>+14.2</td>
<td>+ 9.3</td>
<td>+21.9</td>
<td>−15.6</td>
<td>+ 2.4</td>
</tr>
<tr>
<td>S.D.</td>
<td>±36.0</td>
<td>± 7.6</td>
<td>±28.8</td>
<td>±18.0</td>
<td>± 8.2</td>
<td>±32.8</td>
<td>± 4.6</td>
<td>± 2.2</td>
</tr>
<tr>
<td>S.E.M.</td>
<td>±11.4</td>
<td>± 2.4</td>
<td>± 7.5</td>
<td>± 9.8</td>
<td>± 2.6</td>
<td>±10.4</td>
<td>± 1.5</td>
<td>± 0.7</td>
</tr>
<tr>
<td>( p_1 )</td>
<td>&lt; 0.5</td>
<td>&gt; 0.5</td>
<td>&gt; 0.5</td>
<td>0.45</td>
<td>&gt; 0.5</td>
<td>&gt; 0.5</td>
<td>0.017</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>( p_2 )</td>
<td>&lt; 0.01</td>
<td>0.30</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&gt; 0.5</td>
<td>&lt; 0.01</td>
<td>0.40</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Values given are an average of those obtained at the end of the infusion expressed as a per cent change from those obtained immediately before the infusion was begun.

\( p_1 \) = significance of change as compared with control group infused with normal blood.

\( p_2 \) = significance of change as compared with group of assays of blood obtained from intact anoxic donors.

Average weight of dogs in A was 12.5 Kg.; in B, 13.3 Kg.; in C, 12.6 Kg.; in D, 11.7 Kg.

and the control group breathing room air (\( p_1 \) in table 1, E). In the adrenalectomized anoxic group there was a significant decrease in oxygen consumption that was associated with a smaller and statistically insignificant decrease in arteriovenous oxygen difference. Thus there was no significant change in cardiac output. The per cent utilization of arterial oxygen was increased. No significant changes were noted in stroke volume, heart rate, total systemic resistance, hematocrit, arterial or right ventricular pressures. The absence of the hyperkinetic circulatory state in the adrenalectomized anoxic dogs was not due to the ligation per se, since the ligature control group (table 1, B) responded to anoxia in the same way as the intact anoxic group.

A further statistical comparison was made between the 14 intact anoxic donors and the 9 adrenalectomized anoxic donors (\( p_2 \) in table 1, E). Significant differences in response were observed for arteriovenous oxygen difference, oxygen consumption, cardiac output, total systemic resistance, and arterial hematocrit. The differences in response in arterial systolic pressure and right ventricular systolic pressure and heart rate bordered...
on statistical significance. When the changes in heart rate between the fourth and twelfth minutes of anoxia in the two anoxic groups are compared, the increase in heart rate in the intact group is statistically different from the lack of significant rise in heart rate in the adrenalectomized group.

**Assays.** As in assays done previously with blood from anemic donors, the present assay results are grouped according to changes observed in cardiac output and mean arterial pressure, as shown in table 2.

Nineteen assays were done with blood from intact anoxic donor dogs and the results are summarized in table 2, C. In 11 of the 19 assays the duration of anoxia in the corresponding donors ranged between 7 and 22 min. (average 14.2), which was the same as for the adrenalectomized anoxic donors; these 11 assays are summarized in table 2, B. Ten of the 11 assays showed a type 1 response characterized by a rise in cardiac output and an unchanged or increased mean arterial pressure. This rise in cardiac output averaged 58 per cent as compared with a 4.3 per cent decrease following infusions of normal blood (table 2, A). Stroke volume was also significantly increased. The rise in cardiac output was associated with a decrease in arteriovenous oxygen difference and in total systemic resistance. Changes in oxygen consumption, heart rate, mean arterial pressure and right ventricular end diastolic pressure were not significantly different from the changes noted with infusions of normal blood (table 2, A). Stroke volume was also significantly increased. The rise in cardiac output was associated with a decrease in arteriovenous oxygen difference and in total systemic resistance. Changes in oxygen consumption, heart rate, mean arterial pressure and right ventricular end diastolic pressure were not significantly different from the changes noted with infusions of normal blood (table 2, A). In one of the 11 assays a type 2 response similar to that described for some assays of anemic blood was indicated by a marked fall in blood pressure. An unsatisfactory measure of oxygen consumption was obtained, but the increased arteriovenous oxygen difference suggests that the cardiac output fell. The heart rate decreased and the right ventricular end diastolic pressure remained unchanged.

Assays were done with blood removed from 8 intact donor animals in which the duration of anoxia exceeded 22 min. In 6 cases a type 1 response was observed and in 2 cases a type 2 response was noted. A statistical summary of the total of 16 type 1 and of 3 type 2 responses is shown in table 2, C. When all 19 assays of blood from intact anoxic donors are pooled and statistically analyzed, there is still a significant increase \( p < 0.01 \) in cardiac output of 33.2 per cent ± 11.2.

Ten assays were done with blood from adrenalectomized anoxic donors. The increase in cardiac output and stroke volume and the decrease in arteriovenous oxygen difference and total peripheral resistance most frequently encountered in assays of blood from intact anoxic donors were not seen in the 10 assays done with blood from adrenalectomized anoxic donors (table 2, D). Except for a greater decrease in heart rate, the results observed were comparable to the effects of infusions of normal blood (table 2, A).

**DISCUSSION**

The cardiovascular responses to anoxia in intact dogs are comparable to those reported by other investigators. Adrenalectomy carried out just prior to the anoxic period either prevented or moderated the rise in cardiac output, hematocrit, respiratory rate, heart rate, and arterial and right ventricular systolic pressures, and the fall in arteriovenous oxygen difference and total peripheral resistance.

The suggestion that the rise in cardiac output during acute anoxia is secondary to a decrease in total peripheral resistance referable to the direct vasodilating action of anoxia on peripheral vessels is not supported by these experiments, since the severity of the anoxia revealed by blood oxygen saturations was similar in both groups. However, it should be pointed out that the oxygen consumption fell in the adrenalectomized anoxic group, whereas in the intact anoxic dogs the oxygen consumption did not change. Although this difference was significant only at a 0.058 level, it may be that the low tissue oxygen tension in operated anoxic dogs has less effect as a stimulus when viewed in terms of tissue metabolism.
The fact that a rise in cardiac output observed in intact anoxic dogs is not present in adrenalectomized anoxic dogs is in agreement with the findings of Nahas and co-workers who used unanesthetized dogs, and is opposed to the earlier studies of Harrison and colleagues who used anesthetized intact dogs and anesthetized adrenalectomized dogs.

Nahas and colleagues suggested that the adaptive mechanism involved in their studies of acute anoxic anoxia in chronically adrenalectomized dogs might already be working at a maximum and was incapable of further adaptation because of the presence of an anemia in their animals. However, in the experiments reported here no anemia was present, the control hematocrit in the adrenalectomized series being 55.8 ± 2.8 per cent red cells. Harrison and co-workers made their experiments a few hours after acute surgical removal of both glands, or by tightening ligatures placed about the lumbar adrenal veins a few hours before experiment. They found that if the animals were not in shock the cardiac output rose during anoxia. In the studies reported here no evidence of shock was noted; the control cardiac output and mean arterial pressure in the adrenalectomized group just prior to tightening the ligature were 2.14 ± 0.30 L/min. and 112 ± 8.5 mm. Hg respectively, and the ligation produced no hypotension. Furthermore, Cannon had previously emphasized that adrenalectomy could only be assured by a more complete ligation than that used by Harrison and co-workers.

Other investigators have studied the role of cardiac sympathetic nerves in the cardiac response to acute anoxia, with conflicting results. Since in the present experiments the cardiac output rise in anoxia was abrogated by adrenalectomy, it seems likely that no important role need be assigned these nerves in the anoxic response of the heart.

The results show that blood obtained from anoxic dogs and infused into normal dogs produced cardiovascular changes which are statistically different from the effects observed with comparable infusions of normal blood. The changes in the assay dog are considered due to some transferable agent in the blood of the anoxic donor dog, and it is implied that this agent is responsible for the elevation in cardiac output in the intact dog made acutely anoxic. However, there is no quantitative correlation between the type and degree of positive assay response and any measured change in the intact anoxic donor. This is not unexpected, since each assay and donor dog was different and was subject to biologic variations in response.

Similarities between the type 1 assay response and the changes observed in anoxic anoxia suggest that the type 1 response is the physiologic response of the normal dog to the active agent, whereas the type 2 response is an unfavorable homeostatic change when considered in relation to compensatory adjustments during anoxia, and might be caused by high concentrations of some agent.

The results of assays of blood from dogs with anoxic and anemic anoxia are qualitatively similar. However, there is no reason to assume that the transferable agent is the same in each case, especially when one considers the nonspecific nature of the assay response. The mechanisms of action of the agent in the assay dog are not known, but evidence can be found for a direct myocardial action and/or a direct or indirect effect on peripheral vessels. In this regard Beyne found a vasodilatation in the isolated dog leg perfused with anoxic blood.

The transferable humoral agent demonstrated in the blood of intact anoxic dogs that is capable of increasing the cardiac output of assay dogs is not demonstrated in the blood of adrenalectomized anoxic dogs. These assay results, together with the results in the donor dogs, suggest that the humoral agent is either produced in the adrenal gland or requires the presence of adrenal secretions for its production, release, or activation. In this respect we tend to favor the explanation that the humoral agent arises from the adrenal gland, and specifically from the adrenal medulla, for the following reasons.
ADRENAL GLAND DURING ANOXIA

It is known that the blood levels of catechols are increased in anoxia of this degree and duration, and that infusions of adrenaline into dogs will produce most of the cardiovascular changes seen in intact anoxic dogs and in assays of blood from these dogs. The effects on cardiac output of infusions of noradrenaline in anesthetized dogs are still controversial. Until this controversy is settled, and if medullary hormones are involved, we would favor adrenaline rather than noradrenaline as the main agent responsible for at least the cardiac output response in donor and assay dogs.

There is no evidence that adrenal corticoid levels are increased during short periods of severe anoxia in man and animals. However, one could argue that at least a normal rate of elaboration of adrenal corticoids during short periods of anoxia was important, in view of the potentiating effects these hormones have on the vascular reactivity to various pressor agents. Although in certain doses some corticoids appear to have a cardiotonic action, the increase in amplitude (but not the rate) caused by adrenaline in the perfused guinea pig and rat heart is not augmented by corticoids. Furthermore, it is generally held that adrenal corticoids can persist for some time after bilateral adrenalectomy, and Remington has shown that no significant change occurs in stroke index during the first two hours after bilateral adrenalectomy, although within the first 2 hours after operation a decrease in blood pressure and an increase in heart rate occur. Finally, Nahas and colleagues found that adrenalectomized dogs maintained on cortisone and D.C.A. did not increase their cardiac output during severe anoxia of 3 to 5 min. duration. The possibility that the adrenal glands are indirectly involved in the production, release, or activation of some other agent involves speculation unwarranted at this time.

SUMMARY

Anoxic anoxia induced in intact anesthetized dogs with 6 per cent oxygen in nitrogen for 15 min. produced a rise in cardiac output, stroke volume, heart rate, respiratory rate, hematocrit and arterial systolic and right ventricular systolic and mean pressures, and a fall in arteriovenous oxygen difference and total peripheral resistance. These changes were prevented or moderated in a similar series of acutely adrenalectomized (ligation technic) dogs, in which the degree of oxygen desaturation of arterial and mixed venous blood was comparable to that produced in intact anoxic dogs.

Blood removed from intact anoxic dogs and infused into normal assay dogs at 0.5 ml./Kg./min. produced a significant rise in cardiac output in the assay dog, a rise which was associated with a decrease in arteriovenous oxygen difference and an unchanged oxygen consumption and arterial pressure. No rise in cardiac output is seen in assay dogs similarly infused with normal blood or blood removed from acutely adrenalectomized anoxic dogs.

It is suggested that the transferable agent demonstrated is responsible for the cardiac output elevation and for many of the other cardiovascular changes in acute anoxic anoxia. The possibility that the agent arises from the adrenal medulla is discussed.

SUMMARIO IN INTERLINGUA

Anoxia anoxic, induce in intacte anesthesiate canes per medio de 6 pro cento de oxygeno in nitrogeno durante 15 minutas, produceva augmentos del rendimento cardiace, del volumine per pulso, de frequentia cardiace, del frequentia respiratori, del hematocterite, del tension systolic arterial, del tension systolic dextero-ventricular, e del tension medie e reductiones del differentia arterio-venose de oxygeno e del resistentia total peripheric. Iste alterationes esseva prevente o moderate in un simile serie de canes, acutemente adrenalectomisate per le technica a ligation, in que le grado de dissaturation oxygenic de sanguine arterial e de sanguine venose mixte esseva comparabile a illo producute in intacte canes anoxic.
Sanguine obtenite ab intacte canes anoxie e infusionate in normal canes de essayo a 0,5 ml/kg/min produceva un significative augmento del rendimento cardiac in association con un reduction del differentia arterio-venose de oxygeno e non-alterate consumption de oxygeno e non-alterate tension arterial. Nullo augmento del rendimento cardiac es notate in canes de essayo similemente infusionate con sanguine normal o con sanguine obtenite ab acutemente adre-nalectomisate canes anoxie.

Es stipulate que le transferibile agente assi demonstrate es responsabile pro le augmento del rendimento cardiac e pro multes del altere alterationes cardiovascular que occurre in acute anoxia anoxic. Es discutite le possibilitate che le agente in question ha su origine in le medulla adrenal.

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