EARLY BLOOD CHANGES IN DOGS FOLLOWING INTRAVENOUS PENTOBARBITAL ANESTHESIA

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In one of a series of rare earth toxicity studies, it was found that a marked leukopenia occurred in dogs anesthetized with pentobarbital sodium (Somnopentyl®) following the intravenous injection of rare earth salts. This finding was in addition to the known anticoagulant effects of these compounds. The rare earths were injected as chlorides which ionize readily or as complexes. The chelations were accomplished with sodium citrate or ammonium versinate, which stabilize the solubility of rare earth salts in the pH range of body fluids. In spite of these differences in binding characteristics it was noted that a leukopenia developed consistently regardless of the form of the compound used. Because of the similarity in results, a control study was made of the effects of the anesthetic on blood. In these experiments the procedures used for rare earth toxicity studies were duplicated except for the administration of the rare earths. Information in the literature of the effects of barbiturate anesthesia on the blood constituents was surprisingly meager and in some instances contrary to our findings. For this reason, the control studies were expanded to include 12 dogs with the findings reported here.

MATERIALS AND METHODS

Twelve normal adult mongrel dogs were studied in this series. Pentobarbital sodium was injected into the cephalic vein to produce surgical anesthesia. The dose was calculated from the body weight and ranged from 28 to 32 mg./kg., according to individual need. Six dogs were anesthetized with Somnopentyl which was used routinely in the rare earth studies. This preparation contains recrystallized pento- barbital sodium, U.S.P., in a 10 per cent alcohol base and was given in the recommended dose. The remaining 6 dogs were injected with a freshly prepared solution of pentobarbital sodium dissolved in sterile distilled water.

The carotid artery was exposed and cannulated in the anesthetized animal for recording blood pressure. Both femoral veins were exposed. The left femoral vein was cannulated and connected to a bottle

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of sterile Ringer’s solution which, in the rare earth experiments, was
used for washing in the salts injected into the tubing just above the
cannula. Blood samples were drawn directly from the exposed right
femoral vein.

A control blood sample was taken before injecting the pentobarbital
sodium. A second sample was taken thirty minutes after anesthesia,
and upon completion of surgical manipulation. This corresponded to
the control blood sample taken just prior to beginning the injection of
rare earth salts which, in those studies, were injected at ten-minute in-
tervals for a total of ten injections. In the studies reported here, 10
ml. of Ringer’s solution was injected at these intervals without rare
earths. Subsequent samples were taken at 40, 60, 90, 130, and 190
minutes after anesthesia. Blood for erythrocyte count, total and dif-
ferential leukocyte counts, hemoglobin determination, and coagulation
time was taken directly from the vein. The differential smear was
stained with Wright’s stain, hemoglobin was determined by the colori-
metric method (Klett-Summerson), and the coagulation time was de-
termined by the Lee and White 4-tube method. Blood taken for pro-
thrombin time, sedimentation rate, and hematocrit was oxalated. Pro-
thrombin time was determined by the Quick method using rabbit brain
thromboplastin (Difeo). The sedimentation rate and hematocrit were
measured by the Wintrobe method. Rectal temperature was taken
with a thermistor probe.

RESULTS

Satisfactory anesthesia was achieved with the dose of pentobarbital
used. Individual variation in response was seen in stretching move-
ments and degree of lightening of anesthesia toward the end of the
experimental period. Activity was great enough in 2 animals to alter
the leukocyte response. No discernible differences were found in
the blood constituents of animals treated with the commercial preparation
when compared to those injected with an aqueous solution of pento-
obarbital sodium. For this reason the experimental results were at-
tributed to the pentobarbital alone and not to the medium of the com-
mercial preparation.

The blood pressure response in the animals showed individual vari-
ation. In all but 2 animals, the blood pressure gradually decreased.
This ranged from a drop of only 4 mm. of Hg to 34 mm. at the end of
160 minutes. The heart rate was generally rapid initially, tended to
decrease in 40 to 60 minutes and then increased again or remained rela-
tively constant at the lower readings. Respiration, which was initially
depressed, increased with time. However, the rate changes were
highly variable from animal to animal.

Changes found in the blood constituents were as follows: A con-
sistent and striking leukopenia was found in all animals which reached
its nadir in approximately 90 minutes following the pentobarbital in-
jection. During this interval of time the count dropped to 20 per cent of the control value. After 90 minutes there was a gradual rise in cell numbers to reach an average value of 39 per cent of the control reading at 190 minutes. The absolute decrease was accompanied by a relative lymphocytosis which reached a peak in 90 minutes then regressed to the control value at the end of the experimental period. The relative decrease of leukocytes and the relative change in differential counts are shown in figure 1. The means with their standard deviation, the actual range of counts and percentage of the control count at the time intervals used are shown as a part of table 1.

According to Beecher (1) all types of anesthesia are followed by a leukocytosis, with the white cell count rise starting almost at once. He also states that differential cell counts indicate that with inhalation anesthesia the polymorphonuclear neutrophiles increase both relatively and absolutely, while the lymphocytes show a relative decrease with absolute numbers remaining the same. These differences from our results emphasize that the barbiturates do not demonstrate their effects in a manner similar to the true anesthetics. Oral administration of pentobarbital sodium in sedative dose apparently does not affect the blood constituents in the same way as intravenous injection. Hardwick and Randall (2) in an extensive study of the effects of orally administered pentobarbital sodium on the blood when administered in labor found no decreased leukocyte counts and no interference with leukocytosis.

A decrease in the number of red blood cells was found. The lowest point was reached in 30 minutes with a reading of 84.6 per cent of the control. The count then gradually rose to the control level in 130 minutes and was 111.9 per cent at 190 minutes. These findings are
consistent with the results obtained by Hausner, Essex and Mann (3). They attribute the change to a dilation of the spleen which reaches a maximum in 20 to 30 minutes. The average time for the spleen to return to normal was found to be 6.5 hours.

Changes in hematocrit and hemoglobin values corresponded with the changes in erythrocyte counts. These are shown in Table 1. On the basis of Hausner, Essex and Mann's findings that the average time for the spleen to return to normal with pentobarbital sodium in dogs was an average of 6.5 hours, the blood fluid shift cannot be attributed to changes in splenic volume.

The sedimentation rate showed a wide variation from animal to animal. However, some significance must be attached to the finding

<table>
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<th>TABLE 1</th>
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**EFFECT OF INTRAVENOUS PENTOBARBITAL SODIUM (28-32 mg./kg.) ON BLOOD VALUES IN 12 DOGS**

<table>
<thead>
<tr>
<th>Postanesthesia Time in Minutes</th>
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<tbody>
<tr>
<td>(Control)</td>
</tr>
<tr>
<td>Leukocytes (thousands/mm.³)</td>
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<tr>
<td>Actual Range</td>
</tr>
<tr>
<td>Per cent of control</td>
</tr>
<tr>
<td>Erythrocytes (millions/mm.³)</td>
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<tr>
<td>Actual Range</td>
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<tr>
<td>Per cent of control</td>
</tr>
<tr>
<td>Hematocrit (ml./100 ml.)</td>
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<tr>
<td>Actual Range</td>
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<tr>
<td>Per cent of control</td>
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<tr>
<td>Hemoglobin (gm./100 ml.)</td>
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<tr>
<td>Per cent of control</td>
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<tr>
<td>Sedimentation rate (mm./hour, corrected to 20°C)</td>
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<tr>
<td>Actual Range</td>
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<tr>
<td>Per cent of control</td>
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<tr>
<td>Coagulation time (minutes)</td>
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<tr>
<td>Actual Range</td>
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<tr>
<td>Per cent of control</td>
</tr>
<tr>
<td>Prothrombin time (seconds)</td>
</tr>
<tr>
<td>Actual Range</td>
</tr>
<tr>
<td>Per cent of control</td>
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</tbody>
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*S.D. = 0 to 6.

that in the controls the rate ranged from 0 to 18, while the range was from 0 to 50 up to 130 minutes. At 190 minutes it approached the control value.

There was some initial increase in the coagulation time but the changes did not appear to be significant on the basis of the number of animals studied. Searles (4) found that coagulation time was shortened by ether.

The prothrombin time showed a decrease which lasted to 130 minutes, at which time it approached the normal. It will be noted in figure 1 that an increase of 30 per cent is shown at that time. In two of the
animals the prothrombin time was found to be 14 seconds and 25 seconds, while the remaining 10 showed ranges of from 5.8 to 8.2 which are similar to the control readings. These findings are consistent with the report of Levy and Conroy (5) who reported that orally administered pentobarbital sodium caused lowering of the prothrombin time.

**Summary**

A study of the early blood changes in 12 dogs following intravenous pentobarbital anesthesia is reported. Blood samples were collected at 30, 40, 60, 90, 130, and 190 minutes. Erythrocyte, total and differential leukocyte counts, hemoglobin, hematocrit, sedimentation rate, coagulation and prothrombin time were compared to controls. A striking and consistent leukopenia was found which reached 20 per cent of the control value in 90 minutes. Transient decreases in erythrocytes, hematocrit and hemoglobin were found. Coagulation time was increased while prothrombin time was decreased. Except for leukocyte counts, these values approached control readings in 190 minutes.

Although the absolute differential white count decreased, there was a relative lymphocytosis which reached its peak in 90 minutes and then returned to normal.

**References**