Adrenal gland homogenates from a Jersey bull with a fascicular nodule converted 4-C\(^14\) progesterone to cortisol three to four times as rapidly as glands from other bulls. Adrenal glands from three bulls of the Norwegian Red and White breed, also with fascicular nodules, converted progesterone to cortisol at rates comparable to glands from bulls without nodules. The adrenals from these three animals converted the 4-C\(^14\) progesterone to cortical steroids similar to, but probably not identical with, corticosterone at faster rates than homogenates from glands of the other groups. Changes in the semen and testes associated with the changes found in the adrenals are described.

Lancaster (6) has reported the presence of adrenal nodules in 10.5% of 57 bulls of normal fertility and in 24% of 46 bulls with lowered conception rates. Cupps et al. (3, 4) found fascicular nodules in the adrenals from some low-fertility bulls. Sperm concentration, sperm motility, and percentage abnormal spermatozoa were variable in these animals, and the semen was further characterized by a low concentration of fructose and an intermediate concentration of citric acid. Injections of large amounts of cortisol or cortisone (4) lowered the fructose concentration and increased the sperm concentration in normal bulls, but did not produce some of the other changes seen in the animals with the fascicular nodules or fascicular hyperplasia of the adrenal.

Hypertrophy and hyperplasia of glomerular zone of the adrenal associated with faulty kidney function (5) has been found in bulls showing tubular degeneration of the testis. This latter condition has been found primarily in older bulls.

This report presents further observations on the function of the adrenal glands from bulls with changes in reproductive efficiency.

**EXPERIMENTAL PROCEDURE**

The experimental animals consisted of a group of eight bulls with lowered fertility. Their ages ranged from three to eight years and averaged five years. Three of the animals (Group I) were of the Norwegian Red and White breed showing various degrees of testicular hypoplasia and fascicular cortical nodules in the adrenals. The other five animals were Jerseys with impaired fertility. Of the Jerseys, two (Group II) had a hypertrophy of the glomerular zone of the adrenal. Two animals (Group III) produced low-quality semen before they were adrenalectomized. Following bilateral adrenalectomy, combined with maintenance therapy, they produced semen of normal quality. One bull (Group IV) had a nodule in the fascicular zone of the adrenal. Glands from the bulls of the Norwegian breed were processed and incubated at the Institute of Reproductive Physiology and Pathology, Norwegian Veterinary School, Oslo, Norway; those from the Jerseys were incubated at the Department of Animal Husbandry, University of California, Davis.

The adrenal glands were collected from the bulls within 30 min following slaughter, placed in plastic bags, and cooled by immersion in cracked ice. Following transport to the laboratory, they were processed using 4-C\(^14\) progesterone according to the method previously described (2).

Small sections of the testes and the adrenals were processed for histological examination using standard methods.

Sulfuric acid chromogens were prepared according to the method of Zaffaroni (8).
RESULTS

Approximately 90% of the radioactivity present in the progesterone was recovered from the incubated mixtures following the preliminary extraction procedures. Recovery of radioactivity following chromatography in the B₅ system of Bush (1) ranged from 35 to 65% and averaged 49% for the group of animals.

The conversion of 4-C¹⁴ progesterone to steroids resembling the adrenal cortical steroids by the various groups of bulls is shown in Table 1.

Figures 1 and 2 are sulfuric acid chromogens (8) of the steroids eluted from the cortisol band and the corticosterone band of the B₅ chromatograms compared with cortisol and corticosterone standards.

Figure 3 shows the testicular hypoplasia found in the bulls of the Norwegian Red and White breed. Semen from one of these bulls

![Fig. 1. Sulfuric acid chromogens of cortisol extract and cortisol standard following chromatography in Bush B₅ system. Extract from cortisol band from bull in Group IV.](image)

![Fig. 2. Sulfuric acid chromogen of cortical extract and corticosterone standard following chromatography in Bush B₅ system. Extract from the corticosterone band. Norwegian Red and White Bull.](image)

![Fig. 3. Testis hypoplasia. Norwegian Red and White bull.](image)

**TABLE 1**

Average radioactivity recovered from adrenal gland homogenates following incubation with C¹⁴ progesterone. Total counts in 5 min per gram of homogenate

<table>
<thead>
<tr>
<th>Expt. group*</th>
<th>No. of animals</th>
<th>Cortisol area</th>
<th>Cortisone area</th>
<th>Corticosterone area</th>
<th>Progesterone area</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>3</td>
<td>4,136</td>
<td>5,115</td>
<td>110,337</td>
<td>10,145</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>2,417</td>
<td>3,522</td>
<td>32,041</td>
<td>15,131</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>3,353</td>
<td>2,569</td>
<td>24,204</td>
<td>6,910</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>14,608</td>
<td>3,162</td>
<td>13,981</td>
<td>1,853</td>
</tr>
</tbody>
</table>

* I—Norwegian Red and White, testicular hypoplasia, adrenal fascicular nodules.  
II—Jersey, adrenal glomerular hyperplasia and kidney damage.  
III—Jersey, low-quality semen.  
IV—Jersey, adrenal fascicular nodule.
METABOLISM OF PROGESTERONE

was extremely thin, and too few spermatozoa were present to obtain a reliable cell count.

The fascicular nodules found in the adrenals from these animals are shown in Figure 4.

![Fig. 4. Fascicular nodules, adrenal gland. Bull from Group I.](image)

DISCUSSION

Conversion of progesterone to cortisol was fairly constant in the bulls except for the Jersey with the fascicular nodule. In this animal the conversion was three to four times that found in the other bulls. This bull produced semen with a high sperm concentration and low fructose concentration typical of other Jersey and Holstein bulls with similar nodules.

The high conversion rate of progesterone to cortisol found in the homogenate, and the production of semen with similar characteristics by injections of supplemental cortisol into normal bulls, provide additional evidence that the abnormally high secretion of cortisol is responsible for the production of semen with these characteristics.

The changes in the characteristics of the semen from bulls showing this condition occur gradually. For example, when the first evidence for a high cortisol secretion in one bull was noted the values for the various seminal characteristics were as follows: motility, 80%, abnormal spermatozoa, 5%, live spermatozoa, 85%, concentration of spermatozoa, \(2.02 \times 10^9\) per milliliter, and fructose 255 mg per 100 ml. Three years later the motility was 10%, the abnormal spermatozoa 23%, live spermatozoa 36%, spermatozoa concentration \(1.9 \times 10^9\) per milliliter, and fructose concentration 266 mg per 100 ml. The decline in semen quality was gradual.

The sulfuric acid chromogen provided further evidence that the cortical extract moving at this rate on the chromatogram was cortisol and represented the conversion of progesterone to cortisol by the gland homogenates.

The adrenals containing the cortical nodules from the bulls of the Norwegian Red and White breed converted the radioactive progesterone to materials traveling with corticosterone more rapidly than the Jersey bulls, normal cows of the Norwegian Red and White breed, or cows with cystic ovaries of the Norwegian Red and White breed (2). Whether the increased conversion of the progesterone to more polar steroids by this group of bulls is associated with the testicular hypoplasia or if it is a breed or sex difference cannot be determined from the available data.

Attempts to identify the compound or compounds (Figure 2) moving at the same rate as cortisol were not successful. The sulfuric acid chromogen was very similar to corticosterone, but not identical with it because the material from the gland extract lacked the absorption band at 240 \(\mu\)m and the broad band between 450 and 475 \(\mu\)m. In the Bush B2 system 17-hydroxydeoxycorticosterone and possibly 18-hydroxydeoxycorticosterone migrate at the same rate as cortisol. Thus, these compounds may have contributed to the chromogen shown in Figure 2. Unfortunately, not enough material was available for further purification procedures.

In the Bush B2 system aldosterone travels at approximately the same rate as cortisol. On theoretical grounds the adrenals from animals in Group II should have converted the progesterone to aldosterone and related compounds faster than bulls in the other groups. This is expected because the adrenals from the animals of Group II showed hypertrophy of the glomerular zone and there was evidence that their kidneys were damaged. Wettstein et al. (7) using the same incubation medium did not find an increased formation of aldosterone by homogenates of normal cow adrenals when progesterone was used as a precursor. Deoxycorticosterone, however, when used as a substrate with homogenates of normal adrenal glands, increased the amount of aldosterone formed with this incubation medium, indicating that progesterone is not a satisfactory precursor for aldosterone formation under these experimental conditions.

The bulls in Group III converted progesterone to cortisol at a rate comparable to the older animals. These results were not expected, because animals of similar breeding appeared to
produce several steroid hormones at subnormal rates. Their secondary sex characters developed more slowly than normal animals, and they responded to supplemental cortisol injections with an increased growth rate (5). Without cortisol the average weight gain was 0.6 lb per day and with supplemental cortisol the daily gain averaged 1.1 lb. Presently, an explanation for this discrepancy is not available. Many possibilities exist and two are suggested. The biosynthetic defect may occur before progesterone is formed. Under these circumstances, the homogenates could convert progesterone to cortical steroids at a normal rate, even though the animals normally produce them in subnormal amounts. Secondly, the lowered production rates found in these animals may be of such magnitude that the experimental technique used is not precise enough to measure them.

REFERENCES


(2) Cupps, P. T. Unpublished.


