Renal Hemodynamics, Electrolyte Excretion and Water Metabolism in Pregnant Sheep Before and After the Induction of Toxemia of Pregnancy

By N. S. Assali, M.D., Louis Holm, M.D., and Donald L. Hutchinson, M.D.

Renal hemodynamics, electrolyte excretion and plasma level of glucocorticoids were studied in pregnant sheep before and after the experimental induction of toxemia. Marked renal ischemia occurred in the animals which developed toxemia. This abnormality occurred concomitantly with an increase in plasma corticoids. Despite the renal ischemia, arterial pressure remained the same. There are some similarities between the toxemia of the sheep and that of human pregnancy.

A syndrome variously called toxemia of pregnancy, twin-lamb disease or ketosis of pregnancy has been known to occur in pregnant sheep during the latter part of gestation. Clinically, this syndrome is characterized by anorexia, disturbances of the central nervous system and of vision, oliguria, stupor, convulsions and coma. Blood and urine abnormalities are stated to be: proteinuria, nitrogen retention, ketonemia, hypoglycemia, eosinopenia and low plasma carbon dioxide content. The disease is very often fulminating and occurs more frequently in well nourished pregnant ewes with multiple or large fetuses which are subjected to a sudden reduction in nourishment. Death of the animal occurs unless the pregnancy is terminated either spontaneously or by cesarean section. Recent reports have indicated that this syndrome can be reproduced experimentally in pregnant ewes and that the experimentally induced toxemia does not differ from that which occurs spontaneously.

The presence of oliguria, proteinuria and nitrogen retention suggested that a disturbance in renal function might underlie the pathogenesis of this disease. Parry and Taylor have studied renal function in sheep with experimentally induced and spontaneous toxemia, using the single injection technique of creatinine and para-aminohippurate (PAH) clearances. They found a markedly reduced renal plasma flow and glomerular filtration rate in both conditions.

The present studies were aimed at investigating renal hemodynamics, excretion of electrolytes, water metabolism and plasma levels of glucocorticoids in the same pregnant animal prior to and following the induction of toxemia. It was thought desirable to repeat the renal studies because the single injection technique employed by Parry and Taylor has been questioned and secondly, recent evidence has indicated that exogenous creatinine clearance at a low plasma level may not be a true measure of glomerular filtration rate in the sheep. Furthermore, we hoped that by studying the same animal during normal pregnancy and after toxemia had been induced, we could detect early changes in renal function which might elucidate the pathogenesis of this disease and reveal any commonalities between the toxemia of the sheep and that which occurs in human pregnancy.

METHOD

Twenty Suffolk-Hampshire cross bred ewes of approximately the same period of gestation were selected for this study. They were confined on the farm of the University of California at Davis, and their basal diet consisted of good quality alfalfa. Control studies were carried out on 10...
of the 20 pregnant animals. Thereafter, these animals, together with the other 10 pregnant ewes, were subjected to experimental induction of toxemia according to the technic of Philipson. This procedure consisted essentially of increasing the plane of nutrition by feeding the animals high grade alfalfa ad libitum and by incorporating grain mixture. Abrupt caloric restriction was then imposed on the animals by substituting straw for the alfalfa-grain mixture.

Table 1.—Data on Urine Flow, Glomerular Filtration Rate, Renal Plasma Flow, Plasma Sodium and Urinary Excretion Before (N) and After (T) Induction of Toxemia

<table>
<thead>
<tr>
<th>Sheep no.</th>
<th>Weight (Kg)</th>
<th>V.F.* (ml./min.)</th>
<th>GFR* (ml./min./Kg)</th>
<th>RPF* (ml./min./Kg)</th>
<th>Plasma Na* (mEq./L)</th>
<th>Urine excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>T</td>
<td>N</td>
<td>T</td>
<td>N</td>
<td>T</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>97</td>
<td>60</td>
<td>70</td>
<td>3.1</td>
<td>1.7</td>
</tr>
<tr>
<td>4</td>
<td>74</td>
<td>27</td>
<td>70.5</td>
<td>8.5</td>
<td>3.4</td>
<td>2.1</td>
</tr>
<tr>
<td>17</td>
<td>65</td>
<td>5</td>
<td>57.3</td>
<td>3</td>
<td>3.1</td>
<td>1.6</td>
</tr>
<tr>
<td>20</td>
<td>63</td>
<td>18</td>
<td>60.0</td>
<td>4.8</td>
<td>1.6</td>
<td>1.5</td>
</tr>
<tr>
<td>8</td>
<td>84</td>
<td>1</td>
<td>10.0</td>
<td>1.7</td>
<td>7.5</td>
<td>154</td>
</tr>
<tr>
<td>9</td>
<td>94</td>
<td>6</td>
<td>11.8</td>
<td>1.4</td>
<td>5</td>
<td>150</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>60</td>
<td>9.8</td>
<td>1.5</td>
<td>8</td>
<td>144</td>
</tr>
<tr>
<td>11</td>
<td>85</td>
<td>5</td>
<td>60.0</td>
<td>0.9</td>
<td>2</td>
<td>87</td>
</tr>
<tr>
<td>15</td>
<td>68</td>
<td>2</td>
<td>1.5</td>
<td>2</td>
<td>12</td>
<td>148</td>
</tr>
<tr>
<td>181</td>
<td>74</td>
<td>6</td>
<td>11.1</td>
<td>1.7</td>
<td>5</td>
<td>153</td>
</tr>
</tbody>
</table>

* The differences between the normal and the toxemic values are highly significant.  
† Early toxemia.  
‡ No water for 6 to 12 hours.

The studies were all performed in unanesthetized animals which were maintained in the prone position by being suspended in a hammock with the limbs extended through openings in the canvas. During the normal pregnant stage, all of the animals had free access to water except sheep no. 11, 15 and 19 (table I). These animals had no water for a period varying from 6 to 12 hours prior to the clearance collections. During the stage of toxemia, the animals continued to have free access to water although their ability to drink was impaired when the disease became severe.

After the animal was suspended in the hammock, a Foley catheter was inserted into the bladder which was completely emptied. Control blood samples were obtained for assay of glucose, carbon dioxide, eosinophils and 17-hydroxycorticosteroids. Thereafter, a priming dose of inulin, PAH and creatinine calculated for each animal according to body weight was injected over a period of 2 min. through a polyethylene tube inserted into the external jugular vein. This was followed by a maintenance solution given at a constant rate and aimed at maintaining a plasma level of approximately 200 mg./L. of inulin, 30 mg./L. of PAH and 10 to 30 mg./L. of creatinine. An equilibration period of 30 to 45 min. was allowed after which 3 to 5 30-min. collections were obtained from each animal. Blood samples were withdrawn at the midpoint of each collection.
FIG. 1. Comparison of the urine flow, GFR and RPF in 4 sheep before and after the induction of toxemia. Note the striking decrease during toxemia.

period. Completeness of urine collections was achieved by exerting suprapubic pressure and by injecting air into the bladder. For determinations of body water, an accurately measured amount of deuterium oxide varying between 40 and 45 ml. was injected through the infusion tubing over a period of 1 to 2 min. Blood samples were collected every 30 to 60 min. for the first 5 to 8 hours. Further blood samples were collected from some animals after 10, 15 and 24 hours and 3, 7 and 14 days. These samples served to determine the turnover rate of the injected deuterium oxide.

A loop of the carotid artery was exteriorized under local anesthesia and mean arterial pressure was measured with a mercury manometer.

Inulin, PAH, creatinine, Na, K, Cl, glucose, carbon dioxide, eosinophils, hematocrit and plasma levels of 17-hydrocorticosteroids were analyzed by methods described elsewhere.*1 We are indebted to Dr. Albert A. Plentl, Columbia University, for analyses of deuterium oxide concentration.

RESULTS

The results are shown in tables 1 to 4 and figure 1. The figures represent the average of all the collections obtained from each animal.

Urine Flow and Solute Excretion. In the normally pregnant sheep which had ingested water freely, urine flow varied from 3.5 to 11.8 ml./min. and solute excretion from 607 to 1930 µOsm/min. (table 1). Sheep no. 11, 15 and 18, whose fluid intake was restricted, excreted urine at a rate of 0.9 to 1.5 ml./min., but their total solute excretion was of the same range as the former group.

The 4 sheep which developed toxemia excreted urine at a rate of 1.6 to 3 ml./min. and their total solute excretion varied from 380 to 690 µOsm/min. (table 1). These values were significantly lower than those of the same animals when they were normal. Sheep no. 4 which was studied 3 times, excreted urine at a rate of 8.5 ml./min. when normal, 3.4 in early toxemia and 2.4 when the toxemia became more severe (table 1).

Glomerular Filtration Rate and Renal Plasma Flow. Glomerular filtration rate (GFR) was estimated from the inulin clearance. Exogenous creatinine clearance at a plasma level varying between 1 and 3 per cent was consistently higher than inulin clearance, and, therefore, could not be used as a measure of filtration rate. These findings were in agreement with those of Ladd et al.*1 in the non-pregnant sheep.

In the normally pregnant sheep which had free access to water, GFR varied from 1.4 to 2.1 ml./Kg./min. and renal plasma flow (RPF) varied from 5 to 12.7 ml./Kg./min. (table 1). The values for the normally pregnant animals deprived of water were within the same ranges. In the sheep which developed toxemia, GFR was never higher than 1 ml./Kg./min. (table 1). Even in the sheep with early toxemia (no. 4) GFR was still far below the values obtained from the same animal before toxemia was induced.

Likewise RPF in the toxemic animals was consistently below those of the normally pregnant animals regardless of whether the ewes were hydrated or not. Filtration fraction in toxemia was slightly lower than during normal pregnancy. Statistical analyses of the data on GFR and RPF was made by computing analysis of variance and the rank test

*We are indebted to Dr. W. J. Dixon of the Department of Preventive Medicine and Public Health for the statistical analyses.
for all of the clearances collected from the normal and the toxemic sheep. The difference in GFR and RPF between the normal and toxemic stage was highly significant (p<.01).

Figure 1 compares the values for urine flow, GFR and RPF in the 4 sheep which were studied before and after the induction of toxemia. It is evident that in each instance the changes from the normal to the toxemic stage were dramatic.

**Mean Arterial Pressure.** Mean carotid pressure in the normally pregnant sheep varied from 110 to 128 mm. Hg. It did not change following the induction of toxemia.

**Plasma and Urine Electrolytes.** During the normal pregnant stage, plasma Na varied between 144 and 154 mEq./L, plasma Cl between 103 and 109 mEq./L and plasma K between 3.6 and 5.8 mEq./L. The 3 animals deprived of water had plasma electrolytes which were within this range. In the toxemic phase, plasma Na rose in each instance whereas Cl and K remained within the normal ranges (table 1, values for Cl and K were not listed).

The excretion of electrolytes showed a marked variation from animal to animal and in the same animal from one collection to another, both in the normal and the toxemic stage. In general, during normal pregnancy the animals excreted significantly and consistently more potassium than sodium. This was thought to be due to the ingestion of large quantities of alfalfa in which potassium is present in high concentrations. The concentration and excretion of sodium were completely inconsistent and were unrelated to the urine flow. For instance, sheep no. 11 and 18 (table 1) with nearly the same urine flow excreted markedly different quantities of sodium, although they were on the same diet. On the other hand, sheep no. 9 and 11 with markedly different urine flow had nearly the same sodium excretion.

During the toxemic stage, the excretion of sodium became slightly more consistent than during normal pregnancy. Potassium excretion decreased probably because of a smaller content of this cation in the diet employed to induce toxemia.

Table 2 shows the values for whole blood glucose, plasma HCO₃, eosinophil counts, packed cell volume and plasma levels of 17-hydroxycorticosteroids in 4 sheep before and after the induction of toxemia. Blood glucose decreased in 2 animals, increased in 1 and remained the same in 1. Likewise the changes in plasma HCO₃, eosinophil count and packed cell volume were inconsistent. Plasma levels of 17-hydroxycorticosteroids increased in each of the 3 animals in whom these substances were assayed.

**Water Metabolism.** The purposes of the deuterium oxide studies were to record total body water of the animals and to calculate the disappearance rates of the administered deuterium oxide in normal pregnancy and in the toxemic state. Unfortunately, the disease was of such a fulminating nature that serial samples could not be obtained after toxemia was produced. Therefore, the data listed in tables 3 and 4 represent water metabolism of the group of sheep in the last trimester of normal pregnancy.

Uniform distribution of deuterium oxide occurred between 2 and 3 hours after intra-
TABLE 3.—Total Body Water and Fat Content of Normal Pregnant Ewes

<table>
<thead>
<tr>
<th>Sheep no.</th>
<th>Body weight (Kg.)</th>
<th>Deuterium oxide space (L.)</th>
<th>Deuterium oxide space (%)</th>
<th>Per cent fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>70.5</td>
<td>30.6</td>
<td>43.4</td>
<td>40.7</td>
</tr>
<tr>
<td>20</td>
<td>63.6</td>
<td>28.4</td>
<td>44.6</td>
<td>39.1</td>
</tr>
<tr>
<td>18</td>
<td>76.4</td>
<td>33.1</td>
<td>43.3</td>
<td>40.8</td>
</tr>
<tr>
<td>17</td>
<td>65.4</td>
<td>29.5</td>
<td>45.0</td>
<td>38.5</td>
</tr>
<tr>
<td>15</td>
<td>68.2</td>
<td>27.0</td>
<td>40.4</td>
<td>44.8</td>
</tr>
<tr>
<td>12</td>
<td>60.9</td>
<td>31.9</td>
<td>52.4</td>
<td>28.5</td>
</tr>
<tr>
<td>11</td>
<td>85.5</td>
<td>40.0</td>
<td>46.8</td>
<td>35.0</td>
</tr>
<tr>
<td>9</td>
<td>94.6</td>
<td>41.6</td>
<td>43.9</td>
<td>40.0</td>
</tr>
<tr>
<td>3</td>
<td>80.9</td>
<td>44.3</td>
<td>54.7</td>
<td>25.3</td>
</tr>
<tr>
<td>8</td>
<td>84.1</td>
<td>63.9</td>
<td>75.8</td>
<td>—</td>
</tr>
</tbody>
</table>

* Deuterium oxide space (%) =

Deuterium oxide space

\[
\text{Body wt. Kg.}
\]

\[
\frac{\text{Deuterium oxide space} \times\text{Body wt. Kg.}}{0.732}
\]

† Per cent fat =

\[
100 - \frac{\text{Deuterium oxide space}}{\text{Deuterium oxide space}}
\]

The results of the serial samples obtained at 30 min. intervals showed no significant decrease in deuterium oxide content of the sera after 3 hours. Therefore, the concentration of the 3 hour sample was used for the calculation of total body water.

The "total body water" or "deuterium space" varied between 40.4 and 54.7 per cent of total body weight (average 46.1 ± 4.6) (table 3). Animal no. 8 had unexplained high values of 75.8 per cent (table 3). There are no reports of studies on total body water with deuterium oxide in pregnant sheep available in the literature to serve for comparison. Hansard and Lyke measured total body water in mature nonpregnant sheep using labeled 4-iodo-antipyrine and antipyrine (A.N.P). Their average total body water was about 55.8 per cent of total body weight. It is not possible to state whether the difference between our values and those observed by Hansard and Lyke was due to the difference in technic of measuring body water or to the difference between pregnant and nonpregnant animals.

The formulas which have been used to estimate the fat content of the total body in animals and humans have not been used in venous administration. The results of the serial samples obtained at 30 min. intervals showed no significant decrease in deuterium oxide content of the sera after 3 hours. Therefore, the concentration of the 3 hour sample was used for the calculation of total body water.

† H.L. =

\[
\frac{\text{Deuterium oxide space}}{\text{Deuterium oxide space}}
\]

† T.T. =

\[
\frac{\text{Deuterium oxide space}}{\text{Deuterium oxide space}}
\]

\[
\text{per cent fat} = 100 - \frac{\text{Deuterium oxide space}}{\text{Deuterium oxide space}}
\]

With the pregnant state. However, the agreement among animal species is surprisingly good and it maybe reasonable to apply the mean value of water in lean body mass (73.2 per cent) to normally pregnant sheep. Assuming a constant ratio of fat and lean body mass in these pregnant animals, it is possible then to calculate the percentage of fat from the equation:

\[
\text{per cent fat} = 100 - \frac{\text{Deuterium oxide space}}{\text{Deuterium oxide space}}
\]

Table 3 shows that the fat content of these animals when calculated in this manner was extremely high. This is not too surprising as the animals have had optimal caloric intake and limited activity. This might offer further evidence to the effect that the total body water in the normally pregnant sheep was not increased and that these animals were not edematous.

Following the initial body water determination, samples of venous blood were withdrawn at intervals of 24 to 48 hours for a period of 7 to 14 days. Table 4 shows the

TABLE 4.—Disappearance Constants, Half Life of Deuterium Oxide, Turnover Time, and Total Turnover in Pregnant Ewes Before Toxemia

<table>
<thead>
<tr>
<th>Sheep no.</th>
<th>Disappearance constant in days</th>
<th>Half life in days</th>
<th>Turnover time in days</th>
<th>Total turnover in L./day</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>.081</td>
<td>8.6</td>
<td>12.3</td>
<td>2.5</td>
</tr>
<tr>
<td>20</td>
<td>.097</td>
<td>7.1</td>
<td>10.3</td>
<td>2.8</td>
</tr>
<tr>
<td>17</td>
<td>.087</td>
<td>7.9</td>
<td>11.5</td>
<td>2.6</td>
</tr>
<tr>
<td>12</td>
<td>.091</td>
<td>7.6</td>
<td>11.0</td>
<td>3.0</td>
</tr>
<tr>
<td>9</td>
<td>.110</td>
<td>6.3</td>
<td>9.1</td>
<td>4.6</td>
</tr>
<tr>
<td>8</td>
<td>.081</td>
<td>8.6</td>
<td>12.4</td>
<td>5.2</td>
</tr>
<tr>
<td>15</td>
<td>.126</td>
<td>5.5</td>
<td>7.9</td>
<td>3.5</td>
</tr>
<tr>
<td>18</td>
<td>.145</td>
<td>4.8</td>
<td>6.9</td>
<td>4.8</td>
</tr>
<tr>
<td>11</td>
<td>.193</td>
<td>3.6</td>
<td>5.2</td>
<td>7.7</td>
</tr>
<tr>
<td>3</td>
<td>.240</td>
<td>2.9</td>
<td>4.2</td>
<td>10.6</td>
</tr>
</tbody>
</table>

* Disappearance constant =

\[
\frac{\log \text{deuterium oxide} - \log \text{deuterium oxide}}{\text{Disappearance constant}}
\]

† H.L. =

\[
\frac{\text{Disappearance constant}}{1.00}
\]

† T.T. =

\[
\frac{\text{Disappearance constant}}{\text{Disappearance constant}}
\]

† Total turnover = (TBW) (disappearance constant) (100).
late disappearance constant and its related values. There was rather a wide variation in the disappearance constant and its related values in these pregnant animals when compared with normal human pregnancy at term. This would suggest that the water turnover in these normal pregnant animals is fairly rapid which speaks against a significant defect in water metabolism.

**Discussion**

The present data show clearly that a renal disturbance is associated with toxemia of pregnancy in the sheep. The decreases in urine flow, GFR and RPF were of the same magnitude as those found by Parry and Taylor despite the fact that the technic utilized by these authors was somewhat different from ours. These findings indicate the presence of severe renal ischemia involving the glomeruli. The lower total solute excretion by the toxemic animals also suggests the existence of an impaired tubular concentrating ability of the kidneys. Since in neither our animals nor in those studied by Parry and Taylor could specific renal pathologic lesions be demonstrated at autopsy, it appears likely that the disturbance is largely functional.

It could be argued that the impairment in renal function found in the toxemic animals was related to a certain degree of dehydration which might have occurred during the period of starvation. This hypothesis seems unlikely for the following reasons: first, the normally pregnant animals which were studied during water deprivation had urine flows which were similar or even lower than those of the toxemic animals. Nevertheless, their renal plasma flow, glomerular filtration rate and total solute excretion were within the normal ranges and were significantly higher than those of the toxemic animals. Second, evidence of dehydration should have been reflected in the changes in the hematocrit. However, in the 4 toxemic animals, the changes in hematocrit were variable and did not reflect consistent hemococoncentration. Similar findings were observed by Parry and Taylor who also concluded that dehydration did not play a major role in the renal disturbance of the toxemia of the sheep.

In view of these findings, it is interesting to speculate about the similarity between the toxemia of the sheep and that of human pregnancy. Clinically, the following factors are common to the 2 diseases: (a) sporadic occurrence in the later part of gestation, (b) higher incidence in the short, obese individuals (spontaneous and induced toxemia occurs in short obese sheep), (c) higher frequency with large or multiple fetuses (of the 8 animals which developed toxemia, 6 had twins), (d) prominence of nervous system disturbances including severe visual disturbances, (e) presence of oliguria and edema in a large number of cases, (f) lack of specific pathologic findings at autopsy, (g) striking improvement in the mother's condition upon termination of pregnancy. Laboratory findings common to the 2 diseases are proteinuria, nitrogen retention and mild and inconsistent acidosis. Eosinopenia and hypoglycemia which are not present in human toxemia are occasionally observed in the toxemia of the sheep but as shown by Parry and Taylor and confirmed by these and other data to be reported by one of us (L.H), these findings are by no means constant or pathognomonic.

The present data on renal function add more to the similarity between the 2 diseases. The degree of renal ischemia and decreased filtration rate found in the toxemic sheep was slightly more marked than that found in women with toxemia of pregnancy, but this difference could have been due to the more fulminating nature of the disease in the sheep. In the case studied in early toxemia (sheep no. 4) the changes in renal function were closely similar to those of pregnant women.

One striking difference between the 2 diseases is the lack of hypertension in the toxemia of sheep. Normal blood pressure was found consistently by Parry and Taylor in spontaneously occurring and experimentally induced toxemia, regardless of the degree of the disease. Our findings are in agreement with those of these authors. It is difficult to
ASSALI, HOLM AND HUTCHINSON

explain the absence of hypertension in the presence of a marked renal ischemia such as observed in these animals. Goldblatt and his co-workers\textsuperscript{14} were able to produce experimental renal hypertension in the nonpregnant sheep. This would seem to rule out the problem of species difference. A second possibility is that pregnant sheep respond differently from the nonpregnant ones to renal ischemia or that they may elaborate some antihypertensive substances. This latter possibility is now being investigated.

Little can be said about the excretion of electrolytes in either the normal or toxemic sheep. Despite the effort which was made to keep the diet of these animals constant, a marked variation in electrolyte excretion occurred. Whether the variation was due to a difference in the electrolyte content of the various batches of alfalfa, barley and hay or to inherent properties of the sheep cannot be asserted from these studies, since there are no data available in regard to water and electrolyte excretion in this animal with which ours could be compared. Studies are now in progress to investigate sodium and water metabolism in these animals with radioactive isotopes.

Although it would be difficult to interpret the high levels of plasma sodium observed in the toxemic animals in view of the irregular behavior of electrolyte excretion, it is reasonable to assume that these levels reflect sodium retention. Dehydration can be excluded as being the cause since the changes in hematocrit did not reflect hemoconcentration and because of the absence of any significant change in plasma potassium. Under these circumstances, one might be led to believe that hyperactivity of the adrenal cortex might be involved in this disease and might be responsible for the elevation of the ratio of plasma sodium-potassium. Although assays for the mineralcorticoids were not performed in these studies, the few results on plasma levels of glucocorticoids suggest an adrenocortical hyperactivity. Indeed, this hypothesis does not seem illogical since the disease can be induced experimentally by stressful stimuli such as starvation. Undoubtedly, starvation may produce a series of metabolic events which, although at present very obscure, might have an important relation with the cause of the disease. However, it is possible that starvation might stimulate the hypothalamic-pituitary-adrenal axis and might lead to some of the manifestations observed in this disease. Evidently, many studies are necessary to elucidate these various points.

**SUMMARY**

Renal hemodynamics, excretion of water and electrolytes, and plasma levels of 17-hydroxycorticosteroids were investigated in pregnant sheep before and after the experimental induction of toxemia. A marked decrease in urine flow, renal plasma flow, glomerular filtration rate and total solute excretion was found in the animals which developed toxemia. These findings provide additional evidence to support the similarity between toxemia in humans, and in sheep. Clinical and pathologic findings constitute other factors common to both diseases. Lack of hypertension in the presence of renal ischemia in the toxemic sheep offers the only striking difference.

Electrolyte excretion was inconsistent and erratic in both the normal and toxemic sheep. Increased plasma levels of glucocorticoids suggest in the toxemic animals adrenocortical hyperactivity.

**SUMMARIO IN INTERLINGUA**

Le hemodynamic renal, le excretion de aqua e del electrolytos, e le nivellos del 17-hydroxycorticosteroides del plasma esseva investigate in oves pregnante ante e post le induction experimental de toxemia. In le animales que disveloppava toxemia, marcate augmentos esseva constatatate in le fluxo de urina, le fluxo de plasma renal, le intensitate del filtration glomerular, e del excretion total de solutos. Iste constatationes supporta addicionalmente le postulato del similitude de toxemia human con toxemia ovin. Observations clinic e pathologic revela altere factores que le duo conditiones ha in commun. Le absentia de hypertension in le presentia de
ischemia renal in ovse toxemica representant le sol differentia.

Le excretion de electrolytos esseva irregu-
lar e erratic in ovse tanto normal como etiam toxemic. Le augmentate nivellos plasmatic
de glucocorticoides observate in le animales
corn toxemia suggerave le presentia de hyper-
activitate adrenocortical.

REFERENCES
1. PARRY, H. B.: Toxemia of pregnancy in the
domestic animals with particular reference
to the sheep. In Toxemias of Pregnancy: Hu-
man and Veterinary. A Ciba Foundation
Symposium. The Blakiston Co., 1950,
pp. 8-93.
2. —: Induction of toxemia of pregnancy in
3. PHILLIPSON, A. T.: Experimental ketosis in
pregnant ewes. In Toxemias of Pregnancy:
Human and Veterinary. A Ciba Founda-
tion Symposium, The Blakiston Co., 1950,
p. 94.
function in sheep during normal and tox-
5. —, AND TAYLOR, W. H.: Renal clearances of
creatinine and p-aminohippurate in normal
pregnancy and toxemia of pregnancy in the
6. SMITH, H. W.: The kidney structure and
function in health and disease. New York,
Oxford University Press, 1951, p. 57.
7. LADD, M., LIDDLE, L., GAGNON, J. A., AND
CLARKE, R. W.: Glomerular and tubular
functions in sheep and goats. J. Appl.
Physiol. 10: 249, 1957.
8. ASSALI, N. S., KAPLAN, S. A., FORDON, S. J.,
AND DOUGLASS, R. A., JR.: Renal function
Invest. 32: 44, 1953.
9. —, MONK, A., ULLRICH, R., YOSKIAN, J.,
AND SINGH, B. P.: Effects of inhibition of
renal carbonic anhydrase by Diamox in
normal and toxemic pregnancies. J. Lab.
10. —, GARSIP, J. B., AND YOSKIAN, J.: Blood
levels of 17-hydroxycortcosteroids in normal
and toxemic pregnancies. J. Lab. &
11. HUTCHINSON, D. L., PLENTL, A. A., AND
TAYLOR, H. C., JR.: The total body water
and the water turnover in pregnancy stud-
ied with deuterium oxide as isotope tracer.
12. HANNSB, S. L., AND LYKE, W. A.: Measure-
ment of total body water in sheep using
18th labeled 4-ido-antipyrine. Proc. Soc.
13. KENNEY, R. A., LAWRENCE, R. F., AND MILL-
ER, D. H.: Hemodynamic changes in the
kidney in “toxemia of late pregnancy.” J.
14. GOLDBLATT, H., KAINX, J. R., AND LEWIS,
H. A.: Studies on experimental hyperten-
sion: XIX. The production of persistent
hypertension in sheep and goats. J. Exper.
Med. 77: 297, 1943.
Renal Hemodynamics, Electrolyte Excretion and Water Metabolism in Pregnant Sheep
Before and After the Induction of Toxemia of Pregnancy

N. S. ASSALI, LOUIS HOLM and DONALD L. HUTCHINSON

Circ Res. 1958;6:468-475
doi: 10.1161/01.RES.6.4.468

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1958 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/6/4/468