1963

Pregnancy Disease

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cow between the two years can be explained partially by the increased experience of the inseminator and partially by the extremely wet year in 1962 which caused a high estrogen content of the grass and this contributed to more abnormal estrous cycles.

The advantages expected when the program was started have been partially realized. Increased weaning weights of 35 to 50 pounds per calf, more uniform calves, and improvement of the herd through better quality replacement heifers are the advantages achieved so far.

### Figure 2
Heat detection results from the 34 days breeding season used in 1963.

<table>
<thead>
<tr>
<th>Total Number of females</th>
<th>Age</th>
<th>Number Detected</th>
<th>% Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>83</td>
<td>1</td>
<td>52</td>
<td>62.65</td>
</tr>
<tr>
<td>75</td>
<td>2</td>
<td>41</td>
<td>54.6</td>
</tr>
<tr>
<td>226</td>
<td>3-10</td>
<td>209</td>
<td>92.3</td>
</tr>
</tbody>
</table>

### Figure 3
The weight relationship to heat detection in yearlings.

<table>
<thead>
<tr>
<th>Weight range of females</th>
<th>Total number of females</th>
<th>Number detected in heat</th>
<th>% Detected in heat</th>
</tr>
</thead>
<tbody>
<tr>
<td>380-420 lbs</td>
<td>15</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>421-440 lbs</td>
<td>9</td>
<td>2</td>
<td>22.2</td>
</tr>
<tr>
<td>441-460 lbs</td>
<td>6</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>461-480 lbs</td>
<td>14</td>
<td>7</td>
<td>50</td>
</tr>
<tr>
<td>481-530 lbs</td>
<td>34</td>
<td>29</td>
<td>85.3</td>
</tr>
</tbody>
</table>

### Figure 4
The per cent of non-return rate in 21 days from semen used in 1963.

<table>
<thead>
<tr>
<th>Bull</th>
<th>Number of cows served</th>
<th>Number of repeat-services</th>
<th>% non-returns</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>62</td>
<td>20</td>
<td>69.35</td>
</tr>
<tr>
<td>B</td>
<td>7</td>
<td>3</td>
<td>57</td>
</tr>
<tr>
<td>C</td>
<td>41</td>
<td>26</td>
<td>36.6</td>
</tr>
<tr>
<td>D</td>
<td>31</td>
<td>15</td>
<td>51.6</td>
</tr>
<tr>
<td>E</td>
<td>17</td>
<td>5</td>
<td>70.8</td>
</tr>
</tbody>
</table>

### Figure 5
Records comparing the age and the number of services per cow in 1962 and 1963.

<table>
<thead>
<tr>
<th>Age of cows per cow</th>
<th>Number of services</th>
<th>Age of cows per cow</th>
<th>Number of services</th>
</tr>
</thead>
<tbody>
<tr>
<td>1962</td>
<td>1963</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 yr.</td>
<td>1 yr.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.635</td>
<td>1</td>
<td>1.150</td>
</tr>
<tr>
<td>2</td>
<td>1.050</td>
<td>3</td>
<td>1.122</td>
</tr>
<tr>
<td>3</td>
<td>1.383</td>
<td>4</td>
<td>1.181</td>
</tr>
<tr>
<td>4</td>
<td>1.345</td>
<td>5</td>
<td>1.540</td>
</tr>
<tr>
<td>5</td>
<td>1.600</td>
<td>6</td>
<td>1.714</td>
</tr>
<tr>
<td>6</td>
<td>1.000</td>
<td>7</td>
<td>1.363</td>
</tr>
<tr>
<td>7</td>
<td>1.714</td>
<td>8</td>
<td>1.000</td>
</tr>
<tr>
<td>8</td>
<td>1.400</td>
<td>9</td>
<td>1.091</td>
</tr>
<tr>
<td>9</td>
<td>1.330</td>
<td>10</td>
<td>1.388</td>
</tr>
<tr>
<td>7</td>
<td>1.571</td>
<td>11</td>
<td>1.272</td>
</tr>
<tr>
<td>Total</td>
<td>1.432</td>
<td>Total</td>
<td>1.213</td>
</tr>
</tbody>
</table>

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Pregnancy Disease

Ronald C. Huhn*

### History

Pregnancy disease is a highly fatal, acute metabolic disease affecting pregnant ewes during the last few weeks of gestation. It is characterized by ketonemia with fatty infiltration of the liver and is often associated with a low blood sugar. The condition is found wherever sheep are raised; it has been variously called stercoremia, lambing paralysis, pregnancy toxemia, and lamzierteke, ketosis, (2) domzierteke, acidosis, preparturient paresis, and hypoglycemic encephalopathy, (16,18,19) snow blindness, and twin lamb disease. (11) The entity has been widely studied if not always well studied.

### Etiology and Pathogenesis

Because of the various conditions, both internal and external, which are associated with pregnancy disease, its occurrence has resulted in conflicting views concerning its etiology.

### Miscellaneous suppositions

The disease has been diagnosed as a form of rabies. (2) Other viral and bacterial diseases were also considered but, because of the inability of fulfilling Koch’s postulates, were discounted. (4,39) The attribution of the signs of the disease to pregnancy disease. (11)

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toxins absorbed from retained feces (constipation) has occurred. The alleviation of signs once the ewe defecated was seen. I believe that the interpretation of such observations in this way is in the nature of the fallacy of post hoc, ergo propter hoc. Constipation as a cause of pregnancy disease has been disproven for work has shown that the passage of digesta through the gastrointestinal tract increases in rate as pregnancy advances. Thus any constipation and resulting autointoxication would most likely be secondary to the onset of pregnancy disease. Absorption of fetal toxins has also been considered and discounted.

**Role of exercise**

A lack of exercise is often thought to be a precipitating factor in pregnancy disease. The carbohydrate stored as muscle glycogen is inaccessible for use by the rest of the body unless the animal exercises. The glycogen is then released in the form of lactic acid, which can be re-synthesized into glucose to be used by the body. Also, ketone bodies are better utilized during exercise than during non-exercise periods. While lack of exercise cannot be classed as an agent causing pregnancy disease, it can be a precipitating and exacerbative item.

**Ketone bodies as a cause**

The possibility of excess ketone bodies causing the signs of pregnancy disease is remote or nonexistent. The blood ketone level is thought to be the result of a balance between acetyl coenzyme A oxidation, fatty acid synthesis and catabolism, and mobilization of fat reserves. Directly or indirectly, the corticosteroids affect all of these. It is reasoned that the hyperketonemia of pregnancy disease is mediated by the corticosteroids which are released because of the low glucose levels. It is further believed blood glucose and blood ketones would be due largely to the fact that the magnitude of the adrenal response, at any particular time, is a function of the severity of the hypoglycemia and of the period during which it was previously maintained. Thus ketosis is a secondary, nonconsistent lesion found in pregnancy disease. The lack of correlation of ketosis and pregnancy disease suggests strongly that the prime biochemical lesion is not immediately concerned with either the production or utilization of ketone bodies, but that the lesion (ketonemia) is likely to occur in conditions of stress in late pregnancy, which are often associated with a check in nutrition.

**Nutritional factors**

The initial difference between toxemic and normal pregnancy is considered to be a breakdown in the maternal carbohydrate economy, a failure of the glucose forming and sparing adaptations of pregnancy to accommodate to the fetal drain of hexose. The predisposing conditions conducive to this inability are: (1) twin fetuses, (2) lack of food, and (3) impaired efficiency of maternal metabolism.

**Role of the fetus(es)** Fructose (formed at the placenta), glucose, and fatty acids pass the placenta. Fructose formation and transfer was found to proceed at a rate which was independent of the glucose level in maternal blood. Loss from the dam in this form may be looked upon as an obligatory one. The direction of transfer of glucose is affected by the relative magnitudes of the maternal and fetal concentrations. In this way the drain need not be thought of as an obligatory loss.

Twin fetuses require 70% more nutrients than does a single fetus. These requirements may be equal to 20% of the dam’s own needs. Thus, when the ewe is on a poor ration, the fetus(es) are definitely a drain on her system and may be the factor precipitating the symptoms of pregnancy disease. Ewes bearing twins show less post-prandial rise and more fasting drop in glucose level than do ewes bearing single fetuses. The rate of glucose utilization (injected) by fasted pregnant ewes is much faster than that utilized by fasted non pregnant ewes. In fact, with controlled feed intake, the number of fetuses can be determined by referring to the rate of glucose utilization. The significance of or reason for the fetal requirements is more tangible when we con-
sider that 80% of fetal growth takes place during the last five to six weeks of gestation. (39)

**Role of deficient ration** The most constant phenomenon associated with pregnancy disease is a low plane of nutrition. (1) This may be manifested by an inadequate intake or by ingestion of a ration of poor quality (especially in amount of metabolizable glucose). (2,4,8,11,12,26,30) The ration of poor quality may be such that the ewe cannot physically ingest sufficient amounts to supply adequate calories. The reason for inadequate intake may be inaccessibility to the feed (such as in snowstorms), lack of appetite due to some other cause such as a mineral deficiency, or another disease which may render the animal incapable of ingesting proper amounts of feed. Comparative observations of pregnant and nonpregnant ewes have revealed that as the stage of pregnancy advances, the passage of ingesta through the digestive tract increases in rate. (9) The more rapid passage of ingesta would depress the digestibility and absorption of some rations, reducing the energy available to the ewe, and hence, would contribute to under-nutrition in late pregnancy.

**Impaired efficiency of maternal metabolism** The impaired efficiency referred to will be that observed postabsorptively. It may, at times, be only a relative impairment. Basically it should be remembered that little glucose is normally absorbed from the ruminant digestive tract. Glucose for use by the tissues must come from gluconeogenesis (fatty acid metabolism, etc.). This is largely done in the liver. Thus a malfunction of the liver or a lack of "raw products" would predispose to hypoglycemia more than in nonruminants for there is no secondary supply of absorbed glucose to fall back upon.

The nervous system uses glucose as its sole source of carbohydrate. (7) In the event of excessive demand for glucose (by the fetus) associated with a short supply (ration poor in glycogenic substances) the liver and brain are the first to show the signs of hypoglycemia. (14) The neurophysiological signs observed in pregnancy disease are characteristic of cerebral depression. The phylogenetically newer centers (high metabolic rate) are depressed before the older centers (lower metabolic rate) with the peripheral nerves being extremely resistant. The signs are comparable to those shown by a decorticated higher animal (quasi-hypoglycemic decoration). The symptoms of hypoglycemic cerebral depression, (progressive depression of cerebral cortical and cerebellar centers responsible for receiving stimuli from extero-and intero-receptors and initiating appropriate responses, release of subcortico-diencephalic centers from cortical control, and, in some cases, depression of mid-brain centers) similar to those encountered in pregnancy disease cases can occur after only brief periods of hypoglycemia. (16,18,19) Blood glucose levels of 12–20 mg.% for twenty-four hours can result in pregnancy disease. The critical level is determined by: (1) the adrenalin state, (2) genetic susceptibility, (3) environmental factors (such as temperature), (4) stage of pregnancy, and (5) the rate of development of hypoglycemia. Variances in these factors are probably responsible for the differences observed in clinical cases of the disease. It is thus concluded and agreed upon by several research workers that the induction of pregnancy toxemia is in nearly all cases due to hypoglycemia. (14,16,18,19,23,26) The low blood sugar almost invariably results from a combination of low diet source and high fetal requirements.

Once the cerebral depression is incurred, normoglycemia and even hyperglycemia may occur without remission of signs. One worker feels that this is because of irreversible brain damage. (16) Another worker has presented a more extensive hypothesis; it is based upon the fact that corticosteroids depress glucose utilization by the brain in addition to their stimulation of gluconeogenesis. The sequence (he feels) is this: fetal demands—hypoglycemia—release of some corticosteroids—insufficient gluconeogenesis (signs of pregnancy disease may come here—hypoglycemic encephalopathy)—continued hypoglycemia—release of more corticosteroids (in excess of what the liver can detoxify)—depression of glucose metabolism in brain plus gluconeogenesis—
continued signs of pregnancy disease in presence of normal or above normal glucose levels.(24,25,26,27,29,31,32,34) A case has been observed in which a pregnant ewe with normal blood glucose levels developed signs of pregnancy disease. The ewe was found to have a very high blood steriod level.(13,15)

The true role of the adrenal hormones in relation to pregnancy toxemia has not been completely determined. They function in relation to hypoglycemia, but are also released in response to psychic and physical stimuli which may or may not be related to hypoglycemia.(20,24,25,26,27,29,32,33,34)

Symptoms

The animals affected are ewes in the last four to six weeks of pregnancy. These ewes are nearly always carrying two or three fetuses. The condition often affects many in the flock.(2,4)

Whether viewed as a hypoglycemic encephalopathy or as a steroid hormone induced inhibition of glycolysis by the brain, it remain that the symptoms can be viewed as the results of a progressive inhibition of the more complex functional centers of the brain. This may result in a temporary release of the less complex reflex areas of the central nervous system.

The first observed deviation from normal is an attitude of lethargy and anorexia. The ewe will stand away from the flock and will show no fear. Salivation and chewing motions may be noticed. The animal will not eat food put before it and may not drink water even though its lips are immersed. As the condition worsens, the animal may wander, walking slowly with a staggering gait. Muscular twitching of the neck and head, ears, lips, eyelids, and nostrils will be evident. Secretory disturbances such as mild scours, loss of saliva (hypersecretion or inability to swallow), snuffling respiration and nasal exudate are observed. Untreated animals become extremely ataxic, appear blind, and may “go down.” The affected animal may remain in the position in which it fell or may experience convulsions in which running movements and other spastic limb movements as well as opisthotonus may be noticed. Death may ensue in one to ten days. This may be variously attributed to: (1) depression of cardiac and respiratory centers (rare), (2) circulatory embarrassment, (3) hypostatic congestion, (4) renal damage and sequelae there of, (5) dehydration and (6) starvation (due to anorexia). The possibility of a bacterial debacle due to lowered resistance would seem imminent. The condition is afebrile. (1,2,3,4,5,8,11,16,39)

Lesions

Lesions primary to the disease consist of a fatty infiltration of the liver producing a yellow clay-colored organ; the kidney may be fatty with the presence of a diffuse glomerular and tubular nephritis. Sequelae occurring secondary to the primary condition could result in innumerable lesions.(5,11,39)

Diagnosis and Differentiation

The diagnosis of pregnancy disease should not be difficult if one considers the individual (predescribed) signs shown by the animal in association with the nutritional plane and psychic or physical stimuli which might have induced or exacerbated the symptoms. Other conditions which must be distinguished from pregnancy disease are: (1) hypocalcemia, (2) presence of Corenurus cerebralis (coenurosis), (3) acute fascioliasis, (4) dystocia, or (5) various viral or bacterial encephalitides.(11,39)

Treatment and Prevention

Upon reflection, it will be remembered that the etiology of pregnancy disease, the metabolic pathways involved, and the pathogenesis of the condition are still controversial factors. Therapy, therefore, must still be somewhat symptomatic. The close relationship of the disease to a low nutritional state (i.e., a tentative identification as a hypoglycemic encephalopathy) would lead to the postulation that any therapy which induces hyperglycemia (reverses hypoglycemia) should induce recovery provided it is initiated before irreversible damage has occurred.(16,18,19,37) If this latter provision is not made, the carbohydrate deficiency may be negated with-
out alleviation of clinical signs, causing many therapeutic agents to be discounted as ineffective, while they may have value if used at the proper time. (3,4,10,17,21,24,36,37) It should also be remembered in evaluating experimental treatments that it is difficult to interpret data obtained from untrained animals. (28)

Of treatments tried, glucose and/or glycerol given early seems to be the best. (4,17,37,39) Glucagon, a hyperglycemic and glycogenolytic compound acting hormonally, has been tried. (21) Corticosteroids and A.C.T.H. have been reported as effective (3,21) and ineffective. (10) Treatment must be continued until recovery is complete including complete return of appetite. Rumen inoculation capsules, multiple vitamins, molasses, and other appetite stimulators may be used. (3,19) The fetuses may be aborted or taken by cesarean section to effect a remission of signs.

Preventive measures include: (1) stepping up the feed intake during the last few weeks of pregnancy, (2) avoiding sudden changes in feeds and avoiding starvation, (3) proper exercise, (4) proper sheltering of animals, and (5) culling to remove undesirable susceptible animals. (11,19,39)

Apercu

The condition in sheep variously termed but most often called pregnancy disease has been discussed. The etiology is in controversy but two hypotheses, that of a hypoglycemic encephalopathy and that of a steroid-induced diabetic-like syndrome, have been advanced recently. The symptoms follow those of a progressive depression of the higher centers of the cerebrum (highly metabolizing centers being depressed before the more slowly metabolizing ones). Lesions are confined to the liver (fatty infiltration) and kidney (varying degrees of nephritis) primarily, with lesions due to secondary sequelae varying widely. Treatment and prevention are aimed at regaining or maintaining caloric homeostasis.

BIBLIOGRAPHY


