Uterine Changes Associated With Impaired Fertility in the Dairy Cow

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Abstract

Uteri from 55% of a group of repeat breeder cows contained abnormal uterine glands. Morphologically, these glands were characterized by enlargement of the lumen, various degrees of degeneration of the glandular epithelium, and a localized modification of the stoma accompanied by infiltration of either eosinophils or lymphocytes or both. The lesion was localized and was caused by occlusion of the endometrial gland.

Introduction

Many dairy cows that fail to conceive, repeat-breeders, have ovaries and accessory reproductive organs that appear to be functioning normally when examined grossly. Histological observations reveal that uteri from some of these animals contain abnormal uterine glands surrounded by a fibrotic area of stoma. These abnormal glands have been described as endometrial glands with fibrous rings, as cuffed uterine glands, or as areas of periglandular fibrosis. They have been associated with leucocytes of different types and have been found in animals having nonpurulent endometritis (4). Also, presence of these glands is evidence that animals either have or have had severe metritis (1).

The purpose of this report is to describe in further detail uterine conditions associated with the presence of these abnormal glands in animals with impaired fertility and to suggest a hypothesis concerning their probable relationship to lowered fertility.

Materials and Methods

Animals for this study were loaned to the Department of Animal Science by cooperating dairymen—animals culled from the departmental herd for various reasons—and a group of sexually mature heifers and cows of beef breeding slaughtered for a genetic study. These beef animals form the control group of Table 1. Animals from dairymen were selected

Table 1. Incidence of uterine abnormalities in cows with different reproductive histories.

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cows</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Sterile</td>
<td>69</td>
<td>23</td>
</tr>
<tr>
<td>Cross anomalies</td>
<td>47</td>
<td>14</td>
</tr>
<tr>
<td>Absent</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>Present</td>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>Control</td>
<td>11</td>
<td>4</td>
</tr>
</tbody>
</table>

*Sterile cows were subdivided into two groups on presence or absence of gross abnormalities which, potentially, could cause the sterility. Of the nine animals with gross abnormalities, three had cystic corpora lutea, three had cystic corpora intera, two had adhesions of the oviduct to the ovary, and one had an occluded cervix. The 4 had cystic ovaries, 1 had an occluded cervix, and 1 had occluded oviducts.

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because they had failed to conceive from four or more breedings and were considered sterile by their owners. Animals loaned to us came from herds that were under veterinary supervision and, in most cases, animals were selected for grossly normal reproductive tracts. Animals were transported to the campus and were dried off if they were milking. They then were screened for infectious disease and were bred artificially to bulls of normal fertility. If they did not conceive to first or second service, they were slaughtered at all stages of the estrous cycle, and a section of the uterus was fixed in Zenker-formal fixative. Following fixation the tissues were processed and stained with hematoxylin-eosin-azure II. Animals in the pregnant group consisted of animals loaned by the dairymen that conceived and animals from the station which were slaughtered for experiments on lactation. Duration of pregnancy ranged from 30 to 260 days. Serial sections from a uterus containing the abnormal glands were examined to study details of the abnormality.

Results and Discussion

Lengths of estrous cycles in animals which did not conceive and in pregnant animals were essentially the same, and a histogram of the individual cycle lengths was similar to that reported for dairy cows by Asdell (2).

Changes in the uterus and the incidence of abnormal glands are in Table 1. Enlarged uterine glands with periglandular fibrosis were in 23 of 69 (33.3%) of the sterile animals, in 1 of 16 pregnant animals, and in none of 24 controls (2.5% for combined pregnant and control groups). The difference in incidence of abnor-

![Fig. 1. Massive infiltration of eosinophils into the endometrium X 200.](image)
mal glands in sterile animals and in combined pregnant and control groups was significant ($P<.05$) as measured by Chi-square. All of the sterile animals with cuffed glands had eosinophils, lymphocytes, or a combination of both in the endometrium. In some of the animals the eosinophils were distributed throughout the endometrium, being most abundant in the compact zone (Fig. 1); in others they were localized around the abnormal glands (Fig. 2). In animals whose uteri contained lymphocytes only the lymphocytes were localized around the abnormal glands (Fig. 2). Generally, when both eosinophils and lymphocytes were present, they were localized around the affected glands. Secretion occurs in some of these abnormal glands (Fig. 4), and some of them contain numerous large mononuclear cells (Fig. 5).

Endometrial glands in the cow are simple-branched tubular glands with a variable amount of coiling, particularly in the branched portions, and morphological changes in the glands and endometrium in these abnormal uteri are caused by occlusion of the lumen of the affected glands (Fig. 6). Although occlusion may occur in any part of the gland, morphological characteristics suggest that in most cases the lumen is blocked in the region of the compact zone of the endometrium.

The number of abnormal glands per section was variable in different animals, ranging from a single abnormal gland to all of the glands in the section.

The presence of eosinophils and lymphocytes singly or in combination is closely asso-
associated with the presence of modified uterine glands. An analysis of variance showed a highly significant interaction between the presence of these two types of leucocytes and presence of the abnormal glands. Eosinophilic infiltration of the endometrium of the cow has been reported under several different conditions. Murphy (5) found large numbers of eosinophils in the endometrium of cows during the entire estrous cycle with greatest concentration about the 5th day of the cycle. Laszlo (4) reported eosinophilic infiltration in cases of non-purulent endometritis. Both of these investigators found abnormal uterine glands in the animals with eosinophils. Skjerven (6) found a relationship between eosinophils in the uterus and the interval from parturition. Uterine eosinophilia occurs following death of the early embryo (3). According to Weber (8), uterine eosinophilia was not present in heifers during the estrous cycle, nor was it in pregnant and control animals. All of these observations indicate that high concentrations of eosinophils are associated with abnormal conditions in the uterus. They probably play an important role in the destruction of the secretions of the occluded glands that are reabsorbed into the endometrium. Lymphocytes also appear to be active in modification of the morphology and activity of the occluded glands.

If 11 animals (3 with inactive ovaries, 4 with cystic ovaries, 2 with adhesions of the oviduct, and 2 with occluded tracts) are eliminated from the sterile group in Table 1, 20 of 58 sterile animals exhibit abnormal uterine glands combined with leucocytes and 12 of 58...
animals exhibit infiltration of leucocytes in the presence of normal glands. Thus, 32 of the 58 sterile animals have a combination of abnormal glands and leucocytes or leucocytes alone. If some of the uterine sections failed to reveal the uterine abnormality because of its localized nature, the incidence of this condition probably is greater than reported in these data, but its extent cannot be estimated.

The nature of reproductive failure in these animals was not studied, but as a group they resemble animals reported by Tanabe and Casida (7), who reported both failure of fertilization and early embryonic death in affected animals.

On the basis of our conditions, the following hypothesis is suggested to account for events which occur in the affected uteri. Trauma to the endometrium either as the result of parturition or from uterine infection is associated with reorganization of the endometrium. In some instances during the subsequent healing process lumens of some of the glands become occluded. These occlusions prevent glandular secretions from reaching the lumen of the uterus and they are trapped within the glands. The increased pressure within the gland causes a modification of the connective tissue in the stroma surrounding the gland. This increased intraglandular pressure probably causes a resorption of the secretory material from the gland, and the morphological differences between the uteri probably reflect progressive changes which develop during the process. If the lesions are limited in number and the glands are functionally inactivated, the uterus may recover to such an extent that fertility is
restored. If the damage is too extensive, normal function of the uterus is impaired to the extent the animal becomes permanently sterile.

Functional uterine changes caused by eosinophils and lymphocytes probably are responsible for changes in the uterine environment which interfere with successful fertilization and implantation and account for the delay in conception and successful gestation in affected animals in which temporary infertility occurs.

References

Fig. 6. Occluded area of an endometrial gland. Arrow indicates area of occlusion. Note the presence of normal endometrial glands adjacent to the abnormal gland × 200.