STUDIES on uterine defensive mechanisms and inflammatory responses evolved from attempts to induce pregnancy in luteal phase animals by depositing semen in the uterine lumens after artificial ovulation or by transferring ova through the cervixes and into the uterine lumens (Black et al., 1953b; Rowson, Lamming and Fry, 1953). Invasion of the uterine lumen during the luteal phase of the estrous cycle was usually followed by infection and pyometra. This type of reaction did not follow invasion of the uterus during the follicular phase of the cycle, suggesting that uteri of luteal phase animals were more susceptible to uterine infection than were uteri of estrous animals.

Several investigations followed on inflammatory responses in uteri of rabbits and cattle. Inflammation was induced by depositing semen or bacterial suspensions in the uterine lumen. At autopsy 1 or 2 days later, the uteri of estrous animals usually contained little pus and few bacteria, indicating the operation of a highly effective uterine defense mechanism; uteri of luteal phase animals contained relatively large amounts of pus and greater numbers of bacteria, indicating impaired bactericidal capabilities despite the severe leukocytic response (McDonald et al., 1952; Black et al., 1953a, b, 1954; Rowson et al., 1953). The endocrinological basis for the difference between follicular and luteal phase animals was due primarily to inhibition of defensive capabilities by progesterone; uteri of ovariectomized animals and estrous or ovarioectomized estrogen treated animals all had highly effective bactericidal capabilities. In much of this work, the opportunity was present for differential degrees of drainage through the cervix to play a part in the varying defensive capabilities of the uterus. However, even when the cervix was ligated to prevent drainage, uteri of estrous rabbits had much more effective defenses than did uteri of pseudopregnant rabbits (Black et al., 1954).

Impetus for work on uterine defensive mechanisms was provided by reports that uteri of luteal phase cows of low fertility showed lesser leukocytic response and greater bactericidal capabilities than did uteri of luteal phase virgin heifers (Black et al., 1953b, 1954).

The remainder of this paper will be concerned for the most part with inflammatory responses during the first 2 to 8 hr. of induced inflammation. The irritant was almost always a suspension of bacteria. Inflammatory responses were usually measured by the number of leukocytes entering the uterine tissues and lumens within a given period of time. Effectiveness of uterine defensive mechanisms was measured by clearance of bacteria from the uterine lumens.

Consideration will first be given to the defensive mechanisms that are known to operate in the uterus during the early phases of the inflammatory response. Each one is influenced by the ovarian status of the animal.

**Uterine Defensive Mechanisms**

**Drainage.** Once bacteria gain entrance to the uterine lumen, it would be reasonable to expect that drainage through the cervix would be a more effective defense mechanism in estrous animals, with their motile uterus, patent cervix and copious cervical secretions, than in luteal phase animals, with little uterine motility, relatively closed cervixes and scant cervical secretion. In line with this reasoning, Black et al. (1954) reported that drainage had contributed more to the uterine defenses of estrous than of pseudopregnant rabbits by 24 hr. after bacterial inoculation of the uterine lumen. Also, Winter et al. (1960a) found that more bacteria were cleared from the uterus by drainage in follicular phase than in pseudopregnant rabbits, particularly during the first few hours after inoculation.

Although drainage from the uterus is undoubtedly a powerful defensive mechanism under natural circumstances, at least in follicular phase animals, the role of this factor under experimental circumstances is difficult.
to assess. Therefore, most of the studies to be cited below were conducted with uterine horns ligated at each end in order to eliminate drainage as a factor.

Leukocytes and Phagocytosis. It has been somewhat difficult to establish the precise role of leukocytes and importance of phagocytosis in clearing bacteria from uterine lumens for the following reasons: at 1 to 2 days after inoculating the uterine lumen, the seeming inability of great numbers of leukocytes in uteri of luteal phase animals to have been as effective in clearing bacteria from the uterus as smaller numbers of leukocytes in estrous animals; during the first few hours after inoculation, the difficulty in quantitating the phagocytic activity of leukocytes, particularly when Gram-negative bacteria were used as the irritant; the near impossibility of ruling out the operation of major defensive mechanisms other than phagocytosis.

Investigations on possible bases for the persistence of larger numbers of bacteria in uteri of luteal phase than of estrous animals have not shown the difference to be due to differential nutritional properties of uterine contents (Hawk et al., 1957; Broome and Lamming, 1959a), to differences in bactericidal activity of blood plasma (Broome, Lamming and Woodbine, 1959), or to rapid local production of antibodies in estrous rabbit uteri (Broome and Lamming, 1959b).

Hawk et al. (1957) found that, as early as 4 hr. after inoculation of ligated rabbit uteri, only a fraction of the bacteria could be recovered from estrous rabbits while nearly all of the bacteria were recovered alive from pseudopregnant rabbits. It was soon ascertained that the influx of leukocytes into the uterine lumen in response to bacterial inocula occurred earlier in estrous than in luteal phase rabbits, sheep and cattle (Hawk, 1958; Broome, Lamming and Smith, 1959; Hawk, Turner and Sykes, 1961a; Hawk et al., 1964). Intense leukocytic responses, with the migration of tens or hundreds of millions of polymorphonuclear neutrophilic leukocytes into the uterine lumen, occurred between 2 and 4 hr. after uterine inoculation in estrous rabbits and heifers and between 4 and 8 hr. in estrous ewes. The development of a leukocytic response of similar intensity in luteal phase animals, required more than twice as much time in each species (Winter et al., 1960a; Hawk et al., 1960c; Brinsfield, Hawk and Leffel, 1963; Hawk et al., 1964).

In both estrous and luteal phase animals, the influx of large numbers of leukocytes into the uterine lumen was accompanied by intense bactericidal activity. The following facts suggest strongly that phagocytosis by polymorphonuclear leukocytes constitutes the major defensive mechanism against bacteria deposited in the lumens of ligated uterine horns: the consistent association in rabbits, sheep and cattle between the influx of leukocytes into the uterine lumen and clearance of most bacteria from the uterus; the observation of large numbers of phagocytized leukocytes in some experiments, particularly when Gram-positive bacteria were used as the irritant (Broome et al., 1960); the lack of bactericidal activity when leukopenia was induced or the leukocytic response was suppressed experimentally in rabbits (Hawk et al., 1960b; Winter et al., 1960b).

The earlier work on uterine defensive mechanisms had shown that uteri of luteal phase animals contained greater numbers of both leukocytes and bacteria at 1 or 2 days post-inoculation than did uteri of estrous animals. Winter et al. (1960a) and Broome et al. (1960) reported the same situation and considered that it might be due to such factors as bacterial multiplication, less effective bactericidal activity of leukocytes in uteri of luteal phase animals or greater activity of non-leukocytic bactericidal factors in uteri of follicular phase animals. The slower mobilization of leukocytes in luteal phase animals, allowing time for bacterial multiplication to occur, might be a major factor.

Killingbeck and Lamming (1963) and Lamming and Haynes (1964) found that uterine flushings from luteal phase rabbits and cows contained substances which markedly inhibited phagocytosis of starch granules by polymorphonuclear leukocytes. The active substances were polysaccharides which seemed to effect the surface of leukocytes (Killingbeck, Haynes and Lamming, 1963). These substances were not present in uterine flushings from estrous rabbits or cows, suggesting that their presence might be related to endocrine control of the susceptibility of the uterus to infection.

Since most bacteria disappear from the uterine lumens of luteal phase rabbits, sheep and cattle once the leukocytic response develops, there is little evidence that phagocytosis inhibiting substances interfere greatly with bactericidal activity in uterine lumens.
of luteal phase animals. Broome et al. (1960) failed to detect any difference in the phagocytic activities of leukocytes in uteri of estrous and luteal phase rabbits. Nevertheless, if substances which inhibit the phagocytosis of starch particles can also inhibit the phagocytosis of bacteria in utero, the presence of such substances might explain the persistence of bacteria in uteri of luteal phase animals in the face of massive leukocytic responses.

Similar to endocrine effects on leukocytic responses to bacterial inocula, leukocytic responses to semen deposited in uterine lumens are slower in luteal phase than in estrous hamsters, rabbits and cows (Marcus, 1966; Howe, 1967; Mahajan and Menge, 1967).

**Non-Cellular Bactericidal Factors.** Non-cellular bactericidal substances accumulate in the uterine lumen during the development of an inflammatory response. Cell-free inflammatory exudates from estrous rabbits were bactericidal in pseudopregnant rabbit uteri and in vitro (Hawk, 1958). Exudates from pseudopregnant rabbits became bactericidal at a later time interval as the leukocytic response developed (Hawk et al., 1960b; Winter et al., 1960a).

The non-cellular factors seem to originate in leukocytes; cell-free uterine exudates began to have bactericidal capabilities as leukocytes migrated into the uterine lumen (Hawk, 1958; Hawk et al., 1960b); the bactericidal factors in the exudates were more heat stable than bactericidal factors in blood serum; extracts of leukocytes had bactericidal properties similar to those of non-cellular exudates when tested in vitro against Escherichia coli; both exudates and extracts lost bactericidal capabilities in the same temperature range and neither one lysed the bacteria that were killed (Hawk, 1959).

The importance of non-cellular factors in uterine defenses against bacteria is not clear. In many instances in which bacteria in uterine flushings were enumerated both by colony and microscopic counts, the colony counts accounted for only a small percentage of the bacteria deposited in the uterus while the microscopic counts accounted for all of them; the discrepancy suggested that many bacteria had been killed in the uterus (Hawk, et al., 1960b). Thus it seems likely that non-cellular factors have some value in holding bacterial numbers in check until phagocytosis occurs. The range of bacterial species against which such a defensive mechanism might have value is not clear, since non-cellular factors were highly bactericidal against E. coli but had little bactericidal activity against Staphylococcus aureus (Winter et al., 1960a).

None of the studies on uterine defensive mechanisms have ruled out the possibility that non-cellular bacteriolysis mechanisms operate in intact uteri against some bacterial species.

**Localized Effect of Ovarian Hormones on Induced Leukocytic Responses**

It is known that ovarian hormones can influence the effectiveness of various defensive mechanisms of the body, such as the spread of infectious agents through skin (Sprunt, 1941), phagocytic activity of the reticuloendothelial system as measured by phagocytosis of circulating carbon particles, production of gamma globulin and protection against experimental infections (Nicol, Vernon-Roberts and Quantock, 1965). Of various hormones tested for effects on the phagocytic activity of the reticuloendothelial system, estrogens are strong stimulants and progesterone is a mild stimulant.

Hormonal effects on general body defenses might influence the course of chronic infections in the uterus and the spread of infectious agents from the uterus, but it seems unlikely that ovarian steroids control acute inflammatory responses in the uterus by affecting general body defenses. The stimulatory effect of progesterone on the phagocytic activity of the reticuloendothelial system certainly differs from its inhibitory effect on uterine defensive mechanisms.

Acute inflammatory responses of the type induced experimentally in the uterine lumen have been induced in other body cavities. After bacterial inoculation of the peritoneal or pleural cavities as well as the uterine lumens of rabbits, the uteri of estrous and pseudopregnant rabbits differed in bactericidal activity 28 hr. later but peritoneal or pleural cavities did not (Hawk et al., 1955). At 4 hr. after inoculation of pleural cavities, there was no evidence of differences between estrous and pseudopregnant rabbits in leukocytic responses, bactericidal activity in the pleural cavities, or bactericidal properties of cell-free pleural exudates (Hawk, et al., 1960c). Most bacteria had been cleared from the pleural cavities of both kinds of rabbits.

In a study on possible effects of ovarian
TABLE 1. ENDOCRINE EFFECTS ON THE INTENSITY OF INDUCED ACUTE LEUKOCYTIC RESPONSES

<table>
<thead>
<tr>
<th>Species</th>
<th>Endocrine state</th>
<th>Relative leukocytic responses</th>
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<tbody>
<tr>
<td>Rabbits</td>
<td>Estrous</td>
<td>++++</td>
</tr>
<tr>
<td></td>
<td>Pseudopregnant</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Ovariectomized</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ovariectomized, estradiol injected</td>
<td>++++</td>
</tr>
<tr>
<td></td>
<td>Ovariectomized, progesterone injected</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Ovariectomized, estradiol+progesterone injected</td>
<td>+</td>
</tr>
<tr>
<td>Cattle</td>
<td>Estrous</td>
<td>++++</td>
</tr>
<tr>
<td></td>
<td>Luteal phase</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Ovariectomized</td>
<td>+</td>
</tr>
<tr>
<td>Sheep</td>
<td>Estrous</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Luteal phase</td>
<td>+</td>
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<tr>
<td></td>
<td>Ovariectomized</td>
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<tr>
<td></td>
<td>Ovariectomized, estradiol injected</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Ovariectomized, progesterone injected</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Ovariectomized, estradiol+progesterone injected</td>
<td>+</td>
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</tbody>
</table>

* Relative responses derived from numbers of leukocytes flushed from uterine lumens 4 hr. after bacterial inoculation of rabbits and cattle and 4, 6 and 8 hr. after inoculation of sheep. References: Hawk et al., 1960a; Brinsfield et al., 1963; Brinsfield et al., 1964; Hawk et al., 1964.

status on inflammatory responses in mammary glands of non-parous ewes, no evidence was obtained that development of leukocytic and vascular responses and bactericidal activity were delayed in luteal phase ewes (Hawk, Righter and Brinsfield, 1963; Righter, Hawk and Brinsfield, 1963). In fact, inflammatory responses developed slightly faster in mammary glands of luteal phase and estrous ewes than ovariectomized ewes. The developing mammary glands of the luteal phase ewes were almost certainly under the influence of endogenous progesterone.

The studies cited above suggest strongly that suppression of leukocytic responses by progesterone is restricted to the uterus.

Comparative Roles of Estrogen and Progesterone in Regulating Acute Leukocytic Responses

During the first 4 hr. of induced uterine infection in rabbits and cattle, greater numbers of leukocytes enter the uterine lumens of estrous or ovariectomized estradiol treated animals than ovariectomized untreated animals, indicating that estrogen intensifies the acute leukocytic response (table 1). Leukocytic migration into the uterine lumen occurs faster in ovariectomized animals than in luteal phase or ovariectomized progesterone treated animals, indicating that progesterone delays the leukocytic response (Hawk et al., 1960a; Hawk et al., 1964).

In sheep, as in the other species, leukocytic responses are slowest during the luteal phase (table 1). Unlike in the other species, however, responses are quicker in ovariectomized ewes than in estrous ones (Brinsfield et al., 1963). It appears that leukocytic responses are no faster in ovariectomized ewes than in ovariectomized cattle or rabbits, but rather that responses are delayed in estrous ewes. The injection of estradiol into ovariectomized ewes raised the leukocytic responses above those of ovariectomized ewes (Brinsfield, Hawk and Righter, 1964), indicating that estrogen had the same intensifying effect on the response that it had in the other species. Injection of a small amount of progesterone plus estradiol into ovariectomized ewes suppressed the responses to a level comparable to those of estrous ewes (table 1), suggesting that delayed leukocytic responses in estrous ewes were caused by some action of endogenous progesterone. The progesterone might be that secreted during the previous luteal phase, with lingering effects exerted during estrus because of the relatively short follicular phase that precedes estrus in sheep (Stabenfeldt, Holt and Ewing, 1969).

Consideration of Sites at Which Ovarian Hormones Might Control Leukocytic Responses

The numbers of polymorphonuclear and mononuclear leukocytes in uterine tissues and in the circulation before and during the acute inflammatory response did not differ between estrous and pseudopregnant rabbits (Broome et al., 1960). In sheep, the numbers of leu-
kocytes in endometrial tissue or in the uterine lumen were no less in luteal phase than in estrous ewes 2 hr. after inoculation of the uterine lumen, the numbers being small in each type of ewe (Brinsfield et al., 1963). There is thus no experimental evidence that slower leukocytic responses in luteal phase rabbits and sheep are due to the initial presence of fewer leukocytes in uterine tissues or to fewer leukocytes available in the circulation.

In cattle, the number of polymorphonuclear leukocytes both in the endometrium and in the circulation increase around the time of estrus (Skjerven, 1956; Moberg, 1955). Infiltration of the endometrium by phagocytic leukocytes at this time probably improves the defensive capabilities of the uterus. However, these leukocytes represent only a very small percentage of the massive number of cells that enter the uterine lumen in response to a bacterial inoculum and could not account for the differing responses of estrous and luteal phase animals. The number of circulating neutrophilic leukocytes might affect the number that enter the uterine lumen over a period of time, but it is doubtful that fewer circulating neutrophils in luteal phase cattle could account for the delay in the initial response in these animals.

Evidence has been reported, based on relative numbers of leukocytes in endometrial tissues and uterine lumens of estrous, ovarioectomized and pseudopregnant rabbits, that endogenous progesterone slows the migration of extravasated leukocytes through the endometrium as they move toward the uterine lumen (Hawk et al., 1960a, 1961b; Broome et al., 1960). This can presumably account in part for the relatively slow influx of leukocytes into uterine lumens of pseudopregnant rabbits.

No evidence was found that the rate of migration of extravasated leukocytes was slowed in luteal phase ewes or heifers (Brinsfield et al., 1963; Hawk et al., 1964). The small numbers of leukocytes in uterine tissues of ewes and heifers during the first 2 hr. of induced infection, compared to the massive numbers of leukocytes entering the uterine lumens as the inflammatory response develops, indicate that ovarian hormones control the development of leukocytic responses mainly by controlling the time and intensity of leukocytic migration out of the endometrial vascular system.

Studies on Physiological Mechanisms by Which Ovarian Hormones Might Control Leukocytic Responses

The means by which endogenous or exogenous estrogen intensifies acute leukocytic responses is not known, but enlargement of the uterus and increased blood flow through the endometrium would have to be considered as possible major factors. Estrogen does not necessarily intensify leukocytic responses through the same physiological mechanisms by which progesterone delays the responses.

Progesterone might delay the migration of large numbers of leukocytes out of the endometrial vascular system by having such effects as the following: delay the transmission of chemical signals from the uterine lumen to circulating leukocytes, delay activation of the mechanism that causes leukocytes to stick to vascular endothelium prior to migrating through the vascular walls, cause normal changes in the vascular endothelium or basement membrane which retard leukocytic emigration during inflammatory responses, or prevent changes in vascular walls during an inflammatory response which might facilitate the rapid emigration of large numbers of leukocytes. None of these points has been studied intensively, and the means by which progesterone delays the leukocytic response have not yet been established.

There is no evidence that substances which might attract leukocytes into the uterine lumen are lacking in pseudopregnant rabbit uterii. Cell-free uterine exudates taken from estrous, ovarioectomized and pseudopregnant rabbits during the early stages of induced infection were tested for leukotaxic properties in rabbit skin or uteri (Hawk et al., 1961b); exudates from pseudopregnant rabbits actually attracted a greater leukocytic response than did exudates from the other rabbits.

Injections of heparin into the systemic circulation did not alter leukocytic responses in the uterus, thus failing to suggest that ovarian hormones might influence leukocytic emigration by controlling fibrin formation in the uterine vascular system (Hawk, Turner and Brinsfield, 1963a).

Heap, Robinson and Lamming (1962) washed the uterine horns of estrous and pseudopregnant rabbits injected with estradiol or progesterone before inoculating the uterine lumens with *E. coli*. Washing the uterus in-
CREASED THE LEUKOCYTIC RESPONSE IN PSEUDO-PREGNANT AND IN OVARIECTOMIZED PROGESTERONE INJECTED RABBITS BUT NOT IN THE OTHERS. THE RESULTS WERE INTERPRETED AS SUGGESTING THAT THE WASHING REMOVED SOME SUBSTANCE FROM UTERI OF PROGESTOGEN-INFLUENCED RABBITS WHICH WOULD OTHERWISE INHIBIT THE LEUKOCYTIC RESPONSE. SUBSEQUENT WORK HAS SHOWN THAT POLYSACCHARIDE SUBSTANCES ARE PRESENT IN FLUSHINGS FROM LUTEAL PHASE RABBIT AND COW UTERI BUT NOT IN FLUSHINGS FROM UTERI OF ESTRUS ANIMALS (LAMMING AND HAYNES, 1964). IT SHOULD BE NOTED THAT IN THE ORIGINAL WORK ALL RABBITS WERE AUTOPSIED AT 8 HR. POST-INOCULATION, WHICH PROBABLY ALLOWED AMLE TIME FOR LEUKOCYTIC RESPONSES TO DEVELOP FULLY IN ESTRUS AND OVARIECTOMIZED CONTROL RABBITS; UNDER SUCH CIRCUMSTANCES, AN EFFECT OF WASHING COULD PROBABLY BE DETECTED ONLY IN PROGESTOGEN-INFLUENCED RABBITS.


RESULTS OF WORK ON WASHING UTERINE LUMENS ARE NOT INCONSISTENT WITH THE POSSIBILITY THAT SOMETHING IN THE UTERI OF LUTEAL PHASE ANIMALS CAN DELAY THE LEUKOCYTIC RESPONSE SOMEWHAT, PERHAPS BY DELAYING TRANSMISSION OUT OF THE LUMENS OF CHEMICAL MEDIATORS REQUIRED TO INITIATE THE RESPONSE. INSUFFICIENT EXPERIMENTATION HAS BEEN DONE TO CONCLUDE THAT SUCH FACTORS CONSTITUTE THE MAJOR MEANS BY WHICH PROGESTERONE DELAYS ACUTE LEUKOCYTIC RESPONSES.

WHETHER OVARIAN HORMONES MIGHT CONTROL ACUTE LEUKOCYTIC RESPONSES BY CONTROLLING VASCULAR FUNCTION IS DISCUSSED IN THE FOLLOWING SECTION.

VASCULAR RESPONSES OF THE ENDOMETRIUM TO INFLAMMATORY STIMULI


<table>
<thead>
<tr>
<th>TABLE 2. ENDOCRINE EFFECTS ON ENDOMETRIAL VASCULAR FUNCTION</th>
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<tr>
<td>Species and endocrine state</td>
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</tr>
<tr>
<td><strong>RABBITS</strong></td>
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<tr>
<td>Estrous</td>
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<td><strong>SHEEP</strong></td>
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<tr>
<td>Estrous</td>
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<td>Luteal</td>
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<td>Ovariectomized, estradiol injected</td>
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<td>Ovariectomized, progesterone injected</td>
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<tr>
<td>Ovariectomized, estradiol+progesterone injected</td>
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</table>

* Relative degrees of blueness of endometrium (rabbits) and relative degrees of blueness or amounts of dye extracted from endometrium (sheep).
* Relative increases in blueness of endometrium 2 and 4 hr. after bacterial inoculation of rabbit uteri and 6 hr. after inoculation of sheep uteri. References: Hawk et al., 1963b; Hawk et al., 1963; Brinsfield et al., 1964.
During acute phases of inflammatory responses in animal tissues, the vascular endothelium generally increases in permeability. The increase in permeability can be measured by increased extravasation of circulating vital dye (Spector and Willoughby, 1963). During acute inflammation in rabbit uteri, the exudation of circulating dye into the endometrium increased appreciably in ovariectomized and estrous does. It did not increase in pseudopregnant does (table 2), indicating that endogenous ovarian hormones of pseudopregnancy suppressed the vascular response to inflammatory stimuli in the uterine lumen (Hawk et al., 1963b).

During the acute inflammatory response in sheep uteri, coloring of the endometrium increased greatly in ovariectomized ewes (table 2). It did not increase in luteal phase or estrous ewes or in ovariectomized ewes injected with estradiol, progesterone or both steroids (table 2). These results indicated that endogenous ovarian hormones as well as exogenous estradiol or progesterone could suppress the endometrial vascular response in the ewe.

The relative levels of vascular function in estrous, ovariectomized and pseudopregnant rabbits, after the marked increase in vascular function in ovariectomized rabbits, were correlated with the rates of leukocytic response (tables 1 and 2). Whether a cause and effect relationship might be involved is not known.

Ovariectomized sheep, with marked increases in vascular function, had good leukocytic responses, while luteal phase and estrous sheep, with no apparent increases in vascular function, had delayed leukocytic responses (table 2). However, ovariectomized ewes injected with ovarian hormones had no such relationship between vascular and leukocytic responses. Ovariectomized ewes injected with estradiol and those injected with progesterone in addition to estradiol had similar vascular characteristics, yet estradiol alone intensified leukocytic responses and progesterone injected with estradiol inhibited the responses (table 1). It is, therefore, questionable whether progesterone delays leukocytic responses in the sheep uterus by suppressing changes in vascular function.

Discussion

It is not known how the effect of progesterone in delaying the initial leukocytic responses to irritants in the uterine lumen relates to the pregnancy maintaining actions of progesterone. Neither is it known whether maintenance of vascular stability by ovarian hormones during acute inflammatory responses reflects the operation of some pregnancy maintaining mechanism. If the effect of progesterone on acute inflammatory responses represents only a side effect to some primary action of the hormone, then that side effect may be inconsequential with regard to survival of embryos. On the other hand, it is possible that suppression of uterine irritability is directly essential for safeguarding pregnancy.

In a symposium concerned largely with reproductive physiology of the postpartum animal, it seems appropriate to note the lack of work on factors that influence inflammatory responses of the uterus during the postpartum period. The defensive capabilities of the uterus relative to challenges by invading microorganisms during this period are not known. Theoretically, the endocrine state of the postpartum female before the first ovulation should be reasonably good for efficient operation of defensive mechanisms because of the lack of luteal progesterone. However, the relationships between defensive capabilities of the uterus and the ability of microorganisms to persist in the uterus may be completely different in postpartum animals from those in the cycling and ovariectomized animals used in the studies covered in this review. During the postpartum period, there is probably ample opportunity for microorganisms to enter the uterus through the patent cervix, insufficient uterine tone and motility to cleanse the uterus by drainage, and perhaps a sluggish response of defensive mechanisms to the presence of infectious agents, even in the absence of corpora lutea. It is even possible that effects of any endogenous estrogens secreted during this period might promote a uterine environment better suited to the maintenance of infection, with resulting chronic inflammatory responses, than would be the case without the action of any ovarian hormone.

Ovulation within the first few weeks postpartum presumably makes the uterus even more susceptible to the establishment and persistence of uterine infection. Infection in postpartum cows can cause the maintenance of corpora lutea (Lynn, McNutt and Casida, 1966), which would probably tend to delay the termination of infection even further.
Literature Cited


uterus to instillation of semen at different phases of the estrous cycle. Amer. J. Vet. Res. 13:419.

DISCUSSION

Comment: Wagner

I would like to add a couple of comments. In regard to Dr. Marion’s presentation, on the persistence of the remnants of atretic follicles, he mentioned that these apparently do not remain in the ewe. We have not done an exhaustive study, but in the postpartum sow it appears that all one finds are the remnants of the zona pellucida from the ovum, with virtually no connective tissue remnants remaining. In fact, there is merely a hole in the ovary containing the remnants of the ovum. Concerning the other comment in regard to the response of the postpartum uterus; in these uteri at about 10 to 14 days, one can almost always find large numbers of polymorphonuclear cells migrating into the lumen. Whether this is a markedly increased response, as one would expect to find in an estrous animal, I have no way of evaluating, but there are certainly large numbers of these polymorphs present and moving into the lumen regularly.

Question: Grosvenor

Dr. Hawk, I didn’t see in any of your slides any indication of a measurement of intraluminal temperature, and I wonder if subtle changes in intraluminal temperature might not, perhaps through related changes in the vascularity of the uterine endometrium, be important here?