HISTOLOGIC STUDY OF THE ENDOMETRIUM DURING PREGNANCY*

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Although the significance of chorionic villi and decidual cells is well known, little attention has been paid to the endometrial glands during pregnancy. Not infrequently, during the microscopic examination of an endometrium in which chorionic villi or decidua are not in evidence, the question of pregnancy is raised purely on the basis of certain changes that are manifested in the glands.

This investigation was undertaken to determine the reliability of such changes in connection with the question of pregnancy. Hence, a study was made of endometriums in cases of abortion, normal uterine pregnancy, extra-uterine pregnancy, and also in two cases in which examination of an agravid uterus revealed early loss of tissue.

As far as we have been able to ascertain, Leopold (1877) was the first to observe sinuous glands in the endometrium during pregnancy. Opitz (1899) described in detail the changes in the endometrial glands during pregnancy. He found that early in pregnancy the glands formed papillary processes which projected into the lumens and that the intervening stroma was scanty. The individual cells lining the glands were swollen and poorly stained. Later in the course of pregnancy, the papillary projections and the greater part of the epithelium disappeared and the glands were lined by one layer of cells. Opitz (1900) reported the results of a histologic study of the endometrium in 140 cases of abortion. He said that the glands were so typical

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in forty cases that a diagnosis could be made from them alone. He felt that the desquamation of the cells was a degenerative process secondary to abortion. Seitz (1903) said that pregnancy did not exist in one case in which the glands were considered typical of pregnancy according to the criteria used by Opitz. Opitz (1903) argued that the endometrial glands in the case described by Seitz were not typical of pregnancy because the interglandular stroma was too thick and the glands were not sufficiently numerous.

Teacher (1930) said that the earliest change in the development of the decidua was the formation of papilliform growths in the glands which became saw-toothed. He believed that the purpose of these glands was to nourish and aid the implantation of the ovum.

Boehmerus (1752) was the first to observe the formation of decidual tissue in the uterus in cases of ectopic pregnancy. Numerous writers (Schumann, 1921; Graves, 1928) have expressed the opinion that decidual tissue is formed in the uterus in every case of ectopic pregnancy, but that it is not uncommonly expelled as a cast at the time the tubal rupture occurs. Geist and Matus (1929) found uterine decidua in twenty-three of thirty-nine cases of extra-uterine pregnancy. Siddall and Jarvis (1937) studied the endometrium from thirty-eight cases of proved ectopic pregnancy. Decidual tissue was present in the uterus twenty-one times; it was present in all cases in which bleeding from the uterus had been present for less than eleven days. Moritz and Douglass (1928) were able to find decidual tissue in the endometrium in only eight of fifty-three cases of ectopic pregnancy. In twenty-nine of the remaining cases, the endometriums were in the so-called resting stage and in sixteen cases there was cystic hyperplasia of the endometrium. In a small proportion of the cases the authors were unable to obtain any history of uterine bleeding or expulsion of casts; they, therefore, concluded that decidual tissue was not formed in the uterus in all cases of ectopic pregnancy.

Knepper (1936) described a peculiar necrosis of the decidual
cells in the endometrium, which was present in the last half of uterine pregnancy but was constantly absent in the decidual cells of the endometrium in forty-seven cases of extra-uterine pregnancy. He did not say how frequently decidual tissue was formed in the uterus during extra-uterine pregnancy.

Hartje (1907) pointed out that glands similar to those found in pregnancy are found in the endometrium immediately preceding menstruation. Hitschmann and Adler (1908) proposed the term "decidual glands" for these glands and considered their presence as an indication of the premenstrual stage. O'Leary and Culbertson (1928) described decidua and tortuous saw-toothed glands which were present late in the menstrual cycle and which were similar to the glands of pregnancy which were described by Opitz. They believed that they were caused by an increased secretion of the glandular epithelium with the resultant dilatation and crowding of the glands.

Teacher (1930) expressed the opinion that the proliferation of the premenstrual phase corresponded to an early formation of decidua. He noted that all degrees of changes in the stromal cells, including definite decidual formation, could occur. Rock and Bartlett (1937) observed that after the twenty-fifth day of the menstrual cycle the stroma became edematous and the cells become large and had pale vesicular nuclei, which gave them the appearance of decidual cells. These changes he termed as the "predeciduum."

The findings in this paper are based on a study of the endometrium in 111 cases of intra-uterine pregnancy, twenty-seven cases of extra-uterine pregnancy (twenty-six cases of tubal pregnancy and one case of abdominal pregnancy), and two cases in which the uterus was agravid. In most of the cases of intra-uterine pregnancy the endometrium was examined early in the course of the pregnancy. The presence of chorionic villi was the criterion for the assumption of pregnancy in the first two groups of cases. In one case a biopsy revealed decidual tissue but no chorionic villi; the pregnancy continued and a full-term baby was delivered. No attempt was made to choose a selected
series of cases of uterine pregnancy; the cases included in this series are consecutive cases in which the existence of pregnancy was incontrovertible. In eighty-six cases of uterine pregnancy the endometrium was obtained by curettage either following incomplete abortion or in the course of therapeutic abortion, which was performed for obvious reasons. The most common indication for therapeutic abortion in these cases was pulmonary tuberculosis. In twenty-five cases of uterine pregnancy the uterus was available for study. In nine of these cases the pregnancy was an incidental finding at necropsy. In the remaining sixteen cases the uterus was removed surgically because of serious complications, such as multiple leiomyomas and rupture. In eighteen of the cases of extra-uterine pregnancy specimens of the endometrium were obtained by curettage, for diagnostic purposes, preliminary to exploratory laparotomy; in nine cases the uterus and the fallopian tube were removed because of multiple leiomyomas.

One piece, and occasionally several pieces, of endometrium from each patient was sectioned by the fixed frozen technic and stained with hematoxylin and eosin. Since the existence of pregnancy had been proved by the finding of chorionic villi, we selected only those sections in which the endometrial glands were evident. The results of the study of the endometrium were tabulated according to decidual formation, flattening of the endometrial glands, thinning of the interglandular connective tissue, papillary infoldings of the glands with serration or scalloping of the free border of the cells lining the glands, and degeneration of the cells lining the glands. Where it was possible the endometrium was compared with one of the phases of the menstrual cycle which have been described by Herrell and Broders (1935). They divided the normal menstrual cycle into four phases, each of which normally lasts seven days. These phases are the early and late proliferative phases and the early and late differentiative phases. The duration of the pregnancy was estimated either clinically or from the length of the fetus, if it were available.
RESULTS

Uterine pregnancy

In sixty-seven of the 111 cases of uterine pregnancy microscopic examination of the endometrium revealed a picture that was more or less comparable to the late differentiative phase of the menstrual cycle. The appearance of the glands varied a great deal depending upon the presence and amount of the decidual reaction. Where this decidual reaction was marked, the glands had lost their papillary infoldings, the glandular spaces were narrowed as if the decidua had encroached on them, and the lining

Fig. 1. Endometrium in a case of uterine pregnancy; the glands are surrounded by decidual tissue and the lining epithelium is flattened and one layer in thickness (hematoxylin and eosin × 90).
epithelium consisted of one layer which was flattened and in places was almost impossible to detect (fig. 1). In thirty-seven cases in which the foregoing change occurred it was impossible to compare the glands with those found during any part of the normal menstrual cycle. Many variations between the typical

Fig. 2. Endometrium in a case of uterine pregnancy; the glands show the transition from the typical "glands of pregnancy" to glands which are surrounded by decidual tissue and lined by a single layer of low cuboidal epithelium (hematoxylin and eosin × 100).

"glands of pregnancy" and this appearance were seen (fig. 2). In seven cases the endometriums differed in appearance from the endometriums in the group of sixty-seven cases and the group of thirty-seven cases. In three of the seven cases the endometrium was comparable to that of the late proliferative phase of
the menstrual cycle; in two cases there was evidence of a late proliferative phase and an early differentiative phase; in one case there was an early differentiative phase and in another case there was evidence of an early differentiative phase and late differentiative phase of the menstrual cycle.

Fig. 3. Endometrium in a case of early uterine pregnancy; the glands show the typical saw-tooth appearance but very little interglandular stroma (hematoxylin and eosin × 50).

Decidual tissue was found in the endometrium in seventy-six cases. This varied from a slight swelling of the stromal cells to a marked formation of decidua.

The so-called glands of pregnancy were present in the endometrium in sixty-two of the 111 cases (fig. 3). They were evidenced either by their papillary infoldings or serration of the
free border of the glands, or both. The changes in the glands of the endometriums in these cases were manifested to such an extent that one could say with reasonable certainty that one was dealing with the "glands of pregnancy," irrespective of the presence of decidual tissue or chorionic villi. In thirty-six cases

![Fig. 4. An endometrial gland in a case of uterine pregnancy; one may note marked degeneration of the lining epithelium with desquamation (hematoxylin and eosin × 210).]

the glands were packed together so closely that there was little stroma or connective tissue between them. This was a characteristic finding, when it was present. The serration of the free border of the cells lining the lumen appeared to be caused by a peculiar degeneration of the epithelial cells characterized by
swollen and poorly stained cytoplasm. This resulted in small spaces between the superficial or free portion of the individual cells and bulbous projections of the cells into the lumens of the glands (fig. 4). The "glands of pregnancy" were found to be most typical in those cases in which decidual formation was minimal; therefore, these glandular changes are most common in early pregnancy. As the decidual formation increased, the glands lost their papillary infoldings and serration (fig. 5), while the lumens of the glands became small. This ironing-out process appeared to be produced by an actual desquamation of the

![Image](https://academic.oup.com/ajcp/article-abstract/8/5/547/1798202)

**Fig. 5.** Endometrium during uterine pregnancy, showing transitional stage of the glands, loss of papillary infoldings and a serration of the free border of the epithelial lining (hematoxylin and eosin × 205).
degenerated epithelial cells (fig. 4). The final result was a regular small glandular space which was lined by flattened epithelium and surrounded by decidual tissue (fig. 1).

In eighteen cases the glands were flattened to such an extent that their longest diameters, instead of being perpendicular to the uterine cavity, were parallel to it. This could be explained on the basis of increased intra-uterine pressure caused by the products of conception.

A study of the basal glands was confined to those cases in which the uterus was available for examination. There were no noticeable variations from normal.

In twelve of the 111 cases it was not possible to presume pregnancy, either as a result of decidual formation or from the appearance of the glands. In two of these cases the patients were eight months and two months postpartum respectively, and menstruation had been resumed. There were two other cases in which prolonged metrorrhagia had followed an incomplete abortion; in these cases it seemed probable that ovulation had taken place. In seven of the twelve cases examination of the endometrium did not disclose a picture that was comparable to the late differentiative phase of the menstrual cycle, which was frequently associated with pregnancy.

**Ectopic pregnancy**

In the twenty-seven cases of ectopic pregnancy, when the changes in the endometrium were compared to the phases of the menstrual cycle the variation was much greater than that observed in the cases of uterine pregnancy. In ten cases the changes in the endometrium were more or less comparable to the late differentiative phase of the menstrual cycle; in 8 cases they were comparable to the late proliferative; in two cases they were comparable to the early differentiative phase and late proliferative phase, and in three cases they were comparable to the early differentiative phase. In four cases the glands were lined by a single layer of flattened epithelial cells and were completely surrounded by decidual tissue. In these cases the changes did not resemble any normal phase of the menstrual cycle. Decidual tissue was present in only five cases.
"Glands of pregnancy," in which there were papillary infoldings and serration, were present in seven cases (fig. 6). In seven other cases there was serration of the free border of the cells but no papillation; this change was not considered to be sufficient for a diagnosis of the "glands of pregnancy." Degeneration and a swelling of the epithelial cells were observed in five cases.

![Image of endometrial glands in a case of extra-uterine pregnancy](https://academic.oup.com/ajcp/article-abstract/8/5/547/1798202)

Fig. 6. Endometrial glands in a case of extra-uterine pregnancy; the typical papillary infoldings and bulbous projections of the cells may be seen (hematoxylin and eosin X 95).

There were markedly thin septa between the glands in two cases; in these cases the glands appeared to face one another. In one case cysts were found in the endometrium. In eleven cases the examination revealed typical decidua or glands of pregnancy, or both. In those cases in which the uterus was available for study, the basal glands did not vary from normal.
The endometrium of agravid women

Specimens of endometrium obtained from two agravid women were studied. The first patient had been passing membranous tissue from the vagina during each menstrual period. Microscopic study revealed decidual tissue, small glands, and slight serration of the free border of the cells, but these changes were not sufficient to warrant a diagnosis of glands of pregnancy.

In the second case the endometrium was obtained by curettage, the day prior to the expected onset of menstruation. Examinations...
tion of the endometrium revealed a very slight decidual reaction. The glands were in the late differentiative phase of the menstrual cycle, but there were papillary infoldings, serration of the free border, and degeneration of the cells, which are typical of the "glands of pregnancy" (fig. 7). In the endometrium there were collections of erythrocytes, which were indicative of early loss of tissue or beginning menstruation.

COMMENT

A picture more or less comparable to the late differentiative phase of the menstrual cycle was the most common finding in the endometrium in cases of uterine pregnancies. This picture was observed in more than half of the endometriums which were examined. These cases, together with those cases in which the glands were lined by a single layer of epithelium and surrounded by decidual tissue comprise approximately 95 per cent of the cases of intra-uterine pregnancy. The variations found in the endometrium in some of the remaining few cases of extra-uterine pregnancy can be explained on the basis of resumption of menstruation following incomplete abortion or delivery.

There was evidence of the late differentiative phase of the menstrual cycle in only ten of the cases of ectopic pregnancy. In the majority of the other cases there was evidence of the late proliferative phase. It is very difficult to explain this observation unless the menstrual periods continued uninterrupted.

The changes of the endometrial glands during pregnancy, as described by Opitz (1903), were marked in sixty-two of 111 cases of uterine pregnancy. These changes also were seen in seven of twenty-seven cases of ectopic pregnancy and in one case in which the uterus was agravid. The "glands of pregnancy" represent a variation of the late differentiative phase of the menstrual cycle. Most characteristic of this variation were papillary infoldings of the epithelium, swelling and degeneration of the cells and serration of the free border of the cells. In addition to the foregoing changes, the glands appeared to be more numerous than they are normally and the interglandular stroma was
very sparse. The apparent increase in glands is most marked early in pregnancy and disappears with the formation of decidual tissue. The epithelial cells were for the most part desquamated and the final result was a small glandular space lined by a single layer of cells with no papillary infoldings. It is evident that the glands have the same significance as does the presence of decidual tissue. They frequently are present in the early stages of a uterine pregnancy, in a small percentage of cases of ectopic pregnancy, and very rarely in cases in which the endometrium of an agravid uterus is examined immediately before menstruation. Their presence cannot be taken as absolute proof of an intra-uterine pregnancy.

Decidual tissue was present in only five out of twenty-seven cases of ectopic pregnancy. In six of the cases in which decidual tissue was not present, there was no history of vaginal bleeding or discharge. In only one case was there a history of the passage of a cast. These findings would agree with those of Moritz and Douglass (1928), who claimed that decidual tissue was probably never formed in the uterus in a number of cases of ectopic pregnancy. In a small number of cases in which the patients are normal, well-formed decidual tissue also is present immediately preceding each menstrual period.

In the majority of early uterine pregnancies in which chorionic villi are absent, one is able to make a correct presumption of pregnancy, even following abortion, with the aid of decidua and the changes in the endometrial glands.

CONCLUSIONS

1. A picture more or less comparable to the late differentiative phase of the menstrual cycle is usually present in the endometrium during the early part of uterine pregnancy; it is less common in extra-uterine pregnancy.

2. The changes in the endometrial glands ("glands of pregnancy") are present in a large proportion of cases of early uterine pregnancy, in a small proportion of cases of extra-uterine pregnancy, and occasionally in the agravid uterus, immediately prior to the menstrual period.
3. The “glands of pregnancy” have the same significance as decidual tissue.

4. Decidual tissue was found in the uterus in five of twenty-seven cases of extra-uterine pregnancy.

REFERENCES

1) BOEHMERTJS: Quoted by Moritz, A. R. and Douglass, Marion.


