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Early implantation and embryonic development of the baboon: stages 5, 6 and 7

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Summary. Implantation stages of the olive baboon, *Papio cynocephalus anubis*, showing embryonic development equivalent to Carnegie stages 5, 6 and 7 of development, were collected by hysterotomy and examined histologically. The younger specimens (stage 5) consisted of a thick trophoblastic plate composed of cytotrophoblast and syncytiotrophoblast with multiple small clefts, and a bilaminar disk embryo with a small slit-like amniotic cavity. An epithelial plaque response was present in the uterine epithelium immediately peripheral to the implantation site, within an area of pronounced uterine edema. The bilaminar embryonic disk consisted of columnar epiblast cells underlying the amniotic cavity, and thickened visceral endodermal cells that form part of the yolk sac. The slightly further developed placenta (stage 6) consisted predominantly of cytotrophoblast including primary villi and syncytiotrophoblast lining large spaces containing maternal blood. Secondary placental villi were present in the oldest group (stage 7), and there was modest decidualization of the uterine stroma. An epithelial plaque response persisted, but varied in extent. The sequence of events in early development in the baboon is similar to that in the rhesus monkey insofar as blood space formation and endometrial responses are concerned. However, the plaque response is not so great as in the rhesus; there is no secondary placenta, and the decidual response is slightly more extensive.

Key words: Implantation – Baboon – Developmental stages – Epithelial plaque – Decidualization (decidua)

Introduction

Early implantation and embryonic development has been studied in a variety of species, including the human and nonhuman primate (Houston and Hendrickx 1968; Hendrickx 1971; Wynn et al. 1971; Schlafke and Enders 1975; Ramsey et al. 1976; Enders and Hendrickx 1980a, 1980b; Enders and Schlafke 1981; Enders et al. 1983; Moore et al. 1985). These studies provide basic information for the study of comparative implantation in primates and aid in the recognition of appropriate models for experimental work. The acquisition of additional information on the control of human implantation depends to a large extent on the study of discrete aspects of the implantation process in the available nonhuman primate species (Enders 1976; Enders and Hendrickx 1980b).

In the human, early attachment of the blastocyst to the endometrium occurs 5 to 6 days after ovulation (Hertig et al. 1956; O'Rahilly 1973). Implantation is interstitial and is followed by a pronounced decidual reaction; there is no epithelial plaque reaction (Ramsey et al. 1976). The placenta is monodiscoid. In the rhesus monkey and baboon attachment of the blastocyst occurs about 9 days after ovulation (Heuser and Streeter 1941; Hendrickx 1971). Implantation in the rhesus monkey is superficial with little decidual reaction, a substantial but transitory epithelial plaque, and the formation of a secondary placental disc (Wislocki and Streeter 1938; Luckett 1974; Enders et al. 1983; 1985). In the baboon, implantation is superficial and the placenta monodiscoid. Epithelial plaque formation and a decidual reaction have been reported either to be absent (Houston 1969) or variable in degree (Luckett 1974). There are blood-filled lacunae in the trophoblast of all three species by day 11 of pregnancy, representing 2 days post attachment in the baboon and rhesus monkey and 4 to 5 days in the human (Enders et al. 1983). Large intraluminal cells present in maternal blood vessels at the junction with the implantation site are also present in all three species; however, their number reaches a maximum at week 12 of pregnancy in the human, and can be seen early, on day 16 and 17, in the rhesus monkey and baboon, respectively (Ramsey et al. 1976). In the marmoset monkey, the only New World species studied in detail, embryo attachment occurs 12 days post ovulation. Implantation is superficial, with a small epithelial plaque and stromal decidual reactions (Hearn 1983; Moore et al. 1985).

Several morphologic similarities between the baboon and human suggest the appropriateness of this nonhuman primate as a model for aspects of human implantation (Hendrickx and Enders 1980; Enders and Hendrickx 1980b). The purpose of this study is to provide histologic detail on early stages of implantation in the olive baboon representing Carnegie stages 5–7 and to compare these findings to similar stages in other primates.

Materials and methods

Twenty-five female and five male olive baboons (*Papio cynocephalus anubis*) were individually caged under uniform conditions at the Institute of Primate Research, Nairobi, Kenya. Animals were fed twice daily with nutritionally bal-

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Table 1. Comparison of developmental stage with gestation age based on sex skin deturgescence and LH peak

Specimen number	Gestational age (days)		Stage	Location of implantation site
	Sex skin[a] deturgescence	LH peak[b]		
576	12	12	5	Dorsal, central
578	12	11	5	Ventral, central
750	12	–	5	Dorsal, central
552	17	17	6	Dorsal, cranial
580	11	13	6	Dorsal, left, cranial
563	14	–	7	Ventral, left, cranial
564	14	14	7	Dorsal, central, cranial

[a] The third day prior to deturgescence is designated day 0 of pregnancy

[b] The day of the LH peak is designated day 0 of pregnancy

anced commercial primate cubes supplemented once a day with fruits and vegetables. Water was provided ad libitum. Females were trained for unanesthetized blood sampling, use of a transfer cage, and vaginal swabbing. Perineal cycles were followed daily and females were mated daily, beginning approximately five days prior to sex skin deturgescence and continued daily until deturgescence had occurred.

Before mating, a blood sample was taken from the female between 8:00 and 9:00 a.m. and serum samples were stored at −20° C in 1 ml aliquots until the time of assay for LH. The female was then transferred to the male's cage for six hours. At the end of each mating period, the female was allowed to enter the transfer cage where a vaginal swab was taken, and an eosin-stained smear was made and examined for the presence of sperm.

The assay employed for the measurement of LH in baboon serum (0.1 ml) was the World Health Organization (WHO 1981) system for monkey gonadotrophin with a rhesus monkey LH preparation (WP-XV-20) as standard, ^{125}I cynomolgus LH (WP-XV-63-2429) as tracer and anti LCG (R13) as antiserum. Serial dilutions of standards were included in the assay over the range 80-1.25 ng/0.2 ml and the antiserum was used as a final dilution of 1:40000.

The day of ovulation (day 0 of pregnancy) was estimated to be three days prior to deturgescence of the perineum (sex skin) (Hendrickx 1971). This estimate was retrospectively compared with day of ovulation designated by peak urine LH levels (Table 1). A laparotomy was performed between estimated days 11 and 15. The uterus and ovaries were exteriorized and the presence of a corpus luteum noted. A hysterotomy was performed by making a midline incision in the myometrium of the ventral uterine body through the fundus to the dorsal aspect. A small cut was made in the endometrium at the fundus and the two sides of the uterus were slowly separated. The luminal surface of the endometrium was examined for evidence of a conceptus which appeared as a discrete slightly raised, red site. If present, the location of the site was noted and it was then excised. The tissue was immediately placed in cold buffered 3% glutaraldehyde and then post-fixed in 2% osmium tetroxide, dehydrated in a graded alcohol series, and embedded in epon araldite resin. The implantation sites were sectioned at approximately 1 μm and stained with azure B for light microscopic examination.

A total of seven specimens: three stage 5 (576, 578, 750), two stage 6 (580, 552) and two stage 7 (563, 564) staged according to Hendrickx (1971); O'Rahilly (1973); Hendrickx and Sawyer (1975), were studied.

Results

Stage 5

Three implantation sites were collected at estimated day 12 of gestation and classified as stage 5 on the basis of the following morphologic features: a thick trophoblastic plate primarily composed of cytotrophoblast and syncytiotrophoblast with incompletely expanded lacunae, and a bilaminar embryonic disc with a small slit-like amniotic cavity but lacking an expanded secondary yolk sac cavity (Figs. 1–4).

Trophoblast and placenta

The dome-shaped implantation site protruded slightly above the endometrial surface. It was composed of pale staining cytotrophoblast proximal to the blastocyst cavity and darker staining syncytiotrophoblast. The cytotrophoblast cells had distinct large nuclei with prominent nucleoli. Syncytiotrophoblast lined irregular spaces which contained red blood cells and were most extensive on the fetal side of the placenta (Figs. 1, 2).

Overlying the cytotrophoblast, especially near the embryonic disc, a few spindle-shaped mesenchymal cells were evident interposed between cellular trophoblast and the extraembryonic endoderm. The trophoblast intruded a short distance into the endometrial stroma and extended into adjacent endometrial glands, frequently obliterating the lumina but not usually penetrating into the stroma surrounding the glandular epithelium.

Endometrium

An epithelial plaque response was evident in the uterine surface epithelium immediately peripheral to the implantation site. This focal thickening of the epithelium was characterized by clusters of large pale-staining cells with occasional interspersed columnar epithelial cells. The arrangement of the large plaque cells along the basal border of the epithelium resulted in an undulating profile (Fig. 1). At the periphery of the epithelial plaque, localized superficial edema separated the columnar surface epithelial cells from the underlying subepithelial stroma (Fig. 3) In two specimens, the continuity of uterine surface epithelium with trophoblast was interrupted by a multinucleate mass which formed a transition zone between these two structures (Fig. 3).

Embryo

In two of the earlier specimens, the embryos were oriented parallel to the endometrial surface. In one (750), the embryonic disc was situated in an indentation, and was oriented perpendicular to the endometrial surface. At stage 5 the embryo was bilaminar, consisting of two plates of cells, a slightly thicker, regularly arranged epiblast and a more irregular embryonic endoderm (Figs. 2, 4). Both layers were composed primarily of columnar cells with some cuboidal cells at the periphery of the embryonic disc. The amniotic

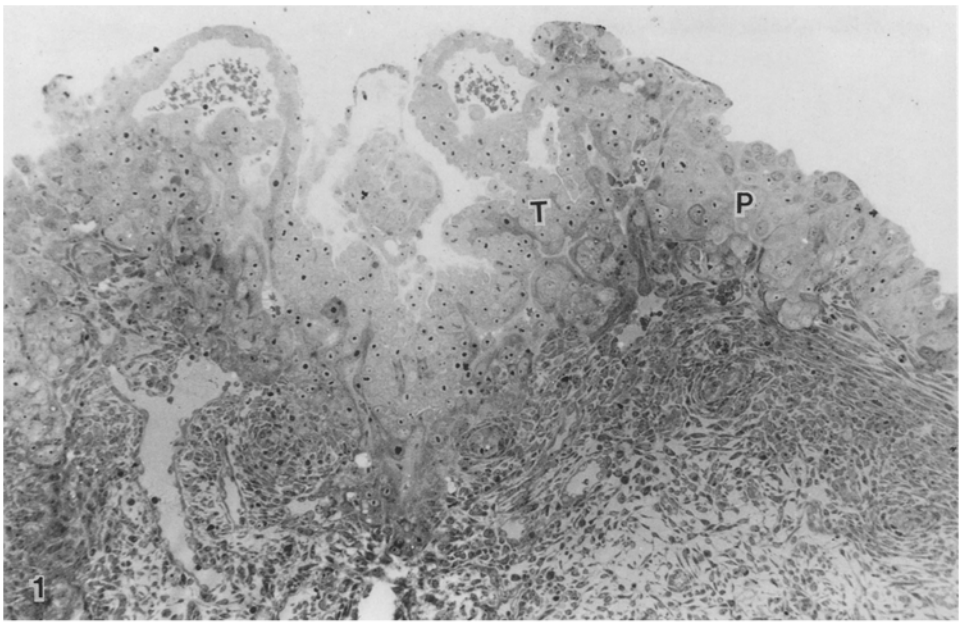


Fig. 1. Stage 5 (750). The dome-shaped implantation site protrudes slightly above the endometrial surface. An epithelial plaque (*P*) is present immediately peripheral to the trophoblast (*T*) of the implantation site. × 120

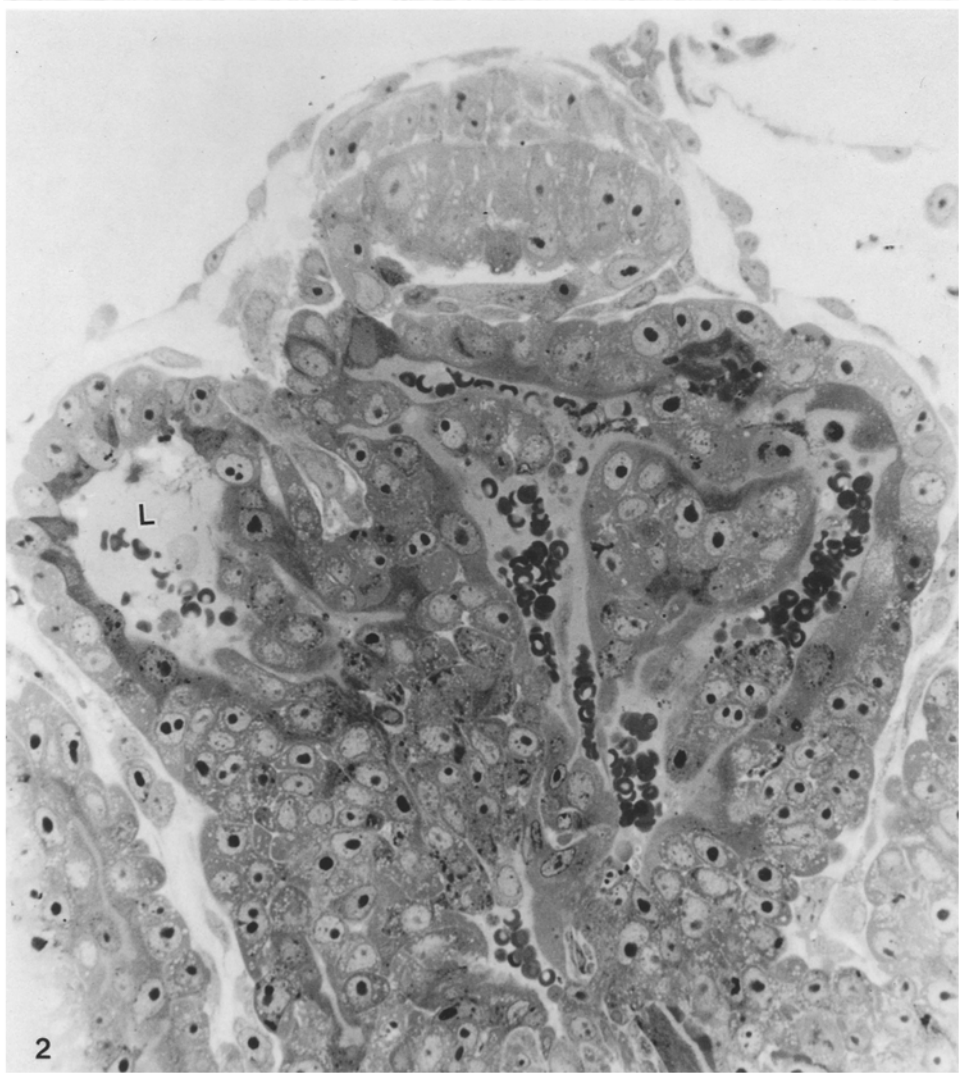


Fig. 2. Stage 5 (576). Broad lacunae (*L*) lined by a layer of syncytiotrophoblast are present on the embryonic side of the trophoblast plate. × 420

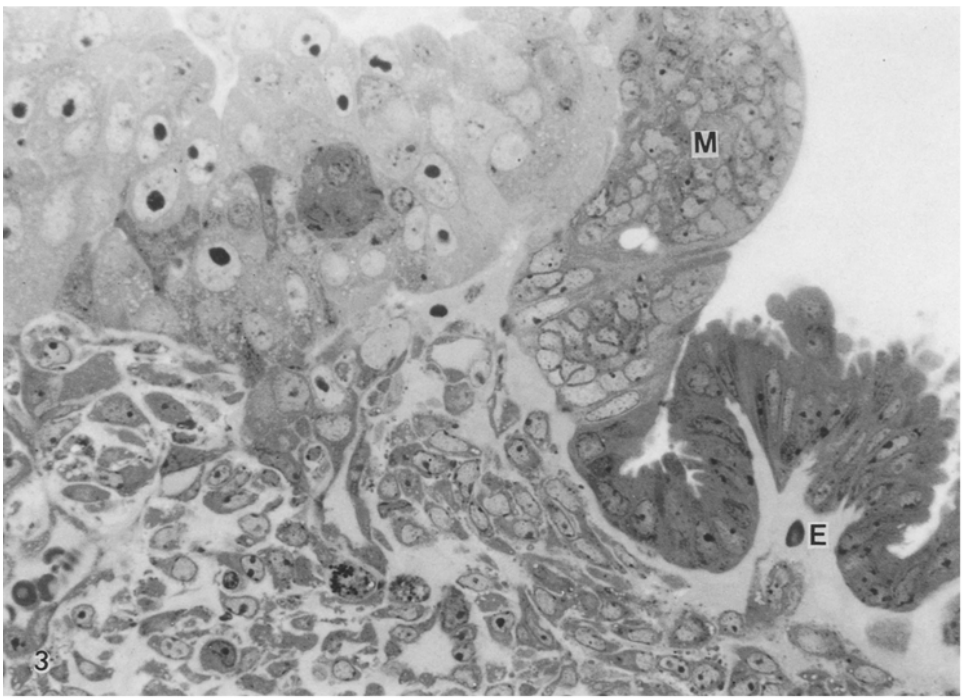


Fig. 3. Stage 5 (576). Superficial edema (*E*) is present in the endometrium at the periphery of the implantation site. A multinucleate mass (*M*) is interposed between the cytotrophoblast and the uterine epithelium. × 520

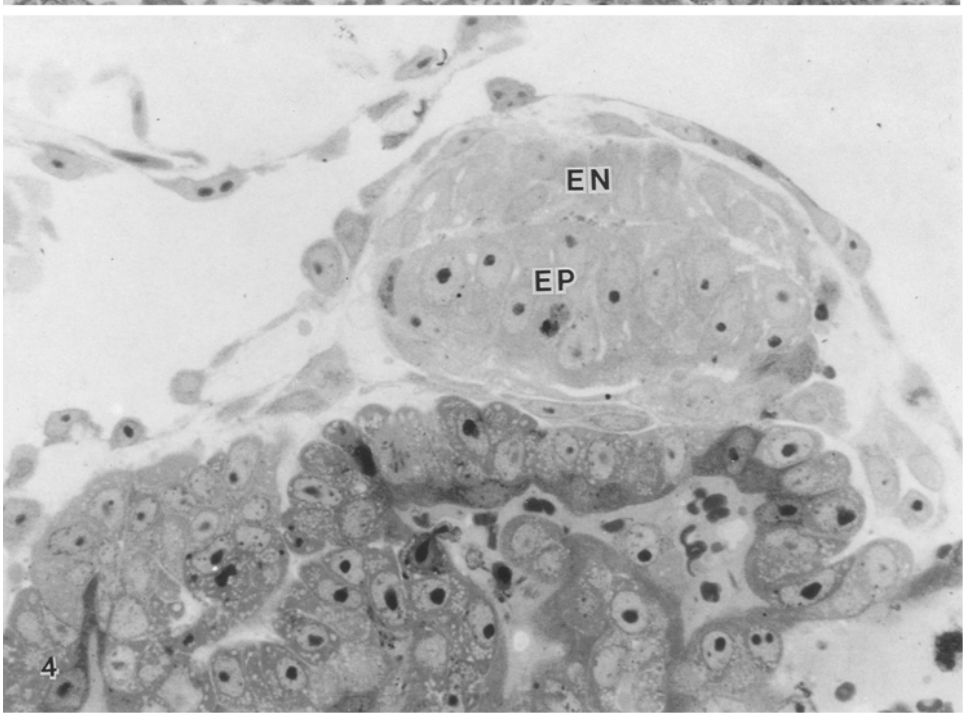


Fig. 4. Stage 5 (576). The bilaminar embryo consists of thicker regularly arranged epiblast (*EP*), and the irregular visceral endoderm (*EN*). × 520

cavity was present as a narrow cleft between the epiblast cells and the amniotic epithelium, a layer of cells that varied from low cuboidal to squamous.

One "abnormal" specimen (578) was judged to be abnormal on the basis of degenerative changes, including trophoblastic cell death, hemorrhage, and leucocytic infiltration. While the embryonic epiblast appeared normal, the endoderm was indistinct, no amnion formation was evident and the endometrium lacked a plaque response.

Stage 6

Two implantation sites were classified as stage 6 on the basis of the following morphologic features: large well-defined bilaminar embryonic discs with distinct but still unexpanded amniotic cavity, endoderm bordering the secondary yolk sac cavity and a placenta with primary chorionic villi alternating with extensive blood spaces (Figs. 5–8).

Trophoblast and placenta

Both implantation sites protruded well above the endometrial surface and extended beyond the area of junction forming a pedunculated broad base of attachment (Figs. 5, 6). Abembryonic trophoblast and primary yolk sac endoderm were in close apposition, each consisting of a layer of squamous cells.

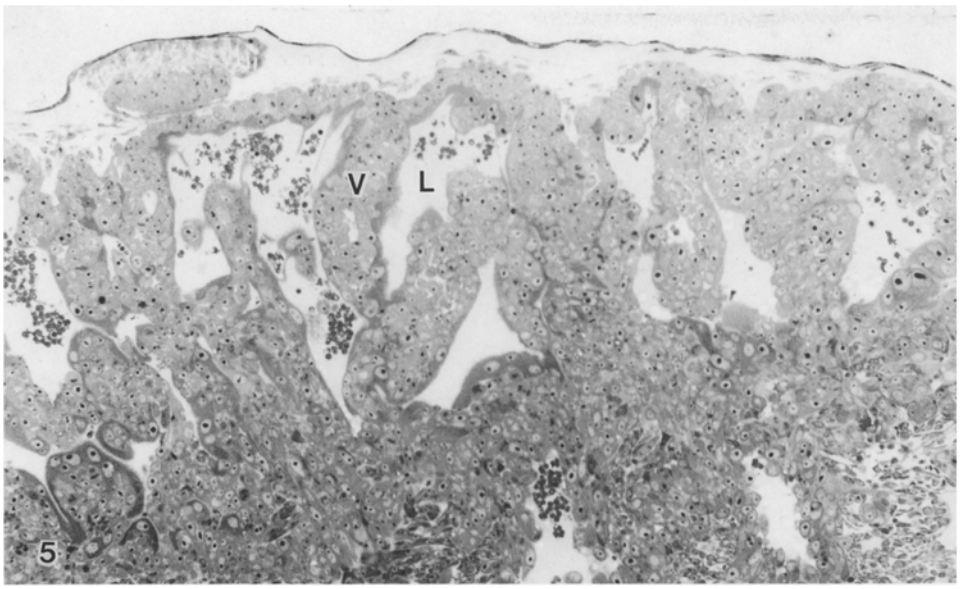


Fig. 5. Stage 6 (552). The trophoblastic plate is composed of radially arranged primary villi (*V*) which separate blood-filled lacunae (*L*) that are lined by syncytiotrophoblast. ×120

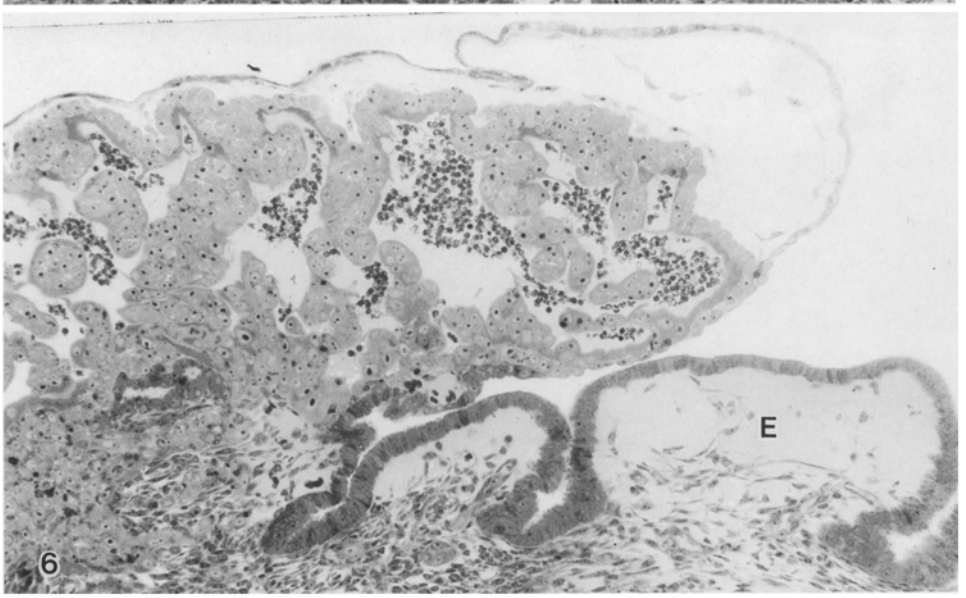


Fig. 6. Stage 6 (552). There is marked superficial edema (*E*) peripheral to the implantation site. Most of the thickness of the developing placenta is above the surface of the endometrium. ×120

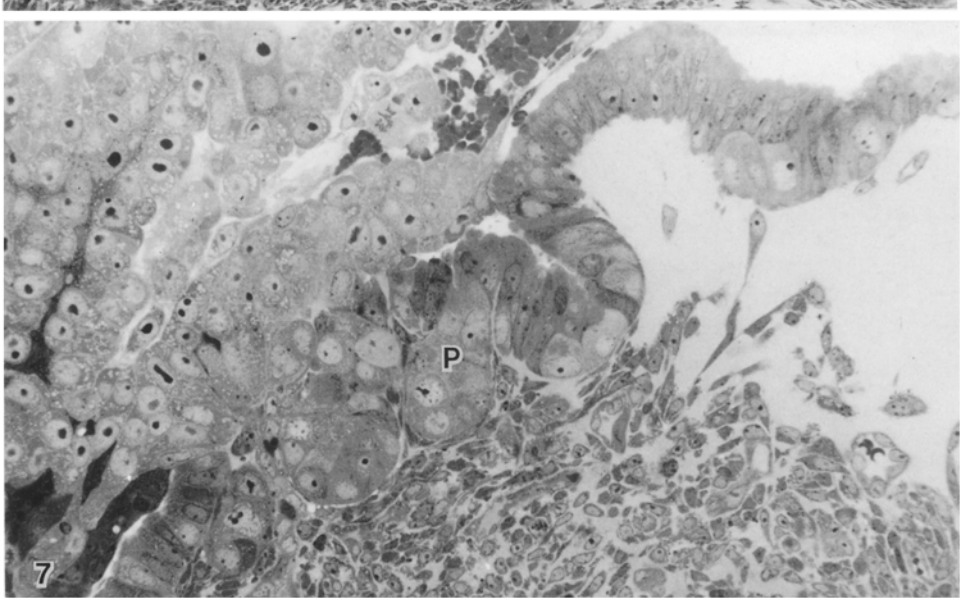
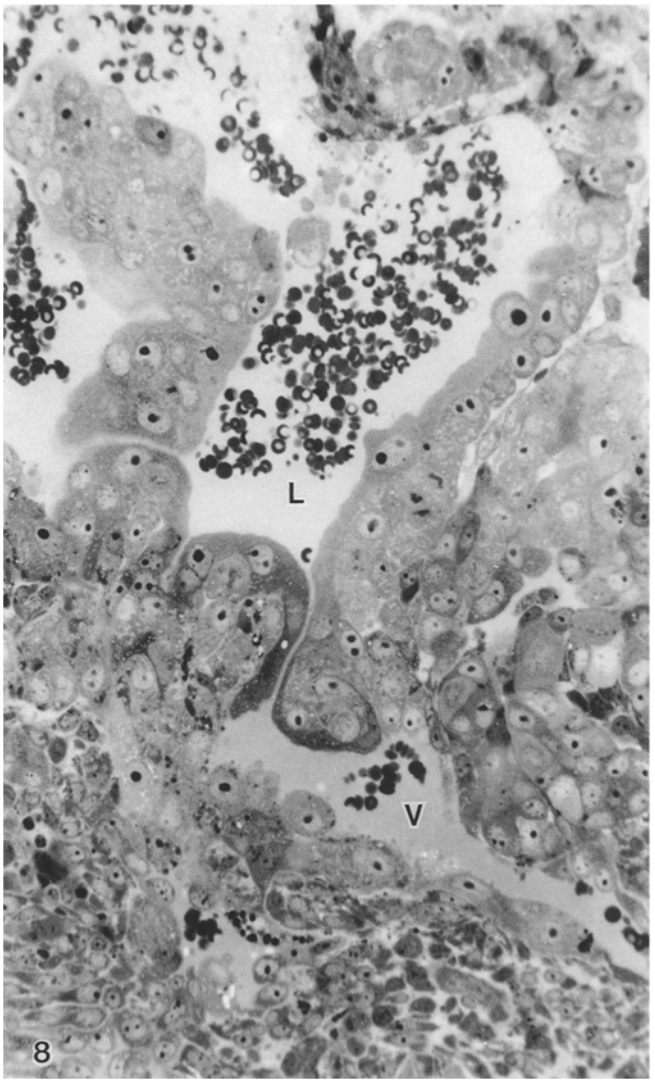


Fig. 7. Stage 6 (580). There is an epithelial plaque (*P*) at the periphery of the implantation site as evidenced by focal thickening of the surface epithelium resulting from the presence of clusters of cells along the basal lamina. These cells have pale cytoplasm and large nuclei. Marked edema results in separation of epithelium from the underlying stroma at the periphery of the implantation site (*E*). ×320



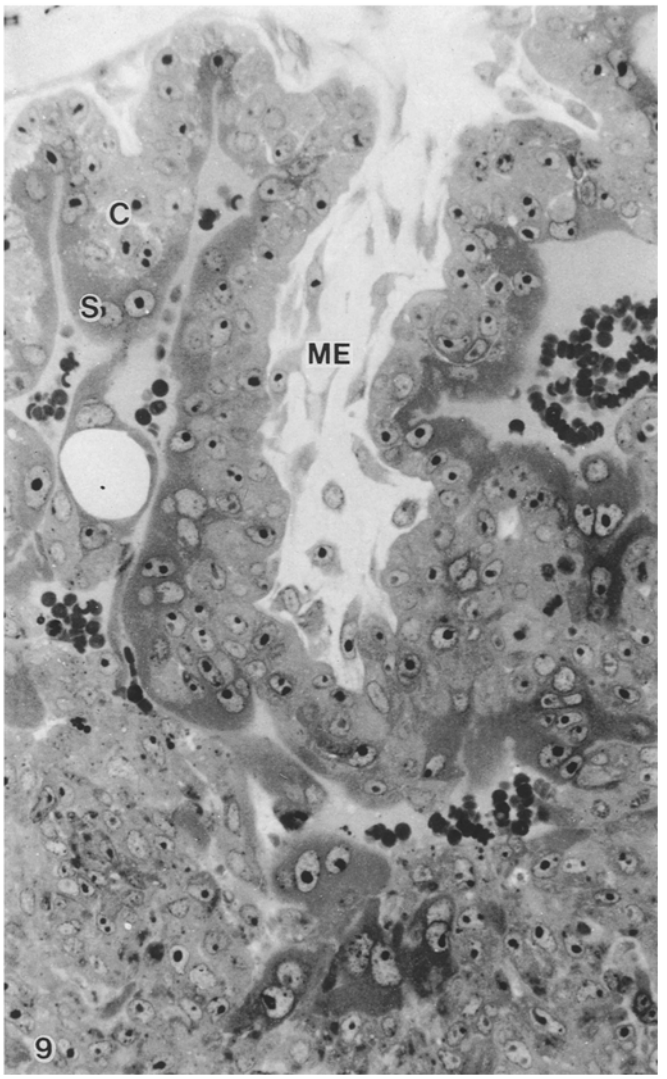


Fig. 8. Stage 6 (580). There is continuity between an endometrial blood vessel (*V*) and a lacuna (*L*) of the trophoblast. This blood vessel is lined by large cells with finely vacuolated cytoplasm. × 320

Fig. 9. Stage 7 (564). Secondary villus formation is present in the form of mesodermal columns (*ME*) in many of the villi. (*C*, cytotrophoblast; *S*, syncytiotrophoblast). × 320

The trophoblastic plate was now composed of perpendicular cords (primary villi) of pale-staining cytotrophoblast overlain by a dark-staining layer of syncytiotrophoblast that lined the blood-filled lacunae. These villi extended from the embryonic (chorionic plate) surface to the maternal (basal plate) region where the cytotrophoblastic cells form an incomplete cytotrophoblastic shell. Presumptive mesodermal cells were present in the forming chorionic plate but no distinct secondary villi were evident.

Endometrium

Marked superficial edema was present peripheral to the implantation site (Figs. 6, 7). The distinct epithelial plaque reaction at the immediate periphery of the implantation site resulted in an acinar arrangement of the plaque cells (Fig. 7). Beneath the implantation site, large thin-walled venules were observed in the endometrial stroma. The continuity of maternal vessels with the lacunae was difficult to discern, indicating a narrowing of vessels near the confluence with the lacunae. In one series of sections where a maternal vessel was directly confluent with a lacunae, the entrance to the lacuna was narrow and some of the cells of the vessel were large and vacuolated (Fig. 8).

Embryo

The bilaminar embryos were located on the central aspect of the implantation site, oriented parallel to the endometrial surface. The epiblast was pseudostratified with the mitotic figures toward the amnion. The visceral endodermal cells were shorter and more irregular than the epiblast. The secondary yolk sac was unexpanded and although extraembryonic mesoderm was present, there was no indication of intraembryonic mesoderm.

Stage 7

Two specimens were collected at 14 days of gestation and classified as stage 7 on the basis of the presence of secondary villi, decidualization of the uterine stroma and expansion of the amnion (Figs. 9–12).

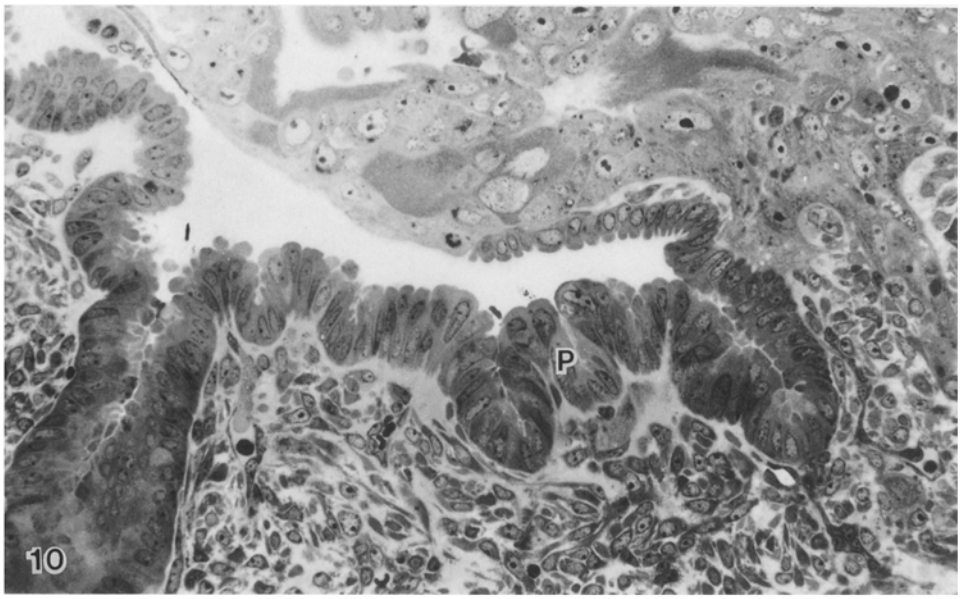


Fig. 10. Stage 7 (564). A mild epithelial plaque (*P*) is present at the periphery of the implantation site, consisting of slight hypertrophy of surface epithelial cells. Note the superficial position of the placental disc. × 320

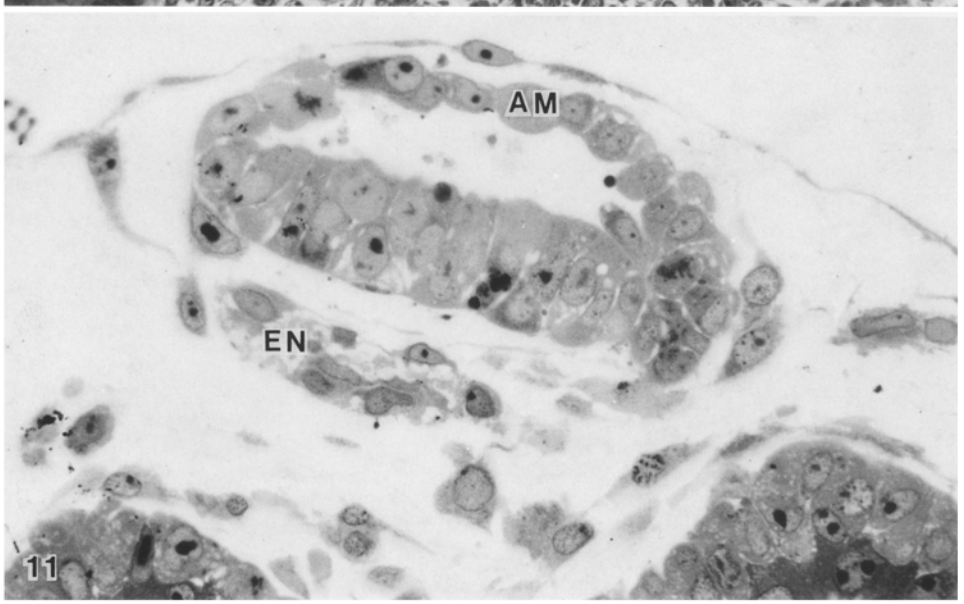


Fig. 11. Stage 7 (564). The orientation of one embryo was reversed with the endoderm (*EN*) facing the trophoblast plate and the amnion (*AM*) positioned toward the adluminal trophoblast. × 520

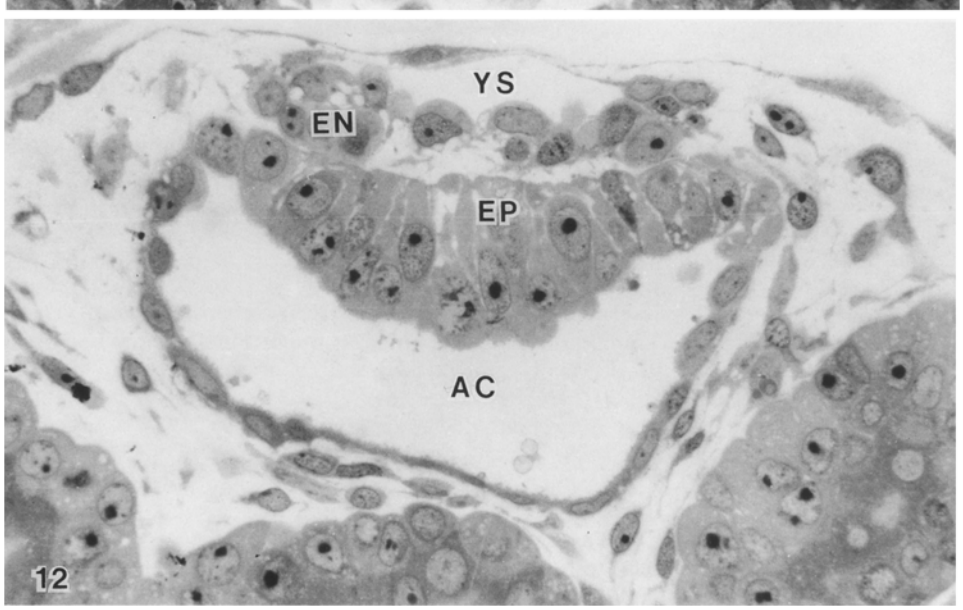


Fig. 12. Stage 7 (563). In a normally-oriented embryo, the thick epiblast (*EP*) faces a prominent amniotic cavity (*AC*). There is a one- to two-cell transition from epiblast to amniotic epithelium. The endodermal layer (*EN*) is composed of a single to double layer of irregular cells, and the secondary yolk sac (*YS*) is enclosed by a single layer of squamous parietal endodermal cells. × 520

Trophoblast and placenta

The implantation site was more distinctly pedunculated and overlapped the uterine surface, including reflection of the uterine luminal epithelium (Fig. 10). The abembryonic trophoblast formed a convex dome over the implantation site. This trophoblast remained low cuboidal to squamous, except for occasional clusters of enlarged cells near the confluence with the cytotrophoblast at the periphery of the site. An inner layer of squamous endodermal cells was present beneath the abembryonic trophoblast, and no extraembryonic mesoderm was present at this location. A meshwork of mesodermal cells extended over the forming placental disc, protruding toward the maternal surface as secondary villi. These tend to be most extensive near the embryo. The largest of the secondary villi have several short branches. At the tips of secondary villi, adjacent to endometrial stroma, cytotrophoblast cell cords converged and formed a thick cytotrophoblastic shell interspersed with syncytiotrophoblast.

Endometrium

A patchy epithelial plaque reaction and reduced peripheral edema were evident in both implantation sites. An early decidual response in the stroma adjacent to the implantation site was characterized by increased size and area occupied by the still-spindle-shaped stromal cells. Several of the vessels entering the implantation site were expanded by the presence of numerous large polygonal cells, occupying the lumen and part of the wall of the vessel. Such vessels were now thicker than many of the glands, but the lumen was tortuous.

Embryo

Both embryos from this stage had a convex embryonic shield, formed of pseudostratified epiblast cells whose apical ends protruded into the amniotic cavity (Figs. 11, 12). However, one of the embryos was reversed in orientation, in that the secondary yolk sac, rather than the amnion, faced the chorionic plate (Fig. 11). The visceral endodermal cells, constituting the portion of the secondary yolk sac within the embryo, were irregular in shape, and showed extensive basal processes on their border towards the epiblast. The parietal layer of the secondary yolk sac of the normally oriented embryo was squamous (Fig. 12).

Discussion

Implantation in the baboon is superficial and central, with formation of a single discoid villous hemomonochorial placenta (Noback 1946; Houston and Hendrickx 1968; Houston 1969). There has been uncertainty regarding some early implantation events, such as epithelial and stromal responses to the implanting blastocyst (Houston 1969; Luckett 1974; Ramsey et al. 1976). An early decidual cell reaction was evident in the stage 7 material described here, which is consistent with observations of Houston (1969) and Hendrickx (1971). Nests of proliferating surface epithelium have been observed peripheral to the placental disc and opposite the unattached abembryonic wall of a 20-day chacma baboon, *Papio ursinus* (Gilbert and Heuser 1954) but epithelial proliferation had not been reported at any stage in other *Papio* species (Houston 1969, 1971; Hendrickx 1971). In our current series, an epithelial plaque response was present in all stages with the exception of the single degenerating conceptus, although there was considerable variation in extent of the epithelial plaque.

Several factors may have contributed to the confusion concerning the presence or absence of an epithelial plaque reaction in baboons. The relative lack of shrinkage and increased resolution obtainable with plastic-embedded material certainly makes visualization of the plaque response easier. In addition, there has been a tendency to group all endometrial responses to the blastocyst or to trauma as decidual (or deciduomal) reactions (see, for example, Wheeler et al. 1983). As suggested by Luckett (1974), both species and individual animal variation in extent of plaque reaction, together with its limited duration, all contribute to differences in observations. The small plaque response of the baboon is thus intermediate between species such as the rhesus monkey, with an extensive plaque response, and others such as the human that lack a plaque response.

It has been suggested that epithelial and stromal responses may participate in the restriction of penetration of trophoblast (Wislocki and Streeter 1938; Wynn 1965; DeFeo 1967; Cowell 1972). It has also been suggested that epithelial and stromal responses may have a supportive function either by secretion or as histiotroph (Amoroso 1952; Boving 1963; Ramsey 1976; Enders et al. 1985). The glycogen-rich plaque cells and the stromal cells could provide nutritive and growth factors for the implanting blastocyst, and the level of the response, whether epithelial or stromal, may reflect the extent of stimulation by the trophoblast and the sensitivity of the endometrium rather than acting as a barrier to implantation.

Intravascular cells, characterized as large pale cells, were observed in baboon implantation sites near the confluence with trophoblastic lacunae. Similar cells were seen lining other endometrial blood vessels adjacent to the implantation site. The presence of intravascular cells has been extensively described in human, rhesus monkey and baboon, and has been interpreted as being of cytotrophoblast origin (Ramsey 1976; Ramsey et al. 1976). Our observations did not resolve this point, and the contribution of endogenous endometrial cells, especially endothelial cells cannot as yet be discounted.

An inflammatory reaction to the early stages of implantation has been reported in the rhesus monkey and human (Hertig 1968; Enders 1976; Enders and Schlafke 1979; Enders et al. 1983, 1985). We did not uniformly find an accumulation of leucocytes in the endometrium adjacent to the trophoblast. The only significant leucocytic infiltration was seen in the specimen with degenerative changes in trophoblast, which may represent an inflammatory response to tissue debris.

Our current observations confirm that the developmental stages 5, 6 and 7 of the baboon embryo are morphologically similar to those in the rhesus monkey (Heuser and Streeter 1941; Hendrickx and Sawyer 1975; Enders et al. 1983, 1986). During these stages the bilaminar embryonic disc thickened and the amnion increased in size. There was variation in amount and conformation of visceral endoderm, which may be related to the age of the embryo and precocity of formation of secondary yolk sac. Embryos with altered orientation, similar to the one reported here, have been reported (Hertig 1968; Gilbert and Heuser 1954; Hendrickx and Binkerd 1980). The reasons for such malposition in embryo orientation are not clear. It has been speculated that some disruption in orientation might result from the

presence of defects in the endometrial surface, and mechanical disruption at surgical excision can be considered a possibility (Hendrickx 1971).

On the basis of conceptions following single mating, Hendrickx (1971) concluded that ovulation most often occurs three days preceding sex skin deturgescence. Subsequent studies incorporating hormonal data have suggested that sex skin deturgescence is more likely to occur one to two days after ovulation (Wildt et al. 1977; Shaikh et al. 1982) and ovulation has been shown to occur 12–24 h after the LH peaks (Parkin and Hendrickx 1975). The results of embryo staging based on sex skin deturgescence according to Hendrickx (1971) and the LH peak obtained in this study were in agreement. These limited data suggest that in a fertile cycle, ovulation is more likely to occur three or more days before sex skin deturgescence.

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References

Amoroso EC (1952) Placentation. In: Marshall's Physiology of Reproduction vol 2, Longmans London

Boving BG (1963) Implantation mechanisms. In: Hartman CG (ed) Conference on physiologic mechanisms concerned with conception. MacMillan Pergamon Press New York, pp 321–396

Cowell TP (1972) Control of epithelial invasion by connective tissue during embedding of the mouse ovum. In: Tarin D (ed) Epithelial mesenchymal interactions in carcinogenesis. Academic Press, New York, pp 435–463

DeFeo VJ (1967) Decidulization. In: Wynn RM (ed) Cellular biology of the uterus. Appleton-Century-Crofts New York, pp 191–290

Enders AC (1976) Cytology of human early implantation. Res Reprod 8:1–2

Enders AC, Hendrickx AG (1980a) Morphological basis of implantation in the rhesus monkey. Prog Reprod Biol 7:270–283

Enders AC, Hendrickx AG (1980b) Implantation in nonhuman primates. I. A comparison of morphological events. In: Kumar TC Anand (ed) Nonhuman primate models for study of human reproduction. Karger, Basel, pp 99–108

Enders AC, Schlafke S (1979) Comparative aspects of blastocyst endometrial interactions at implantation. In: Maternal Recognition of Pregnancy. Ciba Foundation Series 64, pp 3–32

Enders AC, Schlafke S (1981) Differentiation of the blastocyst of the rhesus monkey. Am J Anat 162:1–21

Enders AC, Hendrickx AG, Schlafke S (1983) Implantation in the rhesus monkey: Initial penetration of the endometrium. Am J Anat 167:275–298

Enders AC, Welsh AO, Schlafke S (1985) Implantation in the rhesus monkey: Endometrial responses. Am J Anat 173:147–169

Enders AC, Schlafke S, Hendrickx AG (1986) Differentiation of the embryonic disc, amnion, and yolk sac in the rhesus monkey. Am J Anat 177:161–185

Gilbert C, Heuser CH (1954) Studies in the development of the baboon (*Papio ursinus*). A description of two presomite and two late somite stage embryos. Carnegie Contrib Embryol 35:11–54

Hearn JP (1983) The marmoset monkey. In: Hearn JP (ed) Reproduction in new world primates. MTP Press Lancaster, pp 182–223

Hendrickx AG (1971) Embryology of the baboon. The University of Chicago Press, Chicago, pp 45–67

Hendrickx AG, Enders AC (1980) Implantation in nonhuman primates. II. Endocrinology. In: Kumar TC Anand (ed) Nonhuman primate models for the study of human reproduction. Karger, Basel, pp 109–115

Hendrickx AG, Sawyer RH (1975) Embryology of the rhesus monkey. In: Bourne G (ed) The rhesus monkey, Vol II. Academic Press, New York, pp 141–169

Hendrickx AG, Binkerd PE (1980) Fetal deaths in nonhuman primates. In: Embryonic and fetal death. Academic Press, New York, pp 45–69

Hertig AT, Rock J, Adams EC (1956) A description of 34 human ova within the first 17 days of development. Am J Anat 98:435–493

Hertig AT (1968) Human trophoblast. AH Thomas Springfield, Illinois, pp 157–164

Heuser CH, Streeter GL (1941) Development of the macaque embryo. Contrib Embryol 181:23–31

Houston ML (1969) The villous period of placentogenesis in the baboon (*Papio* sp.) Am J Anat 126:17–30

Houston ML (1971) Comparative development and evolution of the placenta in primates. In: Contrib Primatol 3:152–155, Karger, Basel

Houston ML, Hendrickx AG (1968) Observation on the vasculature of the baboon placenta (*Papio* sp.) with special reference to the transverse communicating artery. Folia Primat 9:68–77

Luckett WP (1974) Comparative development and evolution of the placenta in primates. Contrib Primatol 3:152–155

Moore HDM, Gems S, Hearn JP (1985) Early implantation stages in the marmoset monkey, *Callithrix jacchus*. Am J Anat 172:265–278

Noback CR (1946) Placentation and angiogenesis in the amnion of a baboon (*Papio papio*). Anat Rec 94:553–567

O'Rahilly R (1973) Developmental stages in human embryos. Part A. Embryos of the first three weeks (stages 1 to 9). Carnegie Institution of Washington Publication 631, p 167

Parkin RF, Hendrickx AG (1975) The temporal relationship between the preovulatory estrogen peak and the optimal mating period in rhesus and bonnet monkeys. Biol Reprod 13:610–616

Ramsey EM (1976) Vascular anatomy. In: Wynn RM (ed) Biology of the uterus, Plenum Press, pp 59–76

Ramsey EM, Houston ML, Harris JWS (1976) Interactions of the trophoblast and maternal tissues in closely related primate species. Am J Obstet Gynecol 124:647–652

Schlafke S, Enders AC (1975) Cellular basis of interaction between trophoblast and uterus at implantation. Biol Reprod 12:41–65

Shaikh AA, Celaya CL, Gomez I, Shaikh SA (1982) Temporal relationship of hormonal peaks to ovulation and sex skin deturgescence in the baboon. Primates 23:444–452

Wheeler AG, Hurst PR, Poyser NL, Eckstein P (1983) Uterine histology and prostaglandin concentrations and utero-ovarian venous steroid and prostaglandin concentrations during the luteal phase of the menstrual cycle in baboons (*Papio* spp.) with or without an IUD. J Reprod Fertil 67:35–46

Wildt DE, Doyle LL, Stone SC, Harrison RM (1977) Correlation of perineal swelling with serum ovarian hormone levels, vaginal cytology, and ovarian follicular development during the baboon reproductive cycle. Primates 18:261–271

Wislocki GB, Streeter GL (1938) On the placentation of the macaque (*Macaca mulatta*), from the time of implantation until the formation of the definitive placenta. Contrib Embryol Carnegie Inst 27:1–66

World Health Organization (1981) W.H.O. Special programme of research development and research training in Human Reproduction. Programme for the provision of matched assay reagent for the radioimmunoassay of hormones in reproductive physiology. Method Manual (5th ed)

Wynn RM (1965) Electron microscopy of the developing decidua. Fertil Steril 16:16–26

Wynn RM, Panigel M, MacLennan AH (1971) Fine structure of the placenta and fetal membranes of the baboon. Am J Obstet Gynecol 109:638–648

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