The embryo–maternal dialogue during early pregnancy in primates

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Introduction

Implantation and the establishment of pregnancy is a crucial event in the life of any mammal. The uterine epithelium and endometrium must be prepared to receive the embryo, and the embryo must hatch from the zona pellucida, attach to and invade the maternal tissue. The life of the corpus luteum must be prolonged, and adequate channels of communication must be established rapidly. These channels ensure the flow of nutrients from mother to embryo and the flow of embryonic secretions to the mother that are necessary for pregnancy and embryonic differentiation to be sustained.

The sequence of morphological and physiological steps that result in successful implantation has been studied extensively in non-primate species, revealing a bewildering variety of mechanisms and considerable differences between species (Wimsatt, 1975; Perry, 1981; Finn, 1983; McLaren, 1985). In the human and non-human primates knowledge of the peri-implantation period, from fertilization to completion of the luteo-placental shift (Csapo & Pulkkinen, 1978), is limited for good reasons, such as the relative lack of availability of embryos for study, the inaccessibility of the embryo and the long duration of gestation. That the process is prone to failure may be deduced from the high incidence of natural embryonic loss, estimated at about 50% for the human (reviewed by Short, 1979). Considerable embryonic loss may also be seen in some domesticated farm stock (Wilmut, Sales & Ashworth, 1986). Acquisition and testing of the data for primates is therefore a long-term procedure.

On the other hand, an improved knowledge of implantation and early embryonic differentiation in primates is urgently needed for the treatment of infertility and for the development of new approaches to fertility control, as well as for the breeding and conservation of rare primate species. The human population of the world reached $1 \times 10^{12}$ as recently as 1850, now stands at $4-5 \times 10^{12}$ and is expected on moderate predictions to reach $10 \times 10^{12}$ by 2050 (McNamara, 1984). Much of this increase will take place in developing countries that are at present the natural habitats for wild-living primates. It follows that a great deal less space will be available and most primate species will have become rare or endangered over the next 50 years. A fundamental appreciation of the factors affecting early embryonic survival, together with more applied aspects using the new reproductive technologies to accelerate the breeding of rare species and to manage the genetic diversity of small populations, is required to help redress the balance (Hearn, 1985; Moore, 1985; Polge, 1985).

The control of implantation requires study at both systemic and local levels. The former is relatively straightforward through the monitoring of endocrine changes in the peripheral circulation. The latter is more difficult as there are no biochemical studies that describe the complex interactions at the maternal–embryonic junction in primates in vivo and only a few reports that provide information on the peri-implantation development of the primate embryo in vitro (Pope, Pope & Beck, 1981; Hearn, 1983; Fishel, Edwards & Evans, 1984; Hearn & Summers, 1986). It is clear that the primate embryo must commence secretion of chorionic gonadotrophin (CG) at or soon after implantation in order to ‘rescue’ the corpus luteum which will otherwise decline at the end of the
ovarian cycle (Short, 1969; Knobil, 1973; Ross, 1979). Interference with the systemic circulation of CG, by passive or active immunization of the mother with antisera raised against this hormone, will block implantation and terminate early pregnancy before completion of the luteo-placental shift (Hearn, 1976, 1979; Stevens, 1976; Talwar et al., 1976).

Over the past decade, evidence has slowly accumulated from studies in laboratory rodents and agricultural livestock to show that embryos secrete chemicals that signal their presence to the mother, sustain the corpus luteum and promote the necessary nutrients for further development (Heap, Flint & Gadsby, 1979; Heap, Flint & Staples, 1983). The embryo initially depends on an inherent programme of development (Johnson, 1979) which soon requires communication with the mother (Bazer & Thatcher, 1977; Bazer & First, 1983); and the functioning of the paternal and maternal genomes are necessary for normal development (Barton, Surani & Norris, 1984). The precision of these studies has yet to be matched in those with primates although undoubtedly many of the fundamental control mechanisms are similar.

There are, however, dissimilarities between non-primates and primates, including the timing of embryonic development, the support of the corpus luteum, the chemical messages secreted by the embryo and aspects of the morphology of implantation. These are considered further below and illustrated with recent reports from the human, baboon, rhesus monkey and marmoset monkey.

The Primates

There are 180 species of primates of which 43 are prosimians and 137 are the Old World monkeys, New World monkeys, apes and man. The higher primates range in adult size from 150 g for the pygmy marmoset to 150 kg for the gorilla. Few of these species have been studied in any detail and knowledge of their reproductive physiology comes mainly from those that have been investigated for their relevance to biomedical sciences. Table 1 presents a summary of the breeding biology of

<table>
<thead>
<tr>
<th>Species</th>
<th>Ovarian cycle (days)</th>
<th>Gestation (days)</th>
<th>Average no. of young born/year</th>
<th>Sexual maturity (years)</th>
<th>Generation interval (years)</th>
<th>Seasonal breeding*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common marmoset (Callithrix jacchus)</td>
<td>28</td>
<td>144</td>
<td>5</td>
<td>1.5</td>
<td>2</td>
<td>No</td>
</tr>
<tr>
<td>Owl monkey (Aotus trivirgatus)</td>
<td>16</td>
<td>133?</td>
<td>1</td>
<td>1.5–2.0</td>
<td>2–3</td>
<td>No?</td>
</tr>
<tr>
<td>Squirrel monkey (Saimiri sciureus)</td>
<td>9</td>
<td>150</td>
<td>1</td>
<td>3</td>
<td>3–4</td>
<td>No?</td>
</tr>
<tr>
<td>Rhesus monkey (Macaca mulatta)</td>
<td>27</td>
<td>168</td>
<td>1</td>
<td>3–5</td>
<td>4–6</td>
<td>Yes</td>
</tr>
<tr>
<td>Baboon (Papio cynocephalus)</td>
<td>33</td>
<td>184</td>
<td>0.8</td>
<td>5–7</td>
<td>6–10</td>
<td>No?</td>
</tr>
<tr>
<td>Chimpanzee (Pan troglodytes)</td>
<td>37</td>
<td>235</td>
<td>&lt;0.5</td>
<td>7–10</td>
<td>7–15</td>
<td>No</td>
</tr>
<tr>
<td>Man (Homo sapiens)</td>
<td>30</td>
<td>280</td>
<td>&lt;0.5</td>
<td>15+</td>
<td>20+</td>
<td>No</td>
</tr>
</tbody>
</table>

*Of the species listed, the rhesus has a definite breeding season which may be extended but not abolished in captivity. Births will occur throughout the year in captive owl monkeys, squirrel monkeys and baboons, but there are probably seasonal changes in fecundity.
Fig. 1. General endocrine feedback systems in the female primate. The embryo is active in secreting CG from at least the time of attachment, although this may not be apparent from peripheral measurements until embryo-maternal blood vascular connections are formed. By the 7th week of pregnancy, the embryo-placental unit is independent of the corpus luteum.

seven species, including those studied most intensively in laboratory colonies. Figure 1 shows the overall endocrine feedback mechanisms in primate pregnancy, with an implied early autonomy of the embryo through secretion of chorionic gonadotrophin.

**Prostaglandins and the corpus luteum**

The susceptibility of the corpus luteum in non-primates to prostaglandin (PG) F-2α has been well described for many years and the mode of action of prostaglandins on receptors in the corpus luteum is now becoming apparent (McCracken, Schramm & Okulicz, 1984). The primate corpus luteum has long been thought to be insensitive to prostaglandins, as it relies on luteotrophic support that may be neutralized by intra-ovarian secreted oestrogens or prostaglandins, in contrast to the sheep, cow and other species in which prostaglandin secreted by the uterus terminates the life of the corpus luteum (Knobil, 1973; Baird, Baker, McNatty & Neal, 1975). Recent studies of the baboon (R. M. Eley, P. M. Summers & J. P. Hearn, unpublished data) suggest that this is true for Old World species but the marmoset monkey, a New World species, shows an immediate demise of the corpus luteum when treated with a single, intramuscular injection of 0.5 µg cloprostenol (a PGF-2α analogue) after Day 10 of the cycle (Summers, Wennink & Hodges, 1985). The marmoset has a mean ± s.e.m. cycle length of 28.6 ± 1.0 days with a luteal phase of 19.2 ± 0.6 days (Hearn, 1983; Harlow, Gems, Hodges & Hearn, 1983) and hysterectomy does not disrupt cyclicity, at least in the cycles immediately following removal of the uterus (Hearn, 1978).

**Implantation**

**Timing**

Table 2 shows the principal stages of implantation and their estimated timing in the human (Hertig, Rock & Adams, 1956), baboon (Hendrickx, 1971), rhesus monkey (Enders & Hendrickx,
Table 2. The principal stages of implantation and their approximate timing (days) after ovulation in the human, baboon, rhesus monkey and marmoset monkey

<table>
<thead>
<tr>
<th>Stage</th>
<th>Human</th>
<th>Baboon</th>
<th>Rhesus</th>
<th>Marmoset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryo enters uterus</td>
<td>3-4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Zona pellucida shed</td>
<td>5-6</td>
<td>7-8</td>
<td>7-8</td>
<td>9-10</td>
</tr>
<tr>
<td>Attachment</td>
<td>6-7?</td>
<td>8-10</td>
<td>8-10</td>
<td>11-12</td>
</tr>
<tr>
<td>Trophoblast differentiates (previllous stages)</td>
<td>7-12</td>
<td>10-25</td>
<td>10-30</td>
<td>12-40</td>
</tr>
<tr>
<td>Tertiary villi</td>
<td>16-17</td>
<td>23-25</td>
<td>23-25</td>
<td>40+</td>
</tr>
<tr>
<td>Decidual reaction</td>
<td>12+</td>
<td>Local oedema (11-14)</td>
<td>Plaque (11-14)</td>
<td>Epithelial 20+ Stromal 30+</td>
</tr>
<tr>
<td>Implantation type</td>
<td>Interstitial</td>
<td>Superficial</td>
<td>Superficial</td>
<td>Superficial</td>
</tr>
</tbody>
</table>

Table 3. Stage of marmoset embryo development at removal from the reproductive tract on Days 1–11 after ovulation

<table>
<thead>
<tr>
<th>Day of pregnancy</th>
<th>Embryos recovered</th>
<th>Stage of embryonic development*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 cell</td>
<td>4 cell</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>9</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*M = morula; B = blastocyst; HB = hatched blastocyst. Intermediate stages are included in the more advanced number.

1980) and marmoset (Hearn, 1980; Moore, Gems & Hearn, 1985). Timings for the human are approximate as the time of ovulation was uncertain and there is limited information at the cellular level. However, it is clear that there is considerable variation between species although the underlying stages of development are, of course, similar.

Table 3 shows the stages of development of marmoset monkey embryos recovered from the oviducts or uteri on Days 1–12 of pregnancy, after ovulation (Day 0) was monitored by measurement of peripheral plasma progesterone (Harlow et al., 1983). In the marmoset the embryo enters the uterus at the 8–16-cell stage on Day 4 (of 8 embryos recovered 3 were in the oviducts and 5 were in the uterus) and hatches on Days 9–10. No embryos were recovered when uteri were flushed after Day 11 and it is now clear that marmoset embryos commence attachment and implantation on Days 11–12 after ovulation (Moore et al., 1985).

Studies based on asynchronous transfer of embryos in mice and sheep show that in these species the uterine environment is hostile to the blastocyst during stages of development normally reached during tubal life. There is a narrow window when implantation can be initiated and asynchronous
development of the embryo results in its loss. The embryo requires to be at the same stage or more advanced than the uterus as more slowly developing embryos have a reduced chance of successful implantation (McLaren, 1985). In contrast, synchronous transfer of embryos from the oviducts to the uterus can be accomplished successfully in rhesus monkeys even at an early cleavage stage (Marston, Penn & Sivelle, 1977) and human embryos formed by in-vitro fertilization developed to successful births when placed in the uterus as early as the 2-cell stage (Edwards, Steptoe & Purdy, 1980). These results suggest that the requirements for synchrony are less rigid in primates than in rodents although the limits to such tolerance and the degree of success have yet to be determined. The capacity of primate embryos for delayed implantation has yet to be tested. Further definition of these limits may improve the success rates of in-vitro fertilization in human and non-human primate pregnancy where success rates to birth are only 10–20% of embryos transferred (Biggers, 1983).

**Morphology**

In primates including man the morphology of implantation is based mainly on incidental observations, usually at uncertain time intervals after fertilization (Hertig et al., 1956; O'Rahilly, 1973; Luckett, 1978). Most primate species (the Ceboidea and Cercopithecoidea studied to date) have a superficial form of implantation while the Hominidae show an interstitial type. Implantation is not a single event but lasts for at least 1 week from attachment of the blastocyst to the uterine epithelium and penetration by trophoblast, to the onset of a decidual reaction in the endometrium. Although similar in the general pattern, there is considerable variation between primate species both in the timing of the process (Table 2) and also in the characteristics displayed by the embryo related to the degree of invasion and the degree of the decidual reaction. Figure 2 gives a diagrammatic interpretation of implantation in the human (O’Rahilly, 1973), rhesus monkey (Enders, Hendrickx & Schlafke, 1983), baboon (Hendrickx, 1971) and marmoset (Moore et al., 1985). Ethical considerations make it extremely unlikely that additional data will be forthcoming from the human and great apes so that comparative investigations in monkeys may provide the only opportunity for sequential studies of the process.

**Fig. 2.** A diagrammatic representation of implantation in primates, which requires further definition from ultrastructural investigations. The human trophoblast sinks under the endometrial epithelium and there is a massive endometrial reaction. In the monkeys studied to date, implantation is superficial, although rapid contact is made with the maternal vasculature. The degree of endometrial response varies in intensity and timing according to the species. Endometrial response; ~ trophoblast–maternal interface; e.p. = epithelial plaque.
In the human and great apes, the trophoblast penetrates the epithelium and invades the stroma. By Day 11 the epithelium grows over the entire trophoblast which has differentiated into cytotrophoblast and syncytiotrophoblast and sunk into the stroma. By about Day 14 the primary villi appear and an extensive decidual reaction develops in the endometrium around the conceptus (Moore, 1977; McLaren, 1985). In all species there is a local reaction to the presence of the implanting embryo but this reaction is less evident in the rhesus monkey in which epithelial cells are transformed to a transient 'plaque' in the vicinity of the embryo. In the baboon there is a more diffuse epithelial reaction over the surface of the uterus covered by the trophoblast, with an increased oedema nearer the initial embryonic site, while in the marmoset monkey there is a distinct epithelial proliferation but it remains at the margin of the implantation site rather than extending into the centre. There is a modest stromal reaction at the later stages of implantation in the marmoset (Moore et al., 1985). The more superficial position of monkey embryos compared with the highly invasive interstitial implantation in the human has been interpreted as more primitive (Hertig et al., 1956) but it may also be argued (Enders et al., 1983) that the trophoblast of monkeys does invade and reach maternal blood vessels rapidly to establish an equivalent morphological position at about the same stage.

Early studies of implantation in primates (Hill, 1932; Heuser, 1940) suggested that the syncytium had cytolytic properties, eroding the epithelium to penetrate the underlying maternal vessels and interstitial tissue. In recent studies of the rhesus monkey (Enders et al., 1983) and the marmoset (Moore et al., 1985), destruction of the epithelium appears less evident and trophoblast at the earliest stage intrudes between adjacent epithelial cells, doing minimal damage. The precise nature of the relationship between syncytium and the endothelium of the maternal capillaries requires further investigation at the ultrastructural level.

Endocrinology

There is a vast literature on the endocrine requirements for implantation in rodents (for succinct reviews, see Finn, 1983; McLaren, 1985) from which it is clear that both oestrogen and progesterone are required in the rat and mouse. The uterus is primed by oestrogen before ovulation, conditioned by progesterone during the first 4 days of pregnancy, and oestradiol is again required for the endometrial changes that facilitate implantation. In the hamster, guinea-pig, rabbit, pig, sheep and ferret, implantation appears to proceed in the presence of progesterone alone but oestrogen improves the success of implantation and the blastocyst itself is thought to secrete oestrogen in several species (Heap et al., 1979). Monoclonal antibodies to progesterone will block early pregnancy in mice (Wang, Rider, Heap & Feinstein, 1984) and ferrets (Rider & Heap, 1986).

Rather less is known about the hormonal requirements for implantation in primates although it is thought that only progesterone is required. Csapo & Pulkkinen (1978) showed that pregnancy continued in women treated with exogenous progesterone after their ovaries were removed, although the ovarioctomies or corpus luteum excisions were probably performed when implantation was well advanced.

Meyer, Wolf & Arslan (1968) ovarioctomized rhesus monkeys within 1–5 days of ovulation, showing that pregnancy proceeded after replacement with progesterone. However, the uterus would by then have been primed by the midcycle oestrogen rise although no ‘new’ ovarian oestrogen would have been contributed. Ross (1979) reported that the pregnancy rate in women treated for infertility due to inadequate luteal-phase levels of progesterone, and undetectable oestradiol-17β, was markedly improved by treatment with exogenous progesterone alone during the luteal phase of conception cycles.

Although the above results suggest that oestradiol-17ß is not required for implantation in primates, in women there are normally elevated levels of oestradiol-17ß during the luteal phase and the period of implantation (Baird et al., 1975). In the chimpanzee (Graham, 1976) there is a marked rise in oestradiol-17ß during the luteal phase, with a profile similar to that seen in women. In the
marmoset the midcycle peak of oestradiol is 1.4 ng/ml (range 0.8–2.2); levels decline to 0.3 ng/ml for 2–3 days after ovulation and then rise again to 0.7 ng/ml (range 0.3–1.6) during the luteal phase. There are occasional spikes of oestradiol during the late luteal phase that go higher (up to 3 ng/ml in a few cases) but whether these are associated with implantation is unknown. In the baboon, rhesus monkey, crab-eating macaque, bonnet macaque and brown capuchin blood concentrations of oestradiol-17β decline after the preovulatory peak and remain barely detectable during the luteal phase. However, this is no proof that oestradiol is not involved in implantation in these species as low, tonic levels may facilitate implantation.

First appearance of chorionic gonadotrophin

Undoubtedly, the first clear signal from the embryo to the mother is the secretion of CG, which appears in the peripheral blood after implantation has begun, probably during the stage of trophoblastic lacunar formation when the necessary channels between embryo and mother have been established. Table 4 summarizes the times after ovulation when CG may be detected.

<table>
<thead>
<tr>
<th>Species</th>
<th>Embryo attachment</th>
<th>CG first detected</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human</td>
<td>6–7?</td>
<td>9</td>
<td>Lenton et al. (1982)</td>
</tr>
<tr>
<td>Chimpanzee</td>
<td>6–7</td>
<td>11</td>
<td>Reyes et al. (1975)</td>
</tr>
<tr>
<td>Baboon</td>
<td>8–10</td>
<td>12</td>
<td>Shaikh (1978)</td>
</tr>
<tr>
<td>Rhesus</td>
<td>8–10</td>
<td>12</td>
<td>Atkinson et al. (1975)</td>
</tr>
<tr>
<td>Marmoset</td>
<td>11–12</td>
<td>14</td>
<td>Hearn (1983)</td>
</tr>
</tbody>
</table>

It would not be surprising to find that CG is secreted by the embryo before it can be detected in the peripheral circulation and preliminary reports suggest that this is the case in the human (Fishel et al., 1984), baboon (Pope et al., 1981) and marmoset (J. P. Hearn, S. Gems, J. K. Hodges & C. Wennink, unpublished data). These studies were of embryos in culture and suggest that CG is secreted from the time of embryonic attachment. Measurement of CG from marmoset embryos cultured from morula and blastocyst stages, through hatching, attachment and outgrowth on a pregrown marmoset fibroblast layer, showed that CG may be secreted after the embryo hatches from the zona pellucida and immediately before it attaches and commences trophoblast outgrowth (J. P. Hearn, J. K. Hodges & S. Gems, unpublished). Levels of CG secreted by individual marmoset embryos increased very rapidly once attachment and outgrowth had occurred to reach production rates of up to 240 mi.u/day per embryo within 3–4 days after attachment. Incubation of hatched blastocysts with antisera to hCG-β subunit, derived from active immunization of female marmosets, prevented embryonic attachment and outgrowth and caused embryo lysis within 2 days. Incubation with antisera that had been heat treated to inactivate complement also blocked attachment and differentiation, but controls incubated with non-specific IgG showed no inhibition of attachment, outgrowth or the secretion of CG. These preliminary results suggest that CG may have a local role in implantation and trophoblastic differentiation in addition to its more widely recognized function in sustaining the corpus luteum.
Chorionic gonadotrophin was considered in the past to be a hormone specific to pregnancy in primates. In the past decade secretion of this hormone has been reported from a wide range of tumours, in normal men and children and in pregnancy of non-primate species (reviewed by Hearn, 1981). The validity of some of these claims has been questioned (Sherman, 1983) as some are probably artefacts of ever more sensitive radioimmunoassays that may recognize biologically inactive fragments of the hormone. However, CG remains as the first clear, defined embryonic signal of pregnancy in primates.

In addition to CG, there is an ever lengthening list of hormonal and non-hormonal embryonic products, including enzymes and pregnancy associated proteins, whose synthesis and secretion is proven but whose biological role remains to be defined (for reviews, see Loke & Whyte, 1983). Inevitably, claims are made for many of these to be important in suppression of the maternal immune response to the fetal allograft, but rigid experimental testing of these hypotheses is difficult to design. One exciting experimental model is through interspecies embryo transfer (Allen, 1982; Hearn & Summers, 1986) but this approach has yet to be developed in primates.

**Preimplantation embryonic signals**

While CG is the first clear signal from embryo to mother in primates, the effects of bi-directional signalling during preimplantation life are now becoming an apparent feature of early embryonic activity in several non-primate species (reviewed by Heap, Rider, Wooding & Flint, 1986). Studies of women suggest that an early pregnancy factor (EPF) can be measured 2–3 days after fertilization (Morton, Rolfe, Clunie, Anderson & Morrison, 1977), but this depends on a rosette inhibition assay whose validity is open to question (Koch & Ellendorff, 1985). Further progress depends on the development of a suitable bioassay or radioimmunoassay.

O’Neill (1985) reported an early pregnancy associated thrombocytopenia in mice that has since been applied to monitor the viability of human embryos after in-vitro fertilization and transfer (C. O’Neill, personal communication). Initial results from preimplantation embryos, studied in vivo and in vitro, of marmoset monkeys suggest a transient thrombocytopenia caused by an embryonic product (J. P. Hearn, C. J. O’Neill & A. A. Gidley-Baird, unpublished) but between-animal variability is high and a more robust assay is required before the findings can be fully confirmed.

**Future developments**

Figure 3 summarizes the relationships between the embryo, uterus and ovary during the peri-implantation period in primates. Much of the available knowledge has come from relatively remote sampling of peripheral plasma or, to a lesser extent, from utero-ovarian vein plasma. Further advances are now possible through the use of embryo culture methods, but there is a need for investigation at the implantation site with ultrastructural histochemistry, local sampling and cell lines, using more precise cell markers and monoclonal antibody or cDNA probes of embryonic antigens. In this way a more fundamental appreciation will be obtained of the support of the corpus luteum, the factors affecting embryonic attachment and trophoblastic differentiation, the causes of embryonic loss or abnormality, and the capacity for embryonic regeneration.

Clearly, no single primate species is an ideal animal analogue for studies in the human. The species used can only be selected as the most appropriate available for the question being asked. On the other hand, the mechanisms of implantation and the embryo–maternal dialogue during early pregnancy in primates are variations on a theme, with many shared endocrine and morphological features that distinguish the primates from non-primate species. In some respects it is encouraging that the great increase in research on early human pregnancy, catalysed by in-vitro fertilization and...
the treatment of infertility, has resulted in a better understanding of this important area in the human than in non-human primates. To this extent the human is becoming the animal model on which some rare primates may have to depend for their future breeding and conservation.

References


