SELECTED PAPERS ON PLANNED PARENTHOOD

计划生育专题论文选集

VOLUME 2

Drugs for Anti-Implantation & Termination of Early Pregnancy

抗着床与抗早孕药物

Selected Papers on Planned Parenthood

Vol. 2

Drugs for Anti-Implantation & Termination of Early Pregnancy

1975

Abstracts

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着床

本文叙述了哺乳类动物孕卵着床过程的一般特征。较详细地阐述了灵长类、啮齿类等胚泡的发育，透明带的作用，着床时胚泡和子宫内膜的关系，以及胚泡在子宫内定向等问题。文章有助于了介不同哺乳类动物孕卵着床中各自的特点。

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着床研究

着床是哺乳类动物生殖的基本过程，不同物种的着床过程有很大区别。本文比较系统地总结了作者对于大鼠着床机制的实验研究，将大鼠着床过程分为两个阶段，对其具体内容作了概括性描述。文中并按研究工作开展的时间顺序，叙述了有关着床机制的一些概念的提出、发展和修正的过程。

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生殖过程中易被调节的环节

本文概述了人体生育过程各环节的生殖生理、包括激素调节和药物影响。对其中易受药物干扰的生殖过程进行了讨论，如宫颈粘液的生理生化，黄体功能，精子在女性生殖道中的获能，受精卵的发育和运行以及着床过程中内膜的变化等等。

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房事后避孕：评论

本文总结了多年来性交后避孕的各种方法，包括雌素和孕素的应用，指出性交后避孕药今后可能发展的新途径，诸如对精子获能、精卵运行、胚泡着床等的干扰以及诱发黄体溶解等。

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房事后避孕

本文综述有关的性交后避孕药物；内容包括：(1) 作用方式，(2) 活性的分离，(3) 甾体化合物，(4)三芳基链烷化合物及三芳基链烯化合物，(5) 茋及联苄衍化物，(6) 含有基础醚基团的茋及联苄衍化物，(7) 二苯茚、二氢萘及有关的化合物，(8) 其他活性物质，(9)展望。

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人类生育控制进展：孕素作为房事后避孕药

为了达到短期推迟妊娠的目的，本工作试用了三种孕素，紧接在性交前后服用。根据在136名育龄妇女试用814周期的初步结果，指出这种用药方式值得进一步加以研究。

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终止妊娠：排卵后雌激素抗着床的应用

作者对猕猴应用雌素终止妊娠的试验达十年以上，在这一工作的基础上又进行了临床的观察。认为在排卵之后服用高剂量雌激素能降低妊娠率至0.8—0.08%。在半数以上的妇女有呕吐现象，除了一例急性肺水肿以外，没有发现其他严重副作用。

Mechanisms Involved in Progesterone Contraception & Estrogen Interception 153

孕激素避孕及雌激素终止妊娠的机制

作者比较了孕激素和雌激素抗生育作用的机制：交配前应用孕激素，通过干扰精子的运行、受精和卵的运行而达到避孕效果。如在交配后用药则效果更好。相反，雌激素必须

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PHYSIOLOGY OF IMPLANTATION

IMPLANTATION

By

Richard J. Blandau

Embryo-endometrial interrelationship leading to implantation has been a subject of great interest to developmental biologists for decades. Although considerable understanding of the process has evolved for several laboratory animals, it is not incorrect to state that it is still impossible to define precisely the exact temporal, physiological and biochemical parameters that lead to successful nidation for any mammal, much less the primates.

Anyone attempting to summarize what is known concerning implantation phenomena on a comparative basis is soon impressed with the diversity of opinion as to how the various factors, systemic, blastocystic, and endometrial, interact in nidation. Specific information remains vague and unsatisfactory. The considerable species differences in the manner in which implantation is accomplished but adds to the dilemma and aggravates the uncertainty.

A uniform feature of the fertilized ovum after it enters the uterine cavity is its transformation into the blastocyst. The morula forms a cavitation that enlarges and expands rapidly to line the zona pellucida. Certain of the cells gather at one pole and form the inner cell mass from which the embryo develops. The layer of epithelial cells on the inside of the zona pellucida comprises the trophoblast. When primitive mesoderm lines the trophoblast, it becomes the chorion.

The trophoblast of the blastocyst is a remarkable membrane that has not received the attention which it deserves: 1) It develops various kinds of attachment cone that initially anchor the blastocysts to the maternal endo-

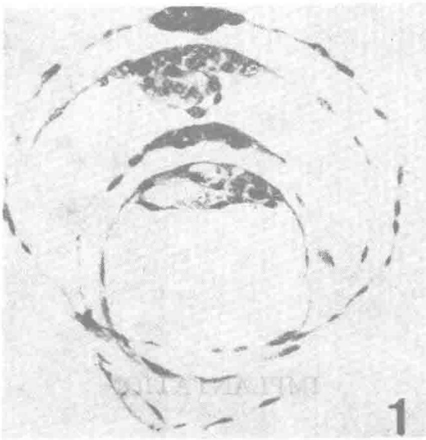

Fig. 1.
Sections of four different free blastocysts recovered from the uteri of the *Macaca mulatta* to show particularly the variations in size and appearance of the normal pre-implanted embryos. × 200 (Courtesy *Heuser & Streeter* 1941).

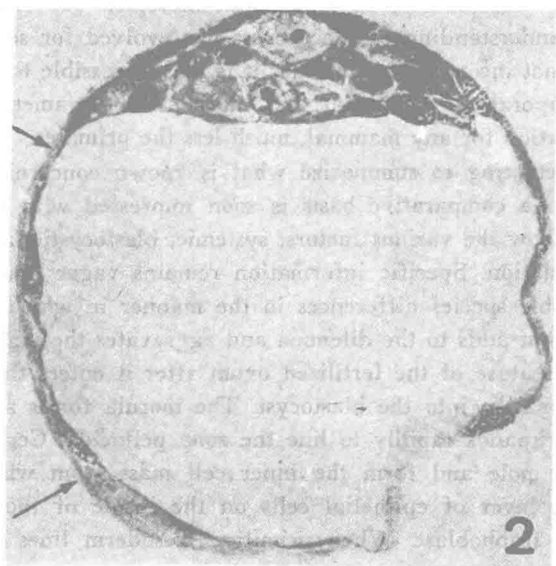

Fig. 2.
Section through an 8-day macaque blastocyst. Note the various cells comprising the inner cell mass, the single layer of trophoblast cells, and the remnants of the zona pellucida (arrows). × 250 (Courtesy *Heuser & Streeter* 1941).

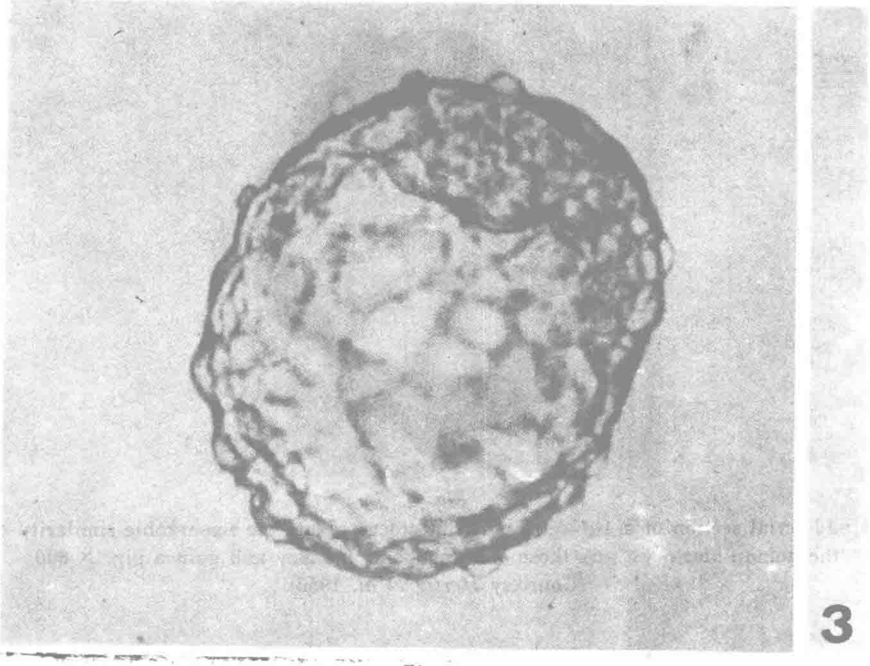

Fig. 3.
A free baboon blastocyst recovered from the uterine cavity at 8 days (estimated fertilization age). (Courtesy *Kraemer & Hendrickx* 1971).

metrium; 2) It acts as a selective membrane that controls materials entering the blastocoelic cavity; 3) It plays a role in controlling the rate of protein metabolism in blastocysts in which implantation is delayed; 4) It is important in the escape of the embryo from the zona pellucida and accomplishes this by a variety of mechanisms in different species; 5) At the appropriate time in development it is transformed into the syncytial trophoblast that, by its adhesiveness and cytolytic capabilities, invades the living maternal endometrial stroma; 6) It may play a critical role in interposing an immunological barrier between foetus and maternal tissues; and 7) With time it will produce and secrete both protein and steroid hormones and develop into a complex endocrine organ, the placenta.

Although blastocysts vary greatly in size and rate of development, they are basically alike in all mammals (compare Figs. 1, 2, 3, 4, 5 & 6). Why blastocysts assume the shape and form that they do in the various mammalian species is unknown. The blastocyst remains free in the uterine lumen for a variable period of time (rat and mouse, 36 to 48 h; guinea pig, 6 days; macaque, 9 days; baboon, 7 to 8 days; cat, 13 days and human, at least 5 to 6 days). In cases of

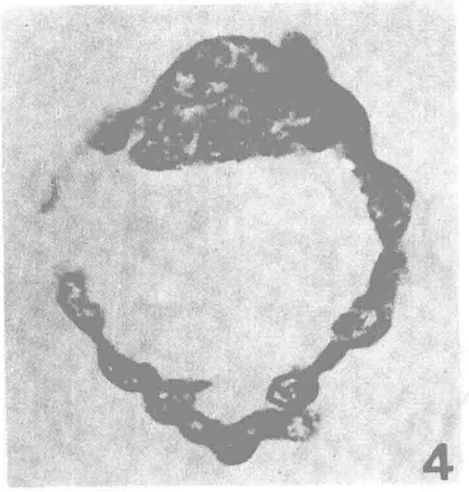

Fig. 4.
A mid-serial section of a 107-cell human blastocyst. Note the remarkable similarity of the human blastocyst and those of the baboon, monkey and guinea pig. × 600. (Courtesy *Hertig et al.* 1956).

delayed implantation nidation may be deferred for days or for even as long as 10 months (European badger, *Meles meles*). Under conditions of delayed implantation the appearance of the blastocysts remains largely unchanged.

Blastocyst development in the non-human primate

Considerable information on the development and appearance of the blastocysts is available for a few primates, namely, the baboon, *Papio cynocephalus* (*Hendrickx* 1971); lesser bush baby, *Galago senegalensis senegalensis* (*Butler* 1959); and macaque, *Macacus rhesus* (*Heuser & Streeter* 1941).

A series of four different macaque blastocysts, in section, is shown in Fig. 1 (*Heuser & Streeter* 1941). All of these were still free within the uterine cavity and were recovered on the 8th and 9th days after ovulation and fertilization. Unfortunately all of the blastocysts recovered in this series were fixed in

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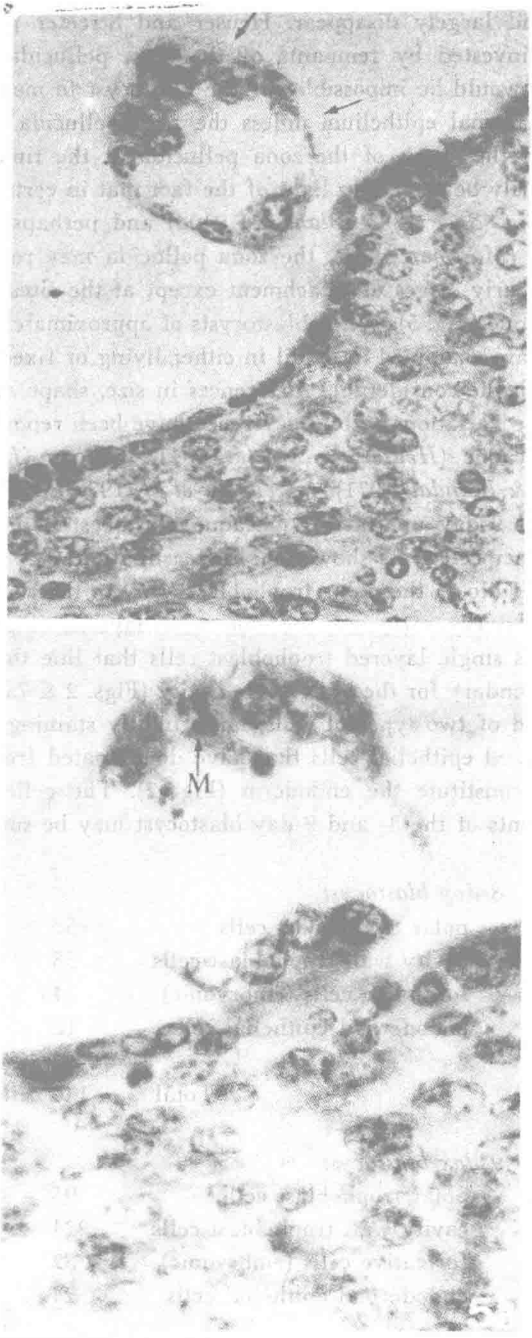
Fig. 5 a & b.
Guinea pig blastocysts found attached to the antimesometrial border in freshly opened cornua on the 6th day after ovulation. They were fixed *in situ*, removed *en bloc*, sectioned and stained. In »a« shrinkage artifact has lifted the blastocyst away from the epithelium. Except for the area of attachment cone the zona pellucida (arrows) is still intact. In »b« note the alterations in the superficial epithelium below the attachment cone and the early invasion of the endometrial stroma by the trophoblastic syncytium. M – embryonic macrophage.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Bouin's fixative, the acid component of which causes the zona pellucida to depolymerize and largely disappear. Heuser and Streeter picture an 8-day blastocyst still invested by remnants of the zona pellucida (Fig. 2). They maintain that it would be impossible for the blastocyst to make effective contact with the maternal epithelium unless the zona pellucida were shed. This interpretation of the status of the zona pellucida at the time of attachment may not necessarily be correct in light of the fact that in certain animals, such as the guinea pig (*Spee* 1883; *Blandau* 1949*a*) and perhaps also in *Citellus tridecemlineatus* (*Mossman* 1937), the zona pellucida may remain largely intact during the early stages of attachment except at the sites of formation of the attachment cone (Fig. 5). When blastocysts of approximately the same stage of development are examined in detail in either living or fixed conditions, one is impressed with the considerable differences in size, shape, and stage of development. These variations in blastocyst size have been reported in a number of animals [macaque (*Heuser & Streeter* 1941), baboon (*Hendrickx* 1971), mouse (*Rumery & Blandau* 1971), rat (*Tachi et al.* 1970), etc.].

In the 8- and 9-day unattached macaque blastocyst both the trophoblast shell and the inner cell mass show some differentiation. The trophoblast may be differentiated into 1) the polar trophoblast (*i. e.*, in the region of the inner cell mass), which very early may become multi-layered (Figs. 7a & b), and 2) the continuous single layered trophoblast cells that line the zona pellucida and form the boundary for the blastocoele cavity (Figs. 2 & 7a). The inner cell mass is composed of two types of cells, large lightly staining cells (formative cells), and flattened epithelial cells that have delaminated from the inner cell mass and now constitute the endoderm (Fig. 2). The cells comprising the various constituents of the 8- and 9-day blastocyst may be summarized:

8-day blastocyst	
polar trophoblast cells	56
cavity wall trophoblast cells	58
formative cells (embryonic)	14
endodermal epithelial cells	12
Total	140 cells
9-day blastocyst	
polar trophoblast cells	95
cavity wall trophoblast cells	224
formative cells (embryonic)	32
endodermal epithelial cells	24
Total	375 cells

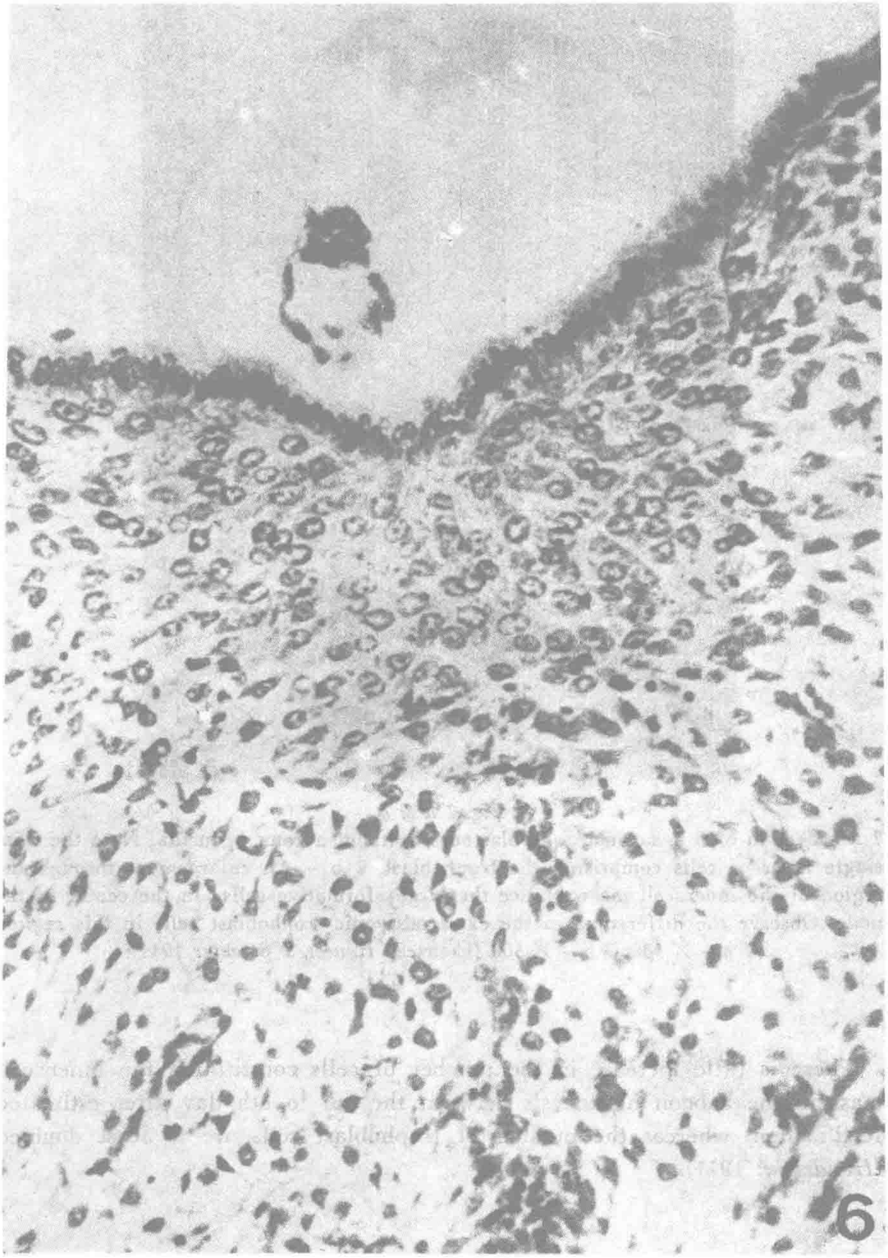

Fig. 6.

A section through the initial site of attachment of a rat blastocyst recovered late on the 4th day after ovulation. The blastocyst has initiated an early decidual response. There is no obvious alteration of the superficial epithelium. The zona pellucida is gone.