

CONTINUED DIFFERENTIATION OF MAMMALIAN EMBRYOS IN UTERO AFTER  
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Previous observations tend to suggest that the development of mammalian embryos beyond stages equivalent to implantation depends somehow on the formation of an intimate cellular contact of the trophoblast with uterine tissues. In vitro culture gives satisfactory results only up to the late blastocyst stage, if attachment is impossible; further development can be obtained if the culture is started with postimplantation stages.

In a series of experiments on interference with implantation by proteinase inhibitor administration in vivo, we used continuous intrauterine infusion of aprotinin (Trasylo) by osmotic minipumps. This treatment effectively inhibits blastocyst activity which is essential for dissolution of the extracellular blastocyst coverings in the beginning of the implantation process. As a result, these coverings remain interposed between trophoblast and uterine epithelium thereby preventing contact formation. While the majority of the embryos manages to hatch mechanically from the coverings so that partial attachment is possible, 25% of them were found completely encased in the coverings at 9 1/2 days post coitum, i.e. 2 1/2 days after implantation would normally have started. These embryos are still completely free in the uterine lumen, but, interestingly, differentiation is not hampered or only slightly retarded. Therefore a condition is found, in this eutherian mammal, which was previously only seen in marsupials, i.e. a free-living conceptus in the uterine lumen with neural tube, somites etc. In contrast to the regular development of the embryo proper, the trophoblast was found to undergo early degeneration from which it was rescued only in cases where it managed to contact maternal tissue. (Supported by Deutsche Forschungsgemeinschaft grant No. De 181/9-4)

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