transplants are capable of providing a bridge through which anatomical continuity of the spinal cord is re-established.

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Growth of trophoblast in mouse lung

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Summary. When blastocysts are introduced into the lungs of mice via the circulation, trophoblast cells grow, as they do in other extrauterine sites.

Trophoblast is naturally deported to the lungs during pregnancy in only 2 species, man and chinchilla[1,2]. In neither species does the tissue proliferate. Trophoblast has been introduced experimentally into the circulation of mice and rabbits using placental tissue from donor animals in the 2nd half of pregnancy[3,4]. This disappears from the lungs without trophoblast growth and, usually, without reaction. We have previously described experiments in which 3.5-day blastocysts or 7.5-day ectoplacental cones have been introduced into the lungs of mice[5,6]. Trophoblasts grew whether they were introduced directly, intravascularly or intrabronchially with 1 exception; trophoblast never showed sustained growth from blastocysts introduced into the circulation in adult mice. There appeared to be an initial growth of trophoblast when mice were killed 3 days after introducing blastocysts[5], but in animals killed on the 4th day, the trophoblast was seen to be dying[6]. Those killed more than 4 days after injecting blastocysts into the lung via the femoral vein showed a reaction involving hyperplasia of all elements of the lung. These results were observed in 27 adult, syngeneic mice whether male or female recipients were used. A series of experiments were designed to investigate the reason for this failure of blastocysts to produce trophoblast in adult lungs. However, during the 2 years in which these experiments were conducted, the results changed and we began to see healthy trophoblast in the lungs of these animals. The re-investigation of this process is the subject of the present report.

Methods. All the experiments were carried out in syngeneic C3H/HeJ mice (Jackson Laboratories) which were housed under standard conditions. Operative procedures were conducted under ether anesthesia and sterile conditions were maintained. The animals were 12–14 weeks old and donor blastocysts were flushed from the uterus with Hanks solution at 3.5 days gestation. The blastocysts were introduced into the lungs of recipient mice via the femoral vein and the animals killed with ether 4–10 days later.

Results and discussion. The results of earlier, published, experiments and of the present study are summarized in the table. In the earlier experiments, up to 3 blastocysts were instilled into the lungs and in animals killed on the 4th day, degenerating trophoblast cells were found in 1 or 2 areas of the lung (fig. A). In animals killed 5–10 days after the experiment no trophoblast remains were found but extensive hyperplastic reaction of the lung was seen[5,6].

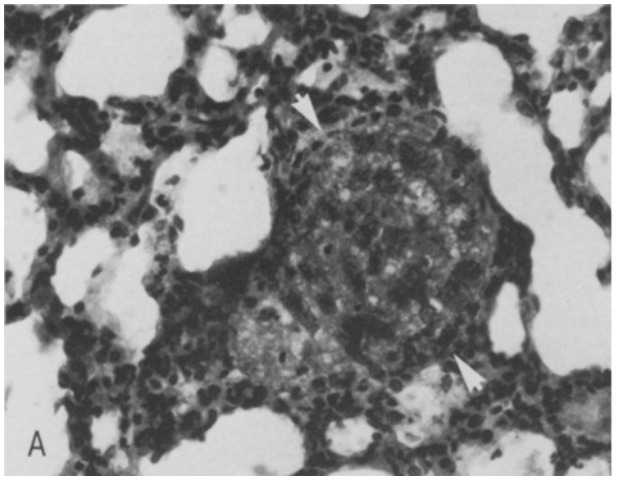
In the 2nd series of experiments, reported here, 3–9 blastocysts were instilled into the lungs via the femoral veins of 20 animals. These were killed 7–10 days later and 15 showed 1–6 areas of trophoblast proliferation in the lungs (fig. B). Giant trophoblast nuclei were seen at the periphery of the mass and small trophoblast nuclei in the core. Both appeared healthy in animals killed up to 10 days after blastocyst injection. Mice were not studied later than 10 days after instillation of blastocysts because this generally represents the day of maximum trophoblast growth in extra-uterine sites[7]. Extensive invasion of the lungs with tissue destruction and bleeding which is frequently observed when trophoblast grows in other organs[7] was not seen in the lungs in these experiments. The 5 mice that were negative for trophoblast growth showed no reaction of the type noted in the earlier experiments. The lungs were normal in these animals and the failures appeared to be technical.

The reason for the different results between the earlier and present studies is not definitely known. The strain of mice and their source remained the same. Blastocyst donors and recipients were syngeneic and the experimental method remained unchanged. The formula of the Hanks solution had not changed but in order to eliminate minor changes, in trace elements for instance, dry Hanks solution from the period covering the 1st experiments was obtained[8] and used for most of the current investigations.

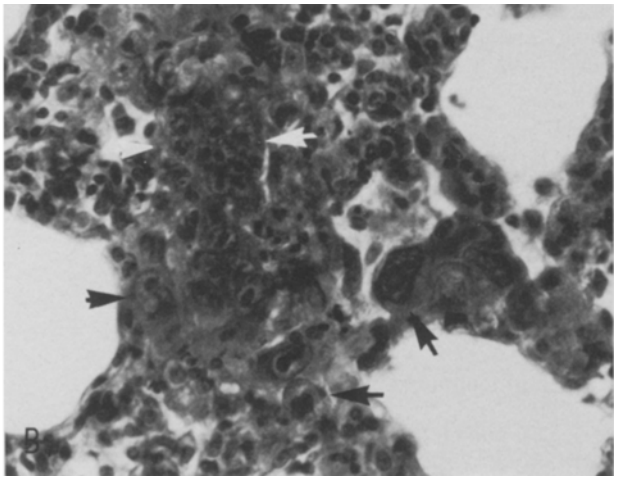
We had been aware that, during the period of the earlier work, mice tended to die after weeks or months in stock, although those used in the actual experiments always appeared healthy. During the later experiments, this high mortality of stock animals had ceased. In retrospect, this 1st period had been marked by endemic outbreaks of murine virus pneumonia. If this was the cause of the change in results, it only affected the growth of trophoblast from 3.5 day blastocysts with the zona pellucida intact. It is possible

Growth of trophoblast in lungs of mice killed 4–10 days after injecting blastocysts via circulation

	No. of animals	Degenerating trophoblast	Lung reaction	Normal trophoblast	Normal lungs
Earlier reports[5,6]	39	5	22	0	12
Present study	20	0	0	15	5



A Trophoblast nuclei in the lung from a mouse killed 4 days after injecting blastocyst into circulation. All the trophoblast cell nuclei, lying within the area indicated by arrows, show marked lysis. ×210.



B Small and giant trophoblast cells in the lung of a mouse killed 8 days after injecting blastocysts into the circulation. The giant trophoblast nuclei are indicated by black arrows and the small nuclei by white ones. ×270.

that the mucopolysaccharide of the zona acted as a focal point of concentration of the virus and that breakdown products affected the growing trophoblast adversely. The initial failure of blastocysts to produce trophoblast giant cells in the original experiments appears, therefore, to have been due to or associated with an endemic infection in the mice.

Thus, the lungs can be added to brain, spleen, kidney, liver, testis, peritoneum and eyes, as organs in which trophoblast grows from blastocysts or ectoplacental cones when they are experimentally implanted[5–7,9]. The lungs do not apparently contain a specific enzyme which protects them from trophoblast growth as has been suggested[10], at least not in mice.

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Rabbits infested with adult *Ixodes ricinus* L.: effects of mepyramine on acquired resistance[1]

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Summary. The results of this work demonstrate that histamine seems to be involved in the expression of the resistance acquired by rabbits to ♀♀ *I. ricinus.* Daily treatment of animals with the H_1-antihistaminic mepyramine inhibited the effects of immunity. This observation applies to the effect of resistance on the weight of engorged ticks, the duration of the blood meal and the success of egg laying and hatching.

In our preceding work, we demonstrated that rabbits infested by ♀♀ *I. ricinus* progressively acquire resistance during repeated infestations[2]. This immunity is manifested by an increase in the average duration of the blood meal, by inadequate feeding and by poor oviposition. The duration of pre-oviposition and embryogenesis can also be prolonged[3]. Experimentally, resistance can be partially transferred by serum from immune animals[4,5]. As described previously, the skin of the animals is rendered sensitive to antigens of tick saliva, resulting in an immediate hypersensitivity reaction[5]. Infested animals show a marked infiltration of cells at the tick attachment site, notably of mast cells and basophils[6]. We have observed that some cells degranulate during a reinfestation. This phenomenon is due, undoubtedly, to a type I hypersensitivity reaction of mast cells, and also to a reaction similar to cutaneous basophil hypersensitivity[3]. Using a degranulation test, we have shown a progressive sensitization of basophils to tick salivary antigens.

In the present study, we have tried to demonstrate the importance of liberated histamine in the biological expression of resistance. After treatment of rabbits, reinfested with ♀♀ *I. ricinus,* with the H_1-antihistaminic drug mepyramine, we compared the duration of the blood meal, weights of engorged ticks, and the success of egg laying and hatching with the results obtained from both primary infestation and reinfestation of untreated, immune animals.

Materials and methods. 12 male rabbits of a Russian race (Himalayan breed, genotype aac^Hc^H) weighing approximately 2 kg were used. They were infested twice at an interval of 3 weeks, with 10 ♀♀ and 10 ♂♂ *I. ricinus,* raised in our laboratory. 4 animals served as controls and these