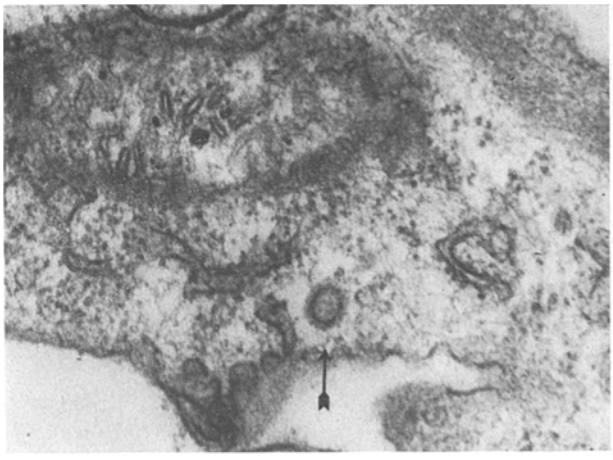

Fig. 2. Viral particles in the cytoplasmatic region. Araldite-Epon; ×50,000.

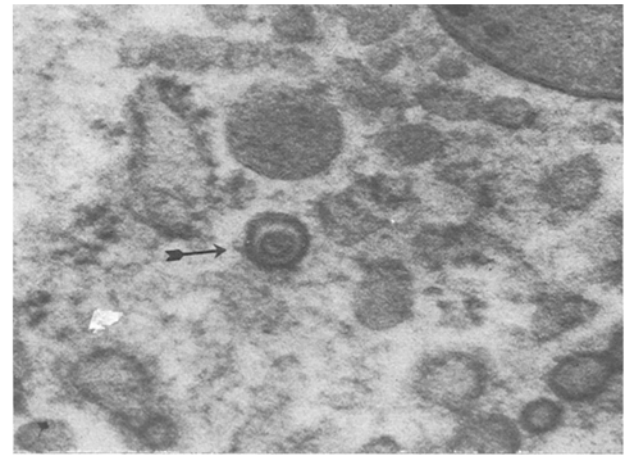

Fig. 3. Viral particles in the cytoplasmatic region. Araldite-Epon; ×100,000.

in the mammary area of female subjects, which regularly ensured, for 3 generations, the reproduction of the neoplasia. The other tests were found to be negative.

The case described above would seem to be the first one in which viral particles have been found in a spontaneous mammary tumour in the rat. However, this does not justify the proposal of any considerations regarding the etio-pathogenesis of the tumour in question. In fact, there is no possibility for correlating the evidential viral particles with the origin of the tumour, that arose spontaneously in the rat, in agreement, among other things, with what is know regarding cancer in the human species[4], even if in our case there is, in addition, the transplantability of the tumour.

Although there have been reports[5,3] of the possibility of inducing leukemias in the rat, with acellular extracts of mammary neoplasias of the same species, it would appear premature to draw any general conclusions, especially since these were cases of neoplasias induced with dimethylbenzo-anthracene. On the other hand, it would seem[1] that the virus isolatable from mammary carcinomas of the rat induced by radiation does not possess the same antigene constitution as the virus of murine leukemia.

As regards our results, we can merely say that, although the neoplasia is found to be transplantable, and inspite of the fact that viral particles have been found in it, it is not possible to conclude that it is of a viral nature. What has chiefly prevented us from doing this has been the absence of results following the inoculation of acellular extracts in numerous subjects.

Riassunto. Per la prima volta viene segnalato il reperto di particelle virali in adenocarcinoma mammario spontaneo del ratto.

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Effects of Placental Lesions on Foetal Growth in Rats

Normal growth of the foetus is dependent upon the functional integrity of the placenta and the maintenance of adequate foetomaternal exchange. Impaired uteroplacental circulation as well as placental insufficiency are commonly associated with foetal growth retardation in humans; thus predisposing to a high incidence of perinatal mortality and morbidity in such neonates, in spite of a full gestational period[1–7]. Experimentally, intrauterine growth retardation was obtained, following reduction of the utero-placental blood flow, in rats by Wigglesworth[8] and more recently in sheep by Creasy et al.[9]. Myers et al.[10] succeeded in inducing a condition of placental insufficiency and growth retardation of the foetal rhezus monkey by surgically interrupting the foetal blood vessels to the secondary placental disc. In the present study, an attempt was made to determine the effects of partial destruction of the placenta upon foetal growth in rats.

Materials and methods. 15 albino female virgin rats, 2 to 3 month-old, were mated. Successful mating was confirmed by sperms in the vaginal smear and this date was considered as day 1 of pregnancy. On day 17, the uterus was exposed through a midline abdominal incision, under general anaesthesia provided by intraperitoneal injection of Evipan-Natrium. The number and condition of conceptuses were recorded. Electrolytic lesions were made in alternating placentas of one uterine horn (experimental horn), while the remaining placentas of the same horn as well as all those of the contralateral horn (control horn) were kept intact. The lesions were made with stainless steel anodal electrodes using a direct current. In this system, the magnitude of the current remains constant and the extent of the lesion is mainly a function of the effective size of the electrode and the duration[11]. The bare end of the electrode measured 0.6 mm in diameter and varied between 3 and 5 mm in length

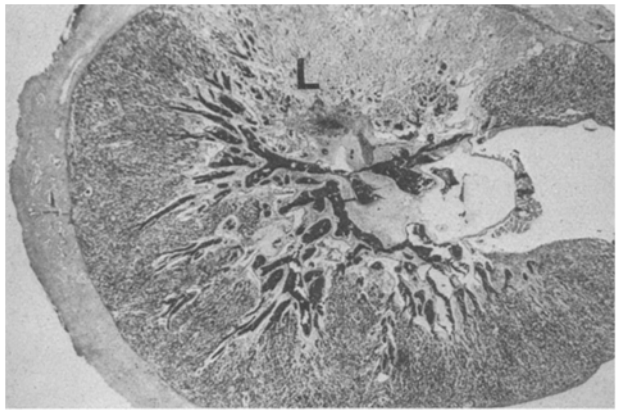

Fig. 1. Section through lesioned placenta near foetal surface. L, area of lesion. H and E. ×10.

Fig. 3. A lesion deep within the placenta. Necrotic and haemorrhagic changes are evident; note haemosider in deposition (arrows). Area of damage extends beyond the immediate path of the electrode. H and E. ×54.

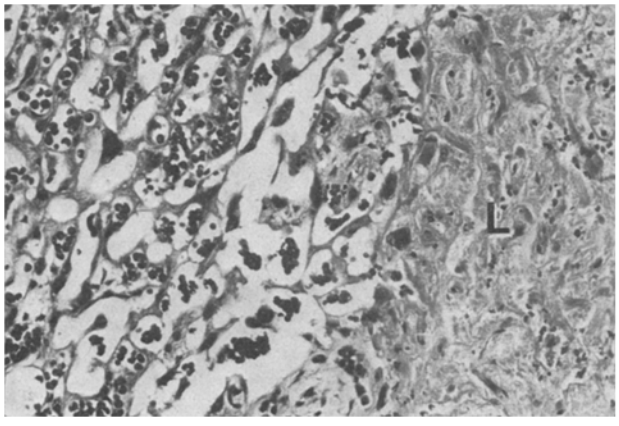

Fig. 2. Junction of lesioned (L) and normal placental tissue. Note loss of normal architecture of placental labyrinth and degenerative changes in villous structures compared to adjoining intact tissue. H and E. ×260.

Fig. 4. Placental lesion near the tapered end of the electrode. Area of damage is less extensive. H and E. ×30.

according to the size of the placenta. The current was applied for 20 sec and maintained at 2.0 mA. 2 such lesions were applied per placenta, by inserting the electrode through the uterine wall, well within the placenta and parallel to its foetal surface. While the current was switched on, the uterine wall was in contact with the insulated part of the electrode. The procedure was conducted aseptically and the abdomen was closed with 4–0 silk. Pregnancy was left to proceed to the 21st day when the mothers were killed by decapitation, followed by immediate removal of the conceptuses. Total body weight, liver weight and brain weight were recorded separately for each foetus. The placentas were fixed for histological confirmation of the lesions.

Results and discussion. This procedure was found to be associated with 87% foetal survival; loss of amniotic fluid being the main cause of death of the remainder. Figures 1, 2, 3, and 4 are photomicrographs illustrating the changes that have taken place as a result of electrolysis and the appearance of lesioned areas as compared to intact placental tissue. Loss of normal architecture of the placenta, haemorrhage, fibrin deposition and degenerative manifestations in villous structures were observed suggesting loss of placental function in the affected area; more of the placental labyrinth was involved than merely the area in the immediate vicinity of the electrode (Figures 1 and 3).

The Table summarizes the effect of these lesions on total body and absolute organ weights of the surviving foetuses. The average body weight was reduced in comparison to that of the control groups. It was 15% less

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Effect of placental lesions* on rat foetal body and organ weights (mean ± SEM)

Placenta	No. of foetuses	Body wt. (g)	Brain wt. (mg)	Liver wt. (mg)
Intact (control horn)	50	3.28 ± 0.05 [a]	159 ± 1.55 [d]	277 ± 5.36 [g]
Intact (experimental horn)	28	3.20 ± 0.08 [b]	151 ± 3.51 [e]	252 ± 7.80 [h]
Lesioned	30	2.80 ± 0.11 [c]	149 ± 2.90 [f]	216 ± 8.99 [i]

* Lesions made on day 17, pregnancy terminated on day 21. (c-a) $P < 0.01$, (c-b) $P < 0.05$, (f-d) $P < 0.01$, (i-g) $P < 0.001$, (i-h) $P < 0.01$.

than the average weight of foetuses in the control horn. The average brain weight was significantly reduced only in comparison with the intact horn controls. However, the effect on the liver was more consistent in that its weight in lesioned conceptuses was significantly less than that in the 2 control groups. Figure 5 represents the average ratios of organ to body weight in the 3 groups of conceptuses. Placental lesions were associated with a significant decrease in the average liver-to-body weight ratio, 71 ± 1.5%, from that of intact horn and experimental horn control groups, 84 ± 0.35% and 81 ± 0.46% respectively. The average brain-to-body weight ratio was not affected. However, when the brain-to-liver weight ratios were calculated (Figure 6), foetuses with placental lesions had a ratio (0.73 ± 0.04) significantly higher than that of each of the control groups (0.58 ± 0.009, 0.61 ± 0.02).

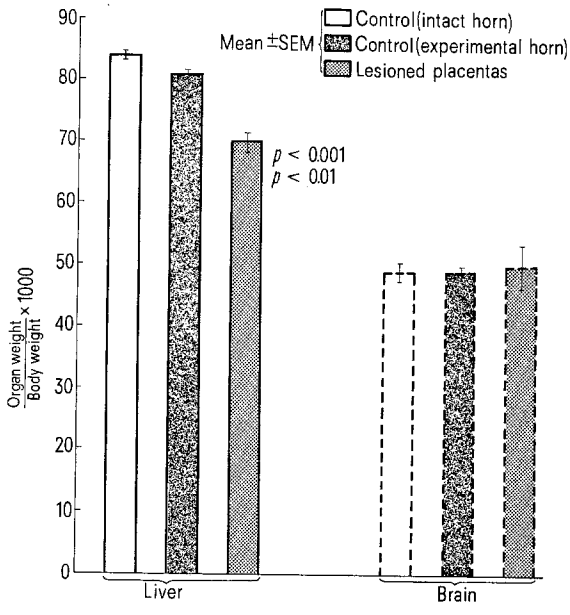

Fig. 5 .Effect of placental lesions on the ratio of organ to body weight in rat foetuses.

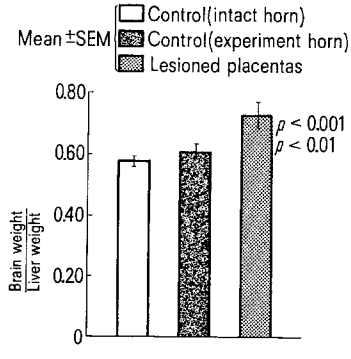

Fig. 6. The average ratios of foetal brain to liver weight in lesioned and control groups.

The data presented show that partial destruction of the placenta in rats, as described in this study, is associated with reduced foetal body weight, significant decrease in liver-to-body weight ratio, and no effect on brain-to-body weight ratio. These findings are indicative of foetal growth retardation as reported by the studies of other investigators in different mammals including humans[8–10, 12]. Moreover, DAWKINS[13] observed a significant increase in brain-to-liver weight ratios in human fetuses with growth retardation and a similar observation was made experimentally in animals[9, 10]. Such effect on the relative growth of these 2 organs was also observed in this study.

It could be concluded, therefore, that in the present experiments a condition of placental insufficiency had been selectively induced in pregnant rats that led to retardation of foetal growth, presumably without interfering with the uterine circulation. Such a method, may be useful experimentally as a model to study the role of the placenta in relation to intrauterine growth as well as an alternative to ligation of the uterine artery for the production of foetal growth retardation in rats.

Résumé. Un état d'insuffisance placentaire a été produit chez la ratte au moyen de lésions électrolytiques effectuées au 17e jour de gestation. Le poids corporel ainsi que le poids du foie des foetus, au 21e jour de la grossesse, présentèrent une diminution; tandis que le poids du cerveau en relation à celui du foie avait augmenté. Ces résultats indiquent que les foetus ainsi traités subissent un retardement de croissance par rapport aux témoins de même âge.

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[14] Acknowledgments. The author wishes to thank Dr. D. G. MONTEMURRO for the use of the electrolytic apparatus and Mr. N. FALCONER and Mr. J. KRCEK for their technical assistance.