EXPERIMENTAL INFECTION OF PREGNANT MICE WITH VIRUSES OF THE TICK-BORNE ENCEPHALITIS (TBE) COMPLEX

*A. Molnárová, *V. Mayer*

Chair of Plastic Surgery, Medical Faculty, Commenius University, 883 26 Bratislava; and *Institute of Virology, Slovak Academy of Sciences, 809 39 Bratislava, Czechoslovakia

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For the expressed viraemia, experimental infections by virulent flaviviruses are expedient models of transplacental virus transmission and of its effects on the foetal development (*1, 2*). These pathogenic capacities were investigated in the E5"14" *ts* mutant of the naturally attenuated Langat TP 21 virus (*3*), in comparison with the virulent P III-E variant of the TBE virus (western subtype), using outbred 20—25 g white female mice (Dobrá Voda breed). The teratogenic effect of the attenuated virus was studied in the offspring of a total of 111 pregnant mice, infected subcutaneously (s.c.) with 10^5 PFU of the *ts* mutant. From 5—9 mice were infected at daily intervals from the 1st until the 18th day of pregnancy, 61 gravid mice received under similar conditions 0.1 ml of a 10% normal mouse brain suspension and 23 pregnant mice were investigated untreated. On the 20th-21st day of prognancy, after the birth, the implantationplaces, the total number and the numbers of dead and resorbed foetuses were estimated. Macroscopic developmental anomalies were inspected in newborn mice. Skeleton defects were investigated by the method od Dawson (*4*). In the progeny of all 3 groups of mice, besides a few stillbirths, resorbed foetuses and foetuses displaying retarded growth, also foetuses with "polydactylia" were observed. But the 6th finger's processus consisted of the soft tissue only. No statistically significant differences between the offsprings of the above 3 groups of pregnanf mice were observed.

Transplacental transmission of the attenuated mutant was studied in 19 mice, given 10^5 PFU of the virus on the 8th day of pregnancy. Two or three gravid mice were bled daily from the 1st until the 9th day after infection (p.i.), killed and their brains and spleens removed. Foetuses were dissected from the same animals aseptically, washed in phosphate buffered saline, pH 7.2, and 2—3 of them pooled. Materials were kept deeply frozen until tested for infectious virus by plaque assay in pig kidney cell monolayers (*3*). In another experiment, 9 mice were inoculated s.c. with a sublethal dose of the virulent virus ($10^{3.9}$ PFU corresponding to about 1—5 sc LD_{50} for mice of the respective age) on the 8th day of pregnancy. From the 2nd until the 6th day, materials from the gravid females were collected as in the preceding experiment. Virus was recovered from foetuses of all 3 mice examined on the 3rd day p.i. The titres varied in individual foetus pools (33—170 PFU per ml) suggesting that some of the virus did not originate from viraemic blood only and that viral invasion of implantation places was asynchronous. The virus in foetuses titered as high as $3.7—9.5 \times 10^3$ PFU per ml on the 4th—5th day p.i. Viraemia was observed only in one mouse on the 3rd day p.i. (53 PFU per ml of blood diluted 1 : 3). Virus (33—26 PFU per ml) was detected only in spleens of mice killed on the 3rd—5th day p.i., i.e. in 44% of all mice examined. Traces of virus (24 PFU per ml) were recovered from the brain of one pregnant mice on the 5th day p.i. Thus, in contrast to the non-invasive E5"14 *ts* mutant, the virulent TBE virus, in spite of the very low infecting dose and an irregular and barely detectable viraemis, localized and grew across the blood-foetal junction in the discoid placenta (haemochorioidal type) before the 3rd day p.i. at least in some foetuses from a given mouse. This situation approached events observed during infection of pregnant mice with St. Louis encephalitis virus (*2*).

References

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