

## VIRAEMIA IN RABIES

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Received July 3, 1980; revised December 30, 1981

The rabies virus spreads to CNS predominantly in neuraxons. Several authors (1, 2) succeeded in isolation of virus from the blood of experimental animals only in the first hours post infection (p. i.). The reports on "true" viraemia in rabies associated with extensive virus replication in the CNS immediately before or at the onset of clinical symptoms are confusing (1-4). To elucidate the reason of this controversy may be important for the understanding of rabies pathogenesis.

Viraemia was studied in outbred white mice weighing 18-20 g inoculated either by intracerebral (ic) or intraperitoneal (ip) routes with two wild type (wt) strains of rabies virus designated "Yak" (5) and "On-5" (6) respectively or by intramuscular (im) route with the attenuated (at) strain ERA. Incubation time was 6-7, 8-14 and 7-10 days respectively. One half of infected mice received no treatment, while the other half of infected animals received cyclophosphamide (CPA) in a dose of 100 mg/kg body weight by ip route on days 0.2 and 5 p. i. CPA is an alkylating compound exerting immunosuppressive effect on both B and T cells. Mice were killed on the 2nd and 4th days of illness. Blood from each mouse mixed with 5 units of heparin was inoculated into 10 mice weighing 6-7 g; in addition, blood was used for the determination of neutralizing antibodies (NA) by means of neutralization tests in mice.

In infected untreated mice NA were regularly found. Viraemia was detected only in 2 out of 5 mice inoculated by ic route. In the latter, the NA titre was lower than 1:10. In animals treated with CPA no NA were detected. Viraemia was found in each animal regardless of the site of virus inoculation. The titres of virus in blood ranged from 0.8 to  $\geq 1.4 \log LD_{50}$  per 0.03 ml, in brain from 4.5 to 6.5  $\log LD_{50}$  per 0.03 ml.

Virus strain (inoculation site)	Virus dose $\log LD_{50}$	No CPA		CPA	
		Viraemia	NA titre	Viraemia	NA titre
"Yak", wt (ic)	5.0	2/5	1:112	5/5	0
"On-5", wt (ip)	3.6	0/5	1:71	5/5	0
"ERA", at (im)	3.7	0/7	1:63	5/5	0

In CPA treated mice inoculated with the "Yak" wt strain by ic route virus was isolated from blood since 2 hr p. i. Neither virus nor NA were detected by day 4 p. i. These results are suggestive for the two phase course of viraemia in experimental rabies. Early after infection a short lasting "resorptive" viraemia occurs due to virus penetration from the inoculation site. The secondary (,true") viraemia related to extensive virus replication in CNS occurs at the onset of or immediately before the appearance of clinical symptoms. The "true" viraemia at the onset of illness is masked by the presence of NA, which at this time reached considerable titres.

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