inoculation. However, the difference between this and the titers obtained with blood pools drawn on the 7th and 8th days after inoculation falls well within the limits of experimental error. Thus, it may be assumed, that the concentration of rabies virus in the blood of infected embryos was fairly constant, the daily fluctuations being of minor importance.

Summary and comments. The Flury strain of rabies virus was inoculated by the yolk-sac route into 7-day-old chick embryos. By means of intracerebral injections into mice, the virus was recovered from the chick-embryo blood secured from the 3rd to the 15th post inoculation day. The similar results obtained in two series of experiments seem to exclude the possibility of a major experimental error. While these experiments do not prove or disprove the infectiousness of mammalian blood from rabies infected animals, they do indicate a completely different mechanism of dissemination of the virus in embryonated eggs.

16574

Reverse Interference Between Simian and Murine Poliomyelitis Virus in Guinea Pigs.*

CLAUS W. JUNGEBLUT.

From the Department of Bacteriology, Columbia University College of Physicians and Surgeons, New York City.

Earlier work has shown that certain strains of mouse-adapted human poliomyelitis virus (Col SK, MM) which have lost the greater part of their monkey pathogenicity will effectively interfere with the propagation of simian virus in rhesus monkeys. Murine infection in mice, on the other hand, could not be significantly influenced by the administration of monkey poliomyelitis virus. Nor was it possible to inhibit regularly the growth of murine virus in minced embryonic mouse brain tissue culture by adding monkey poliomyelitis virus to the medium.[1] Subsequent attempts to arrest the propagation of murine virus (Col SK) in embryonated eggs by previous or simultaneous implantation with simian virus (Aycock) have likewise failed to give unequivocal results.[2]

The question as to whether this viral antagonism is strictly a unilateral reaction—as would seem from the above observations—or whether interference may also be demonstrated in the reverse direction is of more than theoretical interest. In one case the phenomenon would be confined to whatever therapeutic significance it may possess, in the other, it might conceivably lend itself also to diagnostic application. Evidence that such reverse reaction may actually occur under favorable circumstances has already come from the work of Dalldorf and Whitney.[3] These authors reported that hamsters following intracerebral injection with simian virus, or with filtrates of faeces collected from human cases of poliomyelitis, exhibited a well marked resistance towards subsequent intraperitoneal challenge with MM murine poliomyelitis virus.

Previous attempts to demonstrate reverse interference in mice having failed—possibly because of the extreme susceptibility of the albino mouse to murine infection—it was decided to investigate whether the phenomenon could be successfully elicited in a less sensitive animal, such as the guinea pig. Results obtained in a small series of experiments

* Aided by grants from the Philip Hanson Hiss, Jr., Memorial Fund and from anonymous donors.

1 Jungeblut, C. W., and Sanders, M., *J. Exp. Med.*, 1942, **76**, 127; Jungeblut, C. W., *J. Exp. Med.*, 1945, **81**, 275.

2 Jungeblut, C. W., unpublished data.

3 Dalldorf, G., and Whitney, E., *Science*, 1943, **98**, 477.

TABLE I.
Interference Between Simian and Murine Virus in Guinea Pigs.

Experiment	No. of guinea pigs	Blocking injection		Challenging injection			Result	
		Simian virus	Dose	Murine virus	Dose	Route	Paralysis	No paralysis
I	7	RMV	0.1 cc i.c. + 0.5 cc i.p.	MM	1 cc 10^{-1}	i.p.	0	7
	5	Aycock	"	"	"	"	2	3
	7	Control	"	"	"	"	4	3
II	5	RMV	"	"	0.1 cc 10^{-1}	i.c.	0	5
	4	Aycock	"	"	"	"	0	4
	5	Control	"	"	"	"	2	3
III	2	RMV	"	"	1 cc 10^{-1}	i.p.	0	2
	4	Control	"	"	"	"	3	1
IV	6	Aycock	"	"	"	"	0	6
	5	Control	"	"	"	"	2	3
V	5	Aycock	"	"	0.1 cc 10^{-1}	i.c.	1	4
	3	Control	"	"	"	"	2	1
VI	5	Aycock	"	"	"	"	2	3
	5	Control	"	"	"	"	5	0
VII	5	Aycock	"	"	"	"	1	4
	5	Control	"	"	"	"	2	3
Total (Exps. I-VII)	20	Simian	"	"	1 cc 10^{-1}	i.p.	2	18
	16	Control	"	"	"	"	9	7
	24	Simian	"	"	0.1 cc 10^{-1}	i.c.	4	20
	18	Control	"	"	"	"	11	7

are recorded in this communication.

Methods. Two different strains of simian passage virus, *i.e.* the Aycock strain and the RMV strain, were used for blocking injection. The challenging virus was the MM strain of mouse-adapted human poliomyelitis virus. The tests were carried out in young guinea pigs (175 g weight), which are moderately susceptible to infection with MM murine virus by either the intracerebral or intraperitoneal route. The interfering effect was measured by injecting the guinea pigs first with a large dose of 10% glycerinated simian virus suspension (i.c. and i.p.) and, after a uniform interval of 24 hours, challenging the prepared animals intracerebrally or intraperitoneally with approximately 10-100 ID_{50} of freshly harvested murine virus. The interval between the two injections was advisedly held brief to exclude any concurrent effects of immunity. A suitable number of control guinea pigs, challenged with the same dose of MM virus following preparation with 10% glycerinated normal monkey cord suspension, accompanied each experiment. A total of 7 different experiments were run, which are presented in Table I.

It appears from Table I that in every one of the 7 experiments the incidence of paralysis following challenge with MM virus was considerably reduced in the animals prepared with simian virus as compared with the corresponding controls. Experiments I, III, IV, V, and VI were winter experiments with MM virus at the peak of its guinea pig pathogenicity. Experiments II and VI had been conducted in the summer months when murine virus undergoes some seasonal drop in virulence for guinea pigs.[4] Combining the data of the several experimental series, it will be seen that of a total of 44 guinea pigs prepared with simian virus, which were challenged either intracerebrally (24) or intraperitoneally (20) with MM virus, 4 (16%) responded with paralysis to intracerebral challenge and 2 (10%) to intraperitoneal challenge. By contrast, of a total of 34 control animals which received MM virus intracerebrally (18) or intraperitoneally (16), 11 (61%) or 9 (56%), respectively, became paralyzed. In other words, in the prepared group the morbidity rate was approximately one-fourth to one-fifth that observed in the control group. These figures are in close agreement with those previously published by Dalldorf and Whitney,[3] who reported that among a total of 36 prepared hamsters 9 (25%) became paralyzed upon intracerebral challenge with MM virus, whereas among 29 control hamsters, 28 (97%) developed paralysis.

Summary. The above results indicate that reverse interference between simian and murine virus occurs with about the same frequency in rodents as direct interference between murine and simian virus in monkeys. The phenomenon may therefore be said to be reciprocal in character. Adjustments in the quantities of both viruses or variations of the time interval may further improve the efficiency of the reaction. In judging these results it must be borne in mind that successful operation of the interference phenomenon depends upon a delicate balance between the ability of the interfering virus to occupy susceptible cell receptors and the invasive potency of the challenging virus. It is therefore, perhaps, not without importance that the two strains of simian virus employed successfully in this work were passage strains of unusual virulence. One experiment with simian virus of lesser virulence has given less clearcut results. Leaving alone the question of its specificity, it therefore seems doubtful whether this reaction can be used for diagnostic purposes to detect virus in human cases of the disease without resorting to some form of preliminary concentration of the pathological material (faeces, blood, nerve tissue, etc.).

[4] Jungeblut, C. W., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 177.