

shown that as a rule the arm-to-arm circulation time is about the same in both positions of the body; whereas the foot-to-arm circulation time is much longer in the standing still than in the recumbent position. Data on a typical case are recorded in Fig. 1.

Our results are consistent with the theory that in the standing still position, the circulation is slowed only where it is impeded by gravity, *i. e.*, in dependent portions of the body.

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Experimental Herpetic Encephalitis in the Guinea Pig Produced Through the Respiratory Tract.

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In a previous communication¹ we described experimental *herpetic encephalitis* produced by feeding herpes virus to guinea pigs. The brains from such animals, dying after feeding of herpes virus, when injected into rabbits by the intraspinal route produced typical *herpetic encephalitis* and the disease could be passed in series from rabbit to rabbit. Control cultures of the guinea pig brains were without growth. It was noted that the herpes virus was somewhat attenuated following passage through guinea pigs by this method but its virulence rapidly returned by rabbit passage. It was further observed that only about 50% of the guinea pigs so treated with herpes virus died, the others remaining apparently unaffected. The "Beckley" strain of herpes (Flexner) was used in these experiments.

The apparent passage of the herpes virus from the intestine of the guinea pig to the brain, as demonstrated by subsequent passage through rabbits, has led us to consider the possibility of infecting guinea pigs by dropping herpetic brain emulsion into the nostrils of these animals.* In these experiments we have employed the Le Fèvre herpes strain which has been fully described in another publication.²

An emulsion of herpetic (Le Fèvre) rabbit brain was prepared

¹ McKinley, E. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1928, **xxvi**, 21.

* Somewhat similar and likewise positive results on nasal infection in rabbits by herpes virus have been reported by Levaditi and Harvier, Da Fano, Remlinger and Bailly, and Flexner and Amoss.

² McKinley, E. B., and Holden, M., *J. Infec. Dis.*, 1926, **xxxix**, 441.

by emulsifying one gm. of infected brain in 5 cc. of physiologic salt solution. In the first experiment 3 guinea pigs were given 10 drops of this emulsion in each nostril. Three control guinea pigs received a similar quantity of an emulsion prepared with normal rabbit brain. Seven days after treatment one of the guinea pigs became ill and on the eighth day was in coma and had repeated convulsions. The animal remained in this state for 30 hours and was sacrificed late on the ninth day. The brain was removed and placed in 50% glycerol. Three days later an emulsion was prepared (1 gm. of the suspected guinea pig brain emulsified in 5 cc. of saline) and 0.5 cc. of this emulsion was injected intraspinaly into a normal rabbit. The other 2 guinea pigs which had received infected rabbit brain remained well as did the 3 control guinea pigs which had received in each nostril 10 drops of a normal rabbit brain emulsion. The rabbit so injected with the suspected guinea pig brain died with typical herpetic encephalitis 7 days following inoculation. The virus was then passed serially through 6 rabbits and in each case the rabbit so inoculated died with typical symptoms of herpetic encephalitis within 5 or 6 days. In each case control cultures made from the rabbit brains were without growth. Emulsions of normal guinea pig brain injected intraspinaly into rabbits proved to be innocuous.

In a second series we confirmed these results upon a larger scale. Of 12 guinea pigs receiving herpes emulsion intranasally only 2 died. Typical encephalitis was produced in rabbits with the brains from these 2 animals. In this experiment 6 control guinea pigs were used, each receiving 10 drops of normal rabbit brain emulsion intranasally. All remained unaffected. The remaining 10 guinea pigs receiving infected material remained perfectly well after nearly 2 months following treatment.

These experiments indicate that, in certain cases, the virus of herpes may reach the brain of guinea pigs following deposition of the virus in the nares of such animals. That only a few animals so treated become infected is significant. There is without doubt a certain individual resistance to this virus when the animal is infected in this manner. Dmitrieff³ noted that there is a tendency for herpes strains to be reduced in virulence when passed through guinea pigs by intracerebral inoculation. Similar observations were made by Rose and Walthard.⁴ Flexner⁵ states that in guinea pigs the effects of the inoculations vary with the strength or degree of virulence of the virus. He believes that if Dmitrieff and Rose and

³ Dmitrieff, S., *Z. Hyg. u. Infektionskrankh.*, 1926, cvi, 547.

⁴ Rose, G., and Walthard, B., *Z. Hyg. u. Infektionskrankh.*, 1925-26, cv, 645.

⁵ Flexner, S., *J. Exp. Med.*, 1928, xlvii, 23.

Walthard had employed strongly virulent strains their results could not but have been very different. On the whole we feel that there is good evidence in our experiments that even the highly virulent strains, such as the Beckley and Le Fèvre strains, become somewhat attenuated by passage through guinea pigs by the feeding and inhalation methods of infection which we have employed. However destruction of the virus does not take place and the lost virulence of the virus is quickly regained by passage through rabbits. Our experiments would however, we believe, lend support to Flexner's concept that the guinea pig serves to separate weak from strong strains of herpes. Olitsky and Long⁶ have shown that a weak strain, such as the Levaditi C strain, may fail to produce characteristic encephalitis in guinea pigs though the virus may be present in sufficient quantity to permit its detection. These authors also observed that the Levaditi virus failed to elicit signs of infection in guinea pigs following repeated intraperitoneal injections. Judging from our observations on the infrequency of producing infection in guinea pigs by feeding and intranasal inoculations with highly virulent strains we would suspect that infection would be impossible with weaker strains by these methods.

Practically nothing is known concerning the portal of entry of the true virus of epidemic encephalitis in man, and while there is little evidence to support the view that epidemic encephalitis is caused by the herpes virus, the possibility of infection by such a virus through the respiratory tract may prove to be of importance from the epidemiological point of view. The apparent resistance of certain individuals when inoculated in this manner may also have its counterpart in human beings. Since the virus of herpes has so rarely been found in the brains of human cases dying of encephalitis it is suggested that the virus be sought for elsewhere. If the natural infection may take place through the respiratory tract, and if, through some mechanism, the true agent may lose its virulence in the central nervous system and thus escape detection, one might consider the possibility of finding it in some other locality, such as the respiratory tract.

⁶ Olitsky, P. K., and Long, P. H., *J. Exp. Med.*, 1928, *xlvi*, 379.