the diet. The calcium content, on the other hand, is definitely increased. In muscle and heart, the average calcium increase is moderate, being only about 60%. In the kidneys, however, the accumulation is enormous, amounting to a 15 fold average increase. This tremendous increase of calcium in the kidneys probably indicates that metastic calcification forms part of the degenerative process in the kidneys induced by magnesium deprivation. Cramer[3] and the writers have observed the presence of multiple casts, which stain purple with hæmatoxylin and which are probably of a calcareous nature in the kidney sections of deficient rats.

8594 C

Protective Action of Specific Serum Against Experimental Vaccinia in Rabbits.

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It is well established that in certain virus diseases such as poliomyelitis immune serum exercises little or no effect on the progress of the infection, even when administered in large doses several days before the usual onset of symptoms.[1] It is also of limited prophylactic value when administered before intranasal instillation with virus.[2] The therapeutic limitations of immune serum in virus diseases generally may be explained by the fact that cytotropic viruses once established within tissue cells are inaccessible to immune bodies in the plasma. Since viruses are primarily intracellular, rather than intercellular parasites, it would appear that the effectiveness of humoral antibodies is likely to be limited largely to infections in which the virus in transported to distant susceptible tissues by the blood stream, or tissue fluids. In diseases such as poliomyelitis, in which the virus is nerve-transmitted throughout and may gain admission to susceptible tissue without necessarily passing a barrier of immune plasma[3] the prospects of establishing significant protection against infection by the natural or intranasal

3 Cramer, W., *Lancet*, 1932, **223**, 174.

1 Schultz, E. W., and Gebhardt, L. P., *J. Pediat.*, 1935, **6**, 615.

2 Schultz, E. W., and Gebhardt, L. P., *J. Pediat.*, 1935, **7**, 332.

3 Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 728.

route appear little better than those of gaining a therapeutic effect once infection is established. This is borne out by the observations already mentioned.[1, 2] In this paper we deal with a virus (vaccinia*) which although "neurotropic" does not, like poliomyelitis virus, depend on intact nerve paths for its transmission to susceptible cells, but may be disseminated by the blood stream and lead to generalized infection. More specifically, these studies are concerned with the protective action of immune serum in rabbits inoculated with vaccinia virus by the intranasal route.

Halva and Honl[4] 40 years ago reported that serum from immune calves when injected subcutaneously into normal calves conveys some degree of protection against subsequent cutaneous inoculation with vaccinia virus. Since then a number of investigators have reported experimental observations which show quite clearly that immune serum may convey well defined protection against subsequent inoculation with virus.[5] Observations on the protective value of immune serum against intranasally instilled vaccinia virus have apparently not been reported thus far.

Pools of immune serum were prepared from the blood of 11 rabbits hyperimmunized by repeated subcutaneous injection of vaccinia virus (Gallardo strain) following recovery from cutaneous vaccinia. Titration of these pools showed that 1 cc. of serum contained sufficient antibodies to neutralize at least 16,000 minimum skin infecting doses. Preliminary observations on the effectiveness of intranasal instillation as a means of infecting normal rabbits indicated that as little as 10 minimum skin infecting doses sufficed to establish generalized vaccinia in 5 to 6 days. The technic of inoculation was essentially that described by Schultz and Gebhardt[6] for the intranasal inoculation of monkeys with poliomyelitis virus. The total amount of virus instilled intranasally into each animal amounted to about 10,000 minimum skin infecting doses. The immune serum was administered intravenously in all cases. One rabbit received 3 daily injections of 5 cc. each 3, 2

* Gallardo strain.

4 Halva, J., and Honl, I., *Wein. klin. Rundschau*, 1895, **9**, 625, 643.

5 Béclére, A., Chambon and Ménard, *Ann. L'Inst. Past.*, 1899, **13**, 81; Camus, L., *Compt. rend. Soc. Biol.*, 1912, **73**, 197, 294; Haendel, L., Gildemeister, E., and Schmidt, H., *Centralbl. f. Bakt., Abt. I., O.*, 1920, **85**, Beiheft, 125; Hunt, L. M., and Falk, I. S., *J. Immunol.*, 1927, **14**, 347; Andrewes, C. A., *J. Path. and Bact.*, 1929, **32**, 265; Craigie, J., and Tulloch, W. J., *Med. Res. Council, Special Rept. Series*, No. 156, 1931.

6 Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1933, **33**, 1010.

and one day preceding inoculation with virus; 2 rabbits received 2 injections of 5 cc. each, 2 days and again 1 day preceding the inoculation. Eight rabbits received a single injection of 2 cc. per kilo of serum 1, 2, 3, 4, 7, 14, 21, and 35 days, respectively, preceding inoculation. All but one of the animals receiving serum were protected. This animal had received the serum 35 days previously. All of the controls (4 in number) developed generalized vaccinia in 6 to 7 days.

Another series of animals were given serum injections at varying intervals of time *following* intranasal instillations of virus. Five rabbits received 4 cc. of serum per kilo of animal weight 1, 6, 12, 24 and 36 hours, respectively, after inoculation. All were protected, while the controls developed generalized vaccinia on the 6th day. Four additional rabbits received the same dose of serum 24, 48, 72 and 96 hours, respectively, following inoculation. The 2 animals which received the serum within 2 days survived, while the 2 which received the serum later developed generalized vaccinia on the 6th day.

The results suggest that passive immunization is considerably more effective in protecting rabbits against generalized vaccinia following intranasal instillation of virus than in protecting monkeys against intranasal inoculation with poliomyelitis virus. This harmonizes with evidence already available[3] that in poliomyelitis, the virus is transmitted from the olfactory mucosa to the central nervous system by the olfactory nerves essentially out of the reach of immune substances in the blood plasma.

8595 C

Dietary Production of Specific Syndrome of Deficiency in Vitamin B_6.*†

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As a result of recently reported work from many laboratories it appears certain that the factor formerly known as vitamin G

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