TABLE III.
Effect of Vaccine and Antiviral Serum on Intracerebral Infection.

	Vaccinated	Non-vaccinated
Normal serum	8,8,11,S,S,S	6,6,6,7,7,7
Immune serum	S,S,S,S,S,S	10,13,15,15,16,17

satisfactory protection afforded by the combined vaccine and antiserum treatment as compared with the administration of either alone is of interest. Further studies along this line are in progress to explore in greater detail its practicability.

Conclusion. Administration of a single dose of potent antiviral serum intraäbdominally 10-15 minutes after infection is capable of prolonging the life-span of the intracerebrally infected animals, and completely saving the lives of some of the intramuscularly infected animals depending on the dosage of infection and amount of antiviral units given. The combined use of vaccine and antiserum afforded full protection to the animal against 100,000 intracerebral M.L.D. of the virus.

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Effect of Malonate and Iodoacetate on Respiration of Brains of Rats of Various Ages.

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It has been shown that the oxygen uptake of the excised brain of the infant rat is much lower than that found in the adult.[1, 2] Furthermore, during the development of the brain of this animal 3 levels in its metabolism can be distinguished.[3] The lowest level is found during the first week of life; the highest occurs between the fourth and seventh week; the third, or adult level, is reached at about 20 weeks, and is significantly lower than the second level. Parallel changes are found to occur also in the rate of glucose utilization. In contrast to this, the glycolytic activity during the first week is rela-

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1 Himwich, H. E., Baker, Z., and Fazekas, J. F., *Am. J. Physiol.*, 1939, **126**, 601.

2 Tyler, D. B., and van Harreveld, A., *Am. J. Physiol.*, 1941, **133**, 472.

3 Tyler, D. B., and van Harreveld, A., in press.

tively very high, but falls off rapidly, so that at 31 days it is of the same order as that of the adult.[3]

This report, the first of a series concerned with enzymatic activity during the development of the brain, deals with the degree of inhibition produced by malonate and by iodoacetate on the oxygen uptake of brains of rats of various ages.

Methods. Oxygen consumption was measured in Warburg Respirometers using Ringer's-glucose media buffered with phosphate to pH 7.4.[4] The rats were killed by decapitation, the brains quickly removed, and the pallium (cerebral hemisphere minus the corpora striata and olfactory lobes) was separated from the neuraxis. One hemisphere of each animal served as a control, and was minced quickly and suspended in tared vessels containing the media without the inhibitor. The hemisphere of the other side was likewise minced and placed in vessels containing the inhibitor. The mince was distributed in vessels so that approximately the same weight of tissue was in each (150 mg $\pm$20). This necessitated the pooling of several litter mates in the case of newborn rats. The vessels were quickly weighed and placed in the bath at 38°C. This entire procedure—killing, preparing the tissue, weighing the vessels containing the mince, washing the manometers with oxygen, and placing them in the bath, took from 30 to 35 minutes (for 6 vessels). This allowed 15 to 20 minutes for the manometers to reach equilibrium before the initial readings at 50 minutes were taken. In this report, the oxygen consumption found between 90 and 110 minutes after the animal was killed, and expressed as mm^3 of O_2 consumed/g of wet weight of tissue/hour, was used. For comparative results, this procedure has been found to be satisfactory as the oxygen utilization for a given region of the brain of rats of the same age is very constant.

Results. It can readily be seen from Table I that the brain of a newborn rat is comparatively insensitive to malonate. However, an increased sensitivity develops very quickly, so that at 10 days of age the percentage of inhibition is of the same order as that found in the adult. A point of special interest is the residual oxygen uptake found in the malonate exposed tissues. Despite the fact that there is a steady increase in percentage of inhibition during the first 10 days, the residual respiration remains constant at about 550 mm^3/g of wet weight of tissue/hour. Between the tenth and sixteenth day, there occurs an increase in this residual respiration that amounts to 260 mm^3 at 16 days, 410 mm^3 at 31 days, and 300 mm^3 in the adult.

[4] Dixon, M., *Manometric Methods*, The University Press, Cambridge, 1934.

TABLE I.

Age (days)	Control	0.01 M Malonate*	% Inhibition	Age (days)	Control	0.01 M Malonate*	% Inhibition
1	656	547	16.9	10	1080	530	50.9
2	582	507	12.9	16	1500	810	46.0
6	814	590	27.6	31	1900	960	49.5
8	712	559	34.3	Adult	1723	864	50.0

*The final concentration was made up in Ringer-glucose-phosphate media.

The results with iodoacetate (10^{-4} M) show that the brain of the newborn is very sensitive to this inhibitor. The oxygen uptake is reduced 46% in one-day-old rats, as compared with 26% in the adults. Thus, although the newborn is relatively insensitive to malonate, it is extremely sensitive to iodoacetate.

Discussion and Conclusions. Malonate has been assumed to be a specific inhibitor of succino-dehydrogenase.[5] If this assumption is correct, the above results indicate that the brain of the newborn does not depend on the oxidation of succinate to the same extent as does the adult's brain. However, the specificity of the action of malonate has been questioned, and evidence indicates that its effects are more complex and cannot be due primarily to an inhibition of that one enzyme.[6, 7, 8] Irrespective of which enzyme systems are inhibited by malonate, it is clear that, compared with the infant brain, the adult's is more sensitive to this substance. It is interesting to note that the increase in the respiration of the malonate poisoned tissue occurs at about the same time that myelinization is known to begin in the rat.[9, 10] Apparently, this increase is due to a system not very sensitive to malonate.

The results with iodoacetate seem to imply that the brain of the newborn depends, for its aerobic metabolism, on some of the degradation products of glycolysis to a relatively greater degree than does the brain of the adult.

[5] Quastel, J. H., and Whetham, M. D., *Biochem. J.*, 1925, **19**, 525.

[6] Weil-Malherbe, H., *Biochem. J.*, 1937, **31**, 299.

[7] Greville, G. D., *Biochem. J.*, 1936, **30**, 877.

[8] Baumann, C. A., and Stare, F. J., *J. Biol. Chem.*, 1940, **133**, 183.

[9] Koch, W., and Koch, M., *J. Biol. Chem.*, 1913, **15**, 423.

[10] Sugita, N.J., *Comp. Neur.*, 1918, **29**, 1, 11, 241.