able to exert its action (?—bacteriostatic, virustatic or what-not) against the infecting agent when it has invaded the tissue cells as in the case of virus infections. The efficacy of sulphanilamide in specific bacterial diseases may depend partly on its successful attack against extracellular organisms, while the host cells themselves are contributing to the defense against the invading microbes. On the other hand, we may assume from present evidence that viruses find conditions within the tissue cells favorable, rather than unfavorable, for survival and multiplication.

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THE SKIN INFECTIVITY OF POLIOMYELITIS VIRUS

ALTHOUGH controversy exists as to the mode of spread of poliomyelitis, a generally accepted view is that the virus gains access to the central nervous system via the olfactory nerves. This theory is supported by the fact that it has been found easier to infect monkeys intranasally than by other routes, such as the gastro-intestinal, intravenous, sub- or intra-cutaneous route. A fact which does not appear to be well known, however, is that this generalization as to infectivity via different routes does not apply equally to all strains of the virus. For with some strains of poliomyelitis virus, monkeys are readily infected on intracutaneous inoculation of doses which are not particularly large. This is illustrated by our results shown in Table 1 to which we will again refer.

The literature also furnishes evidence of this fact. In France during the course of some immunization experiments Erber and Pettit[1] inoculated subcutaneously serum-virus mixtures (which represented a pool of four different strains of virus) into 13 monkeys, and 12 of these animals succumbed to poliomyelitis as a result of this inoculation. Later two of these four strains were found to have this property of infectivity by the subcutaneous route. Levaditi *et al.*[2] have noted that as many as 10 out of 17 animals were infected subcutaneously from poliomyelitis vaccines. Further preliminary evidence bearing on this question may be found in the description of a strain (our Wfd. strain), which we reported in 1936, which in its early passages was peculiarly infective by the cutaneous route.[3] It had been isolated in the 1934 epidemic in southern California. Later two other new strains showing cutaneous infectivity were isolated in California, one by Howitt[4] and one by Kessel and his coworkers.[5]

It next seemed important to determine how frequently this property of intracutaneous infectivity could be found. Was it a rare or a common property of strains isolated in Eastern sections of this continent as well as in the West; was it a property of established strains as well as fresh strains? To this end we have examined a number of strains of virus from various sources during the last two years, and the results, which form the substance of this note, appear in Table 1.

TABLE 1
CUTANEOUS INFECTIVITY OF ELEVEN STRAINS OF POLIOMYELITIS VIRUS*

	Name of strain	Source		No. of monkey passages	Result
Established strains	Park	N. Y. C., ?	1916	Many	1/7†
	Aycock	Vermont,	1921	"	0/6
	Flexner	N. Y. C.,	1931	11–18	1/7
	We.	New Haven,	1931	9–15	0/7
	McC.	Los Angeles,	1934	3–10	0/7
	Wfd. (a)	" "	1934	3– 7	6/10
	" (b)	" "	1934	8–16	4/17
	Hub.	Boston, Mass.,	1936	4– 5	0/4
	Gr. (b)	Memphis, Tenn.,	1936	4– 5	0/2
Fresh strains	Gr. (a)	Memphis, Tenn.,	1936	1– 2	1/3
	Fx.	Toronto,	1937	(Human)	1/1
	Ah.	"	1937	"	1/1
	McL. (a)	"	1937	"	2/2
	" (b)	"	1937	1	0/1

* The same dose was used with all 11 strains, *viz.*, 2 cc of a 10 per cent. suspension of spinal cord given intracutaneously (and rarely subcutaneously) in 8 or 10 piqures in the shaved skin of the flanks or abdomen.
† 1/7 indicates that seven monkeys were cutaneously inoculated and that, of these, one was infected with clear-cut experimental poliomyelitis.

Eleven different strains were investigated. They have been arbitrarily divided into two major groups—established strains and fresh strains. Established strains are those which had been passed in series (by intracerebral inoculation) through more than three monkeys.[6] Two of these established strains (Park and Aycock) were quite old and had been through many monkey passages (perhaps 100 or more). Four fresh strains were tested, the recent (1937) epidemic in Toronto having furnished us with three of them.[7]

Most of our established strains, are (or were) of high intracerebral virulence and most of them infect by the intranasal route, but from Table 1 we note that cutaneous infectivity is seldom a prominent feature, except in one strain, the Wfd. strain, which, so far, has not been infective intranasally. At first about 60 per

1 B. Erber and A. Pettit, *Comp. rend. Soc. de biol.*, Paris, 117: 1175–1178, 1934.
2 C. Levaditi, C. Kling and P. Haber, *Bull. Acad. méd.*, Paris, 3e Série, 115: 431–440, 1936.
3 J. D. Trask and J. R. Paul, *Jour. Bacteriol.*, 31: 527–530, 1936.
4 B. F. Howitt, SCIENCE, 85: 268–270, 1937.
5 Personal communication from F. D. Stimpert.
6 A description of six of these established strains has been given in a recent article by the authors, *viz.*, J. D. Trask, J. R. Paul, A. R. Beebe and W. J. German, *Jour. Exp. Med.*, 65: 687–704, 1937.
7 For these three strains we are particularly indebted to Dr. L. N. Silverthorne, of the Hospital for Sick Children, Toronto, Canada.

cent. of the animals inoculated intracutaneously with this strain were infected. Later (after the seventh passage) this property seemed to decrease and about 25 per cent. were infected. But, among the seven other established strains, cutaneous infectivity was not at all pronounced; in fact, it was quite uncommon. In 40 tests there are only two instances (5 per cent.) in which monkeys were infected by these seven other strains from our so-called established group.

Somewhat in contrast to this is the action of the fresh strains. The number of animals tested is small but large enough to indicate a substantial degree of intracutaneous infectivity of not only human material (*i.e.*, prior to its first passage) but also of the virus during its first two passages. In fact, all the few fresh strains which we so far have tested have shown this property in at least a third of the inoculated animals, and the total percentage of animals cutaneously infected in this particular series is about 60 per cent. This appears all the more remarkable when one recalls the difficulties of getting human poliomyelitis virus established in the monkey by the intracerebral route in its earliest passages, and when one also considers that in the present experiments almost the same dose has been used for these intracutaneous as for the intracerebral inoculations. It remains to be seen whether this apparent difference between the behavior of fresh and established strains is a coincidence or not.[8]

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THE EFFECT OF COPPER IN THE PRODUCTION OF NUTRITIONAL ANEMIA IN RATS

DISCREPANCIES in the bioassay results from different laboratories relative to the availability of iron in foodstuffs have been variously explained by Elvehjem and coworkers[1,2,3] and by Smith and Otis.[4] Elvehjem believed that failure to effect complete depletion of iron storage in the experimental animals was the reason for these discrepancies, while Smith and Otis postulated a sex difference in the ability of anemic rats to utilize iron, and attributed differences in results from various laboratories to ignorance of this fact. Mitchell and Hamilton[5] concluded from their paired-feeding studies that the sex difference noted by Smith and Otis was partially, or entirely, the result of a greater intake of the anemogenic basal diet by the male rats. Smith and Otis[6,7] in recent papers have suggested and attempted to prove that copper administration during the depletion period is necessary to assure complete exhaustion of the iron reserves. They believe that failure to completely eliminate these potentially available iron reserves in the depletion period has often resulted in invalid conclusions being drawn from subsequent curative data. They contend that part, at least, of the hemoglobin response was due to the copper of the food under assay rather than to its available iron content.

In this laboratory we have had occasion to deplete large numbers of rats for hemoglobin regeneration studies. Two small groups of these were depleted in the usual way, except that whole milk powder (Klim) was substituted for whole fresh milk, while other groups received in addition to this same basal diet a daily supplement of 0.05 mg copper as copper sulfate. The results are shown in Table I. Whereas Smith and Otis found that by supplementing the basal diet with copper, beginning at the fourth or at the sixth week of depletion, an immediate and sustained increase in hemoglobin occurred, we have found that the trend of hemoglobin values during the depletion period is not significantly affected by the presence of copper in the basal depletion ration.

TABLE I

SHOWING COMPARATIVE HEMOGLOBIN DECREASE IN RATS FED WHOLE MILK POWDER WITH AND WITHOUT COPPER

Supplement to basal diet	No. of rats used	Sex	Initial hemoglobin (gms/100 cc)	Decrease in hemoglobin (gms/100 cc)		
				In 3 weeks	In 5 weeks	In 7 weeks
None	10	M	12.26	5.59 ± .55	8.44 ± .20	9.08 ± .20
None	10	F	12.18	3.85 ± .58	8.31 ± .31	9.03 ± .36
0.05 mg Cu as $CuSO_4$.	10	M	11.77	4.84 ± .33	8.01 ± .27	8.48 ± .30
0.05 mg Cu as $CuSO_4$.	10	F	11.77	5.18 ± .40	8.25 ± .27	8.78 ± .21

To determine the effect of subsequent iron feeding upon anemic rats depleted with and without copper, five animals from each of the previous groups were fed a daily curative supplement, consisting of 0.1 mg Fe as $FeCl_3$, 0.05 mg Cu as $CuSO_4$ and 0.04 mg Mn as $MnCl_2$, for a period of six weeks.

According to Smith and Otis,[8] at this level of iron

[8] Aided by grants from the President's Birthday Ball Commission for Infantile Paralysis Research.

[1] C. A. Elvehjem and A. R. Kemmerer, *Jour. Biol. Chem.*, 93: 189–195, 1931.

[2] C. A. Elvehjem, E. B. Hart and W. C. Sherman, *Jour. Biol. Chem.*, 103: 61–70, 1933.

[3] W. C. Sherman, C. A. Elvehjem and E. B. Hart, *Jour. Biol. Chem.*, 107: 383–394, 1934.

[4] M. C. Smith and L. Otis, SCIENCE, 85: 125–126, 1937.

[5] H. H. Mitchell and T. S. Hamilton, SCIENCE, 85: 364–366, 1937.

[6] M. C. Smith and L. Otis, *Jour. Nutrition*, 13: 573–582, 1937.

[7] M. C. Smith and L. Otis, *Jour. Nutrition*, 14: 365–371, 1937.

[8] *Op. cit.*