person does not inactivate tuberculin whereas the tuberculous individual's blood does partially block the subsequent *in vitro* cytotoxic effect of tuberculin.

Comment. It has long been assumed that the tuberculin which is placed in the skin or other tissues and which produces a delayed tuberculin reaction is localized in that area. The very nature of the tuberculin reaction itself is evidence for this belief. In the experiments reported here some direct evidence for this belief is presented. The leucocytes of man which are the classic model of host cells of the tissue culture worker are capable of reacting with tuberculin in such a way that it no longer has cytotoxic effects on sensitized white cells from tuberculous subjects. Mouse leucocytes, on the other hand, do not react with tuberculin. It is perhaps not a coincidence that the tuberculous mouse shows no intracutaneous reactions to tuberculin[3] as do tuberculous rabbits, guinea pigs and humans. These findings suggest that there is a primary "affinity" for tuberculin of the tissues of some species and not for others. This "affinity" does not depend on the presence of a tuberculous infection but is present in those species capable of developing a tuberculin reaction. This phenomenon may be compared to other tissue tropisms, for example the neurotropic viruses. It also helps to explain some of the differences in cell damage produced in the tuberculin type reaction as contrasted to the cellular changes in anaphylactic phenomenon.

Summary. 1. Suspensions of human white blood cells in homologous fresh plasma will adsorb tuberculin (O.T.) from the plasma.

2. White blood cells from normal persons with a negative intracutaneous reaction to tuberculin as well as white cells from persons with active tuberculosis show this phenomenon.

3. Suspensions of mouse white blood cells in homologous fresh plasma will not adsorb tuberculin from the plasma.

4. There is no difference in the lack of tuberculin adsorption by white blood cells from normal or tuberculous mice.

5. Normal human plasma does not whereas plasma from patients with active tuberculosis does partially inactivate tuberculin under the conditions of these experiments.

6. Tuberculin has been assayed by its *in vitro* cytotoxic effect on white blood cells from tuberculous subjects.

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Failure of Phenosulfazole to Influence the Course of Infection with Murine Poliomyelitis Virus in Mice.

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Sanders, SubbaRow, and Alexander[1] presented evidence to show that a new sulfonamide compound (N-(2-thiazolyl)-phenol sulfonamide, abbreviated as phenosulfazole, trade name "Darvisul") which was synthesized at the Calco Chemical Division of the American Cyanamid Company acted as an effective antiviral substance in mice infected with the Col. SK strain of murine poliomyelitis virus. Drug treatment instituted 24 hours following intraperitoneal injection with virus at various levels of potency apparently brought about a regular and striking reduction in the mortality rate when compared with that among untreated controls. As judged from the protocols, however, the therapeutic effect showed no clear gradations with respect to amount of virus used for infection or

[1] Sanders, M., SubbaRow, Y., and Alexander, R. C., *Texas Rep. on Biol. and Med.*, 1948, **6**, 385.

TABLE I.
Attempted Chemotherapy of Murine Poliomyelitic Infection with Phenosulfazole.

Exper.	Seed virus	Mice	Intraperitoneal infection*							
			10-1	10-2	10-3	10-4	10-5	10-6	10-7	10-8
I	Mouse passage	Drug treated (8-10 g)					10/10	10/10	10/10	8/10
	Stock virus (glycerinated)	Controls " "					10/10	10/10	10/10	8/10
II	Mouse passage	Drug treated (18-20 g)				10/10	10/10	10/10	6/10	
	Stock virus (fresh)	Controls " "				10/10	10/10	8/10	5/10	
III	Guinea pig	Drug treated (14-18 g)	10/10	9/10	10/10	0/10				
	Virus (glycerinated)	Controls " "	10/10	10/10	8/10	0/10				
IV	First return mouse	Drug treated " "				9/10	10/10	9/10	9/10	
	Passage from guinea pig (glyc.)	Controls " "				10/10	10/10	10/10	7/10	
V	Tissue culture	Drug treated " "	9/10	4/10	0/10					
	Virus (8th serial passage) (fresh)	Controls " "	8/10	1/10	0/10					
VI	First return mouse	Drug treated " "				10/10	10/10	10/10	10/10	
	Passage from tissue culture (fresh)	Controls " "				10/10	10/10	10/10	10/10	
VII	First return mouse	Drug treated " "				10/10	10/10	10/10	10/10	
	Passage from tissue culture (frozen)	Controls " "				10/10	10/10	10/10	10/10	

Note: Results are recorded as follows: Numerator = No. of mice paralyzed or dead. Denominator = No. of mice injected. The incubation periods were not significantly different between drug-treated and control animals. They varied in the different experiments between 3-10 days depending on the type and dilution of virus used.

* The infectious dose was 0.1 cc of the indicated virus dilutions in Experiment I. In all subsequent experiments (II-VII) the dose was 0.06 cc.

dosage of drug employed for treatment. Thus, the percentage of drug-treated surviving animals hovered around 50% irrespective of whether the mice had previously been infected with approximately 1000 ID_{50} (10^{-4}) or 1 ID_{50} (10^{-7}). Again, there was no uniform improvement of the survival rate when the total amount of drug, administered in fractional daily doses over a period of 5 consecutive days, was stepped up from 40 mg to 80 mg. The following report deals with an unsuccessful attempt to verify the above results.

The drug (lot 7-8522 and lot 7-8564) was obtained through the courtesy of Lederle Laboratories, Inc. The drug was administered, 16 to 18 hours after intraperitoneal infection, by intraperitoneal injection of 4 daily divided doses as follows: 5 mg, 4 mg, 4 mg, 5 mg. The total amount of drug per diem was therefore 18 mg. This treatment was continued for 4 to 5 days. No symptoms of toxicity were observed with this dosage. Controls received 0.85% NaCl solution instead of drug. The mice were Rockland Swiss albino mice weighing, with one exception, from 14 to 20 g. The age of the animal is important because older mice are usually less susceptible by peripheral inoculation. Col SK murine virus was used in 3 forms: 1) mouse brain passage virus,)2 guinea pig brain virus and virus harvested from first return mouse passage, 3) tissue culture virus and virus harvested from first return mouse passage. One reason for choosing as infecting agent more than one source of virus was the fact that the 3 different strains—and their subpassages—represent stabile and unstabile forms of the same virus, with varying degrees of peripheral invasiveness,[2-4] which might conceivably respond selectively to the drug. Another more practical consideration was our desire to work under conditions identical with those employed by Sanders, SubbaRow, and Alexander, who operated with a seed virus obtained by passage of tissue culture virus to mice. In all other important details we followed closely the procedure described by these investigators. A total of 7 different experiments were run which are summarized in Table I.

From the data given in Table I it appears that phenosulfazole in adequate dosage had no demonstrable chemotherapeutic effect on the course of infection in mice induced with graded doses of Col SK virus under a wide variety of experimental conditions. It will further be noted that the drug not only failed to manifest any direct antiviral effects against the stabile forms of the virus (mouse passage virus, guinea pig virus, tissue culture virus), but likewise failed to display any indirect effects on the unstabile forms of the virus (first return mouse passage from infected guinea pig or tissue culture medium). In other words, there was nothing in our work to indicate that the drug has the power to cause reversion of the high peripheral infectivity of such viral forms to the low level of peripheral infectivity of their parent viral forms, a phenomenon which, if true, might have furnished a possible explanation for the curious observations reported by Sanders, SubbaRow, and Alexander. We are, therefore, at a loss to reconcile our own negative findings with the positive results reported by the earlier investigators.

Conclusions. Phenosulfazole had no demonstrable effect on the course of infection with murine SK poliomyelitis virus in mice.

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2 Sanders, M., and Jungeblut, C. W., *J. Exp. Med.*, 1942, **75**, 631.

3 Jungeblut, C. W., Feiner, R. R., and Sanders, M., *J. Exp. Med.*, 1942, **76**, 31.

4 Schultz, E. W., and White, S. C., PROC. SOC. EXP. BIOL. AND MED., 1948, **68**, 266.