means of both antisera could not be shown by statistical analysis.

Discussion. The term "strain" as applied to GD VII virus when it was first recovered, and later,[5] was not intended to indicate biological taxonomy, that is, as representing descendants from a common stock; it was so called for convenience only, meaning sample of virus isolated. Indeed, the malady from which it was recovered was not clearly one of the original Theiler's disease.[5] It is suggested that it be designated henceforth as Theiler GD VII virus. But this question of classification is not particularly important; what is significant is that the GD VII virus and the disease it induces have features not in common with the original TO Theiler's virus and its disease. The characteristics as here described, when added to others already recorded,[5] such as activity in high dilution (10^{-7}) and greater invasiveness into the host's tissues constitute elements of a picture not that of mouse poliomyelitis—natural or experimental—or its virus.

Conclusion. Additional properties of Theiler's virus—both the original and the GD VII—are described. The GD VII virus§ has been found to differ in several characteristics from the original Theiler's virus; the differences are great enough to make it unusable as a "model" for the study of human poliomyelitis.

§ What applies to the GD VII virus may or may not apply to the FA virus which was not available for study (*Cf.* reference 5).

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Comparative Effects of Thromboplastin, Lecithin, and Saline on Mortality of Mice Following Experimental Burn Shock.*

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Recent investigations on the systemic chemotherapy of shock resulting from standardized experimental burns have disclosed that isotonic saline solution[1,2] and a fraction from commercial liver extract[2] will significantly increase the mean survival time of groups of treated mice over control groups.

The purpose of this report is to present evidence for the existence of a principle in a commercial cattle brain extract (Thromboplastin, USP) which is effective in prolonging the survival time and in decreasing the mortality of mice which have been subjected to experimental burns.

Method. White male mice ranging in weight from 20 to 25 g were divided, at random, into 3 groups each of which was injected intraperitoneally (approximately one-half hour prior to the application of trauma) in doses of 0.8 cc per 100 g as follows: (1) saline, 0.9% NaCl solution; (2) lecithin, 1% suspension made by homogenizing soybean lecithin with physiological saline solution in a Waring blendor; and (3) thromboplastin (Local-Cutter) diluted to a 1% homogeneous suspension with isotonic saline.

The mice were fasted 12 hours preceding the experiment, and neither food nor water was given once the test was started. This was done in order to minimize the number of variables since nutrition might conceivably be a factor and administration of food or water might influence survival time. A uniform degree of trauma in the mice was attained by immersing each etherized animal completely up to the

* Part of the experiments were carried out at the University of California through the courtesy of Dr. Ernest W. Page.

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2 Prinzmetal, M., Hechter, O., Margoles, C., and Feigen, G., *J. Am. Med. Assn.*, 1943, **122**, 720.

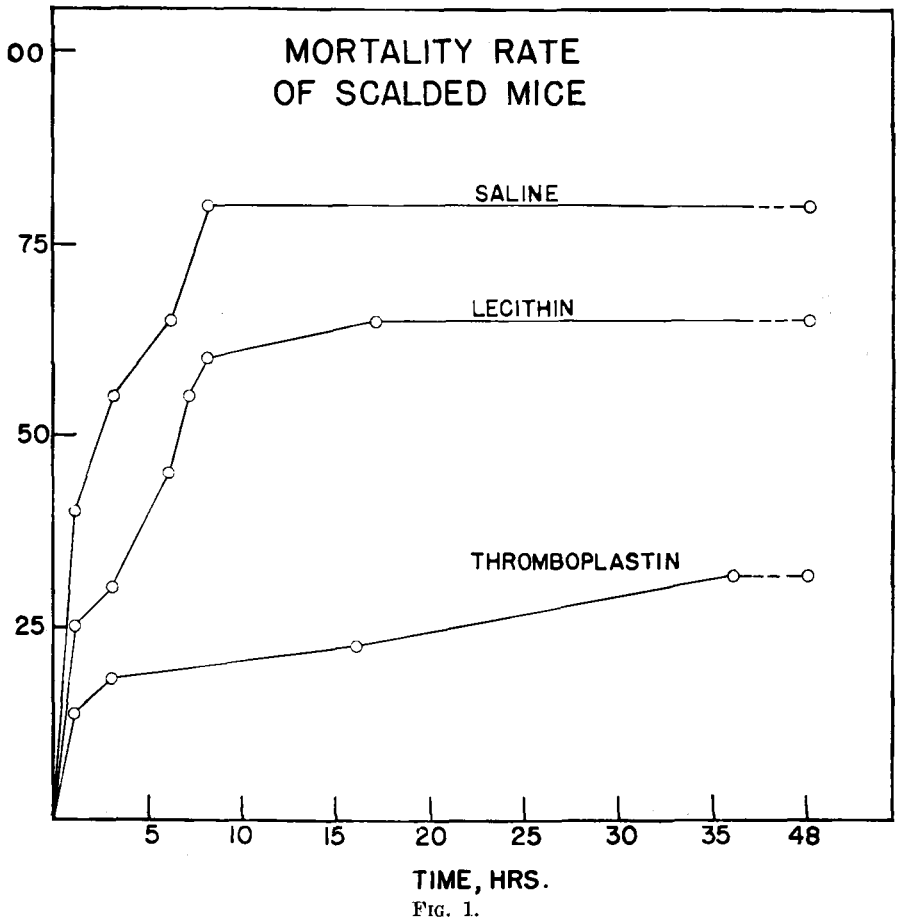

FIG. 1.

region of its neck in water thermostatically controlled at 60 ± 0.25°C for a period of 15 seconds. The animal, upon being withdrawn from the water bath, was laid gently on cotton batting and "blotted" of any excess water. At the conclusion of the scalding, every group was placed in a separate cage for observation and the time of death of each mouse was recorded.

A short time following their withdrawal from the hot water bath, the animals became dyspneic, exhibited a decrease in peripheral circulation, as evidenced by a decline in skin temperature, became stuporous and finally died. Postmortem changes regularly included profound visceral and pulmonary congestion. Hemorrhagic adrenals and hematuria were frequently observed.

The experiment was terminated at the end of a 48-hour period, because mice surviving beyond this time would be dying no longer from the effects of the scald, but would be succumbing to infections and other morbid changes.

Results. Fig. 1 shows the time-mortality characteristics for each of the 3 groups of mice, based upon a 48-hour experimental period. Each observed point represents the ratio of a number of mice dead at that point to the total number of mice used in the entire group.

Comparison of times for 50% mortality brings to light the following differences among the 3 groups: Group 1, about 3 hours; Group 2, between 6 and 7 hours; for Group 3, a 50% mortality was never reached within the 48-hour period.

Statistical analyses, based on the proportion of decedents to survivors, were carried out by

TABLE I.
Statistical Analysis of Data Based on χ^2

Group	Mice: Lived	Died	Total	% survived	Avg survival time in hr*	Chi² (χ^2)	"P"†
1	4	16	20	20	11.8 ± 4.3		
3	15	7	22	68	36.9 ± 4.2		
Total	19	23	42			9.92	<0.01
1	4	16	20	20	11.8 ± 4.3		
2	7	13	20	35	19.6 ± 5.0		
Total	11	29	40			1.13	<0.30

Group 1 received saline, Group 2, lecithin, and Group 3, thromboplastin.
* Including a standard error of the mean calculated as follows:

$$\frac{\sqrt{\frac{\Sigma d^2}{n}}}{\sqrt{n}}$$

where "d" is the deviation and "n" is the number of cases minus one.
† Values below 0.05 are considered significant.

the method of R. A. Fisher.[3] The degree of independence of one group from another is expressed by chi² (χ^2) for a given number of degrees of freedom; in this case, one. Survivors are those mice which were alive at the expiration of 48 hours. P is the probability of this value of chi² occurring by chance for one degree of freedom.

Treatment of the data in this manner shows that although lecithin does not differ significantly from saline in protecting the animals, there is an unmistakable superiority of thromboplastin over saline in saving lives of animals to a 48-hour level.

Discussion. Shock, as the result of burns, is characterized by the increased transudation of fluid and serum proteins from the vascular to the extravascular compartment due to changes in the permeability of the capillary endothelium. The increase in capillary permeability is generally ascribed to the action of some "toxic factor" which is elaborated from the products of tissue destruction at the site of trauma. The presence in the circulation of such a factor is presumably responsible for much of the visceral damage found at autopsy following death from burns. The organs most constantly damaged are those receiving the greatest blood supply; namely, the liver, spleen, kidneys, lungs, and members of the reticulo-endothelial system generally. Liver damage, usually characterized by central necrosis and fatty infiltration is considered an important cause of death after a severe burn.

Evidence has been presented by several investigators[4-9] that regardless of initiating factors, a prominent finding in shock is the decrease in blood platelet concentration and the increase in the coagulation time of the blood. This decreased coagulability of the blood has been ascribed by Quick[4] to the production of an anticoagulant which resembles heparin in its action, though Eagle's finding[5] that addition of platelets to shock blood would not cause clotting indicates that Quick might have been dealing with an antithrombin rather than an antiprothrombin.

The failure of lecithin to be effective as

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[5] Eagle, H., Johnston, C. G., and Ravdin, I. S., *Bull. J. Hopk. Hosp.*, 1937, **60**, 428.

[6] Kopeloff, N., and Kopeloff, L. M., *J. Immunol.*, 1941, **40**, 471; 1939, **36**, 83, 101.

[7] Kinsell, L. W., Kopeloff, L. M., Zwemer, R. L., and Kopeloff, N., *J. Immunol.*, 1941, **42**, 35.

[8] Schultz, E. W., PROC. SOC. EXP. BIOL. AND MED., 1924, **22**, 343.

[9] Krueger, A. P., and Schultz, E. W., PROC. SOC. EXP. BIOL. AND MED., 1925, **23**, 153.

thromboplastin argues that the action of thromboplastin is a specific one. The thromboplastin, although relatively crude, was prepared for its cephalin content. Thus, the effect of thromboplastin is due either to the action of cephalin or to some other substance present in the rather crude extract. Since the two phospholipids are closely allied structurally, the possibility of a caloric influence is eliminated, for these substances are virtually isodynamic and any other material contained in the crude extract which might have this effect would be so low in its concentration as to be negligible from this standpoint.

Data on the mechanism of action must await purification of the active principle. However, the experiments of Glenn, Peterson, and Drinker[10] recently reviewed by Cope[11] prove that thromboplastin is absent in burn edema fluid. In the light of our results this fact would indicate that the function of the injected thromboplastin is to augment the supply of this substance and thus to prevent excessive transudation and fluid loss. An experiment performed to determine whether the material was effective if administered after shock had ensued yielded equivocal conclusions. The animals treated with thromboplastin seemed to die faster than saline-treated animals, indicating that the material was toxic to shocked mice. The crude saline extract of cattle brain contains substances which are inactive as far as *normal* mice are concerned, but such compounds as histamine, which are present in these preparations, will become markedly harmful if they are administered at a time when the animal's normal detoxifying systems have been deranged by burn shock. Further purification is necessary to establish whether the toxicity of the crude preparation is responsible for its lack of efficacy when administered after shock has once been established, or whether some physiological intermediate present in normal animals but damaged in shocked mice, is blocked so that administration of a precursor is ineffective.

Conclusions. 1. Mice injected intraperitoneally with a 1% suspension of thromboplastin in isotonic saline solution showed a greater mean survival period than mice injected with either isotonic saline or with a 1% suspension of lecithin in isotonic saline. 2. Mice receiving thromboplastin showed a higher ultimate survival rate than those receiving either lecithin or saline. 3. Analysis by chi^2 showed a significant difference between thromboplastin and saline but not between lecithin and saline. 4. Intraperitoneal injection of thromboplastin one hour after traumatization of the animals seemed to exert a toxic effect.

The authors wish to express their appreciation to Mr. Frank Lanni for the figure.

10 Glenn, W. W. L., Peterson, D. K., and Drinker, C. K., *Surg.*, 1942, **12**, 685.

11 Cope, O., *J. Am. Med. Assn.*, 1944, **125**, 536.

14851 P

Nutritional Macrocytic Anemia: Response to a Substance Other Than the Anti-Pernicious Anemia Principle.*

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Recent publications[1-7] indicate a difference

* The expenses of this investigation were defrayed in part by the J. K. Lilly gift to the Harvard Medical School.

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2 Wills, L., and Evans, B. D. F., *Lancet*, 1938, **2**, 416.

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