from which a tumor emerged providing the most fertile soil for its subsequent propagation.

Summary. When mice were inoculated with 3 carcinogenic compounds, they developed a transient antineoplastic (AN) response which was demonstrable by tissue culture technic. This AN phenomenon appeared to be chemically and genetically specific. The duration of the AN response to the 3 agents may represent the latent period of carcinogenesis, since the AN phenomenon disappeared when the tumor emerged. The interpretation of the AN phenomenon on an immunological basis is discussed.

1. Pollard, Morris, and Bussell, R. H., PROC. SOC. EXP. BIOL. AND MED., 1953, v83, 671.
2. ———, *Tex. Rep. Biol. and Med.,* 1953, v11, 48.
3. Hewitt, H. B., *Brit. J. Cancer,* 1953, v7, 384.
4. Fagraeus, A., *J. Immunol.,* 1948, v58, 1.
5. Roberts, S., and White, A., *Endocrinology,* 1951, v48, 741.
6. Ehrich, W. E., and Harris, T. N., *J. Exp. Med.,* 1942, v76, 335.
7. Stavitsky, A. B., *Fed. Proc.,* 1952, v11, 482.
8. Leob, Leo, Jr., *Medical Research,* 1901, v6, 28.
9. Andervont, H. B., *Pub. Health Rep.,* 1934, v49, 620.

Received March 22, 1954. P.S.E.B.M., 1954, v86.

Topical Protection against Inflammation by a Preceding Local Inflammation in Adrenalectomized Rats.* (21046)

ERNESTO SALGADO AND RUDOLF HOENE.† (Introduced by Hans Selye.)
From the Institute of Experimental Medicine and Surgery, Université de Montréal, Canada.

Acquisition of topical protection against inflammatory reaction to blood-borne irritants such as egg-white or dextran has been shown in the rat-paw after local pre-irritation with various irritants(1). Further, it has been demonstrated that thermally pre-irritated tissues display topical protection against a subsequent strong thermal irritation leading to inflammation and necrosis in normal tissues (2). One of the authors reviewed earlier data on acquired topical protection against tissue injury and studied mechanisms underlying the acquisition of topical protection against blood-borne irritants and against thermal and X-irradiation injury(3). Recently, an interesting contribution concerning this subject was made by Arteta(4). He observed that adrenalectomy prior to local pre-irritation (peptone injection in the rat-paw) prevented the development of topical protection; thus, the pre-irritated paw displayed apparently undiminished inflammatory reaction to egg-white intraperitoneally injected 24 hours after pre-irritation. However, topical protection could be demonstrated in adrenalectomized rats, if cortisone was intraperitoneally injected 1 hour after the local pre-irritation, the egg-white being given 24 hours later. On the basis of this finding, Arteta advanced the theory that a topical pre-irritation evokes a General Alarm Reaction, and that "the steroids of suprarenal source which are produced during this reaction may move from the blood to the inflamed tissue due to the increase of capillary permeability which takes place in the inflamed area, accumulating there and modifying the tissue's conditions and the degree of resistance of the capillary wall." The preferential accumulation of antiphlogistic steroids in inflamed areas seems to be an intriguing suggestion in connection with the mode of action of these steroids. Some hesitation was felt, however, in accepting this view as an explanation of the mechanism underlying acquired topical protection. Therefore, further investigations were made on the problem of acquired topical protection to intraperitoneally injected egg-white and to thermal

* Supported in part by a grant from the Ministry of Health of the Province of Quebec.

† Fellow of the Canadian Life Insurance Officers Assn.

TABLE I. Acquisition of Topical Protection in Adrenalectomized Rats.

Groups*	1st irritation Inj. in right hind paw	2nd irritation Intraper. inj. 24 hr later	% degree of protection in pre-irritated right paw (mean ± stand. error)
I†	Peptone 4%, .25 ml	Egg-white .5 ml	64.7 ± 8.2
II†	*Idem*	" 20% 1.0	94.6 ± 3.1
III†	Dextran .12%, .2 ml	" .5	96.6 ± 2.5
IV†	*Idem*	" 20% 1.0	95.3 ± 2.5
	Heating right hind paw	Heating both hind paws, 48 hr later	
V‡	47°C, 2 min. 15 sec.	49°C, 2 min.	77.4 ± 1.9

* 6 animals in each group.
† Adrenalectomy 6 hr prior to 1st irritation.
‡ " 10 days " " " " .

injury in adrenalectomized rats.

Methods. Male Sprague-Dawley rats weighing between 100 and 120 g were used. Bilateral adrenalectomy was performed under ether anesthesia and subsequently the animals were allowed 1% saline as drinking fluid and Purina Fox Chow *ad libitum*. Peptone and dextran (Macrodex) were injected beneath the plantar aponeurosis of the right hind paw. Heating [immersion of the paw(s) into water under compression of the blood vessels], evaluation of the degree of inflammatory reaction, and assessment of the protection in the pre-irritated paw were made as described earlier(2).

Results. In corroboration of Arteta's findings(4), whose experimental conditions were adhered to in Group I, only negligible topical protection was observed in some of the adrenalectomized animals in this group (Table I). If, however, the amount of egg-white injected intraperitoneally for the second irritation was reduced (Group II), or if dextran was used for topical pre-irritation (Groups III and IV and Fig. 1A), the pre-irritated right paw displayed maximal topical protection against the hyperergic egg-white reaction in all adrenalectomized animals. In rats adrenalectomized 10 days prior to a thermal pre-irritation of the right hind paw (Group V and Fig. 1B), marked topical protection was observed against subsequent stronger thermal injury.

On the basis of these results, it is not very likely that the acquisition of topical protection depends upon extravasation of antiphlogistic corticosteroids. Since adrenalectomized rats become more susceptible to substances which cause anaphylactoid inflammation [dextran(5,6), globin(6)], one possible alternative to the interpretation given by Arteta (4) could be the assumption that intraperi-

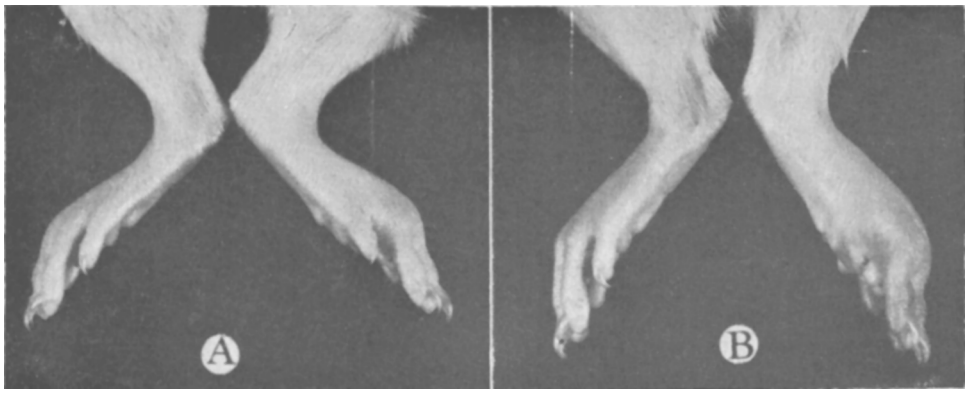

FIG. 1. Acquisition of topical protection in adrenalectomized rats. Left: Animal of Group III, 2 hr after intraperitoneal injection of egg-white; pre-irritated right paw protected; (adrenalectomy 6 hr prior to pre-irritation). Right: Animal of Group V, 14 hr after heating of both paws; pre-irritated right paw protected; (adrenalectomy 10 days prior to pre-irritation).

toneal injection of undiluted egg-white leads to a *maximal* increase in capillary permeability in the paws, and that, in this situation, the protective effect of certain inflammatory substances used for pre-irritation might become less evident.

Summary. 1. Topical protection against hyperergic inflammation by a preceding local inflammation, and topical protection against thermal injury by a preceding local thermal irritation can be demonstrated even in rats adrenalectomized before pre-irritation. 2. Acquired topical protection, therefore, is not likely to depend upon the topical extravasation of antiphlogistic corticosteroids into pre-inflamed areas.

1. Hoene, R., Labbé, P., and Selye, H., PROC. SOC. EXP. BIOL. AND MED., 1952, v79, 65.
2. Hoene, R., *ibid.*, 1954, v85, 56.
3. ———, 1954, Thesis, University of Montreal.
4. Arteta, J. L., PROC. SOC. EXP. BIOL. AND MED., 1954, v85, 162.
5. Briot, M., and Halpern, B. N., *Compt. rend. Soc. de biol.*, 1952, v146, 15.
6. Swingle, W. W., Fedor, E. J., Maxwell, R., Ben, M., and Barlow, G., *Am. J. Physiol.*, 1953, v172, 527.

Received March 29, 1954. P.S.E.B.M., 1954, v86.

Susceptibility of Mice to Infection with the Mahoney Strain of Type 1 Poliomyelitis Virus.* (21047)

ULRICH KRECH. (Introduced by Jonas E. Salk.)
From the Department of Bacteriology, School of Medicine, University of Pittsburgh.

A line of the Mahoney strain Type 1 poliomyelitis virus has been adapted by Li and Schaeffer(1) to produce intraspinal infection in mice. This strain has been used to demonstrate neutralizing antibodies in serum specimens(2), and also to demonstrate resistance upon challenge of mice immunized with Mahoney virus(3). Since the intraspinal inoculation is a rather traumatizing procedure and the non-specific response due to trauma, depending on the skill of the operator, is considerable, a line adapted to the intracerebral route might therefore be advantageous. Furthermore, increasing adaptation might eventually result in a line pathogenic to mice following peripheral inoculation.

It is the purpose of this report to give details of the procedure that resulted in a line of Mahoney virus pathogenic via the intracerebral route. This strain will also induce paralysis in a small proportion of mice following intravenous inoculation.

Materials and methods. Virus. Mahoney strain virus adapted for intraspinal infection of mice was kindly provided by Drs. Li and Schaeffer as 10% cord suspension representative of the 35th mouse passage. This material was used for intraspinal titration in mice and as the inoculum for tissue cultures. Four-week-old Swiss albino mice, CFW strain, were employed as routine. Tissue culture fluids from criss-cross passages 3, 4, 6 and 7 were identified as Type 1 poliomyelitis virus: a) by neutralization test in tissue cultures using homotypic antibody for poliomyelitis types,

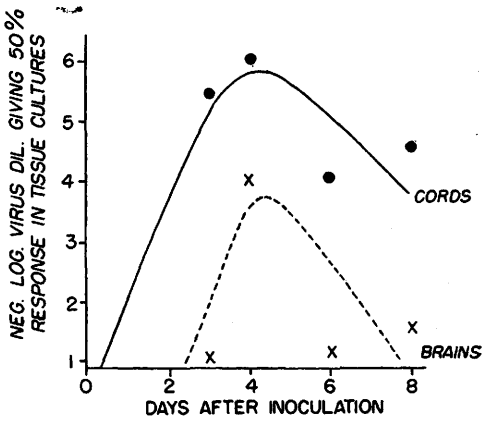

FIG. 1. Distribution of virus in brains and cords of paralyzed mice at various intervals after intravenous inoculation of the 4th criss-cross passage fluid.

* Aided by a grant from The National Foundation for Infantile Paralysis.