To provide simpler experimental conditions, an electric current having parallel isopotential lines and appropriate current density must be passed up or down the polar axis of the root and must coincide with the orientation of the general axis of the inherent electric field of the root as well as that of gravity.

An apparatus was designed to comply with this requirement and to maintain the roots under normal conditions of growth except for the applied current. Three sets of roots were used in each experiment: (1) control roots, (2) roots through which an electric current was passed upward, and (3) roots in which the same current was passed downward. Since individual roots vary slightly with respect to the threshold of current density for reversible inhibition of growth and also in their rates of elongation, each experiment involved 3 or more duplicate sets of roots. Preliminary experiments led to a choice of a current giving an IR drop of 40 mV/mm, with the root immersed in tap water as the growing medium and the current passed upward through 25 mm of the apical end of the growing root. This gives complete inhibition of growth. The same current passed downward gives a very slight inhibition of growth, Fig. 1, or none at all. At 37.8 mV/mm, complete but reversible growth inhibition is obtained with ascending currents.

Most experiments were divided into 3 periods: normal growth rate, current passing, and current off. The growth of each root was recorded under the microscope throughout the experiment.

Regions of the Growing Root Affected by the Electric Current. To determine what region of the growing root apex is involved in the growth response and inhibited by the current, a set of roots was marked in the usual way by means of particles of India ink. The results of one experiment are drawn to scale in Fig. 1. Ordinates are mm length, abscissa hours. I, II, and III are triplicate sets. A current of 40 mV/mm was passed up roots A, down roots B, and the right-hand group were controls. It is evident from the measurements that the growth process under these conditions was prevented by an ascending current in both the region of active cell division and the region of cell elongation.

The inherent E.M.F.'s generated by the root are so oriented that the ascending current, which causes inhibition, opposes them. An applied current (field) of like intensity, but oriented with, rather than against the inherent one, has little or no effect. A detailed report of all experiments will be presented elsewhere.

15178 P

Effect of Induced Pain on Pain Threshold.*

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Relief of pain by counterirritation is common experience and frequently was utilized therapeutically by the older physicians. The number of experimental studies reported in the literature is too small to permit conclusions to be drawn regarding mechanisms involved in the phenomenon which thus remains but poorly understood. Therefore reinvestigations on a larger group of subjects appeared desirable.

Methods. Pain threshold determinations were performed in a group of 14 normal human subjects, men and women, ranging in age between 19 and 45 years. The algesimetric method employed has been described in detail elsewhere.[1] It consisted of applying an

* This work was aided in part by a grant from Whitehall Pharmacal Company.

[1] Goetzl, F. R., Burrill, D. Y., and Ivy, A. C., *Quart. Bull. Northwestern Univ. Med. School*, 1943, **17**, 280.

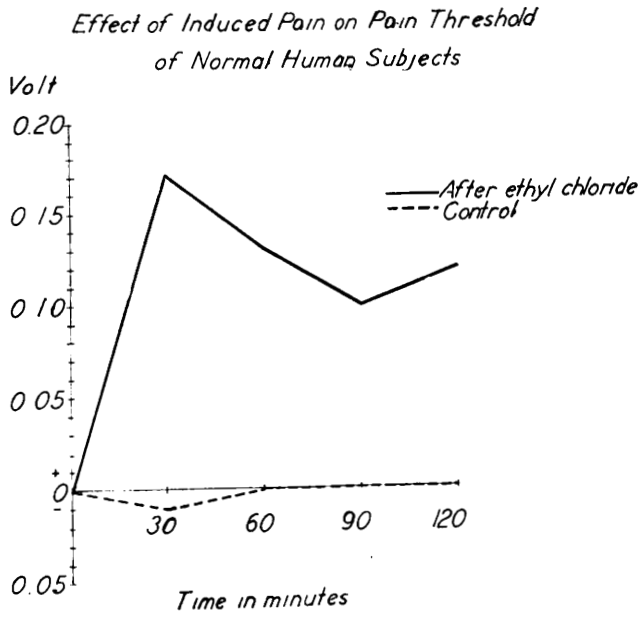

Fig. 1

alternating current to a tooth through a metal filling and noting the voltage at which the subject first experienced a painful sensation. Such voltage was considered an expression of the pain threshold level.

Pain was produced by spraying ethylchloride to an area of one square inch over the anterior surface of the subjects' tibiæ for a period of 20 seconds. At that time pain of burning or aching character was complained of in all instances. Pain thresholds were determined shortly before and at 30-minute intervals for 2 hours after the application of ethylchloride.

Results. Fig. 1 shows the averages of the values obtained in the determinations of pain threshold, expressed in terms of the mean changes in voltage required to produce a painful sensation in the subjects' teeth. The control values were obtained from 34 control tests in the 14 subjects and were found to be between 0.2 and 1.8 volt. Values after application of ethylchloride were obtained from 21 experiments in 11 of the 14 subjects. Analgesic effects were observed in all instances. The greatest variation in pain threshold during control periods in every subject was significantly smaller than the smallest change of threshold following application of ethylchloride. Therefore the curves presented give an indication of the results obtained for each subject.

In the control determinations the mean change in threshold value for the entire group was minus 0.003 volt; the corresponding value for the period following application of ethylchloride was plus 0.129 volt.

Comment. The observations reported are in partial agreement with results obtained by other authors.[2] They, however, employed different algesimetric procedures and different types of induced pain. Also, their studies were made on only 3 subjects and the results were expressed in percentages rather than in actual changes in threshold values. The pain threshold was reported to be elevated by induced pain by approximately 30%.

It is interesting, also, to compare the present results with those obtained previously in studies on analgesic effects of morphine sulfate in normal human subjects using the pres-

[2] Hardy, J. D., Wolff, H. G., and Goodell, H., *J. Clin. Invest.*, 1940, **19**, 649.

ent method.[3] Not all of the subjects tested showed an elevation in pain threshold following administration of 0.016 g of morphine sulfate, which for the entire group produced a mean increase of only 0.0218 volt.

The fact that for producing analgesic effects in the present experiment ethylchloride had to be applied until pain developed indicated that pain rather than cold was the sensation responsible for elevating pain thresholds. The mechanisms involved in producing the analgesic effects cannot yet be stated with certainty. Distraction, changes in local blood supply and other short lasting effects of induced pain cannot fully explain the phenomenon because the pain induced in our subjects lasted for 2 to 3 minutes at the most while the analgesic effects were noticeable for a period of 90 to 120 minutes.

In additional investigations, the possibility is being examined whether epinephrine might be the agent involved in producing analgesic effects following induced pain. The trend of thought seems logical in view of the facts that epinephrine is released by pain from the adrenal glands[4] and that it possesses marked analgesic properties when injected in man or dog.[5]

Summary. Experiments have been made in normal human subjects which demonstrate that induced pain of short duration produces long lasting analgesic effects.

[3] Ivy, A. C., Goetzl, F. R., and Burrill, D. Y., *War Medicine*, 1944, **6**, 67.

[4] Cannon, W. B., *Bodily Changes in Pain, Hunger, Fear, and Rage*, New York, D. Appleton and Co., 1929.

[5] Ivy, A. C., Goetzl, F. R., Harris, S. C., and Burrill, D. Y., *Quart. Bull. Northwestern Univ. Med. School*, 1944, **18**, 298.

15179

Effect of Adrenocorticotropic Hormone (ACTH) on Hypophysectomized Adrenal-demedullated Rats.*

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Ingle[1] has raised the question of the possible role of the adrenal medulla in the response of the adrenal cortex to adrenocorticotropic hormone. In the present study the problem of the relationship between the two parts of the adrenal has been approached by comparing the effectiveness of adrenocorticotropic hormone as a stimulant of the cortical tissue when administered in the presence or absence of the medullary tissue.

Methods. Male rats were adrenal-demedullated† at 25 days of age and the adrenal cortex was allowed to regenerate for 16 days. The animals were supported for the first 13 days of this period by 1% NaCl in the drinking water. The rats were then hypophysectomized, at 41 days of age. Pure ACTH[2] was injected for 15 days, beginning on the day of hypophysectomy, in an effort to maintain the adrenal cortical tissue. The cortical response of the doubly operated animals was compared with that of an equal number of rats hypophysectomized at the same age, in which the adrenal was intact. The daily dose of ACTH, 0.2 mg, was divided into two intraperitoneal injections of 0.5 cc each.

At autopsy the sella turcica of all hypophysectomized rats was searched under 10-fold magnification for remnants of pituitary tissue.

* Aided by grants from the Research Board of the University of California, the Rockefeller Foundation, and the Josiah Macy, Jr., Foundation.

[1] Ingle, D. J., *Endocrinol.*, 1942, **31**, 419.

† The adrenal medulla and all cortical tissue except a few cells adhering to the capsule were enucleated.

[2] Li, C. H., Evans, H. M., and Simpson, M. E., *J. Biol. Chem.*, 1943, **149**, 413.