

results of the present series of experiments. As was pointed out by Spiegel and Spiegel-Adolf, the convulsive reactivity may be increased by 2 mechanisms, pericellular increase of the concentration of ions on the one hand, increase of the permeability of the cellular surface films on the other hand. While the effect of hypochloremia belongs to the second group, hyperchloremia probably acts according to the first mentioned mechanism.

Summary. Experiments on rabbits and cats showed that hypochloremia increases the convulsive reactivity

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Negative Effects of Cysteine Hydrochloride on Regression of Carcinoma in Line A Albino Mice.

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Cysteine hydrochloride injected directly into the Jensen rat sarcoma has been reported to produce complete regression of the tumor.¹ Recurrence did not occur within a period of 6 months, and reinoculation with the same tumor or with Emge sarcoma² was not possible after regression of a cysteine treated tumor. Acids adjusted to the same pH as the cysteine hydrochloride solutions and injected in equivalent volumes were reported to be rapidly absorbed from the tumor and, except for a small area of necrosis, to produce no cytological change.³

After the experiments here described had been completed, further work was reported⁴ on the treatment of 3 different rat tumors, and on the Brown-Pearce rabbit carcinoma. This confirmed the earlier observations that direct injection of cysteine hydrochloride into Jensen's rat sarcoma and an adenofibroma of rats caused complete regression and cross immunity between the two. Treatment administered by other route was practically ineffective except that it prolonged the average life of rats bearing the Walker tumor by 11.1 days.

¹ Connor, C. L., Carr, J. L., and Ginzton, L., *Proc. Soc. Exp. Biol. and Med.*, 1936, **31**, 374.

² Carr, J. L., *Proc. Soc. Exp. Biol. and Med.*, 1936, **35**, 341.

³ Carr, J. L., *Proc. Soc. Exp. Biol. and Med.*, 1936, **35**, 343.

⁴ Carr, J. L., Connor, C. L., and Ginzton, L. L., *Am. J. Cancer*, 1936, **31**, 428.

Experiments with cysteine hydrochloride were carried on in this laboratory over a period of several months. Spontaneous and inoculated carcinomata in Line A albino mice were used. Thirteen spontaneous mammary gland tumors were directly injected from 1 to 6 times at intervals of 4 to 6 days. Ten mice received 15 mg cysteine hydrochloride in 0.15 cc distilled water at each injection and 3 were similarly treated with 10 mg in 0.1 cc. Central necrosis and extrusion of necrotic tissue occurred in 10 of these, as described by Carr. In 3 cases no extrusion of material occurred, and the tumors appeared to be only slightly affected by the treatment. In these animals death followed within 3 to 4 weeks with no evidence of regression. Of the 10 tumors in which necrosis was present: 3 regressed completely, but the mice died within 1 week after the first injection; 1 regressed completely, with no recurrence at the time of death 45 days later; 5 regressed partially, but the outer shell of tumor tissue which remained continued to grow, as evidenced by the presence of mitotic figures. In 1 mouse with 2 tumors, injections were made into 1 tumor only; this tumor regressed but reappeared after 3 weeks. During this period the second tumor continued to grow. After recurrence of the first tumor, the second tumor was injected and partial regression of this tumor took place without influencing the growth of the first tumor.

Since the action of the cysteine hydrochloride seemed to resemble so closely that of a caustic substance, injections of hydrochloric acid of the same pH and in equivalent volumes were tried and found to produce the same effect as cysteine hydrochloride. Following these tests, cysteine hydrochloride solutions were neutralized by the addition of NaOH, and 4 mice with spontaneous tumors were injected with this solution. In only one of these was there any marked regression, but mitotic figures were found in the outer areas of the tumor in sections taken at autopsy on the nineteenth day after treatment. None of these mice survived a period of 6 weeks.

Inoculated carcinomata in 19 mice behaved in a similar manner following injections with cysteine hydrochloride and with neutralized solutions. Central necrosis occurred in many but the edges or base of the tumor continued to grow. In a series of 20 mice doubly inoculated with adenocarcinoma 478, injections of cysteine hydrochloride were given into one tumor only. The treated tumors became necrotic and large portions of them were sloughed off, but no complete regressions occurred and growth continued at the base and edges. The growth of the untreated tumor was not affected by the necrosis of the tumor on the opposite side.

Summary. Cysteine hydrochloride injected directly into spontaneous and inoculated carcinoma caused necrosis and extrusion of necrotic material but produced permanent regression in only one animal. Partial regression of one tumor was without effect on the growth of a second untreated tumor.

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Some Effects of Anesthetic Mixtures Dissolved in Oil on Motor Nerves in the Cat.

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Since the introduction of local anesthetic substances dissolved in oil by Yeomans, Gorsch and Mathesheimer,¹ mixtures patterned after the original have been extensively used by proctologists.² Recently the use of these substances has spread to other clinical specialties.^{3, 4} Injections of the various mixtures regularly produce anesthesia lasting from several days to as much as one month, and occasionally longer.⁵ Variable amounts of muscular relaxation for similar periods are also obtained.

The usual explanation for the prolonged effect is gradual release of the anesthetic materials from the oily vehicle whereby a long continued depressant effect on the functional activity of the nerve endings is obtained.^{1, 6} However, on the basis of Donaggio's⁷ work with long continued application of aqueous local anesthetic solutions, one might expect irreversible organic changes leading to nerve degeneration. Degeneration as a result of the injection of local anesthetics in oil has been suggested in only one⁸ of the many clinical papers examined, and apparently no animal experiments followed by histological examination of the nerves have been performed.

In this laboratory cats were injected in an attempt to determine

¹ Yeomans, F. C., Gorsch, R. V., and Mathesheimer, J. L., *M. J. and Rec.*, 1928, **127**, 19.

² Green, W. W., *Tr. Am. Proct. Soc.*, 1937, **38**, 153.

³ Hollander, E., *Arch. Neurol. and Psychiat.*, 1938, **40**, 743.

⁴ Hunter, G. W., *Am. J. Obst. and Gynec.*, 1939, **38**, 318.

⁵ Block, L. H., Greene, B. L., and Wiltrakis, G. A., *Illinois M. J.*, 1938, **73**, 238.

⁶ Manheim, S. D., and Marks, M. M., *Am. J. Surg.*, 1938, **39**, 86.

⁷ Donaggio, A., *Gior. ital. di anest. e di analg.*, 1937, **3**, 325.

⁸ Steinberg, N., *New England J. Med.*, 1936, **215**, 1019.