40% by the end of 8 hours' incubation (37° C.), then gradually fell to approximately 5% by the end of 36 hours. After the 36th hour the *albus* percentage again rose, reaching about 18% by the 168th hour. Curve C in the same figure records data from a mixed broth culture originally containing 60% *albus* individuals. This curve shows the same type of fluctuations in *albus*-percentage. Identically the same fluctuations were noted when mixed cultures were grown in filtrates or centrifugates from 24-hour to 5-day *albus* or *aureus* broth cultures.

Since all of these fluctuations are predictable from the observed differences in "growth-vigor" and longevity in pure-line *albus* and *aureus* dissociates, such percentile fluctuations furnish no evidence of existence of a specific hormonal antagonism between white and orange dissociates of *S. aureus*.

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Action of Compounds Related to Cysteine on the Regression of Jensen's Rat Sarcoma.

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Since the report[1] of the effect of cysteine hydrochloride on Jensen's sarcoma in rats, attempts have been made to determine the active portion of the cysteine structure responsible for the tumor regressing action. This has been studied by injecting into the tissue of the Jensen rat sarcoma several acids with the same pH as the cysteine hydrochloride solutions, fractions of the cysteine molecule, and compounds built up from the cysteine molecule.

In the first group, hydrochloric acid, sulphuric acid, and acetic acid were tried, and also because of its sulphur content rather than acid properties, sodium thiosulphate. The acids were adjusted to the same pH as the solutions of cysteine hydrochloride and were injected in equivalent volumes. All the acids were rapidly absorbed from the tumor tissue. Except for a little central hyperemia in the tumor and occasionally a small focus of necrosis in the center of the tumor mass, no cytological changes were noted. There was no influence

1 Connor, C. L., Carr, J. L., and Ginzton, L., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 374.

apparent upon the tumor growth. In the case of sodium thiosulphate no effect whatever was noted.

Because of the similarity between cysteine and alanine, the latter was injected directly into tumor tissue in dosages equivalent to the effective cysteine dose. Since the alanine formula is identical with cysteine, excepting for the removal of the S-H radical, it was felt that any differences in effect might be ascribed to the sulfhydryl group. Whereas 50 mg. of cysteine hydrochloride in 1 cc. of water causes early necrosis and often complete regression of a sarcoma nodule 2.0 cm. in diameter, a similar dose or double the dose of alanine has no effect. In fact, 200 mg. of alanine were tried daily for 5 days in the same tumor and no appreciable effect was noted either upon the tumor or upon the host.

The mercaptan radical was then injected in the form of ethyl mercaptan. Because of its low boiling point the drug was injected quickly, being withdrawn from a cold bottle into an iced syringe and placed immediately in the center of the tumor by hypodermic needle. Sublethal injections of 0.001 to 0.002 cc. per kilogram of this substance were given over a period of one week and while the animals appeared somewhat toxic and dizzy, no effects were noted upon the tumor growth during the time of injection and upon post-mortem examination no more necrosis was observed in these tumors than in untreated tumors of a similar size.

Following the recent publication by Schubert[2] regarding compounds of thiolacids with aldehydes, it was felt that a combination of cysteine and formaldehyde might prove to be an effective chemical for tumor control. Accordingly, the compound was made in the manner described by Schubert and after purification was injected into Jensen's sarcoma in rats. Thirty-three mg. of this substance were injected into sarcoma nodules in 150-gm. white rats for 5 successive days. In none of these animals were there any appreciable effects on tumor growth and in none of them either during life or at post-mortem was there any apparent tumor necrosis. Subsequent experiments with homocysteine, glutathione and other sulphur-bearing amino acids are being tried and will be reported. Cystine has given uniformly negative results. Cysteine hydrochloride, on the other hand, has been consistent in causing necrosis and regression in the Jensen rat sarcoma. Studies on the effects of cysteine hydrochloride upon human tumors are in progress.

[2] Schubert, M. P., *J. Biol. Chem.*, 1936, **114**, 341.