The treatment of disease is essentially an attempt at the reconstruction of health. As health is relative there is always room for improvement, even though obvious disease is absent. It should be possible to make apparently well people healthier. That healthy babies can be made healthier has been demonstrated by the pediatricians. Such guidance can, and should, be applied to adults. For this type of medical science and service, the name "constructive medicine" has been suggested.[3]

Galdston proposed the term "eubiotic medicine" for the same general concept. It is our feeling that constructive medicine is a preferable term because it will be understood by more people, and because it more simply portrays the objective of approaching an optimal state of health.

Constructive medicine attempts to improve the intrinsic vigor, resistance, and endurance of an individual. It must be applied individually, for it involves direct effort on the part of the patient and something more than the mere control of the environment. One significant aspect of this idea is that it should reduce the great human inertia against preventive activities. To the average individual prevention has a negative connotation. It suggests rules and prohibitions and long series of "don'ts." Furthermore, the actual accomplishments of prophylaxis are demonstrable only statistically. Statistics have little emotional appeal to the average man or woman. We can not prove that this or that measure actually prevented a disaster befalling this or that person. Most people, if left to their own devices, prefer to gamble rather than take the trouble to protect themselves. Therein lies the strength of public health control of the environment; no effort is involved on the part of the individual in obtaining clean, safe food and water.

Constructive medicine, on the other hand, can produce results clearly demonstrable to the individual patient. Improved vigor from better nutrition and raised hemoglobin levels, greater work efficiency[4] and euphoria aided by properly applied mental hygiene are notable to the patient. Constructive medicine is not a panacea which can prevent all ills and quickly make us into a race of supermen. One of the major limitations of good constructive medicine is that it is expensive, for, to be properly applied, it must be individualized. With older persons individualizaton becomes increasingly imperative. Nevertheless, the potential benefits are valuable at almost any price. Though the hope of avoiding all illness or injury is a vain and unobtainable wish, we must not forget that if a man be in really good health prior to an acute infection, or injury, his chances of survival and his speed of recovery are greatly augmented. It is a fundamental principle of geriatric medicine that in mature adults the prognosis in an acute illness is profoundly affected by the condition of the patient before the acute disorder.[5] Lastly, it is possible that all medical therapy could be improved by an attitude which stresses the reconstruction of health, rather than limiting itself to the treatment of disease. We need to be less concerned with the disease and more with the patient.

EDWARD J. STIEGLITZ

WASHINGTON, D. C.

[3] E. J. Stieglitz, *Annals Int. Med.*, 18: 89, January, 1943.

SPECIAL ARTICLES

THE FAILURE OF PURIFIED PENICILLIN TO RETARD THE GROWTH OF GRAFTS OF SARCOMA IN MICE[1, 2]

THIRTY-FOUR Bagg albino inbred mice, weighing 19 to 20.5 grams, were implanted with a small graft of a sarcoma native in this strain. During the ten years that this tumor has been transplanted the grafts have grown and brought about the death of every one of the implanted mice of this strain.

Two of the implanted mice were not treated, but were kept as controls. Thirty-two were injected hourly with a solution of Merck's purified salt of penicillin dissolved in normal salt solution. They received doses equivalent by weight to those listed by Merck as most favorable for human beings. The ampules, Merck Lot 193, contained 10,000 Oxford units. The material was stored at 4° C and each ampule was opened as needed.

During the first 72 hours following the implantation of the tumor graft the 32 mice received 120,000 units of penicillin in graded doses as follows: 8 received 8,000 Oxford units each; 8 received 4,000 units each; 8 received 2,000 units each and 8 received 1,000 units each. At the end of this time four mice from each lot were selected for further treatment, and the others received no more injections. The sixteen mice

[1] Aided by a grant made to Dr. Warren H. Lewis from the International Cancer Research Foundation.

[2] The purified Merck's penicillin was supplied by the Office of Scientific Research and Development; the Squibb penicillin was obtained from Lieutenant-Colonel Lind and Captain Romansky, of the Walter Reed General Hospital, and the calcium salt of penicillin was obtained from Dr. Lockwood, of the University of Pennsylvania.

[4] E. J. Stieglitz, Proceedings 8th annual meeting Industrial Hygiene Foundation of America, November 11, 1943.

[5] E. J. Stieglitz, editor, "Geriatric Medicine: Diagnosis and Management of Disease in the Aging and the Aged." Philadelphia: W. B. Saunders Company. 1943.

selected received 40,000 units in the next 24 hours in graded doses of 5,333, 2,666, 1,333 and 666 units each.

At the end of 96 hours the tumors were growing in all the mice. Therefore, two mice were selected from those that had received 8,000 units in the first 72 hours and 5,333 units in the following 24 hours. They were injected during a period of 37 hours with 20,000 units each, amounting to 540 units an hour.

From the above results it can be seen that the 32 mice received from 33,333 units each to 1,000 units each. At the end of seven days all the treated and the untreated mice had tumors of approximately the same size. Fourteen days after the experiment was begun two of the treated mice were dead and the others, both the controls and the treated ones, were moribund.

When it was found that the purified penicillin failed to retard the growth of sarcoma *in vivo* we prepared roller tube tissue cultures similar to those used by Ivor Cornman.[3] In these we found that the purified penicillin failed to damage the sarcomatous or the normal cells even when 120 and 160 units were added to the roller tube culture.

We then decided to compare the action of a more highly purified colorless sodium salt of penicillin (Merck Lot 4R263, 14,000 Oxford units in 9.216 mg) with that of a yellow sodium salt of penicillin (Squibb, Lot 87225).

The pieces of tissue were arranged in test-tubes in a row as follows: kidney, sarcoma, spleen, sarcoma, muscle, sarcoma and heart followed by sarcoma. When the tissue had grown for 24 to 30 hours the medium was withdrawn, fresh medium added and then into each tube was added a known number of units of penicillin dissolved in normal salt solution.

Twenty-four hours later the sarcomatous and the normal tissue were growing abundantly in the cultures that had received 20, 40, 53, 60, 80, 100, 120 and 160 units of the highly purified penicillin. In some experiments the tubes were given a second dose of 80 or of 160 units; nevertheless, the cells continued to grow for a number of days. In the tubes that received the yellow penicillin both the normal and the sarcomatous cells were growing abundantly in the tubes containing 20, 40 and 53 units, respectively, but in the tubes containing 60 and 80 units the tumor cells were damaged while the normal cells were growing. In the tubes that had received 100 and 120 units the tumor cells were killed and the normal cells were damaged.

The tube tissue culture experiments were repeated several times and in each instance they showed that the highly purified penicillin failed to damage the growing normal or the growing sarcomatous cells while the yellow penicillin used in proper dosage damaged the growing sarcomatous cells without injuring the normal cells. These experiments confirm the observations of Ivor Cornman.[3]

From our studies we surmise that the factor present in the less purified sodium salt of penicillin which damaged the sarcoma cells is lost in the highly purified product.

In addition to our studies with the sodium salts we tested one calcium salt. One hundred thousand units of a somewhat yellow colored calcium salt of penicillin, prepared by the Commercial Solvents Corporation, were tested on four mice that had been implanted 48 hours previously with grafts of sarcoma. The four mice tolerated injections of 250, 500, 500 and 750 units, respectively, every two and one-half hours for 28 doses. As the tumors were growing the injections were increased to 1,000 units every two hours. Totally the mice received 11,500, 24,000, 24,000 and 31,000 units, respectively, during 38 injections over a period of 5 days. At the end of 8 days the growing tumors were equally large in the 4 treated and the 4 untreated control mice.

MARGARET REED LEWIS
DEPARTMENT OF EMBRYOLOGY, CARNEGIE INSTITUTION OF WASHINGTON, AND THE WISTAR INSTITUTE OF ANATOMY AND BIOLOGY, PHILADELPHIA

[3] SCIENCE, 99: March 24, 1944.

SYNTHESIS OF TWO NEW CARBOHYDRATES WITH BACTERIAL PHOSPHORYLASE

THE synthesis of two carbohydrates, which appear to be new analogues of sucrose, has been effected by the use of a phosphorylase preparation from the bacterium *Pseudomonas saccharophila*. This enzyme preparation catalyzes the reversible reaction:

sucrose + inorganic phosphate $\rightleftharpoons$ glucose-1-phosphate + fructose,

and has previously been shown to have no action on trehalose, maltose, raffinose, glycogen or starch.[1,2,3,4] Attempts to substitute phosphoric esters of fructose or aldose sugars for fructose have met with no success, nor could any reaction be observed between fructose and maltose-1-phosphate.[5] However, when either *l*-sorbose or *d*-ketoxylose (crude mixture of xylose and ketoxylose) was added together with glucose-1-phosphate to the enzyme preparation, there was evidence of a reaction similar to that observed in the synthesis of sucrose and characterized by the liberation of inorganic phosphate accompanied by a decrease in the

[1] M. Doudoroff, N. Kaplan and W. Z. Hassid, *Jour. Biol. Chem.*, 148: 67, 1943.
[2] M. Doudoroff, *Jour. Biol. Chem.*, 151: 351, 1943.
[3] W. Z. Hassid, M. Doudoroff and H. A. Barker, *Jour. Am. Chem. Soc.*, 66: 1416, 1944.
[4] H. A. Barker, W. Z. Hassid and M. Doudoroff, SCIENCE, 100: 51, 1944.
[5] The maltose-1-phosphate was recently synthesized chemically by W. R. Meagher and W. Z. Hassid (unpublished).