$$HO_2 + HC1 \longrightarrow HOC1 + OH$$

 $HO_2 + HC1 \longrightarrow H_2O + C1O$
 $HO_2 + Cl_2 \longrightarrow HOC1 + C1O$

and, in addition, no one has considered the possible chain breaking abilities of hydrogen peroxide itself:

$$H + H_2O_2 \longrightarrow H_2 + HO_2$$

 $Cl + H_2O_2 \longrightarrow HCl + HO_2$
 $HO_2 + HO_2 \longrightarrow Ending the chain$

In conclusion, then, it might be said that, while considerable clarification of our views of the photo combination of hydrogen and chlorine has occurred, there are many aspects of the problem which must be solved before anything like a complete picture can be obtained.

- ¹ Rodebush and Klingelhoefer, these Proceedings, 18, 531 (1932).
- ² Kimball and Eyring, J. A. C. S., 54, 3883 (1932).
- ³ Bodenstein, Trans. Faraday Soc., 27, 413 (1932).
- ⁴ Thon, Z. Physik. Chem., 127, 327 (1926).
- ⁵ Bodenstein and Unger, Z. Physik. Chem., B11, 253 (1931).
- ⁶ Cremer, Z. Physik. Chem., 128, 285 (1927).
- ⁷ Ritchie and Norrish, Nature, 129, 243 (1932).
- ⁸ Lavin and Bates, J. A. C. S., 55, 81 (1933).
- ⁹ Salley and Bates, J. A. C. S., 55, 110 (1933).
- ¹⁰ Frankenburger and Klinkhart, Trans. Faraday Soc., 27, 431 (1931).
- ¹¹ Professor Bodenstein in a private communication has informed the author that the result of a study of these reactions is being published from his laboratory.

REVERSIBLE COAGULATION IN LIVING TISSUE. XI*

By Wilder D. Bancroft, Robert S. Gutsell** and John E. Rutzler, Jr.

BAKER CHEMICAL LABORATORY, CORNELL UNIVERSITY

Read before the Academy, Tuesday, November 15, 1932

It has been pointed out, in several of the reports¹ that have been made during the progress of the investigation of reversible agglomeration in living tissue, that sodium rhodanate antagonizes alcohol physiologically. This fact has been utilized successfully in the experimental treatment of seven cases of chronic alcoholism. Much the same theoretical and practical considerations apply here as in the treatment of morphinism. Therefore, other than to point out that at the present time it is impossible to cure the chronic alcoholic who indulges merely because of the euphoria that is produced, it is not necessary to go into the theoretical details. Sodium rhodanate will help to prevent a return to the use of alcohol by

those individuals who are nervous or sleepless when not using the intoxicant, or those with maniac depressive tendencies who cannot adjust to society adequately.

Since alcohol is easier to obtain, cheaper, less insidious and easier to break away from, than morphine, the chronic alcoholic is not deterred morally, socially and intellectually from a relapse so strongly as the morphine addict. Largely for this reason, a good prognosis is not indicated in so large a percentage of chronic alcoholics. Mark Twain said that to abstain from drinking is not to vow never to take another drink; rather to decide never to want another drink.

Case 1.—This case deals with the same person as the case of drug addiction reported in paper number ten of this series.² On March 18th J. H. came to us in a state of hypomania, having been in a state of alcoholic intoxication for a period of a week. He claimed that during this day he had consumed a quart of whiskey. He was dirty, dishevelled, oblivious to those around him and intoxicated. His speech was poorly coördinated; his face was gray, and exhibited nervous tension; he was thoroughly disgusted with himself. The hypomania, also an agglomerated condition, was brought on by the use of alcohol; on September 9th, the same reaction was caused by sodium amytal, another agglomerating agent. So morphine, alcohol and sodium amytal all brought about the same reaction.

Twenty grains of sodium rhodanate were given to the patient at 9:30 p. m. Bisodol was also administered. While under observation, the patient was subjected to psychotherapy without hypnosis. Thirty minutes after the sodium rhodanate was administered, the hypomanic state disappeared; and the patient was much quieter. At this time ten grains more of sodium rhodanate were given. Soon, the lines left his face and the grayish cast disappeared.

One hour after sodium rhodanate was first exhibited, the patient was entirely sober. He spoke and behaved soberly in all respects. At this time he was given Bisodol again. A bottle of whiskey was shown to him; this sickened him so that he vomited. He returned to his home cool, collected and steady. The patient took ten grains more of sodium rhodanate upon retiring, and slept well during the night. After this episode, his indulgence in alcoholic inebriety slowly subsided. Furthermore, all statements to the contrary, by unqualified professional men, the patient has not returned to the habitual use of morphine in practically one year.

Case 2.—F. P. M., 32 years of age, presented himself for treatment. For two and one-half to three years he had been a steady drinker, using about a quart of whiskey and an undetermined amount of beer each day. The patient was able to work; but he was nervous, restless and unsteady. In addition, he did not sleep well. During the twenty-four hours preceding the beginning of peptization therapy, the patient claimed to have consumed a quart of whiskey and several glasses of beer. Fifteen grains of sodium rhodanate every six hours were prescribed.

The first night after the beginning of the treatment, the patient slept uninterruptedly for nine hours. When seen during the day, he was steadier and feeling better. The patient was not given alcohol at any time. The second night he slept for eleven hours, after having had three grains of sodium rhodanate in the afternoon, and one grain at bedtime. Further than that, he dozed during the afternoon at frequent intervals; he was relaxed, and making up for some of the wear and tear on his nervous system which had occurred concomitantly with two and one-half years of agglomeration due to alcohol. The patient was steadier again than on the preceding day, happy, and

contented. So, three days after the start of peptization therapy, the signs of chronic alcoholism had disappeared. The third night he was given two grains of sodium rhodanate; he slept for eight and one-half hours. During the day he felt even better than he had the day before. The fourth night only one grain of sodium rhodanate was prescribed.

During the fourth night he slept well, and felt exceedingly well the following day. After that, he took five grains of sodium rhodanate every other night for two doses. This was followed by one five-grain dose, after which the patient used the drug only intermittently. When two weeks had elapsed, he was very well, perfectly steady and sleeping satisfactorily. Frequently he refused alcoholic beverages when they were offered to him; the patient smoked one-half of a package of cigarettes in a day, in comparison with a package and a half a day before treatment. He sat and read newspapers for hours; formerly he could concentrate only enough to read the headlines. Two months later the patient was in excellent condition.

Case 3.—I. H., 52 years old, had been a chronic alcoholic for about five years; in addition he used morphine occasionally. His initial condition was one of nervousness, sleeplessness, slight jealousy of his own comfort and an apparent need for alcohol. Nervous tension was visiblehis on face. He tended to a hypomaniac reaction in that he switched from thought to thought without completing many of them. He was distractable. Examination of the heart showed a mitral stenosis and regurgitation of long duration. This case, along with cases 4 and 6, illustrates the fact that theoretical acumen is a prerequisite to an understanding and successful application of these methods. The thing cannot be handled empirically.

The patient took ten grains of sodium rhodanate the first night and "slept better than he had for years." He was somewhat relaxed during the following day, and was given only five grains of the peptizing agent. Before retiring the second night he was given ten grains of sodium rhodanate. He did not sleep much during the night. The interesting thing here is that despite the sleeplessness the patient was calm and not at all nervous. According to the theory, this means that the "sleep center" was overpeptized; and at the same time the sensory nerves were peptized back to normal. Thus, he was sleepless but not nervous. Larger doses of the peptizing agent should result in general over-peptization, and thus uneasiness. The patient was given five grains of sodium rhodanate after breakfast, and again after lunch. This was followed by ten grains after dinner. His condition was much improved during the day; he felt very well, and appeared to be relaxed, physically and mentally. Thus, on the third day the patient was practically back to normal. He was restless during the third night, as predicted.

Throughout the fourth day the patient had no complaints; and his general condition was much improved. He was given fifteen grains of sodium rhodanate during the day. This was a reduction of five grains over the previous day. As a result, he slept better. For the next three days he remained in statu quo due to a heavy cold in the head and throat. No alcohol was administered at any time during the treatment. The first and second of these nights he slept fairly well on a total of twelve grains of sodium rhodanate during the days. On the seventh day, his cold was worse; he was not given any sodium rhodanate during the day. At night he could not sleep, and so he was given fifteen grains of the peptizing agent. A good night's sleep followed.

The rest of the treatment consisted in building up the patient, and working to determine the optimum dose of sodium rhodanate. This was finally fixed at seven and one-half grains shortly after supper. By the ninth day the patient was in comparatively excellent condition; he was calm, quiet, not nervous and relaxed. His speech was slower; and attempts to distract him failed utterly. He was sleeping satisfac-

torily. The signs of chronic alcoholism had disappeared entirely by the time he was sent home after fourteen days of treatment.

So, by following the theory and interpreting it, this patient was straightened out and his immediate problems solved. Reports received several months later indicated that he had not returned to the habitual use of alcohol.

Case 4.—H. H., 57 years of age, had been addicted to the use of alcohol for approximately forty years. The complete story of this case requires too much detail for presentation here; so, only a few of the salient features will be recorded. Upon admission to the hospital his skin was dry and flushed with acne on the nose and cheeks. The conjunctivae were injected and sore; his gums were swollen and red. There was a severe, chronic, chemical pharyngitis as a result of chronic alcoholism. The heart presented frequent extra-systoles. There was a coarse tremor of the extended tongue held in the mid-line. There was a tremor of the hands and arms. He was irritable, restless, wanted whiskey and could not sleep well.

The patient presented a definite physical and mental need for whiskey. The mental need for whiskey suggested that the chronic alcoholism was in response to a schizoid personality. Later events brought this out clearly. He was not very tractable. After six hours of observation, during which six ounces of whiskey were administered, because of lack of cooperation, the patient was given ten grains of sodium rhodanate. This did not quiet him much; two more ten-grain doses were administered before the middle of the next morning. These also failed to quiet him much. During this time, frequent small doses of whiskey were necessary to control the patient. It was considered to be unwise to dose the patient heavily with the peptizing agent because of the heart condition. The alternative was to administer sodium amytal, or some other innocuous agglomerating agent, and at the same time to reduce the amount of alcohol taken. In this way an agglomerating agent to which he had not become addicted was substituted for the one to which he was addicted. In this way he was shown that it was not necessary to have alcohol. When he realized that alcohol was not a necessity, the sodium amytal was discontinued, and his system peptized by small amounts of sodium rhodanate. Actually, sodium amytal in three-grain doses as needed to allay restlessness, was given for one day; then veronal was substituted for amytal, and administered for four days. During the next six days the patient was given seven and one-half grains of sodium rhodanate a day in divided doses. At the end of the treatment he was calm, tractable and not nervous; he slept well at night.

He was discharged with instructions to take seven and one-half grains of sodium rhodanate a day for about two weeks. Instead of following instructions, the patient took more than thirty-five and perhaps as much as sixty grains a day for five days. This over-peptized him to such an extent that he was returned to the hospital at the end of the five days suffering from an acute visual and auditory hallucinatory psychosis. He was tractable, but did not know where he was. The hallucinations were somewhat systematized. From what has preceded it is not difficult to see that agglomeration therapy was strongly indicated. During the first day he was given ten grains of veronal and three grains of sodium amytal; the second day he was given fifteen grains of veronal. On the third day he was somewhat clearer mentally. The veronal was discontinued; since the progress back to normal was slow, even with the use of an agglomerating agent, it was thought best to allow the patient to slide back to normal without agglomeration therapy other than two grains of caffeine citrate every six hours.

The patient was coherent and lucid on the sixth day; he was much improved mentally. He continued to improve during the next four days. On the tenth day he became somewhat irrational in the evening. So, a grain and a half of sodium amytal was ordered every eight hours. In order to improve his general health, and steady his nervous system more he was kept in the hospital an additional ten days. During this

time, one and one-half grains of sodium amytal were given every eight hours. The patient was in good physical and mental condition when discharged. Because of the schizoid tendency of the patient, which means that he would be over-peptized if not given artificial agglomeration, he was instructed to take a small amount of sodium amytal each day for a month or so after returning home. In five months nothing further has been heard from the case, which may mean anything.

Case 5.—M. P., 54 years old, had been a chronic alcoholic for many years. This was accompanied by nervousness, restlessness and insomnia. Upon his admission to the hospital, a particularly indulgent period of alcoholic intoxication came to an end. The patient was very much depressed; his hands trembled, and the muscles twitched. In lieu of whiskey, the patient was quieted with sodium amytal during the first fourteen and one-half hours. Six grains of the agglomerating agent were given at about midnight, four hours after admission to the hospital. At 10:30 the next morning, three grains more of sodium amytal were given. This quieted the patient in the same general manner as alcohol would have. However, when he was awake, he was nervous and restless. This shows that the sodium amytal did not bring about any essential improvement.

So, in the afternoon of the first twenty-four hours of his stay in the hospital, twenty grains of sodium rhodanate were given in a single dose. This quieted the patient somewhat; and he went to sleep again. He was nauseated in about an hour after the dose of sodium rhodanate; therefore, ten grains of sodium bicarbonate were given before each of the following doses of the peptizing agent. Two hours after the first dose of sodium rhodanate, fifteen grains more were given. This was followed by ten grains four hours later. The first two doses quieted him somewhat but he was still very restless and shaky. He became considerably more quiet after the ten-grain dose.

The patient slept most of the second evening. He grew restless around midnight; so, fifteen grains of sodium rhodanate were administered. The second night he was restless a good deal of the time, although he slept for four hours.

During the second day the patient was given fifteen grains of sodium rhodanate; he was restless and nervous in short spells. His appetite improved and he was quiet most of the day. He slept for five hours during the night. When he was not sleeping, he was not at all restless. In the morning of the third day he was very quiet, had no complaints, and was neither restless nor nervous. His hands were much steadier and the mental depression, of which he complained in the beginning, was absent. During the day he partook of the regular diet and seemed to enjoy eating. The patient passed a comfortable day. Twenty grains of sodium rhodanate were administered during the period.

The fourth night, following the third day, was passed comfortably. He was given twenty grains of sodium rhodanate during the fourth day; he was in very good condition on this day. From that time on there were no unusual occurrences. The patient slept six to eight hours a night, ate well, was not nervous or restless, and had no need for alcohol. The patient and his family stated that his recovery was attended by less nervousness, and was much more rapid, than had ever been the case on other similar occasions. The dosage of sodium rhodanate was decreased slowly so that at the end of the treatment, eleven days after admission to the hospital, he was not taking any of the drug. Upon discharge, he was instructed to use it when nervous, restless or sleeping poorly. So, in two and one-half days the patient was improved to a degree that usually required four days for attainment. He was treated for the additional time in order that his nervous system might be stabilized.

Case 6.—H. R., 43 years of age, drank in the neighborhood of ten quarts of corn whiskey in a week. The case was one of acute rather than chronic alcoholism. The patient stopped drinking two days before the services of a physician were required.

When first seen at 9:00 A. M., he behaved abnormally; he was excited, confused, talked wildly, was very nervous and definitely hallucinated. The diagnosis of delirium tremens was made immediately. In order to quiet the patient as soon as possible practicably, he was given six grains of sodium amytal. He was told that the agglomerating agent would quiet him and put him to sleep. He coöperated by lying down and attempting to go to sleep. Fifteen minutes later he arose; all of the symptoms were very much exaggerated. The reason for that state of affairs was that the sodium amytal merely acted to agglomerate further the tissues that were already agglomerated by alcohol. Enough sodium amytal would have put him to sleep, under which condition the above reaction would not have been apparent.

He left the house and walked down the road to where there was a collection of building material; there he started to build a house. Deeming him a menace, the authorities lodged him in jail. When visited professionally, just after five o'clock, he was with the other prisoners and was frightening them. He acted wildly, jumped around, yelled, laid on the floor, jumped up on the table and acted insane in all his actions. Twenty grains of sodium rhodanate were administered, by mouth as usual, at 5:30 p. m.; he was removed to the hospital. Twenty grains more of sodium rhodanate were given at seven o'clock. He then went to bed and behaved better. At this time he was very much confused; but, in contrast with his behavior earlier in the day, he was only mildly hallucinated. He was relatively quiet. Since he was not progressing so well as desired, another twenty-grain dose of the peptizing agent was given at 9:15 p. m. At this time he was behaving better than he had been.

The patient became noisy again at midnight. The theory called for more sodium rhodanate and so twenty grains more (a total of eighty grains) were administered. At 1:00 A. M. this was supplemented by thirty grains of sodium bromide, a weaker peptizing agent. He quieted down and went to sleep shortly thereafter. When seen in the forenoon he was normal mentally, quiet and not at all nervous. The patient ate heartily for the first time in a week. He passed a quiet day, remaining in bed. No more medication was given. The patient went home on the second day in good condition. This was a rather rapid recovery from delirium tremens.

Case 7.—C. D., aged 42 years, strong, well and a hard worker, was treated for acute alcoholic intoxication and insomnia. When first seen he was very nervous, belligerent and pugilistic. Under the pressure of nervousness from overwork he had reached a point where small amounts of alcohol affected him much more than usual. Twenty-five grains of sodium rhodanate were administered at three o'clock in the morning. In a short while he became less pugilistic and more tractable. About thirty minutes later he was given twenty grains more of sodium rhodanate; that made him more quiet and less nervous. In another half hour the twenty-grain dose was repeated along with a dose of sodium bicarbonate. Following that he slept and stayed in bed sleeping and resting quietly most of the day. The day after the episode, the patient was not noticeably nervous, in contrast to his condition before becoming intoxicated.

The night following the episode the patient slept better than he had for a long while; forty-five and one-half grains of sodium rhodanate were given during the day. The next night he again slept well; thirty grains of sodium rhodanate were used. There were no further signs of nervousness. Being a transient, the patient went on his way at this juncture, with instructions to use twenty grains, or less, of sodium rhodanate nightly to try to procure the desired sleep.

At different times during the past eleven months, five people have been sobered quickly after having become intoxicated with alcohol. In these cases single doses of fifteen to twenty-two and one-half grains of sodium rhodanate were used. There was no sudden transformation from a state of intoxication to normal; but a decided alleviating effect was demonstrated.

Thus, twelve cases of alcoholic intoxication have been dealt with successfully by applying peptization and agglomeration therapy. No claim can be made, at present, that chronic alcoholism can be cured by peptization therapy; but our experience has been that, with the use of sodium rhodanate, the habit of alcoholic over-indulgence can be checked a good deal. It has been demonstrated that chronic alcoholism can be broken up and the patient returned to normal more rapidly than is usual in medical practice, if one knows the theory back of the action of alcohol. The limitations to the use of sodium rhodanate and peptization therapy are the same as those that have been found to supervene in the treatment of chronic morphinism.³

The general conclusions of this paper are:

- 1. Chronic alcoholism is benefited by treatment with sodium rhodanate, peptization therapy.
 - 2. Such a treatment tends to return the patient to normal very quickly.
- 3. The patient can then sleep a normal amount and has no physical need for alcohol, provided his general condition of health does not interfere.
- 4. All chronic alcoholics on whom sodium rhodanate can be used safely can be cured if there is only a physical need for alcohol.
- 5. Since there are many nervous, mental and social causes which tend to lead to a return to alcohol, a period of close observation by the physician and the coöperation of the patient is essential in effecting a cure. Although the craving has been broken, there is nothing to prevent the patient from relapsing unless he determines not to.
- 6. If the need for alcohol is brought about by an inadequate personality, chronic alcoholism cannot be combated successfully with the meager facilities at our disposal.
- 7. Delirium tremens has been relieved effectively and quickly solely by the use of peptizing agents.
- 8. Single episodes of alcoholic intoxication can be dealt with to great advantage by the use of sodium rhodanate.
 - 9. The treatment has not been, and probably cannot be, standardized.
- 10. The same general theory underlies the treatment as that which gave rise to a successful treatment for morphinism.
- * This work is done under the program now being carried out at Cornell University and supported in part by a grant from the Heckscher Foundation for the Advancement of Research established by August Heckscher at Cornell University.
 - ** M.D.
- ¹ Bancroft and Rutzler, *Proc. Nat. Acad. Sci.*, **17**, 105 (1931); **17**, 186 (1931); *J. Phys. Chem.*, **35**, 1185 (1931); **35**, 3036 (1931).
 - ² Bancroft, Gutsell and Rutzler, Proc. Nat. Acad. Sci., 18, 8 (1932).
 - ⁸ Bancroft, Gutsell and Rutzler, J. Phys. Chem., 36, 2011 (1932).