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MERCUROCHROME-220 SOLUBLE AND  
GENTIAN VIOLET

BACTERICIDAL EFFICIENCY BY INTRAVENOUS  
ROUTE \*

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In March, 1924, Young and Hill<sup>1</sup> published some very interesting results in the treatment of septicemia and local infections by intravenous injections of mercurochrome-220 soluble and gentian violet, reporting a series of twelve cases. The series was divided into two groups. The first group included seven cases of local and generalized (bacteremic) infections with either staphylococcus or colon bacillus, and one case of chronic pyelitis due to *Bacillus lactis-aerogenes*. These patients were treated by intravenous injections of mercurochrome-220 soluble. The second group was composed of five cases of staphylococcic infection of both the local and bacteremic type, including some cases with multiple pyemic abscesses. The patients in this group received intravenous injections of gentian violet. Cures were obtained in all twelve cases.

In June, 1924, Whitman<sup>2</sup> reported equally remarkable results from the intravenous injections of mercurochrome in ten cases of chronic and subacute gonorrhoea. He said: "The rapid subsidence of symptoms in all, and the abrupt termination of symptoms in some cases was almost incredible."

In August of the same year, Young and Burkhaug<sup>3</sup>

\* From the Departments of Internal Medicine and Pharmacology of the University of Oregon Medical School.

1. Young, H. H., and Hill, Justina H.: Treatment of Septicemia and Local Infections by Mercurochrome-220 Soluble and by Gentian Violet, *J. A. M. A.* **82**: 669 (March 1) 1924.

2. Whitman, W. A.: Mercurochrome-220 Soluble Intravenously in Chronic Gonorrhoea and Its Complications, *J. A. M. A.* **82**: 1914 (June 14) 1924.

3. Young, H. H., and Burkhaug, Konrade: The Cure of Scarlet Fever Complicated with Erysipelas and Streptococcus Septicemia by Intravenous Injection of Mercurochrome-220 Soluble, *J. A. M. A.* **83**: 492 (Aug. 16) 1924.

reported cures in two cases of scarlet fever complicated with erysipelas and streptococcus septicemia that were treated by intravenous injections of mercurochrome.

Both mercurochrome and gentian violet were used in dosage varying from 2 to 5 mg. per kilogram of body weight. In two instances, doses of 7.5 mg. and of 8 mg. of mercurochrome per kilogram of body weight were used by Young and his collaborators.

The present paper presents a report of an investigation into the bactericidal efficiency of mercurochrome and gentian violet, administered by the intravenous route. The investigation consisted of two parts:

1. A study was made of the clinical results obtained from the use of intravenous injections of mercurochrome and gentian violet in five cases of sepsis, including one case of staphylococcus bacteremia, one case of streptococcus bacteremia, one case of colon bacillus bacteremia, and two cases of subacute gonorrhoea.

2. An experimental study was made of the effects of exposure of cultures of staphylococcus, streptococcus, and of colon bacillus to mercurochrome-220 soluble and to gentian violet, respectively, in dilutions which represent the highest concentration obtainable in the human body from the largest doses of the dyes that are regarded safe clinically.

#### CLINICAL OBSERVATIONS

Mercurochrome and gentian violet, in freshly prepared solutions, were employed in doses of from 5 to 7 mg. per kilogram of body weight in three cases of septicemia and in two cases of local gonococcal infections. The results obtained are indicated in the following case reports:

CASE 1.—R. D., a man, admitted, Feb. 20, 1924, complained of headache, pain in the joints and fever. The present illness was of six weeks' duration, though the patient did not go to bed until a few days previous to admission, when the symptoms became decidedly worse. On the day of admission, the patient was found dull and listless, with a temperature of 100.5 F., pulse 88 and a blowing systolic murmur at the apex. The leukocyte count varied from 9,600 to 22,200, with a differential count of from 86 to 93 per cent. neutrophils. The further clinical course of this patient is indicated in Chart 1. After the isolation of *Streptococcus hemolyticus* from the blood, mercurochrome was administered intravenously on

three successive days. There was no improvement in the clinical condition, and a blood culture taken after the mercurochrome therapy again yielded an abundant growth of the streptococcus. Death occurred several days after the last injection of mercurochrome, and the diagnosis was confirmed by a necropsy.

CASE 2.—J. U., a man, admitted, June 12, 1924, complained of chills, fever, sweats and generalized pain. The present illness began three weeks previous to admission, with fever and pain across the small of the back. On the second or third day after the onset, severe chills occurred, which continued at irregular intervals for two or three days. Then, after several afebrile days, there followed similar recurring periods of chills and fever. The clinical course of this patient after admission to the hospital is indicated in Chart 2. A blood

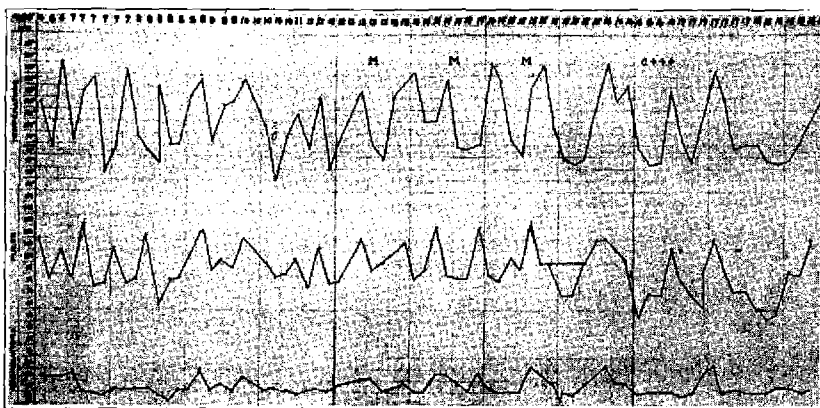


Chart 1.—Clinical record in Case 1: M, mercurochrome, 5 mg. per kilogram; C + + +, strongly positive blood culture.

culture, taken June 16, yielded an abundant growth of *B. coli-communior*. After two intravenous injections of mercurochrome, a negative culture was obtained from the blood. However, since the patient still seemed critically ill and since the temperature had begun to rise again, the mercurochrome therapy was resumed. Three more intravenous injections of 5 mg. per kilogram of body weight were given on three successive days. A blood culture taken on the day after the last injection of mercurochrome again yielded an abundant growth of the colon bacillus. Notwithstanding the positive culture, the patient's condition suddenly improved two days after the last injection, and complete recovery ensued.

A superficial examination of this record might lead one to attribute the recovery to the mercurochrome

therapy. A more careful consideration, however, discloses the following facts: 1. The general course of the temperature curve during the mercurochrome therapy is essentially like the temperature record during the three weeks preceding the onset of treatment; namely, alternating febrile and afebrile periods. 2. Although a negative culture was obtained from the blood after the second intravenous injection of mercurochrome, it will be observed that after the fifth injection, the blood culture was again positive, yielding approximately as many colonies per cubic centimeter of blood as did the original culture before any treatment was instituted. It will also be seen that the negative culture was taken during an afebrile period. In view of these facts, it seems reasonable to conclude that the recovery in this case was independent of the mercurochrome therapy.

Spontaneous recovery in *B. coli* sepsis is not at all unusual. Jacob<sup>4</sup> reported thirty-nine cases, with 60 per cent. recoveries. Coleman and Hastings<sup>5</sup> observed three cases, in all of which the patients recovered. More recently, Felty and Keefer<sup>6</sup> of the Johns Hopkins clinic reported a series of twenty-five cases, in seventeen of which the patients recovered.

CASE 3.—H. L., a man, admitted, Oct. 9, 1924, complained of fever, headache, and pain in the back. An abscess in the region between the third and fourth lumbar vertebrae, which apparently followed an attempted lumbar puncture, was opened and drained two days before admission. When first seen by us the patient was irrational, and his general condition seemed quite serious. Cultures from the blood and from the discharging abscess each yielded a growth of *Staphylococcus albus*. Chart 3 shows the clinical course of this case, indicating a progressive bacteremia, as demonstrated by frequently repeated blood cultures, notwithstanding the vigorous prosecution of mercurochrome and gentian violet therapy. The first culture, taken before any treatment was instituted, yielded approximately fifteen or twenty colonies to 1 c.c. of blood. The subsequent cultures taken during the course of treatment showed a steady rise in the number of colonies to the cubic centimeter of blood; until, in the last culture, taken after

4. Jacob, J.: Colon Bacillus Septicemia, *Deutsch. Arch. f. klin. Med.* **97**: 303, 1909.

5. Coleman, Warren; and Hastings, T. W.: Bacillus Coli Communis: The Cause of an Infection Clinically Identical with Typhoid Fever, *Am. J. M. Sc.* **137**: 199 (Feb.) 1909.

6. Felty, A. R., and Keefer, C. S.: Bacillus Coli Sepsis: Clinical Study of Twenty-Eight Cases of Blood Stream Infection by the Colon Bacillus, *J. A. M. A.* **82**: 1430 (May 3) 1924.

the patient had received two intravenous injections of mercurochrome and three injections of gentian violet in doses of 7 mg. per kilogram of body weight, a growth of approximately 100 colonies to the cubic centimeter of blood was obtained. The patient died two days after this blood culture was taken, on the third day after the last injection of gentian violet.

CASES 4 and 5.—Both patients were young men who gave a history of repeated attacks of gonorrhoea. In each instance there was abundant urethral discharge, with gram-negative diplococci demonstrable in the smears. Both patients received five intravenous injections of mercurochrome in doses varying from 5 to 7 mg. per kilogram of body weight. At the end

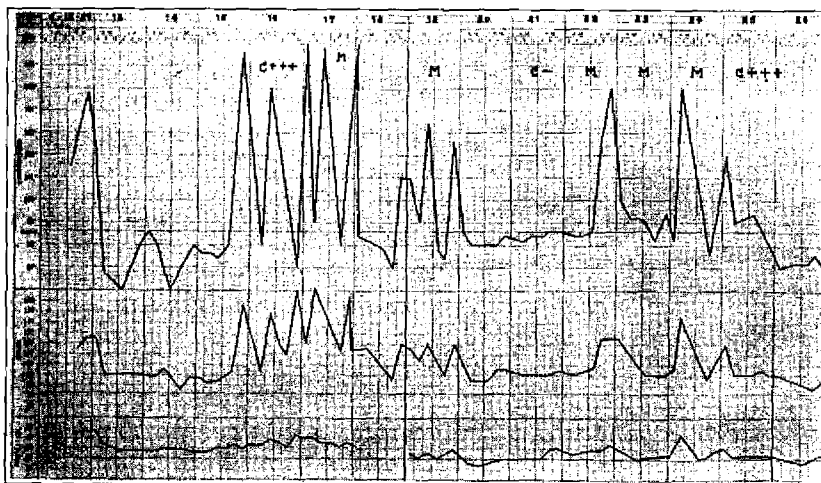


Chart 2.—Clinical record in Case 2: M, mercurochrome, 5 mg. per kilogram; C + + +, strongly positive culture; C —, negative blood culture.

of two weeks, both patients were severely salivated. There was not the slightest improvement in the local infection, the discharge being just as abundant and the organisms just as numerous as before treatment was instituted.

#### COMMENT

Although the cases reported in this paper are comparatively few, the results here indicated are characteristic of the results obtained in eight additional cases known to us, but which were not under our immediate management. Each of the additional cases terminated fatally, apparently uninfluenced by inten-

sive intravenous treatment with one or the other of these dyes.

Further evidence of the inadequacy of mercurochrome and gentian violet as intravenous bactericides is furnished by the following report of an experimental study of the direct action of these dyes *in vitro*:

#### EXPERIMENTAL STUDY

According to results obtained with experimental animals, reported by Young and Hill,<sup>7</sup> 7 mg. of gentian violet per kilogram of body weight approximates the upper range of therapeutic dosage compatible with

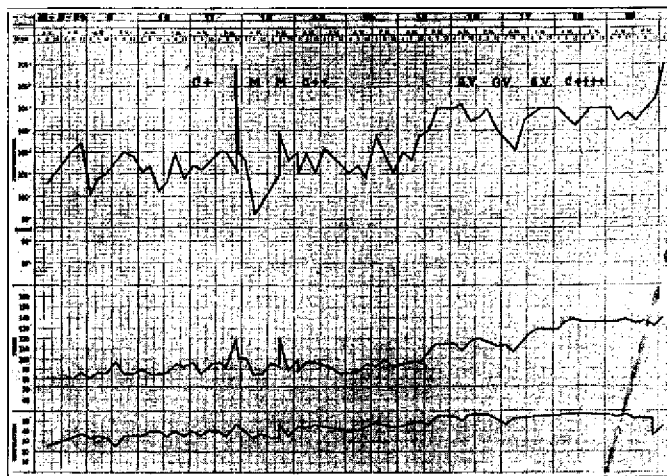


Chart 3.—Clinical record in Case 3: M, mercurochrome, 7 mg. per kilogram; G V, gentian violet, 7 mg. per kilogram; C, blood culture. The plus marks indicate the relative number of colonies per cubic centimeter of blood.

safety, particularly if repeated doses are to be used. Clinical reports indicate that mercurochrome in similar dosage not infrequently causes symptoms of excessive mercurial irritation of the excretory organs (Reed and Lum<sup>7</sup>). An intravenous dose of 7 mg. per kilogram of body weight would give a concentration in the total blood volume of approximately 1:10,000. It was therefore thought advisable to test the bactericidal properties of these dyes in that concentration in contact

7. Reed, A. C., and Lum, D. D.: Toxic Results of Dye Treatment in Septicemia, *J. A. M. A.* **83**:1681 (Nov. 22) 1924.

with organisms recovered from the blood stream of human beings.

Churchman<sup>8</sup> has shown that gentian violet in culture mediums enriched with blood retains its activity against bacteria with but little impairment for several days; but that this activity is rapidly lost in the blood stream, disappearing completely in one and three-fourths hours. In the present study, culture mediums enriched with human blood were mixed with mercurochrome and gentian violet, respectively, in concentrations of 1:10,000. These mediums were inoculated each with a culture of *Streptococcus viridans*, *Staphylococcus albus* and *B. coli-communior*, respectively. Subcultures were then made on blood-enriched broth from each of the tubes after periods of one, two and three hours' exposure.

*Cultural Results Following Exposure to Mercurochrome and Gentian Violet\**

Number of Hours Exposed to Action of Dyes	Mercurochrome-220 Soluble, 1:10,000			Gentian Violet, 1:10,000		
	Streptococcus Viridans	B. Coli-Communior	Staphylococcus Albus	Streptococcus Viridans	B. Coli-Communior	Staphylococcus Albus
1.....	++	++	++	++	++	++
2.....	++	++	++	++	++	++
3.....	++	++	++	++	++	+
24.....	++	+	+	++	++	-

++ signifies luxuriant growth; +, moderate growth; -, no growth.

\* Coleman and Bell's improved gentian violet, and mercurochrome-220 soluble (H. W. D.) were used throughout this work.

The results are indicated in the accompanying table. It will be seen from an examination of the table that both dyes, in the given concentration, were without bactericidal action on any of the organisms tested after three hours' exposure; that in the case of mercurochrome even twenty-four hours' exposure failed to destroy any of the organisms; and that gentian violet, after twenty-four hours' contact with the organisms, exerted bactericidal action on the staphylococcus alone.

SUMMARY AND CONCLUSIONS

1. Clinical observations were made on three cases of bacteremia and two cases of local gonococcal infections treated by intravenous injections of mercuro-

8. Churchman, J. W., and Herz, L. F.: The Toxicity of Gentian Violet and Its Fate in the Animal Body, *J. Exper. Med.* **18**: 579 (Nov.) 1913.

chrome and gentian violet. These observations, which were carefully controlled by cultural checks, seem to indicate that in these five cases the intravascular injection of the dyes in no way interfered with the progress of the infection.

2. Experiments on the effect of dilutions of mercurochrome and of gentian violet on the growth of staphylococcus, streptococcus and *B. coli* in vitro seem to indicate that there was no direct bactericidal action on those organisms from three hours' exposure to mercurochrome and gentian violet in concentrations of 1:10,000, representing the maximal advisable concentration of these dyes in the circulation.

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