

Colloidal Silver in Sepsis

by

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It is a well-known fact that during immunization specific protective bodies are formed, which circulate in the blood and furnish protection against infection or intoxication by neutralizing toxins and destroying bacteria, or preparing them for ingestion by phagocytes. The serological era brought us different seras intended to provoke these actions in another organism.

The sera which were made only for their antitoxic action have given the greatest success, but the bacteriolytic sera failed. Their katabolic action in destroying bacteria was successful; but in destroying them the endotoxins of the bacteria were liberated and the serum failed to neutralize the endotoxins. Hence these sera have been disappointing. All experiments to obtain an immunization against the toxins have failed, so that Wolfe-Risner has claimed it to be impossible. Wassermann explains this failure by the inability to fit amboceptors. The amboceptors are increased during immunization, but the complement remains the same. Since amboceptors without complement remain inactive, even the strongest serum is only slightly effective, in accordance with its complement contents. With the streptococcic immunization sera the inefficiency of the curative effect is sufficiently shown by the numerous methods by which different serologists have endeavored to obtain a perfect serum. The serums of Marmorek, of Aranzon, of Menzer, or of MeyerRuppel have not served their purpose in puerperal fever.

Lavern showed that arsenious acid will destroy trypanosomes in the blood. By a study of the trypanosomes and spirochetes Paul Ehrlich introduced a new phase into therapeutics: chemotherapy in contradiction to pharmaco-therapy.

In the different kinds of sepsis silver is a well-known therapeutic factor; but silver has a great tendency to enter into insoluble combination with the chlorides and phosphates of the blood plasma, which minimizes its antiseptic effect. In 1897 Konig showed experimentally that the antiseptic action of different salts of equal molecular concentration differed according to the degree of dissociation. The more dissociated a solution the greater its antiseptic activity.

Since Lenard discovered the x-rays the study of them by Rontgen and his co-workers, together with the study of the emission of rays from certain metals, has introduced a new theory into physico-chemistry known as the electronic theory. According to this theory the atoms are not the ultimate fractional parts of the molecules, they are only theoretically there. Each atom is composed of several hundred electrons. The hydrogen atom, for instance, has about 800 electrons, each of which is charged with electricity. Whenever a compound goes into solution its molecules are changed into ionized atoms. In every electrolyte there is a perpetual movement of the ions in indefinite directions. When an electrical current is sent through a solution it converts

more of the molecules into ions and they become definitely directed in their wanderings, each ion possessing an electrical charge.

Mercury as a germicide gives a good example of ionic activity. If we study mercuric iodide and mercuric bromide, each containing the same amount of mercury per volume, we find they have a different activity upon living bacteria. It is the individual ionic state which is important and not the quantity of mercury.

Laboratories have prepared by electrolysis a colloidal silver called electrargol. Electrargol is heterogeneous including two essential parts, a liquid medium and solid particles. The solid particles are seen only by the ultramicroscope on a dark ground, as a multitude of (0.1-0.01 mikron) particles moving in the solution, each of these having an electrical charge. Every ion has its own antiseptic power, hence the electrargol combined by these particles represents a larger surface of antiseptic power than other colloidal salts of silver.

What do we expect from an ideal general antiseptic? First, a real and complete katabolic action on bacteria and, second, a protecting influence on the body by stimulation of leukocytes to phagocytosis. From this viewpoint electrargol is ideal.

We obtained virulent streptococci from Parke Davis, made cultures in ascites bouillon, putting five drops of electrargol into each tube. No growth was obtained. We sprayed electrargol onto a growth of bacteria on ascites agar. We transplanted the islands which came in contact with electrargol and those which did not. We obtained growth in our cultural tubes from those that did not come in contact with electrargol spray, but no growth from the others.

As to the stimulation of leukocytosis, we injected rabbits with half c.c. electrargol. The white blood cells raised from 6000 to 10,000-13, the polymorphonuclear leukocytes from 50 or 60 per cent. to 80 or 90 per cent. It is interesting to show that twelve hours after injection there appeared a slight leukolysis (7000 to 6600) but after twenty-four hours the high leukocytosis always appeared.

We used in the following line of experiments 4-pound rabbits and bacteria of uniform virulence. Two classes of animals were studied, those injected with virulent streptococci and those protected by injection of electrargol and later injected with streptococci. Only one animal from each class is noted in this report since each is a fair illustration of what happened to every animal treated.

Rabbit A.—Four pounds. Temperature 96. Leukocyte count 6600 with 34 per cent. polymorphonuclears. Injected with ½ c.c. streptococcus emulsion intraperitoneally. Next day quiet, ate normally, temperature 96.4, leukocyte count 15,000 with polymorphonuclears 76 per cent. After three days restless, leukocyte count 17,000, temperature 102. Blood culture shows streptococci. Dies after seven days.

Rabbit B.—Four pounds. Temperature 96.5. Leukocyte count 8000 with 43 per cent. polymorphonuclears. Injected with 3 c.c. of electrargol. Twelve hours later injected the same amount c-c-) of the same streptococcus emulsion as in rabbit A. Remains quiet, acts normally.

Next day leukocyte count 10,000 with 60 per cent. polymorphonuclears. After forty-eight hours blood culture did not show any growth. After seventy-two hours rabbit is lively, developing no symptoms of sickness. Leukocyte count 9000, animal remains well.

So we see, in vivo as in vitro, that this colloidal silver possesses the requirements demanded in a chemical general antiseptic. Electrargol does not go into insoluble precipitate either with the albumins or with the chlorides of the blood plasma, hence its effectiveness antiseptically is retained in the blood stream. Being a colloid it does not, like a crystalloid, pass through animal membrane by dialysis which would permit of its rapid elimination, but remains long in the tissues performing its antiseptic duties.

We noticed in our patients treated by electrargol another important point. The temperature rises three to five hours after administration. This we believe shows that, after destroying the bacteria, the toxins are liberated into the blood stream and, as foreign albumins, cause the intoxication, this being soon overcome by the action of the drug.

Colloidal silver has, as we know, been used in septic cases before now, and there is much literature on the subject. Collargol differs from electrargol in that it is a chemically made colloid silver, while electrargol is obtained by electrical means; that is, by passing an electrical current through the solution, causing the ions to wander in the solution according to strict physical laws which allow each ion separately to accomplish its germicidal and fermentative action.

Electrargol, in the last few years, has been much used in different septic conditions; not however, so far as I know, in the bacteriemias. Here the results are very satisfactory. Let me cite some of our own cases which were with one exception treated in Providence Hospital.

Case I.—Referred by Dr. George, who later reported to me the following: G. L., pattern-maker. English. March 16, 1915, received slight scratch on dorsum of little finger of left hand. He consulted me the next day with a developing lymphangitis. Glands in the axilla slightly enlarged and tender, headache, etc., had had a chill. Finger was dressed with alcohol and boracic acid and icebag applied. On the 21st, pulse 84, temperature 96, respiration normal. On the 22nd, another chill, pulse 120, temperature 102. Finger was incised, the dressings renewed. A scarlatinic rash made its appearance on the face, neck and chest. Headache intense, complained of dark spots before the eyes. No delirium. On the 23d, A. M., pulse 100, temperature 100; 3 p. M. had another chill, pulse 118, temperature 102.3. The rash had extended over the remainder of the body. On the 24th, A. M., pulse, v.a. 105, temperature 101. He was seen at noon in consultation with Dr. Brown; at 3 P.m., 5 c.c. electrargol was administered intravenously, pulse 120, temperature 103, at 6 p. M., pulse 135, temperature 104. 25th, A. M., pulse 110, temperature 100, headache had disappeared; decidedly better condition, p. M., pulse 100, temperature 101. 26th, A. M., pulse 100, temperature 98.8; p. M., pulse 100, temperature 99.7. 27th, noon, pulse 60, temperature 98.8. The rash had faded. Desquamation had begun—the epidermis of the hands and feet peeling off in large casts conforming to the shape of the fingers and toes. April 5, able to visit me at my office and said he felt able to go back and do light work. April 6, I was called by his mother, who said he had caught a severe cold. He contracted an influenza which kept him in bed for several days. He recovered and is, at present, in good health.

Case II.—Referred by Dr. Meddaugh. Mrs. G. S., aet. twentyfive, housewife. Previous history had nothing of importance. Was confined March 8. On the sixth day, her temperature went up to 100, she was restless, pulse 100, respiration 30. She was admitted into hospital March 15. Temperature suddenly rose to 104, pulse 130, respiration 30, leuokcyte count 13,000 with 83 per cent. polymorphonuclears. In the afternoon she had a chill lasting thirty minutes, another chill at 6 p. M., and another at 10 p. M. Temperature rose after last chill to 106.2. Delirious during the night. On the 16th, she had three chills during the day, each lasting from twenty to thirty minutes, temperature 106.8, pulse 130, respiration 30.

Very cyanotic, restless and delirious. Cervical smears showed streptococci and staphylococci. Treatment only local douches and bromides. On the 17th, electrargol, intravenously, 5 c.c. at 10 A. M. Temperature dropped to 99. On the 18th, chill lasting thirty minutes. Temperature rose to 105, pulse 130, vomiting, perspiration, rash appeared on extremities. On the 19th, electrargol, intravenously 5 c.c., temperature 106, pulse 130. At six o'clock in the morning, temperature suddenly dropped to 97, pulse, 60. On the 20th, electrargol intravenously, temperature rose to 104, pulse 140. After four hours, temperature dropped to 100. Patient still irrational, but no chills. 21st and 22d, no chills, temperature varied from 97 to 102, headache but quiet. 23d, electrargol, intravenously, 5 c.c., temperature 100, pulse 60, respiration 20. 24th, temperature 98, pulse 90, respiration 20, slept well, no rise of temperature. She left the hospital March 28, sixteenth day.

Case III.—Referred by Dr. Haverstock. This case is of interest, because of the exact data of the temperature and pulse after electrargol injection.

Mrs. S. Septic after abortion. Temperature varied between 98 and 105. Staphylococci found by cervical culture and pure streptococci in the blood. She suffered from acute nephritis and acute hemiplegia. Desperate case without any hope. Resistance of the patient on admittance so low that leukocyte count was only 5000 but 90 per cent. polymorphonuclears. Chills every hour, unconscious. The patient could not be saved, but the electrargol injections stopped the chills for forty-eight hours. Previously Van Cotti's vaccine raised the temperature from 102 to 104. Electrargol, intravenously, had following effect: Given at 10.30, temperature 101, pulse 120; 11 o'clock, temperature 102, pulse 120, respiration 24; 12 o'clock, temperature 101, pulse 100, respiration 22; 1 o'clock, temperature 100, pulse 98, respiration 24; 2 o'clock, temperature 100, pulse 94, respiration 22; temperature remained for the next twenty-four hours under 101; again, temperature 104, pulse 130, respiration 30. Electrargol 5 c.c., intravenously, 10 A. M. Na. M., temperature 102.4, pulse no, respiration, 24; 12 M., temperature 102, pulse 108, respiration 24; 1 p. M., temperature 101, pulse 100, respiration 22; 6 P.m. same; 10 p. M. same.

Case IV.—Polish woman, aged nineteen, small in stature. After a prolonged labor, she was instrumentally delivered of a 12½-pound boy. She was torn through the rectovaginal wall nearly up to the cervix. A few days later she developed chills and fever. When admitted to the hospital, her temperature was 105, pulse 130. She was delirious and had no remembrance of her first four weeks in the

hospital. During the first eleven days she was on another service where the usual treatment was carried out. Her condition was desperate. Temperature varying from 98 to 106, pulse 80 to 135. Through the courtesy of the other service we were permitted to try colloidal therapy. Examination: General appearance one of exhaustion. Skin light lemon color with brown spots. Facies septic. Mind a blank. Localized findings negative, other than vaginal injuries. Temperature 104, pulse 90. Culture from cervix showed colon bacillus and a streptococcus, culture from blood staphylococcus aureus. Leukocyte count 9600. Two days later, 9 A. M., temperature 99; pulse 90. Injection electrargol 10 A. M., at noon temperature 102, pulse 105. Next day, temperature 100.8, pulse 100. Injection of electrargol at 12 M., temperature 101.7, pulse 100. Never again above 100. After forty-eight hours the temperature remained normal. Two weeks later the vaginal injuries were repaired, healing by first intention. She made a splendid recovery, leaving the hospital four weeks later in good physical condition. She lately reported that she is several months pregnant.

Case V.—A very interesting result was obtained in the following case, referred by Dr. H. W. Yates. Polish woman, aet. twenty-five. Was admitted to the hospital on July 31, the ninth day after confinement. Temperature 104, pulse 130, respiration 40. Dry tongue, septic facies, restless, leukocyte count 15,000 with 97 per cent, polymorphonuclears. Quinine and brandy had been given every three hours. August 1, temperature 104.4, pulse 120, respiration 30. August 3, electrargol 5 c.c., intravenously, temperature dropped to 99, pulse 110, respiration 24. The next day temperature remained 99, but patient was more comfortable and resting, tongue moist. After a week the leukocyte count was only 6700 showing the prompt effect on the infection by elevation of the temperature in the first hour, followed promptly by a gradual but steady drop.

Thanks are due to my associate, Dr. Nickolas Galdonyi, who directed most of the laboratory experiments, and to Miss Gertrude Beno, my technician, who did much of the detail work in the laboratory.

DISCUSSION.

Dr. Bauchman, Richmond, Virginia.—This is certainly a very interesting paper. It takes me back to 1900 when I visited Crede the younger in Dresden. You are no doubt familiar with the colloid Crede ointment. He invited me to see him operate. He took a probe, stuck it into an abscess, put some of his silver solution on it, and offered me to put it in my mouth. I did not care to do so, but he did put it in his own mouth. He told me that this silver solution would cure any sort of septic trouble.

I am very much interested in this matter, I have seen a few cases of sepsis, and I have used this ointment in the treatment of septic cases. Dr. Brown has given us an intelligent and interesting explanation of the faith Crede had in him. I believe that cases of septicemia which are not of streptococcic origin are going to get well. In streptococcus infection I believe in giving them fresh air and as little interference as possible. I am now speaking of puerperal septicemia. I have discarded the Crede ointment method for some time because I have seen no improvement with it. I have not seen any practical effect from the use of that ointment such as we have here with the method of silver injection recommended and advocated by Dr. Brown. His paper is profoundly interesting to me.

Dr. Henry Schwarz, St. Louis, Missouri.—To me Dr. Brown's paper is the most important contribution to this meeting, for the reason that in cases of puerperal septicemia we are up-to-date absolutely helpless, I care not what system or method of treatment is used. In any case where you have a virulent streptococcus in the blood, the woman is going to die. Take a case that is not of the ordinary streptococcic variety, but the streptococcus is brought from a case that has died of erysipelas or something else. We have tried time and again every new thing that came up; we have tried antistreptococcic sera, and vaccines, and for the reason stated by the essayist, the sera, while they work well on animals and in animal experiments, do not work so well on human streptococci because in animal passage they change their receptors.

We have used the Crede ointment, but that is altogether different from the silver to which Dr. Brown referred. In Credo's ointment we have not been able in our animal experimentation to show exact results which Dr. Brown seems to have obtained.

I would like Dr. Brown in closing to be a little more explicit. I did not quite understand whether he said it was possible to catch up with the infection or not; whether he could give a loop of this culture to the animal and have death follow at the end of forty-eight hours, whereas the other animal, that receives the electrargol six hours after infection has taken place recovers.

In the paper I read at the Syracuse meeting I said we tried to make a streptococcic vaccine, and in our animal experiments we were never able to catch up with the infection. We could immunize the animal by starting immunization weeks ahead. We could immunize a rabbit against streptococci that would kill the control animal at all times, but we were never able to control the infection after it got a good start, be it ever so short. Of course, in the cases of puerperal sepsis, where the streptococci are found in the blood, there seems to be conclusive evidence that in the electrargol we have such a potent agent that it will be the duty of every man in my position to try it out. It will be one of the next things I will do. It is the first time I have heard of this work, and when I hear of such work I take it up immediately.

Some time ago I read in a journal that some man in New York had used formaldehyd injections and had cured septicemia. I think it was Dr. Elbrecht or my assistant who spoke to me about this. We have been working and experimenting ever since, but we have not so far been able to find anything that will stop a streptococcic infection if it is of the right virulence in a puerperal woman.

Dr. Brown (closing the discussion).—Some one has said that the streptococcic cases rarely get well, while the staphylococcus cases recover if left alone. Of course, there is a vast difference in the way in which the two infections act. A staphylococcic infection usually localizes itself. It does not become general. A streptococcic infection never localized itself. In one of these cases, we had a bacteriemia due to the staphylococcus aureus. In two we had a streptococcus. In one of the others the case was not followed out because my assistants were both out of town at that time. The fifth one was a private case, and we did not have the opportunity of studying it as we wished.

A mistake is frequently made by trying to use too many antiseptics, losing sight of the fact that the ionization of the drug is the factor which brings about the good result.

I do not see any hope for treating streptococemia in any other way than by getting at it through the blood stream. Take a rabbit that has recently given birth to its young, and throw into the uterine cavity streptococci, and six minutes later kill the animal, you can demonstrate the streptococcus in the liver. You can see how useless it is to use anything in the way of local means. We must consider the thing systemic and put something that is directly antiseptic in the blood. For this, the electrargol, which is more highly ionized than any other silver salt is probably the one of first choice.

It comes in bulk, also in ampules of 5 and 20 c.c, and with each ampule there is an ampule of normal salt solution which is added to the electrargol, making the electrargol isotonic.

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