

hours in warm water. They are very susceptible to temperatures above 42 to 43° C. and show very little resistance to antiseptics, particularly the silver salts.

The gonococcus secretes no soluble toxin, but contains an endotoxin or toxic "protein" which causes local and general symptoms in both man and animals. Dead cultures produce an inflammatory exudate in the peritoneal cavity of guinea-pigs and mice, resulting in death if the dose is sufficiently large, and when injected into the urethra of man a temporary inflammation results. An actual infection of any sort can not be produced in animals; the cocci are killed without being permitted to proliferate. The endotoxin is fairly resistant to heat, being destroyed only after prolonged exposure to a temperature of 100° C.

In man the mucous membranes and endothelial surfaces are more susceptible to infection than other tissues. The urethra of male and female at all ages, the conjunctiva in the new-born, the vagina, uterus and tubes are probably the most susceptible. Less susceptible are the vagina in older women, especially those who have borne children; the bladder, and in adults the conjunctiva. It is remarkable that there are so few cases of gonorrheal ophthalmia in adults, considering the opportunities for infection. Infection of the mouth, nose and tear sacs is extremely rare. Extension from the urethra to adjacent structures takes place either by way of the surfaces, as in involvement of the prostate, epididymis, glands of Bartholin, uterus, tubes, ovaries, peritoneum, bladder and kidneys, or by way of the lymphatics as in infections of the periurethral tissue or cellular tissue of the pelvis. Infections of the bladder and kidney, and not infrequently the prostate, Fallopian tubes and pelvic tissue are of a mixed character (staphylococcus, streptococcus), but not necessarily so. Arthritis, tenosynovitis, endocarditis, which usually is vegetative but may be ulcerative, are the more common metastatic complications. Less frequent are pericarditis, pleuritis, subcutaneous abscesses and iritis. As to whether the cutaneous phenomena sometimes seen are due to metastases or are of purely toxic origin seems to be undetermined. The blood stream may be infected by way of the lymphatics or local blood vessels (gonorrheal thrombosis).

The influence of the enormous phagocytosis of the cocci on the course of gonorrhea is unknown. Since the ingested cocci usually have a typical form and stain well, it would seem that they resist the action of the leucocytic ferments. Likewise the nuclei of the leucocytes usually stain well, hence there is no evidence of a marked toxicity of the cocci for these cells. The mechanical imprisonment of the organisms by the leucocytes may be of influence in localizing the infection.

During the course of gonorrhea "there takes place a pronounced metaplasia of the epithelium in which the cylindrical cells are changed into a more cuboidal and even pavement form." Following this change the gonococci are limited to the surface of the altered epithelium and penetrate more deeply only in the vicinity of the glands and crypts. "Eventually the gonorrheal process is limited to such isolated points and the gonorrhea thereby enters into a chronic stage" (Observations of Finger, cited by Neisser and Scholtz).

The conditions which cause the subsidence of acute gonorrhea and allow it to persist as a chronic infection have been the subject of much speculation, unproductive for the most part. It is not due to a decrease in the virulence of the cocci since their original infectiousness is retained for others; nor does the local resistance of the mucous membrane reach a high point, since reinfection, or better "superinfection" is possible at any time. A man suffering from chronic gonorrhea and having infected his wife, may again be infected by his wife when the gonorrhea of the latter has become subacute or chronic. It has been suggested that the condition in chronic gonorrhea may be one of "mutual habituation between the mucous membrane and the gonococcus," i. e., a habituation between this particular mucous membrane and this particular gonococcus. Because of prolonged existence under unvarying

conditions, the growth energy of the organism may have become less, whereas, if it is placed in a slightly different medium (transference to another individual), its growth energy (ability to proliferate), becomes augmented, and reinfection of the original host with the same strain becomes possible.

It has often been noted that subsequent attacks run a milder course than the primary infection, but susceptibility is always present.

Mendez, Calvino, and also de Christmas have immunized with the coccus or toxic substances prepared from it. By growing the organism in serum bouillon de Christmas prepared a toxin, the toxicity of which was tested by intracerebral injections in the guinea-pig. Immunization of the guinea-pig resulted in a serum with antitoxic properties. Corroborative work has not been published.

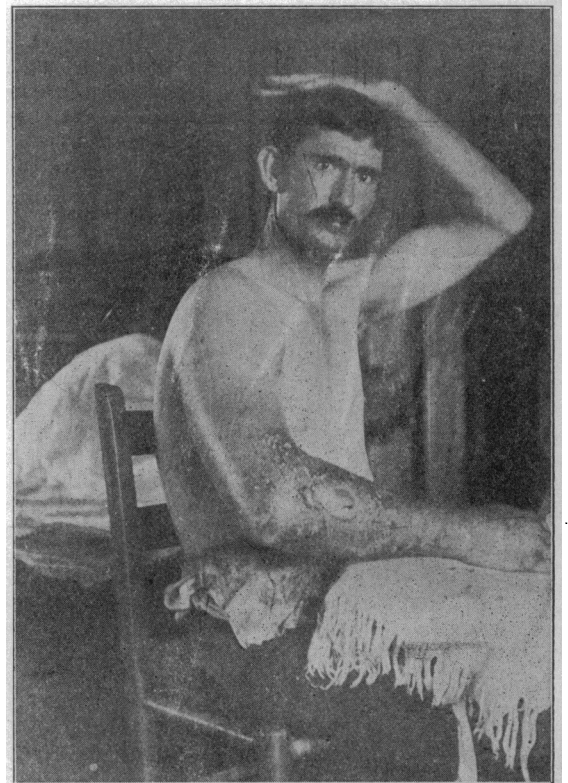
[This series of articles closes with this issue. During the time that they have been appearing in "The Journal" we have received repeated requests to have them reproduced in book form, and the book is now in press. In addition to the subjects considered in the series, the book will contain chapters on infections with the streptococcus, staphylococcus, the diseases of protozoan etiology, and those of doubtful or unknown etiology, including among the latter, smallpox, vaccinia, chickenpox, scarlet fever, measles, German measles, typhus, syphilis, yellow fever, hydrophobia and whooping-cough. The articles, revised and collected in book form, will include a consideration of these diseases from the standpoints of infection and immunity. The book will be ready for delivery in January. The price will be \$1.50.]

### Clinical Notes

#### RATTLESNAKE BITE.

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A man was bitten August 14 by a very large rattlesnake. For about thirty hours it seemed that he was about to suc-



cumb at any time, but he suddenly began to improve. He suffered intensely for twenty-four hours. The accompanying

photograph was taken August 17, about eighty-two hours after the injury. There was only a little sloughing at the point of injection of the poison, but the man was incapacitated for work about thirty days. As to treatment, the arm was corded tightly, an abundance of whisky was given, and hypodermic injections of strychnin 1/40 g. ever forty-five minutes. He has gone to work and has a good arm.

## FATAL CASE OF BLACKWATER FEVER SUPERVENING ON AMEBIC DYSENTERY AND SHOWING MALARIAL PARASITES IN THE BLOOD.\*

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**Patient.**—Lieutenant M. de G., aged 26, Portuguese, was first seen Dec. 20, 1904.

**History.**—The patient had been in Africa two years. The first year and a half of this time were spent on the coast, the last six months in the interior. He has never suffered much from malaria nor blackwater fever. Recently he was again sent to the coast, where he spent three weeks. As he was leaving to return to the interior he was attacked with a sharp diarrhea and passed some blood. He recovered in a few days and continued his journey. He has had some looseness of the bowels, with occasional pains, ever since. After his arrival at Bihi fort he had a relapse of the "diarrhea" and was in considerable distress and very weak. He thought he also had some fever, so he came to me for advice.

**General Condition.**—The patient was thin, weak and feverish. He had no appetite. His tongue was foul. Temperature was 102.4 F., pulse 93, respiration 28. The spleen was slightly enlarged. There was tenderness over the lower bowels. The other organs were normal. At stool there was moderate tenesmus. He had taken no medicine except a diarrhea mixture, ingredients unknown. He considered this the second day of his disease (relapse).

**Examination of Feces.**—The stools were small and unformed, consisting almost entirely of blood and mucus. There was one moderate-sized slough. Under the microscope many amebæ morphologically identical with *Amœba coli* (Lösch) were seen.

**Examination of Blood.**—Both fresh and stained specimens were examined, one of each. In the latter two malarial parasites were seen; both were small intracapsular forms. The result of a differential leucocyte count was as follows (about 50 cells counted):

Polymorphonuclears	51.5 per cent.
Lymphocytes	26 per cent.
Large mononuclear	17 per cent.
Transitional	3 per cent.
Eosinophiles	2 per cent.

The initial and succeeding erythrocyte counts are shown in the chart.

**Examination of Urine.**—The urine was dark but clear. The spectroscope revealed none of the compounds of hemoglobin. There was a trace of albumin.

**Course of the Disease.**—The patient was placed in bed (11 a. m.), and small doses of Epsom salts in solution every hour were prescribed. He was placed on liquid diet with a little brandy. In spite of frequent sponging of the body the temperature steadily rose until 5 p. m., when the hemoglobinuria set in.

**Re-examination of Urine.**—After the hemoglobinuria set in, the urine was re-examined; the color was about like that of porter or stout. There was a dirty-gray sediment, showing under the microscope debris, masses of hemoglobin, and some hyaline and granular casts. The urine was not spectroscoped at first. In later specimens the bands of both oxyhemoglobin and reduced hemoglobin could be seen by shaking up the urine, examining it, adding ammonium sulphid and examining again.

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**Further Course of the Disease.**—*Amœba coli* persisted in the stools (which showed some improvement) throughout the attack, but malarial parasites were not demonstrated in three successive blood examinations. On the morning of the sixth day of the disease the temperature was found to have spontaneously fallen to 101 F. The following day severe hiccoughs set in which nothing availed to control. The patient died at 4:20 p. m. on the twelfth day.

**Treatment.**—The treatment pursued was entirely symptomatic and expectant. The saline routine for the dysentery, liquid nourishment and stimulants were administered for the weakness and the usual ineffectual gamut of sedatives and other devices were tried to control the hiccoughs. Quinin was not administered at any period of the attack as hemoglobinuria was feared from the first.

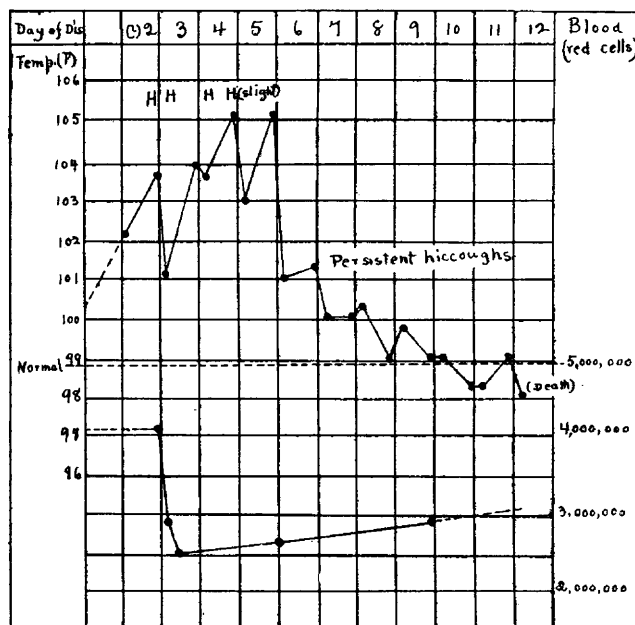


Chart 1.—The blood counts were made on the Thoma-Zeiss hemocytometer. In the first two counts, the blood was also centrifuged and the reading on the hematocrit compared with the result of the actual count. H = hemoglobinuria.

### REMARKS.

1. This is the thirty-fourth case which I have studied more or less carefully in West Africa. Of this series 29 patients recovered.

2. The case just recorded is the only instance in which death occurred during the first attack. This may be explained by the previous and synchronous dysentery.

3. In three cases malarial parasites were seen in the blood immediately preceding the hemoglobinuria. In the present case the return of the dysentery probably brought about an explosion of latent malaria, and the two conditions combined were able to produce the physiologic depression and hypotonicity of the blood that invited the intercurrent hemoglobinuria.

4. The question of the relation between malaria and blackwater fever is of great interest, but too intricate to be discussed in a paper of this kind. I believe that they are related in some way, and I have shown that in southern Angola the geographical distribution of *Myzomyia funesta*, Giles (the principal carrier of *H. præcox* in West Africa), severe malaria and hemoglobinuric fever closely coincide. The precise character of the relation between the two diseases (which is disputed by some) has not yet been shown.