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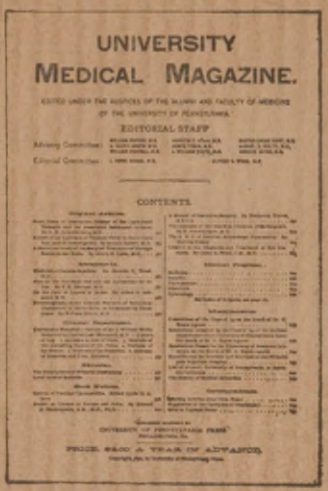

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CONTENTS.

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A STUDY IN SCARLET FEVER: APPARENT TRANSMISSION OF IMMUNITY BY THE INOCULATION OF HUMAN BLOOD SERUM.

By Albert S. Ashmead, M.D.,

New York.

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A STUDY IN SCARLET FEVER: APPARENT TRANSMISSION OF IMMUNITY BY THE INOCULATION OF HUMAN BLOOD SERUM.

By Albert S. Ashmead, M.D.,

New York.

On June 1, I was called to attend Willie D., aged 4½ years, whom I found suffering from scarlet fever. He had been stricken two days before with severe vomiting, prostration and high fever. The night of May 31 the eruption had appeared. When I saw him he was wildly delirious; vomiting had persisted all the time; he was restless; temperature 104° F.; pulse, 130; eruption appearing generally over the body, face pale, features pinched, tonsils swollen, fauces and throat intensely red, strawberry tongue. I gave him ten grains of citrate of potash every two hours, and anointed the body with carbolic vaseline, ℥ss to ℥ij, and injected in his fore-arm, just below the elbow, thirty minims of pure blood serum, taken from a blister on the breast of my own child, who had had scarlet fever five years before, having been under the care of Dr. Edward L. Partridge. The sister of my patient, Lizzie D., aged 2 years and 9 months, had never had scarlet fever; she slept with her brother. I injected a portion of the same blood serum into her arm as a preventive. On June 2 the efflorescence on the boy was full and intense, and very dusky; in fact, the most intense eruption I have ever seen; it was complete from head to foot; temperature in axilla, 101° F.; in rectum, 101½° F.; the glands at the angle of the jaw were swollen. A second injection was given the patient, and the girl was also inoculated again. On June 3 the boy's eruption was fading; temperature in axilla, 100° F.; in rectum, 100½° F.; pulse, 120; several scars on the body were very white; boy and girl both injected again. On June 4 desquamation plentiful at the point of insertion of the serum; the eruption has rapidly faded, and almost disappeared; temperature, 100° F. in axilla, 100½° F. in the rectum; boy and girl both injected. June 5, desquamation spreading over legs, arms and neck; throat symptoms disappearing; the only remnant of eruption is over the back and the front of the body; temperature in axilla, 99½° F.; in rectum, $100\frac{2}{10}$° F.; pulse, 120; the boy eats heartily; both boy and girl received another injec-

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tion. June 6, desquamation general, scaling in large sheets; throat symptoms have entirely disappeared; appetite good; temperature in axilla, 99¼° F.; in rectum, 100° F.; both receive an injection. June 7, desquamation rapidly ending; temperature in axilla, $99\frac{2}{10}$° F.; in rectum, $99\frac{8}{10}$° F.; pulse, 108; appetite good; both receive injection. June 8, normal temperature; pulse, 96; no redness in fauces; desquamation ending; appetite excellent; injections repeated. June 9, temperature normal; pulse, 96; desquamation almost ended; the boy passed at one time ten ounces of urine; the passage of urine has been plentiful throughout; injections given. June 11, temperature normal; pulse, 96; desquamation ended, except on the index fingers and calf of one leg; no throat symptoms; child dressed and moving about as usual; no one would take him for a convalescent; injections repeated. June 13, evidences of dropsy in the boy's face; examination of urine shows presence of albumin; specific gravity, 1025; gave him digitalis, tincture of iron and muriate of pilocarpine; ordered hot baths at night, and placed him on an exclusive milk diet. June 15, swelling in the face diminished; no swelling in the legs; very smoky urine; only two ounces of urine passed in the last twenty-four hours. June 16, about the same. June 17, no fever; increased swelling of face; no swelling of legs; passed two and a half ounces of urine in the last twenty-four hours; vomiting. June 18, vomited four times; face very much swollen; some pitting in the legs; three ounces of urine passed in twenty-four hours; some desquamation on one palm; none on the soles; applied a blister of cantharides to the loins, three by six inches; has had a good passage since giving him ten grains of compound jalap powder. June 18, evening; surprising diminution of dropsy; passed five ounces of urine since morning; skin moist; he had two bowel movements; blister opened and dressed. Fifteen minims of this blister serum inoculated in the arm of the sister, and fifteen minims inoculated in a white rabbit; fifteen minims of precipitated albumin from the urine of the boy also inoculated in a second white rabbit.

The analyses of five specimens of urine taken on the third to fifth days of desquamation, give these results:

(1) Specific gravity 1025, strongly acid, oil globules abundant in quantity, a trace of epithelial debris from the kidney, a few epithelial casts, a few granular casts (narrow fragments), a trace of oxalate of lime, a few blood casts (narrow fragments).

(2) Strongly acid, specific gravity 1025, numerous narrow convoluted granular casts, a trace of epithelium from mucous surface of the bladder, diplococci numerous.

(3) Granular casts abundant.

(4) Epithelial fragments, a few broad casts, numerous granular (narrow) casts, a trace of phosphate of lime, a trace of pus corpuscles.

(5) A few granular casts, sulphuric acid .8, water 94 (to f℥i), a trace of urate of soda.

In every one of these specimens the polariscope[1] showed 3 per cent. albumin. In each specimen there were about 2.06 grains urea to the fluid ounce.

June 19, passed in the night three ounces of urine; in the evening, facial dropsy was much diminished; less albumin in the urine; passed two ounces this morning. June 20, five ounces of urine passed since last night's visit; slept well; less dropsy in the face; some in the legs still; albumin steadily diminishing; absolute milk diet continued. An analysis of the blood serum of the patient, which was inoculated into the girl and the rabbit without producing sickness in either, showed streptococci pyogenes in abundance, and leucocytes without ameboid movement. June 21, boy passed eleven ounces of urine. June 22; eighteen ounces of urine passed, rapid convalescence evidenced by the appearance in excessive quantity of urates of ammonia and soda, and acicular uric acid crystals.

June 26, the white rabbit subcutaneously inoculated with the albumin of the urine, and which had been ailing ever since the operation, died.

Examination of the blood serum taken from the boy June 18, by the Doremus' apparatus, showed 4.06 grains of nitrogen to the fluid ounce. Abundant streptococci and spores were seen in the microscope, with $\frac{1}{25}$-inch objective (1500 diameters). Leucocytes in excessive quantity, granular matter well marked and well defined in outline. The streptococci were freely scattered in the field of observation.

Thomas K., aged 6 years and 8 months, on the eleventh day of desquamation, fingers peeling like gloves; one fold of skin *en masse* from the buttocks; throat symptoms very intense; diphtheritic membrane on one tonsil; no albumin in urine. Blood serum examined under the microscope on the thirteenth day of the disease; 1000 diameters ($\frac{1}{16}$-inch homogeneous immersion lens) shows leucocytes with ameboid movement, granular matter not marked, and indefinite in outline; no streptococci; urine neutral; specific gravity 1010, ninety-seven parts of water. Ten minims of this serum was inoculated into the little girl, the sister of the first case of scarlet fever. No infection resulted.

Blood serum in the second case of scarlet fever, seventeenth day of the disease, 1000 diameters ($\frac{1}{16}$ inch homogeneous immersion objective) shows in the leucocytes protoplasmic movement very active, very

[1] Wentskie-Schiebler. Franz Schmidt and Hoensch, Berlin.

distinct; granular matter well marked. Doremus' apparatus shows in this serum 1.23 grains of nitrogen to the fluid ounce. Examination of the urine of the same case, on the same day, gives specific gravity 1012, acid, 95 parts of water, urate of soda and oxalate of lime, and no albumin by one to 40,000 test, Millard's solution.

Examination of a drop of blood of this case on the same day (seventeenth), that is at the full stage of desquamation, 1000 diameters ($\frac{1}{16}$-inch objective homogeneous immersion) shows the leucocytes actively at work; ameboid movement very distinct; granular matter well defined; fibrin coarse in texture, excessive in quantity; red corpuscles slightly plastic and in irregular masses or hummocks and not inclined to form nummular rolls. It is now sixty days since the first boy developed scarlet fever. His serum when inoculated into his sister, who had never had scarlet fever and whose association with her brother has been of the closest kind throughout, no isolation whatever being made, sleeping with him, fondling and kissing him, did not communicate the disease.

It may be objected that this test was not a fair one, as the immunized blood serum from my own child was also inoculated into the boy, and that if there was any protective principle it might have acted on the boy as well as on the girl. I therefore used a further test. I took the blood serum of the second case of scarlet fever and inoculated it in the girl. She did not take scarlet fever.

There are in the first case of scarlet fever the following points of interest from a clinical point of view: The quick fall of temperature following the first insertion of immunized blood serum, its continuance at about 100° F., the early commencement of the desquamative stage, its commencement at the points of inoculation and its early complete ending.

The death of the rabbit inoculated with albumin would at the first blush indicate a toxic principle in the albumin of scarlet fever, but subsequent careful experiments with this same albumin precipitated with alcohol filtered through absorbent cotton, washed with distilled water and evaporated, failed of a toxic result when inoculated in a white mouse, white rabbit and guinea pig. The presence of nitrogen in excess in the blood serum of the two cases with and without the presence of albumin in the urine, evicently has a connection with the disease. The white corpuscles of the blood seem, therefore, to have in scarlet fever the function of carrying nitrogen,[1] the product of decomposing tissue, to the emunctory organs, the skin and kidneys. They

[1] The sweat of man contains 0,452 per cent. albumin. The total nitrogen is more considerable than the nitrogen of the urea in the sweat, the excedent of nitrogen belongs in great part to the albumen with albuminates of the sweat, Gaube, Paris. Hydrozymases and albumen in human and animal perspiration.

are, therefore, not alone phagocytes, they are chemists and scavengers, and in their ameboid movement they encircle particles of foreign matters or organisms, not to feed on them, but to carry them to the dumping grounds of the economy.[1] In their normal emigration through the capillary walls they carry out the refuse and then return from the lymph spaces to their regular habitat.

A poison, like that of scarlet fever, entering from the air into the current of blood through the mouth and lungs, throws possibly an extraordinary amount of work upon the leucocytes, and in the struggle, if there is any interference with their work of elimination through the natural outlet, the skin, such as imperfect desquamation, contraction of the capillaries by cold, too short a period of desquamation, the leucocytes perish and give up their serum albumin to the blood. This albumin probably is the albumin eliminated through the kidneys. The appearance of albumin in scarlatinal urine, therefore, means a destruction of leucocytes. These leucocytes also are carriers of nitrogen, and the appearance of an excess of nitrogen in scarlatinal blood serum means an increase of katabolisim, in the skin especially.

I will give my conclusions as succinctly as possible. It is probable that the first inoculation of immune blood serum gave protection to the girl. Therefore, there was no necessity for repeated inoculation. I think I am justified in believing that the assertion of Ogata and Jasuhara, of Tokio, that even one drop of immune frog's blood, or half a drop of immune dog's blood, is sufficient to protect a mouse from the fatal effect of an anthrax inoculation, states at least a probable fact.

The streptococci had nothing to do with the disease.

The boy's serum, on the eighteenth day, when inoculated into his sister, was not infectious.

The albumin of scarlatinal nephritis is not toxic.

The inoculation of scarlet fever with immunized blood serum is not curative.

The inoculation without infection of the girl with ten minims of blood serum from the second boy, who had not been immunized, apparently proves the immunity conferred by the first inoculation.

I add two practical suggestions: The application of a blister over the kidneys in scarlatinal nephritis is followed by good effect.

The earliest symptom of improvement in this complication is the appearance of urates and uric acid crystals in the urine.

[1] It is an error, I am sure, to consider the nuclein of a white corpuscle, the nitrogenous part of it, as belonging to the corpuscle; it is only a temporary content, which is being carried out of the body. But it is rightly believed that the serum-albumin of a white corpuscle, which is the proteid left after the removal of paraglobulin, is a part of the corpuscle. This may or may not become a tox-albumin. It does become a tox-albumin in the rigor mortis.