

ON THE PRESENCE OF CERTAIN BODIES IN THE SKIN
AND BLISTER FLUID FROM SCARLET-FEVER
AND MEASLES.*

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PLATE XXVIII.

INTRODUCTION.

In the *Journal of Medical Research*, Mallory¹ described certain protozoön-like bodies, which he had observed in the epithelial cells and in the lymph spaces of the skin, in material from autopsies on scarlet-fever cases. He was unable to find them in the living patient.

At a meeting of the New York Pathological Society in April, 1904,² I reported that I had been able to find these bodies in the skin from five scarlet-fever autopsies, but had been unable to find them in the skin taken from four living patients.

During the summer of 1904, Duval³ obtained bodies similar to those of Mallory in blister fluid from scarlet-fever patients. In looking over Duval's specimens I was struck by the close resemblance of many of them to the extracellular forms of the malarial parasite, except that in Duval's specimens these bodies showed no chromatin. His specimens were stained with Wright's modification of Leishmann's stain, which, in my experience, does not always give a good chromatin reaction.

Since April, 1904, I have taken skin from twenty scarlet-fever patients, ten scarlet-fever autopsies, fourteen measles patients, four measles post-mortems, four patients with antitoxin rashes, and from five autopsies on diphtheria cases which had had a rash before death. Skin was taken from two children, one of

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whom had died of broncho-pneumonia, the other of marasmus. The skin from each of these cases was divided into four parts and placed in Petri's dishes. One was kept in the ice-box, one at room temperature, one at 37° C., and one at 56° C. While able to obtain many kinds of degeneration products in sections made from these specimens (removed from the Petri's dishes every twenty-four hours under the four conditions), I did not find a picture similar to that shown in the sections from the material taken after death from the cases of scarlet-fever and measles. Though many of the epithelial cells showed masses of varying sizes in their protoplasm, these inclusions showed a difference in staining reaction, some being more acidophilic than the surrounding cytoplasm, others less so, while some are basophilic to a marked extent.

The histological technique followed for all the material was fixation in Zenker's fluid, imbedding in paraffine, and staining with eosin and methylene blue, the sections being, on an average, four microns in thickness.

The bodies found in the material from scarlet-fever and measles were the same, so far as I could determine, as those described by Mallory. Some were intracellular, others lay in the lymph spaces. For the most part they were made up of a delicate reticulum which stained a light blue, the surrounding protoplasm being pink. Only a very few showed the rosettes Mallory described as being so characteristic. In the sections from measles the bodies were not so focal in location as those in scarlet-fever and were found more often in the lymph spaces of the corium; there were also small bodies which showed no reticulum but did show a central nucleus-like granule, these small bodies being found not only in the autopsy material, but also in that from the living patient.

So I can report that in sections made from the skin obtained after death from all of the fifteen cases of scarlet-fever I have been able to find Mallory's bodies. One of these cases was most interesting in that two specimens of skin were obtained, one within five minutes after death and the other twenty-four hours later; in the section made from the former, no bodies could be

made out, but in that from the latter these bodies were easily found. In the twenty-four cases of scarlet-fever, where the skin was taken during life, no bodies were found, except in one section, where it was thought a single small body was seen, but as I have been unable to find it again, this cannot be considered a positive observation. In the material from the four autopsies on cases of measles, cellular inclusions were found in three, one being negative. In the last case the skin was taken one half hour after death, and no other specimen could be obtained. In the material from the fourteen living patients no such bodies as Mallory describes were found, but all showed the small round nucleated bodies. The specimens of skin from the antitoxin rashes were negative, both from the living and the dead patient.

STUDY OF BLISTER FLUID.

Methods.—The method used to obtain blister fluid was that devised by Duval except for a slight modification. A square of adhesive plaster two and one half inches in size was covered with vaseline on its adhesive side, leaving a margin of one half inch. A piece of blotting paper one half inch in diameter and saturated with aqua ammoniæ fortior, was placed in the center of this square, and the whole applied closely to the skin so as to admit no air. After being on from five to seven minutes, the skin was then exposed to the air, when in a short time a blister formed. The fluid was withdrawn from the blister with a sterile capillary tube. Moist spreads were made by blowing a drop of the fluid upon a clean slide and then placing on it a clean cover slip, under which the fluid was thinly and evenly spread. Smears were prepared and were fixed in absolute methyl alcohol for two minutes, some being fixed while dry, others while still moist. I did not find that it made any material difference as to which method was used.

In examining the smears many different stains were used, including a number of the various modifications of the Nocht-Romanowsky stain. In my experience Giemsa's⁴ stain was most satisfactory, and Hastings's⁵ was almost as good. Hastings's stain was slightly modified; instead of using 100 c. c. of methyl

alcohol to dissolve the dye, I used 50 c. c. of glycerin heated to 60° C., and to this I added the dye, and then 50 c. c. of methyl alcohol which had been previously heated to 60° C. This idea was obtained from Giemsa's method. It permits of a greater concentration of the dye and the glycerin seems to prevent a deposit on the surface of the glass. In using these stains, it is well to over-stain and then decolorize in from fifty to seventy-five per cent. ethyl alcohol or in absolute methyl alcohol which gives a clearer picture.

Blister fluid was taken from eighteen cases of scarlet-fever and from fourteen cases of measles. The bodies of Mallory were found in all the cases of measles and in fourteen out of the eighteen cases of scarlet-fever.

Control Material.—As control material blister fluid was taken from the following cases:

- One case of erysipelas.
- One case of eczema.
- One case of erythema multiforme.
- One case of urticaria.
- One case of congenital syphilis.
- One case of syphilis in the papular stage.
- One case of irritated normal skin.
- One normal individual.
- One case of morbiliform antitoxin rash.
- Seven cases of scarlatiniform antitoxin rash.

Material from pustules of two smallpox patients was also examined.

No bodies were found in the blister fluid from any of the above cases except in the last four of the scarlatiniform antitoxin rashes which were studied. In these four cases the blistering fluid was left on the skin for a longer period and caused a more severe irritation. In the material from these cases, bodies were found which it was impossible to differentiate from those found in the blister fluid of measles and scarlet-fever. In one case after withdrawal of the material a moist spread was made and examined at once. Only a very few of the bodies were found, but a number of leucocytes were present. After six hours in the

thermostat the preparation was examined again when many more of these bodies could be demonstrated. On making a smear and staining with Giemsa's solution, these bodies were indistinguishable from those in the blister fluid of cases of measles and scarlet-fever. In these diseases, the bodies are found in the fluid as soon as the rash appears, but not before, and they can be found from four to six days after the appearance of the rash, but as soon as the rash fades away they disappear, becoming fewer and fewer until the sixth day, after which time not one has been observed. If two blisters are applied for from five to seven minutes to one patient, one blister being over a portion of the rash and the other on an area that has no eruption, the bodies can be found in the fluid over the rash; they are also present, though less numerous, in the fluid from the normal skin if the area is blistered for twice as long. The blister fluid from the rashes of both the measles and scarlet-fever patients contained many more leucocytes than that from the other sources.

Conjunctival secretions from twelve cases of measles were examined. In the two cases where bodies similar in appearance to those in the blister fluid were found, there were numerous leucocytes, whereas in the ten negative cases the leucocytes were very few in number.

The Bodies.—In smears of blister fluid stained with Giemsa's solution bodies of various kinds are found. The ones most commonly met with are those having a pale pink body with dark brown or black granules scattered throughout their substance. While many of these are undoubtedly red blood cells, or fragments of protoplasm of degenerating leucocytes, others are coagulated proteid, because similar structures can be found in smears made from horse serum which contained no cellular detritus. The bodies in which most interest centers are those which have the appearance of protozoa, many of them resembling closely the extracellular forms of the malarial parasite. These bodies have a pale blue protoplasm with one or more granules; the granules, which in staining resemble chromatin, vary in size from a mere point to a particle taking up half of the total diameter of the body. Four times these bodies were found with the granules arranged

about the periphery of the cell and with fine lines running to the center of the body, which gave them the appearance of a malarial rosette. The bodies ranged in size from one to fourteen microns in diameter, the majority being between three and seven microns. Those containing two or more granules were, as a rule, larger than those containing only one. In the moist spreads these bodies contained granules, dancing around in the protoplasm generally faster than the pigment of the malarial parasite. The morphology of these bodies in moist spreads and stained smears was therefore very strongly suggestive of protozoa.

The origin of these bodies, or bodies indistinguishable from them, was clearly made out. Leucocytes were very numerous in the moist spreads, particularly in those made with material from the acute exanthemata. When these spreads were watched in the warm box at 37° C., the pseudopodia of the leucocytes were seen to break off and in a short time assume a round form, each fragment containing one or more granules. When the pseudopodia which contained nuclear material had separated from the leucocytes and had assumed a regular outline, they resembled very closely individual cells. The reason the protoplasm of these bodies takes the weak basic dye instead of the acid dye is probably due to some chemical change that occurs when it separates from the cell. In some cases this protoplasm may be composed of nuclear material. In some of the stained smears leucocytes were found of which the protoplasm assumed this pale blue color, and in which the nucleus was undergoing karyorrhexis; this would indicate a degenerating cell. The nuclear fragments still gave the characteristic chromatin stain. Bodies of the same nature have been found when an emulsion of leucocytes in salt solution was left in the incubator for forty-eight hours, the salt solution having been previously diluted so as to make it hypotonic. The degenerating cells when stained gave some very beautiful pictures. (The differences in nuclear staining are shown in Plate XXVIII, Figs. 31, 32, 33, 34, and 38.)

In this connection it may be of interest to note that Gotschlich,⁶ in a recent paper entitled "Ueber protozoen Befunde (Apiosoma) im Blute von Flecktyphus-kranken," describes a parasite which

he claims to be that of typhus fever. The "parasite" according to his description seems to be very similar to the bodies described by Duval in the blister fluid of scarlet-fever and by myself in the same fluid from scarlet-fever and measles. In an excellent study of the "Blood-Changes in Typhus Fever," by Love,⁷ this author believes the parasite of Gotschlich to be nothing but degenerative changes in the red blood cells, and advances excellent arguments in favor of this hypothesis.

CONCLUSIONS.

I believe that the bodies found in sections of skin from cases of measles and scarlet-fever are part of the protoplasm of the epithelial cells which has been so changed in its chemical nature that its staining reaction differs from that of the surrounding protoplasm. The small round extracellular bodies found in the living patients may arise from degenerating cells, but I cannot demonstrate this origin with certainty.

In sections of control and normal skin, the nuclei of the epithelial cells were often indented by the cell protoplasm, giving them an appearance similar to those indented by Mallory's bodies.

It would seem that if these bodies of Mallory's were protozoa they would have been found in the sections from both the living and the dead skin of scarlet-fever and measles, as they were present in the blister fluid. Their absence is certainly more suggestive of a degeneration than of a protozoön. This view is also borne out by the fact that they were not found immediately after death, but were present in another specimen from the same case removed twenty-four hours later.

It would seem probable also that the bodies found in the blister fluid were the products of degeneration and cytolytic activity, because they were found in the antitoxin rashes as well as in the cases of scarlet-fever and measles.

The histological changes in the skin of these two diseases leads us to expect the presence of cytolytic products both in the blister fluid and in the sections.

It certainly cannot be stated that none of these bodies is a

protozoön, but it can be positively stated that a great majority of them arise from degenerating cells; and in many cases, I think, it is not possible to differentiate a degeneration from a protozoön by the study of its morphology and staining reactions.

The bodies present in blister fluid resemble very closely those granular bodies found in blood under certain conditions, and seen in vaccine lymph and in emulsions of tissues and in exudates. I think, therefore, that they are for the most part, if not wholly, products of degenerating tissue cells and of leucocytes, and within certain limits specific to scarlet-fever and measles.

DESCRIPTION OF PLATE.

Figs. 1, 2, 3, and 4.—Bodies in the epithelial cells from skin taken after death from scarlet-fever patients.

Figs. 5, 6, and 7.—Bodies in the epithelial cells of the skin of fatal cases of measles.

Fig. 8.—Small round bodies with the central nucleus-like point found in the skin taken from living measles patients.

A. The bodies.

B. A nucleus undergoing karyorrhexis.

C. Normal nuclei.

Fig. 9.—A lymphocyte undergoing degeneration.

Figs. 10, 11, and 12.—Polymorphonuclear leucocytes undergoing degenerative changes in blister fluid from scarlet-fever.

Figs. 13-25.—Bodies found in the blister fluid of measles.

Figs. 26-38.—Bodies found in the blister fluid of scarlet-fever.

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