

ON THE APPEARANCE OF CERTAIN AMŒBOID BODIES
IN THE BLOOD OF VACCINATED MONKEYS (RHOESUS)
AND CHILDREN, AND IN THE BLOOD FROM
CASES OF VARIOLA.

AN EXPERIMENTAL STUDY.

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PLATES XXXVIII-XL.

Even prior to the introduction of Koch's improved methods, Cohn had described his micrococcus vaccinae. Chauveau and Sanderson had demonstrated that the active ingredient contained in vaccine lymph could be removed by filtration.

The possibility of making use of solid culture media gave a new impulse to the search for the causative agent of vaccinia and variola, which has been assiduously continued since that time, as a rule, along the line of bacteriological research.

Notwithstanding the many claims of positive results, these have in the end proven groundless; unless one excepts the latest claim of Klein* (1) and Copeman (2) for the discovery, independently, in vaccine and variolous lymph of a short spore-bearing bacillus of peculiar staining properties and which refuses to grow on all of the usual media.

During the past ten years, and more especially during the last half-decade, attention has been turned toward the possibility of the animal nature of the parasite of vaccinia and variola.

Van der Loeff (3), in 1886, mentioned "numerous small bodies capable of independent movement" which he discovered while examining the clear fresh lymph of a calf, as a hanging drop, in a warm chamber. He gives no other description of these bodies which he assigned to the class Rhizopoda.

If the lymph had been taken with antiseptic precautions these bodies were still to be found after months had passed; but if bacterial contamination of the lymph had occurred they were not to be seen after the lapse of one or two weeks. Impure lymph in which these little bodies could

* References to literature are at the end of this article.

not be found was inactive, whereas the inoculation of pure lymph containing them was always followed by success, even at the end of several months. The following year the same observer (4) reported the presence of similar amœboid bodies, only more numerous, in lymph taken from two cases of small-pox at the commencement of the stage of pustulation.

Shortly after van der Loeff had published his observations, L. Pfeiffer (5) called attention to certain unicellular, round or oval bodies constantly present in the lymph of vaccinia and variola, which he believed to be parasites and assigned to the sporozoa (Leuckart), order Monocystis.

These parasites develop in the cells of the Malpighian layer of the skin, rapidly forming into cyst-like bodies. Propagation takes place by the formation of spores within the cyst wall. The mature spore presents the appearance of a minute disc with vacuolation, out of which there appears to be developed an amœba-like embryo having independent movement. In 1888 Pfeiffer (6) found in human lymph numerous pale hyaline discs, without a nucleus, which exhibited rapid amœboid movements. Rieck (7) confirmed Pfeiffer's finding in human, calf's and variolous lymph. More recently (1895) Ogata (8) has made careful microscopic examinations of stained cover-slip preparations of fresh child's lymph. As a result of his studies he finds in humanized, bovine and variolous lymph certain protozoa which belong to the class Gregarinida, family Polycystidæ, genus *Clepsidrina*, and is of the opinion that these are probably the causative agent of vaccinia and variola.

The first attempt to cultivate the supposed parasite of vaccine lymph was made by Guarnieri (9) in 1892. He first studied the changes which occur in the epithelial cells of the skin during the prepustular stage of small-pox. He always found certain small bodies half the size of the nucleus, or much smaller, which occupied the protoplasm of the affected epithelial cells and stained uniformly and regularly. The little bodies were of various shapes, most often roundish, with irregular margins.

Guarnieri next inoculated the cornea of guinea-pigs and rabbits with vaccine lymph and obtained characteristic lesions, due to the development of a parasite within the deep epithelial cells of the cornea. At various periods of development—generally at the end of 48 hours—scrapings from the cornea were made and examined while suspended in a hanging drop of aqueous humor. Thus prepared, Guarnieri always found within the epithelial cells of the affected area little shining, slowly amœboid bodies, which occupied the protoplasm of the cell but did not obtrude upon the nucleus. Stained sections of the cornea, made through

the site of inoculation, examined under 500 diameters, showed that while the superficial cells were not involved, almost every deep epithelial cell contained, besides its nucleus, a small deeply stained body which lay in the protoplasm and was surrounded by a narrow clear zone. Each cell, as a rule, contained one of these bodies, though two or more might be present in the same cell. Examined under one thousand diameters these bodies were seen to consist of a round or oval nucleus, surrounded by a layer of protoplasm which assumed various shapes. Guarnieri considers these bodies to be parasites and assigns them to the protozoa. From the fact that the parasite occupies the protoplasm of the cell, which it destroys as it develops, Guarnieri designates it *Cytoryctes variolæ seu vaccinæ*.

Ferroni and Massari (10), in 1893, reported that after inoculation of the cornea of guinea-pigs and rabbits with croton oil and India ink, small bodies, like those described by Guarnieri, could be found in the epithelial cells, but in smaller numbers. They believe that the so-called parasites of Guarnieri are derived from the nucleus of the cells or from emigration of leucocytes.

In 1894 L. Pfeiffer (11) confirmed Guarnieri's experiments on the cornea of animals, and announced the discovery of the parasite also in the blood of small-pox patients, and in that of vaccinated children and calves during the stage of fever. He described these parasites as amœboid cells, one-half the size of a red blood cell in the calf and one-fourth that of a red blood cell in the child. A nucleus is present which can be stained; sometimes the parasite contains from 2 to 4 nuclei. They are provided with pseudopodia and often with flagella that can be stained with Loeffler's flagella stain. These bodies are not intracellular, but swim free in the blood. The movements of the parasites are different from those of mononuclear and polynuclear leucocytes and resemble closely those of amœbæ. According to Pfeiffer there are two stages in the development of this parasite. The first consists of an infection of the protoplasm of the epithelial cells by those bodies which were first cultivated in the corneal epithelium by Guarnieri. The amœbæ found during the stage of fever in the blood of vaccinated children and in the small-pox blood belong also to this stage. Out of the young form occupying the epithelial cells develops the second stage, which presents itself as a kind of cyst—*Monocystis epithelialis* of Pfeiffer—whose contents divide into a number of spores. The further development of the spore into the young form has not as yet been followed.

The following year (1895) Von Sicherer (12), Clarke (13) and E. Pfeiffer (14) published confirmatory observations of Guarnieri's experi-

ments on the cornea. Von Sicherer pronounces the process to be a local infection of the corneal cells by a parasite, which, while destroying the protoplasm of the cell, leaves the nucleus undisturbed. E. Pfeiffer failed to find these bodies in the corneal epithelium of rabbits inoculated with chemical irritants, such as osmic acid, glycerine, croton oil and lunar caustic; but they were uniformly present in the cornea of rabbits, goats and calves inoculated with vaccine lymph. Pfeiffer also found in the blood of vaccinated calves amœboid bodies which continued their movements for several hours. His description is meagre, but his figure (No. 6) shows homogeneous amœboid bodies of various shapes, generally with one nucleus. These bodies approach in size a red blood cell.

The foregoing embraces a brief review of the results obtained from a microscopical study of the local lesions of the skin in vaccinia and variola, and of the lesions of the cornea produced by inoculation with vaccine lymph. While not conclusive, the weight of testimony points strongly to the appearance within the corneal epithelium, following local vaccination, of certain definite bodies, possessing independent amœboid movements, and which do not appear to be called forth by various chemical irritants.

As regards the claim of L. Pfeiffer that small, free-swimming, nucleated amœboid cells appear in the blood of variola and vaccinia during the stage of fever, which bodies he considers as the much sought parasite of these diseases, nothing confirmatory has so far been published.

At the suggestion of Surgeon-General Sternberg I took up this line of investigation about one year ago, directing attention at first to the microscopical examination of the blood of vaccinated monkeys and calves, and later to that of children and small-pox patients.

The work was begun in April and continued with slight interruptions until September, 1896. Except in the examination of the blood of small-pox patients, I was assisted by Dr. W. W. Gray, of the Army Medical Museum, and Dr. James Carroll, Assistant in the Laboratory of the Army Medical School, to the former of whom my thanks are also due for microphotographs and drawings, and to the latter for daily valuable assistance in the blood examinations covering a period of nearly five months.

The investigation was entirely confined to the study of fresh preparations of blood which were examined with the greatest care, one at least of the observers making use of a mechanical stage for this purpose. During the earlier experiments the blood was examined only at the height of vaccination (seventh and eighth day). In the later experiments the period of examination was extended to cover the time from the day of vaccination to the subsidence of this process, and in several of the experiments the blood was examined during a number of days preceding and following vaccination.

The results obtained are believed to be of sufficient interest to warrant their report.

In all the vaccinations, except one, glycerinated calf's vaccine was used. In the excepted case fresh monkey's vaccine was inoculated.

The examination of the four animals—three monkeys, one calf—first experimented upon was entirely negative. The succeeding experiments gave more encouragement. The following are brief details of some of these:

Experiment V.—Monkey. Vaccinated May 5, 1896. Successful. Daily examinations of the blood were made, beginning on the 4th day after vaccination. These are negative until the sixth day, when a body is found which attracts attention. It is in diameter about one-third that of a red blood cell; its protoplasm consists of very fine granules, these being smaller than those of an ordinary neutrophilic cell. From the periphery of this small body, clear, short, blunt bits of protoplasm are being continually projected and withdrawn. The granular portion of the protoplasm does not at any time flow into these clear pseudopodia, although the body changes its general shape, being sometimes round or oval, or even triangular. At times a round or oval white spot resembling a nucleus appears in its granular protoplasm. It is kept under observation about six hours (cold stage), during which time its amœboid movements continue active, but the body does not change its position. Other bodies of like granulation and size, some quiet, some amœboid, are observed. One of these bodies seen on the 8th day and left in the field of the microscope during the night shows at the end of 23 hours two distinct, long curved processes resembling flagella. Its amœboid movements have ceased and its granular protoplasm appears darker and more condensed. On several occasions a neutrophilic leucocyte is seen to approach one of these bodies, envelop it completely, and then, after

an interval of a few minutes, release the body and pass on. These small granular bodies are found by each of three observers on all slides examined on the 7th, 8th, 9th, 10th and 11th day after vaccination (Photomicrographs 1-6, Plate XXXVIII). Their number is not large, but as many as five can be found on one slide.

They cannot be found on the 12th, 13th and 14th day, although patient search is made.

Experiment VIII.—Calf. Vaccinated May 13, 1896. Successful. Examination of blood from first to eighth day. On the third day after vaccination there are seen a few finely granular bodies, in diameter one-fourth to one-half that of a red cell, which are either quiet or slowly change their general shape without projecting any clear protoplasm. Two similar bodies, however, are actively amœboid. These bodies continue to appear until the seventh day, when they can no longer be found. These small amœboid bodies, both as to appearance and character of movement, resemble closely those seen in Experiment V.

Experiment XI.—Monkey. Vaccination June 6, 1896. Successful. This animal's blood had been examined daily by two observers from May 22nd to June 5th with negative results. There are seen, however, prior to vaccination, from time to time, small, roundish bodies having a slightly greenish refraction and no distinctly granular protoplasm. These are in diameter about one-third that of a red cell and possess amœboid movements. Small, short processes are projected which quickly assume the same greenish color as that of the body proper. They are not to be confounded with the granular bodies seen in vaccinia. After vaccination daily examinations are negative till June 12th (sixth day). On this day the granular amœboid bodies appear in the blood in moderate numbers. They are in all respects similar to those described in Experiment V, except that some of them are smaller, having scarcely a diameter of one-sixth that of a red cell, and some have a slightly coarser and darker granulation. Distinct, clear, blunt processes are projected by these bodies into which, as a rule, the granular protoplasm does not flow, though exceptionally this is seen to take place. Several of these granular bodies are still amœboid at the expiration of thirty hours. On the 12th day a body unlike any heretofore seen in monkey's blood is found. Its diameter measures one-half that of a red cell, and the body consists of a number of dark granules situated in the midst of a clear protoplasm. This body is rapidly amœboid, its clear periphery continually changing form and sometimes assuming rosette shapes (Plate XL, Figs. 1-9). A few granular bodies are present on the 14th day. Examination on the 15th, 16th and 17th days negative.

Thus of eleven animals—9 monkeys, 2 calves—the blood of seven—6 monkeys and 1 calf—contained during the stage of fever attending a successful vaccination certain extra-cellular, small, granular amœboid bodies which did not correspond to any of the normal elements of human blood. A fact which appeared of additional interest was the discovery of quite similar amœboid bodies in my own blood five days after an accidental vaccination on the finger with fresh monkey's lymph. These bodies were present till the 10th day, but could not be found thereafter.

The time of appearance of the bodies in the blood of the vaccinated monkeys was as follows: 5th day, 2; 6th day, 4. There was observed, however, in the blood of one of the monkeys (Experiment 10), 20 hours after vaccination, an amœboid granular body similar to those which had been seen to appear toward the end of the first week after vaccination. No other bodies were found thereafter in this particular animal's blood until the 6th day. The bodies disappeared as follows: 12th day, 3; 13th day, 1; 14th day, 2. In the one positive experiment with the calf they appeared on the 3rd day and could not be found after the 7th day.

As these rather interesting bodies had been found in the blood of the seven animals last experimented upon, it was considered advisable to continue the investigation with vaccinated children. In this second series of experiments the blood of five children was examined—3 white, 2 black. The following are brief protocols of some of these:

Experiment XII.—Child, 4 yrs., white. Vaccination June 23, 1896. Successful. Examination of the blood on the day preceding vaccination is negative. Examination of blood taken thirty minutes after vaccination shows one small, faintly granular body, in diameter one-third that of a red cell, which sends off clear, blunt processes after the manner of the bodies already described in the vaccinated monkey's blood. From this time until the 7th day examinations are negative. On this day there are observed a few pale amœboid bodies, with a diameter one-half that of a red blood cell, containing a few fine, dark dancing granules and which are slowly amœboid. Similar bodies are observed on the 9th day. Examination on 10th, 11th and 12th days is negative.

Experiment XIV.—Child, 2 yrs., negro. Vaccination July 8, 1896. Successful. Blood subjected to daily examinations for one week preceding vaccination, with the result that four days prior to vaccination there is found a finely granular, actively amœboid body, in diameter one-third that of a red blood cell, which sends off clear processes into which the granular protoplasm is not seen to flow. Twenty-four hours after vaccination a similar body is found. The results are then negative until the 7th day, when the small granular amœboid bodies, as heretofore seen in monkey's blood, can be found in all fresh preparations (Photomicrographs 7-12, Plate XXXIX).

Sometimes as many as nine of these bodies are found on one slide. There is also seen on the 9th day a pale, slightly refractive body, with a diameter one-third that of a red cell, which contains one coarse, dark granule centrally situated, while its clear periphery undergoes continual changes of shape (Plate XL, Figs. 10-16). Examination of the blood on the 14th, 15th and 16th day is negative. In this child's blood prior to and during vaccination the small amœboid body with slightly greenish refraction, which has been seen in the normal blood of the monkey, was found on several occasions.

Thus of five children whose blood was carefully studied during the period of vaccination, three (2 black, 1 white) gave a positive and two (both white) a negative result, as far as the finding of the small granular, amœboid bodies was concerned. The case (*Experiment XII*) in which a granular body was seen in the blood taken thirty minutes after vaccination, but did not appear thereafter, is classed as negative. The bodies appeared in two cases on the 6th and in one on the 7th day; they disappeared from the blood in two cases on the 14th and in one case on the 17th day.

When the latter experiments were about completed the occurrence of an epidemic of small-pox on the island of Key West, Fla.,* afforded the opportunity for the microscopic study of the blood of this disease. Unfortunately for these studies, upon my arrival the epidemic had about spent itself, so that only three cases could be examined, with the following result:

* Through the courtesy of Dr. J. Y. Porter, State Health Officer, and Dr. Jos. H. White, Passed Asst. Surgeon, U. S. M. H. Service, officer in charge of the small-pox hospital, Key West, Fla., every facility was afforded the writer in conducting this investigation.

Observation XVII.—White boy, 11 yrs. Discrete small-pox. 7th day of eruption. The same granular bodies, both as to size and amœboid movements, as seen in the blood of vaccinated monkeys and children are found. In addition there are observed on each slide pale, amœboid bodies, few in number, which contain a few fine or sometimes coarse refractive pigment-like granules. The size of these pale bodies is about one-half that of an ordinary red blood cell. They are generally actively amœboid, continually changing their outline and sometimes assuming rosette-shaped forms. These amœboid bodies are present on the 8th day. One of these is kept under observation for several hours. Its granules, few in number, remain centrally situated, while its periphery is rapidly changing, clear processes being quickly projected and withdrawn. It is left in the field of the microscope during the night and fifteen hours later presents the appearance of a quiet round body, in diameter one-half that of a red cell, with a pale, refractive peripheral zone and a granular centre, the latter made up of a number of quite dark refractive granules (Plate XL, Figs. 17–25).

Examination of the blood on the 9th day is negative.

Observation XVIII.—Negro, 11 yrs. Discrete small-pox. 4th day of eruption. The granular amœboid bodies and the pale amœboid bodies, such as have been described in the preceding observation, are found daily from the 4th until the 7th day of eruption. No examination made on the 8th day. On 9th and 10th days the examination is negative.

Observation XIX.—Negro, 70 yrs. Confluent small-pox. 8th day of eruption. No granular amœboid bodies are seen in this blood. Pale, amœba-like bodies are observed. These vary in diameter from one-third to one-half that of a red cell. Kept under observation for a considerable time, they show frequent changes of shape and contain a few fine, dark dancing granules. One body particularly arrests attention. It contains within its pale protoplasm a few very fine pigment-like granules—eight at most can be counted—which are, as a rule, gathered towards the centre, though they may be at times scattered. This body is very active in its movements, remarkably large blunt pseudopodia, as many as four at one time, being rapidly sent forth in various directions. Two hours later it has assumed the form of an oval amœba one-half the size of a red cell and changes its general shape very slowly. The dark granules are no longer gathered towards the centre, but are distributed throughout the body. This patient died the same day, so that further examination could not be made.

Thus of three cases of variola, the small granular amœboid bodies were present in the blood of two and absent in that of one (blood examined on the 8th day of eruption only). Paler amœboid bodies were found in the blood of three, their appearance in one case being as early as the 4th day of eruption. In two cases they were found on the 7th and 8th day of eruption, respectively. In two cases they were not found on the 9th day.

In view of the results obtained from a study of the blood of variola, it was considered advisable to study the blood of variolated monkeys. Hence soon after my return the following experiment was made:

Experiment XX.—Monkey. Variolated August 8, 1896, with fresh lymph taken from a discrete case of small-pox, 7th day of eruption. Successful. This animal's blood had not been examined prior to inoculation. First day's examination is negative. On the 3rd day after vaccination small finely granular amœboid bodies are observed. These are seen on the 4th, 5th and 6th days. There are also found on the 5th and 6th days a few pale amœboid bodies, in diameter one-half that of a red cell. These exhibit active movements and contain a few dark pigment-like granules (Plate XL, Figs. 26–30).

They resemble the pale amœboid bodies seen in the blood of variola. Examination on the 7th, 8th and 9th days is negative.

In view of Pfeiffer's statement that small amœboid cells are to be seen during the stage of fever in the blood of vaccinated children and calves, the discovery in the blood of vaccinated monkeys, also, during the stage of fever, of granular amœboid bodies much smaller relatively than any of the white elements heretofore described in normal human blood, naturally aroused much interest as to their true character. Their disappearance, too, about the end of the second week did not lessen the important and intimate relation which these bodies appeared to bear to the local inflammation. Their minute size, their active amœboid movements, the persistency of the latter, together with the occasional phenomenon of phagocytosis, all seemed to point to the parasitic nature of these bodies, as claimed by Pfeiffer.

The discovery, however, of a similar body in the blood of a monkey within twenty-four hours after vaccination, and in the blood of a child

thirty minutes after vaccination, necessarily raised a doubt as to their causative importance. It seemed possible, after all, that such bodies might be occasionally found in normal blood and that during vaccination they might appear in larger numbers in the general circulation. This led to a thorough search for these diminutive bodies in the normal blood of monkeys and children. As a result of this search there was found in the blood of one monkey and of one negro child, prior to vaccination, a body having the same appearance and size as those seen in the blood of vaccinated animals. The failure to observe this small granular body heretofore in normal blood must be attributed to its extreme scarcity and relatively small size. The tendency, too, to overlook such small bits of protoplasm would be natural, since on casual inspection they might readily be mistaken for parts of a fragmented leucocyte.

The origin of these small granular bodies, rarely seen in normal blood, as well as their possible identity with those bodies observed by Pfeiffer and myself in the blood of vaccinated animals and children and in that of small-pox, must be left to future observation to determine. Their appearance in the general circulation in vaccinia about the end of the first week, in such numbers that a few may be found in every well-made preparation of blood, and their prompt disappearance about the end of the second week, is indicative of their importance, whatever may be their real significance.

The pale amœboid bodies which were observed in the blood of three cases of small-pox and of one variolated monkey will, it is hoped, attract the attention of other investigators. Bodies such as these have not been found, during this investigation, in the normal blood of animals or children.

CONCLUSIONS.

1. The claim of L. Pfeiffer that small granular amœboid bodies are present in the blood of vaccinated children and calves, and in the blood from cases of variola, during the stage of fever is confirmed. A nucleus has not been positively made out in any of these bodies.
2. Granular amœboid bodies, having a diameter about one-third that of a red blood cell, appear, also, in the blood of the monkey

during the active stage of vaccinia and disappear with the decline of the local inflammation.

3. A body of like appearance, granulation and size may occasionally be found in the normal blood of monkeys and children.

4. Pale amœboid bodies, containing a few dark pigment-like granules, are present in the blood from cases of variola and in the blood of the variolated monkey. Bodies of like appearance may occasionally be found in the blood of vaccinated children and monkeys.

DESCRIPTION OF PLATES XXXVIII-XL.

The description accompanies the plates.

BIBLIOGRAPHY.

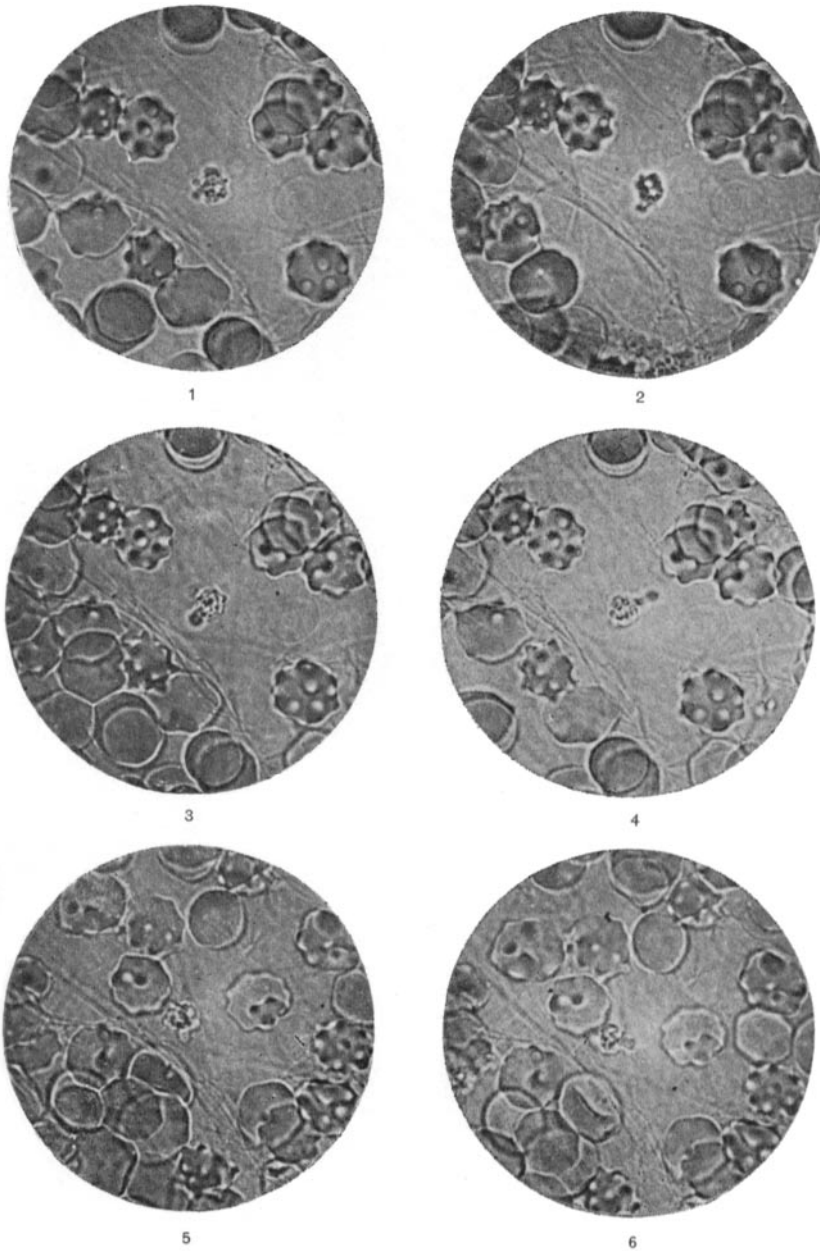
1. Klein, E.—Etiology of Vaccinia and Variola. *Report of the Local Government Board*, xxii (1892-93), 395-400.
2. Copeman, S. M.—Discussion on the Pathology of Vaccinia. *British Medical Journal*, Sept. 22, 1894, 632.
3. van der Loeff, A.—Ueber Proteiden in dem animalischen Impfungstoffe. *Monatshefte für praktische Dermatologie* (1887), vi, No. 5, 189-95.
4. The same.—Ueber Proteiden oder Amöben bei Variola Vera. *Ibid.* (1887), vi, No. 10, 447-9.
5. Pfeiffer, L.—Ein neuer Parasit des Pockenprozesses aus der Gattung Sporozoa (Leuckart). *Ibid.* (1887), vi, No. 10.
6. Pfeiffer, L.—Weitere Untersuchungen über Parasiten im Blut und in der Lymphe bei den Pockenprozessen. *Correspondenz-Blätter des Allgemeinen Aertztlichen Vereins von Thüringen*, xvii (1888), 644-67.
7. Rieck, M.—Ueber einen neuen Parasiten der Pockenprocesse. *Rundschau auf dem Gebiete der Thiermedizin, etc.*, 1887, No. 10, 77-9.
8. Ogata, M.—Ueber die Sporozoa (Gregarinen) der Vaccinelymphe und deren Bedeutung für die Krankheit. *Mittheilungen aus der Medicinischen Facultät der Kaiserlich-Japanischen Universität*, iii (1895), No. 2, Tokio.
9. Guarnieri, G.—Ricerche sulla patogenesi ed etiologia dell' infezione vaccinica e vaiolosa. *Archivio per le scienze mediche*, xvi (1892), No. 22, 403-23.
10. Ferroni, E., and Massari, G.—Sulla pretesa scoperta del Guarnieri riguardo la infezione vaccinica e vaiolosa. *La Riforma Medica*, ii (1893), 602-4.
11. Pfeiffer, L.—Behandlung und Prophylaxe der Blattern. Hand-

buch der speciellen Therapie innerer Krankheiten. Dritte Lieferung, 1894, 229.

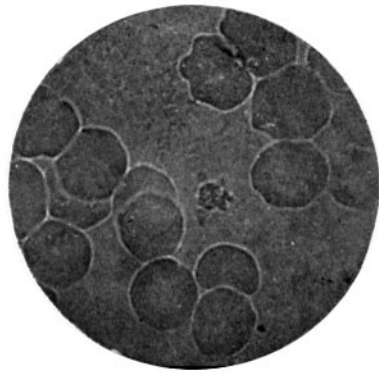
12. Von Sicherer.—Beitrag zur Kenntniss des Variolaparasiten. *Münchener medicinische Wochenschrift*, 1895, No. 34, 492–3.

13. Clarke, J. J.—Einige Beobachtungen über die Morphologie der Sporozoen von Variola, sowie über die Pathologie der Syphilis. *Centralblatt für Bakt. und Parasitenkunde*, xvii (1895), 300.

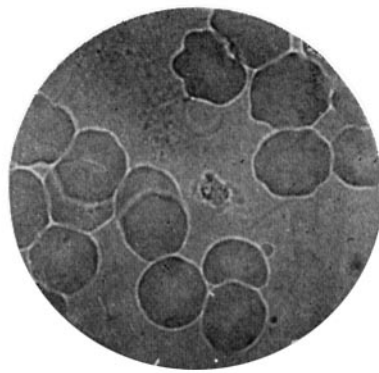
14. Pfeiffer, E.—Ueber die Züchtung des Vaccineerregers in dem Corneaepithel des Kaninchens, Meerschweinchens und Kalbes. *Centralblatt für Bakt. und Parasitenkunde*, xviii (1895), 769.



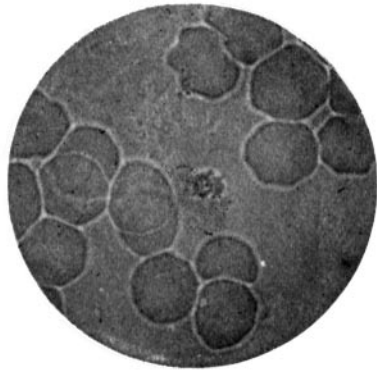
A granular ameboid body, blood of monkey, 8th day of vaccination. Photomicrographs taken at intervals of about thirty seconds. $\times 1000$.



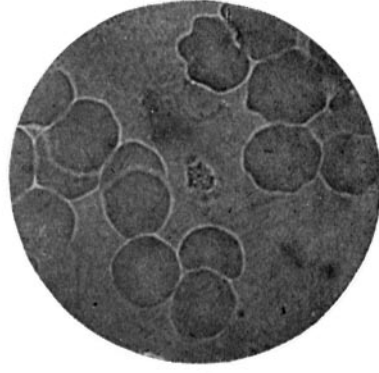
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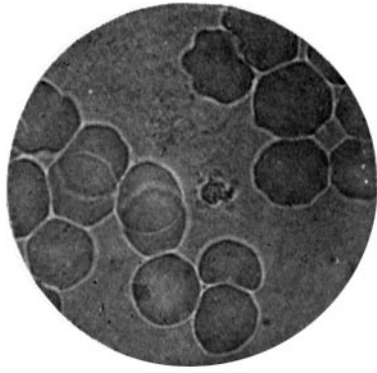
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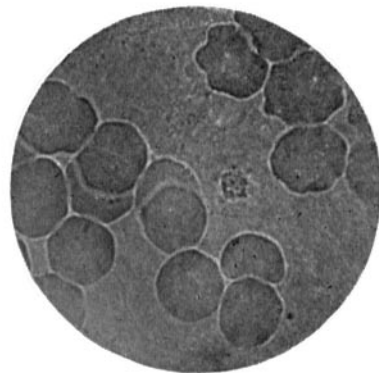
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A granular ameboid body, blood of negro child, 8th day of vaccination. Photomicrographs taken at intervals of about thirty seconds. $\times 1000$.



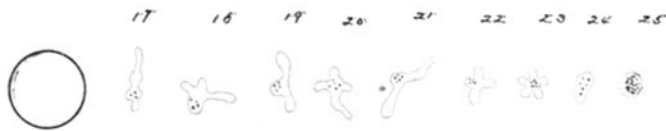
FIGS. 1-9.

Ameboid body, $\frac{1}{2}$ diam. of red cell. Monkey. 12th day of vaccination. $\times 1000$.



FIGS. 10-16.

Pale ameboid body, $\frac{1}{8}$ diam. red cell. Negro child. 9th day of vaccination. $\times 1000$.



FIGS. 17-25.

Pale ameboid body, $\frac{1}{2}$ diam. red cell. Discrete small-pox. 7th day. $\times 1000$.



FIGS. 26-30.

Pale ameboid body, $\frac{1}{2}$ diam. red cell. Monkey. 5th day of variolation. $\times 1000$.