EXPERIMENTAL STUDIES WITH A SPIRAL ORGANISM FOUND IN A WILD RAT.

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Plates 30 to 32.

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The researches of the Japanese on infectious jaundice, seven-day fever and rat-bite fever have brought out the fact, that certain rodents harbor the causative agents of these diseases.

The present paper deals with a spiral organism isolated from a wild rat (*Mus decumanus*) in Mexico City.

The search for it was undertaken on account of the observation of two cases of severe illness in children bitten by rats.

Material.

I saw last year two cases of rat-bite fever with a typical fever course, swelling of the bitten fingers, lymphangitis, lymphadenitis, and a maculopapular exanthem. One was a Mexican girl who was bitten by a rat in the schoolyard. She found the animal lying in a corner and touched it. Apparently the animal was quite sick. The girl was ill for more than six months, but recovered. The second case was a American boy who was bitten by a wild rat which had entered his rabbit cage. He was sick with paroxysmal relapsing fever for 9 weeks. I was called in both cases to do a blood count as the attending physicians took the disease for a peculiar form of sepsis. I made the diagnosis rat-bite fever on account of the fever type and the peculiar exanthem. I found in both cases a moderate polynuclear leucocytosis and signs of a secondary anemia, but no spirochetes. Unfortunately in neither case was I allowed to draw blood from a vein. I decided to examine some wild rats in the hope of finding the microorganism described by the Japanese authors. In one out of the twenty rats I got for examination I found in the blood

a small motile spiral organism with a long flagellum at each end. The animal was killed and emulsions of the internal organs injected subcutaneously into six white rats.

Experiments with White Rats.

Blood from these white rats was examined daily with the dark field, but it was only after 3 weeks, that I found a few organisms resembling those in the original injection material. Blood was taken with a fine needle from the heart of one of the infected rats and injected into six young white rats. 3 days after the injection a few of the organisms were found in the blood of one young animal, 4 days later four were found to be positive and on the 6th day they were found in all. The number slowly increased in the blood for about a week and then slowly decreased again. After 4 weeks only an occasional one was found in the blood. The rats did not show any clinical signs of illness except a transitory swelling at the place where they were injected. Several rats were killed after they had been kept under observation for 4 or 5 weeks. There was a hyperemia of the internal organs with a very few old and fresh hemorrhagic spots in the lungs. With Levaditi's method I found, but only after repeated careful examinations, a few of the spiral organisms in the kidneys and adrenals. In one rat I found several specimens in the wall of a kidney vein. Experiments were now begun with guinea pigs.

Experiments with Guinea Pigs.

Blood was taken from the tail of a rat which was found to have the organisms in the blood and injected with a capillary tube into the scrotum or the labium majus of six guinea pigs. The injected parts became red and swollen within 3 to 5 days with a swelling of the regional lymph glands. The swelling subsided within 3 to 4 days only to light up again afterwards. Between 10 and 14 days after inoculation the organisms were found to be present in the blood by dark-field examination. The number gradually increased for a week to decrease slowly until the death of the animals which occurred between the 26th and the 31st days after inoculation. When the number of organisms was at the highest, there were never more than

eight to ten, in one microscopical field. Although they decreased in number they were found always by direct observation with the dark-field microscope or in stained films (Fig. 3). Between the 15th and 20th day a grayish cloudiness in the form of a ring was found in both corneas of one guinea pig, somewhat resembling an arcus senilis. In a few days the whole cornea became milky and fine vessels entered from the periphery of the cornea. This keratitis cleared up in a few days but was soon followed by a relapse. The conjunctiva became injected and the soft parts surrounding the eye became swollen. The conjunctiva discharged a mucopurulent secretion in which by careful examination a very few motile spiral organisms were found. Dr. Bauer, our hospital oculist, confirmed my diagnosis of parenchymatous keratitis. This keratitis and conjuntivitis appeared in all the infected guinea pigs and was in later experiments found to be a very constant occurrence (Figs. 1 and 2). The hair around the eyes began to fall out, the eyelids became thick and infiltrated, and showed many rhagades; also the hair around the nostrils started to fall out. The guinea pigs now began to lose weight rapidly; there was an extreme progressive atrophy of the whole muscular integument and they screamed when handled as if they had intense pain. Walking became difficult for them; the hind legs especially were stiff and helpless. They died in a comatose condition. Films made with the blood showed marked anisocytosis, polychromatophilia, and nucleated red cells. During the course of the infection all animals had irregular intermittent fever and a paroxysmal relapse was often accompanied by a new cloudiness of one or both corneæ and a new swelling of the primary lesion.

Postmortem Findings.—Extreme emaciation; subcutaneous connective tissue dry, with only a little brownish, gelatinous, fatty tissue. Whole muscular integument atrophic and dry. Some lymph glands, especially those in the mediastinum injected and quite enlarged. Lungs only slightly collapsed, the substance of the lungs somewhat indurated, more or less brownish in color with old and fresh hemorrhagic spots. Heart slightly hypertrophic, myocardium somewhat translucent, endocardium apparently normal. Liver large, congested, somewhat opaque. Spleen dark, hyperemic, enlarged. Adrenals enlarged, with a few fresh and old hemorrhagic spots (not found in all animals). Kidneys hyperemic, showing in two animals a few small irregular contracted scars on the surface. In one of the guinea pigs these scars were found to be quite pronounced, the kidneys having the appear-

ance of a beginning arteriosclerotic kidney. The capsule in this case was quite adherent. The parenchyma of all the kidneys showed always more or less cloudy swelling of the cortex and the boundary between cortex and medulla was not sharp. In the columnæ Bertini fine yellowish spots were to be seen now and then. The whole organ, especially the cortex was pronouncedly hyperemic. Intestines, brain, medula, testicles, and ovaries were apparently normal.

Microscopical Findings. 1. Cornea.—Tissue edematous, connective tissue cells enlarged and increased in number. Between the fibers were polynuclear leucocytes, few lymphocytes, and plasma cells. On the limbus of the cornea there was a dense infiltration with plasma cells and lymphocytes around young vessels, and capillaries entering the substance of the cornea (Fig. 4). Epithelia of the cornea were swollen and the nuclei enlarged. A few mitotic figures were to be found and some polynuclear wandering cells between the epithelia.

2. Eyelids.—Edema and dense infiltration of the mucous membrane with lymphocytes, leucocytes, and plasma cells. The same condition existed in the skin of the eyelids.

3. Lacrimal Glands.—A slight infiltration of the stroma and ducts with lymphocytes and leucocytes was found in all animals.

4. Brain.—Tissue hyperemic and somewhat edematous. In all the animals I found small but very distinct proliferations of neuroglia cells around capillaries in the gray matter just beneath the layer of the large pyramidal cells (Fig. 7). Occasionally such nodules were found in the basal ganglia in the gray matter of the hippocampus and in the cerebellum. They resemble closely the *Gliaherde* found by Duerck in the brain of individuals that had been comatose from malaria. I found in the cerebellum of one animal changes in the molecular layer resembling closely Spielmeyer's *Gliastrauchwerk.*

5. Heart.—The organ proved normal in one animal but in five others there was some cloudy swelling of the muscular fibers but no fatty infiltration. The interstitial tissue increased, and in one animal densely infiltrated with lymphocytes and fibroblasts especially beneath the endocardium.

6. Lungs.—A difference was here to be noted between the animals which died on the 26th day and the animal which died on the 31st day. This difference was one of degree, one lung showing early, the other, advanced changes. The early change was represented by extreme hyperemia of the whole parenchyma of the lung. The capillaries were greatly distended showing a great number of polynuclear leucocytes in the lumen. The septa were enlarged containing polynuclear leucocytes and young fibroblasts which held hemosiderin. The alveolar epithelia were swollen and a slight degree of desquamation was sometimes found, but no pneumonic foci. In the interlobular septa fresh and old hemorrhages were found, and very exceptionally red cells were to be seen in the alveoli. There was a dense infiltration with lymphocytes, plasma cells, and fibroblasts around the small vessels. In the bronchi a slight catarrhal condition was present with desquamation into the lumen. This condition more or less pronounced occurred in five guinea pigs. In the animal which succumbed on the 31st day the microscopic picture resembled, some-

what, the interstitial form of a pneumonia alba. The septa were much enlarged and in some places no alveoli were seen. This disappearance of the alveoli was not due to a hepatization but to a collapse or a compression of the alveolar apparatus by connective tissue very rich in cells, as could be demonstrated through Weigert's coloration for elastic fibers. It consisted of fibroblasts, with comparatively few leucocytes, lymphocytes, and plasma cells. Many of the fibroblasts were densely filled with hemosiderin. Around the small vessels and bronchi there was still a dense infiltration with wandering cells and a pronounced catarrhal condition of the smaller bronchi was present. Endarteritis obliterans was found in a few small arteries. The capillaries and small vessels were distended and hyperemic, containing a few bone marrow giant cells; but not solely on account of compression had the alveolar structure disappeared in many parts of the lung. With Weigert's method an organization of the alveolar apparatus by fibroblasts and desquamated alveolar epithelia containing hemosiderin was found (Fig. 5). Occasionally the fibroblasts were observed to have formed submiliary nodules with radiary arrangement like epithelioid cells. In one instance I saw such a nodule with central necrosis surrounded by giant cells of the Langhans type. The elastic fibers in such organized parts were markedly decreased and their architectonic structure split up.

7. Liver.—The findings in the liver were more uniform. Some cloudy swelling of the liver cells existed within the periphery of the acini hyaline droplets and occasionally fine fat droplets. The stroma was somewhat increased by young connective tissue which showed a moderate infiltration with lymphocytes and leucocytes. Around small branches of the portal vein there was an occasional denser infiltration.

8. Kidneys.—The changes in the kidneys were found to be predominantly interstitial as in the case of the lungs. There was at their beginning a pronounced hyperemia, principally in the cortex. The glomeruli were hyperemic with many polynuclear leucocytes in the capillaries. Some swelling of the epithelia of the tubuli contorti was to be noted and a lesser one of the tubuli recti. An insignificant fatty infiltration existed in the cells of a few tubules with desquamation and desintegration of the epithelia and hyaline cast formation. The retractions in the cortex mentioned in the postmortem findings were formed by scars in which the glomeruli and tubes were atrophic, and some glomeruli completely hyaline and embedded in hyaline connective tissue (Fig. 6). Apparently this represented the final stage in the process which began with a dense infiltration of the interstitial tissue beneath the capsule by polynuclear leucocytes, pseudo-eosinophils, plasma cells, lymphocytes, together with an extravasation of red cells as seen in other parts of the kidneys. Desquamation and proliferation of the parietal part of Bowman's capsule and also hyaline exudate into the capsule were occasionally found. The blood vessels appeared normal except that a moderate swelling of the intima of the vas afferens was occasionally seen. Hemosiderin was found here but only in a few cells near the kidney surface.

9. Adrenals.—Pronounced hyperemia existed especially in the cortex. Occasionally small hemorrhages were present beneath the capsule and some infiltration of the stroma with lymphocytes.

10. Spleen.—This organ showed a marked increase of polynuclear leucocytes mostly eosinophils. A great number of myelocytes and nucleated red cells were found in the spleen of two animals. Hemorrhages and small hemorrhagic infarcts were present in three animals. A good deal of hemosiderin was found in the stroma.

11. Pancreas.—Infiltration of the stroma with lymphocytes and leucocytes was seen in one animal.

12. Spinal Cord.—Not examined.

13. Peripheral Nerves.—No lesions found.

14. Primary Lesions.—This showed a pronounced edema of the connective tissue together with a dense infiltration by leucocytes, lymphocytes, and plasma cells and some desquamation and infiltration of the lymph vessels. There were infiltration and necrotization of the epidermis.

15. Lymph Glands.—Hyperplastic condition of the follicles existed with desquamation and infiltration of the sinuses by leucocytes and lymphocytes.

16. Thyroid Gland.—Atrophic, no gross changes.

17. Salivary Gland.—Some infiltration of the stroma and ducts with lymphocytes and leucocytes. Desquamation of the epithelia of the gland ducts in three animals.

18. Testicles and Ovaries.—Normal.

19. Skeletal Muscles.—There was a pronounced atrophy of the fibers with proliferation of the nuclei of the sarcolemma. Some fibers showed complete loss of the striation and hyaline, and seldom a waxy degeneration. Infiltration of the interstitial tissue with lymphocytes and eosinophilic leucocytes was also present.

20. Bone Marrow.—A marked increase of myelocytes, megalocaryocytes, and nucleated red cells was seen in three animals.

The Organism.

An accurate study of the morphology of the living organism was difficult on account of its very rapid bipolar progression, especially in the blood drop. In secretion from the eyes the movements were not as rapid. The best material for examination was a drop of serum squeezed from the primary lesion after puncture with a fine needle. The organisms were found here in enormous numbers.

With the dark field a fine flagellum was always observed at each end of the body. It was seen as a straight or finely spiral filament. The body measured about 2 to 4 micra in length and specimens from tissue occasionally 5 to 6 micra. The elementary spirals were rigid, regular, and constant in number, measuring about 1 micron in length. Spiral depth 0.6 to 0.7 micron in the center of the body. The body seemed to be round and measured about 0.3 micron in thickness. It was slightly tapered at both ends and the spiral amplitude also decreased somewhat

towards the extremities. Bending of the body was observed. In larger organisms a shallow wave was often seen. I observed three kinds of progressive movement in the dark field: (1) in small individuals which moved very rapidly through the optical field both flagella were seen as straight, motionless filaments in the axial line of the body; (2) a fine very refractile button was seen at the tip of the straight rear flagellum which apparently was the optical effect of the rapid small excursions of the tip; (3) in larger individuals the flagellum was occasionally seen to make undulatory movements and the body deviations from the axial line like a vibrio.

The explanation of the first kind of movement caused me some difficulty on account of the very rapid progression of the organism, the body of which was quite transparent under the dark field. One specimen pushing against a blood platelet furnished me the explanation. It could not move further; the body was seen in rapid spiral movement, the rear flagellum making vigorous large excursions. By slight pressure on the cover-glass the blood platelet was moved aside and the spiral organism now progressed with great rapidity along the field with a straight motionless flagellum at the back end, like a fish which with one rapid stroke of the tail propels itself a great distance. Occasionally the front flagellum was seen bent back along the body of a quickly moving specimen. The rear and front flagella sometimes steered the direction of the movement by quick bending. The flagella measured 2 to 3 micra. Small specimens seemed to have proportionally longer flagella. Living and stained specimens were seen in transversal division. Once I found three individuals arising from one.

I was not able to see more than one flagellum at each end of the organism. In a well lighted dark field I saw *always* one at each end. The organisms stained with Giemsa's solution, Leishman's stain, ordinary aniline dyes and were easily demonstrated with the method of Levaditi and Fontana. Staining of the flagella was only occasionally achieved but they could be easily demonstrated by Burri's method, not so well by Fontana's. Also with these methods the flagella were generally seen as straight or very finely spiral filaments. In living specimens the flagella were probably always in spiral form. In movement they were readily seen in the dark field and gave the impression of a refractile mass, but in stained specimens they could hardly be observed. The organisms are destroyed by 10 per cent saponin, sodium taurocholate, and sodium glycocholate.

I found in the literature only one organism which in form and movement has the same characteristics as that here described, namely *Spirochæta morsus muris* of the Japanese authors. Futaki and coworkers think that their organism is a spirochete belonging to the *Genus treponema.* Adachi succeeded by a special method in staining several flagella at each end of the body of the spiral organism of rat-bite fever and calls it a spirillum. I was not able to demonstrate several flagella in my organism. The fact that I observed bending

of the body indicates that I am dealing with a spirochete. The very constant number of the spirals and their rigidity is characteristic for the *Genus treponema*. The difference between this organism and the treponemata that are well known lies principally in the very rapid movement of the former which is due to the presence of large vigorous flagella. Noguchi denies the presence of true flagella in this whole group of microorganism. The movement of a spironema and a leptospira is comprehensible without the presence of a flagellum. The progression accompanied by axial rotation of a short specimen of a treponema however, in which only occasionally a transient shallow wave may be observed, cannot be explained without motive power in form of a flagellum. The difference between the flagellum of the organism described and the "terminal finely spiral filament" of Noguchi is not an essential one. I classify, therefore, the microorganism I isolated from a wild rat under the *Genus treponema*.

Experiment 1. Transmission Experiments with Biting Guinea Pigs.—A strong male guinea pig 520 gm. in weight, known to me as a fighter was infected with a drop of blood from an infected guinea pig. Spirochetes were found in the blood on the 10th day after inoculation. The same day the animal was placed with a non-pregnant female and another strong male of 460 gm. An hour later the smaller male had a deep bite on a lip. It was then separated for observation and examined daily. The wound healed within a few days without swelling of the surrounding tissues and the animal had no fever. 20 days later it was in good condition and no spirochetes were found in the blood. It was killed 28 days after it was bitten and the examination of the internal organs did not show any pathological changes. On the 17th day after inoculation the larger male showed cloudiness of one cornea and swelling and discharge from both conjunctivæ. It was put with a young male and bit it several times. This animal later developed typical symptoms of the infection and the spiral organisms were easily demonstrated in the blood 11 days after it was bitten.

Experiment 2. Transmission Experiments with Secretion from the Eyes.—A guinea pig was used which showed well developed keratitis and conjunctivitis. With a very fine capillary tube a small quantity of secretion was aspirated from the conjunctival sack and injected

into the labium majus of two guinea pigs. Special care was taken not to produce any lesion of the conjunctiva or of the cornea of the animal while procuring the material. 5 days after the injection the labia were found to be very swollen and appeared to be painful. No spirochetes were found in the blood, but the guinea pigs had fever (101.8°–102°F.) on that day. In a drop of aspirated serum from a swollen part I found a few spirochetes with the dark field. From the 10th and 11th days spirochetes were found in the peripheral blood and the guinea pigs both succumbed later with the typical symptoms.

Experiments with Salvarsan.

Two guinea pigs which had numerous spirochetes in the blood were injected intravenously with neosalvarsan. The next day no spirochetes could be found in the blood, but after 8 to 14 days spirochetes were found in both and the guinea pigs died with the usual symptoms.

Eye Lesions in Rats.

After the finding of living spirochetes in the discharge from the eyes of the guinea pigs and after the positive transmission experiments with this discharge I examined carefully all my white rats which had been infected 4 and 5 months before. The total number of infected rats was twenty-six. Eight of them now showed conjunctivitis, only four had conjunctivitis, keratitis, and iritis with synechia; four, a shrinkage of one or both eyes with iritis; and one, a fresh keratitis. The remaining nine animals were apparently normal.

Dark-field examinations of the secretion from the eyes of these rats resulted negatively. To find out if the eye lesions in rats play a part in the transmission of the disease, the following experiment was carried out. Previous to it I had allowed the rats to bite on wood, toast, and even on iron in order to see whether this would give rise to abrasions. No blood could be found afterwards in their mouths.

Experiment 3. Transmission Experiment with Blood and Discharge from the Eyes of a Rat Infected 4 Months Before.—Four young

guinea pigs were used. A rat was chosen which showed iritis and conjunctivitis and Guinea Pigs 1 and 2 were injected subcutaneously with a drop of discharge of the eye taken with a capillary glass tube, while Nos. 3 and 4 were inoculated with a drop of blood from the rat. Nos. 1 and 2 developed infection with the spiral organism, whereas Nos. 3 and 4 remained well.

Distribution of the Organism.

As already mentioned the organisms were always found in the blood of the guinea pigs, although they decreased markedly in number prior to death of the animals. They could be found with Levaditi's method in every organ by repeated and careful examination but never in great number. In the kidneys and adrenals they were found with greater ease than anywhere else, save in the cornea. Here I found them without difficulty in all six animals and nearly always in great numbers, especially when the keratitis was not very pronounced. When the keratitis was advanced and resorption and organization of the inflammatory exudate by blood vessels had taken place, they were rather scarce, doubtless as the result of an induced immunity. As the normal cornea has no blood vessels the organisms may be supposed to have multiplied there unaffected by circulating antibodies at a time when they are already scarce in the blood stream and in the viscera.

There was another finding most readily to be explained by the development of immunity in the infected animals. While in the central parts of the cornea small, regular organisms were found, in the periphery, where entering blood vessels and dense infiltration with wandering cells appeared, thick, huge, irregular forms such as Kaneko and Okuda have pictured, were met with. The organisms were more numerous at the periphery of the cornea and in the layers near the surface epithelium. Once I found one between the epithelial cells. As already mentioned I found them living in the conjunctival sack and there can be no doubt, that they had passed the cornea.

DISCUSSION.

When I found the spiral organism in a *Mus decumanus* in Mexico City and transmitted it successfully to white rats and guinea pigs, I was convinced, that I was dealing with the spirochete known from the publications of the Japanese workers as *Spirochæta morsus muris*. My organism presents the same morphological aspect and is characterized by the same swift rapid movements. It likewise kills guinea pigs invariably in a comparatively short time and produces inflamation of the injected part after between 3 and 5 days with a swelling of the regional lymph glands. Also it causes the same irregular intermittent fever, has the same low virulence for white rats, increasing in their blood for a short time to decrease slowly again, without producing clinical symptoms, though it could be recovered again after many weeks and months from the blood or viscera. But in spite of all this and the observation of two typical cases of rat-bite fever in Mexico City, I am not at present able to state positively, that I have been working with *Spirochæta morsus muris* because of the lack of precise tests for the identification of the latter. A comparison of the pathological findings in my guinea pigs with those in human rat-bite fever speaks strongly, however, in favor of the view that both are caused by the same organism.

Blake has found acute ulcerative endocarditis, subacute myocarditis, interstitial nephritis, glomerular and interstitial hepatitis, and hemorrhagic infarct of the spleen in the human subject. With the exception of the endocarditis I found the same changes to be more or less pronounced in all my guinea pigs. Kaneko and Okuda found in their first human case interstitial and glomerular nephritis as well, but they assume that this nephritis existed before the patient became ill with rat-bite fever. The gross changes in the organs of Blake's case they attribute to the infection with a streptothrix which he isolated from his case. But when one considers the changes in my guinea pigs it seems possible that the rat-bite spirochete played a prominent part in the pathology of both cases.

Manson reports the frequent occurrence of keratitis in human rat-bite fever and the finding of the spirochete in the eye. The mode of infection in rat-bite fever is not evident from the work of the Japanese authors. Since they never found the spirochetes in the mouth of infected rats, they assumed that transmission must take place as result of hemorrhage from the gums of the biting animals. I think that the experiments reported in the present paper give a more reasonable explanation of the transmission of the spirochetes. These indicate a direct relationship

between the occurrence of eye lesions and transmission through bites. The absence of such lesions would explain why I did not contract the disease in spite of several bites I received from infected rats. Experiment 3 shows clearly that hemorrhages from the gums of a biting animal is an unlikely method of transmission. The two guinea pigs inoculated with rat blood did not get sick, whereas the two others injected with discharge from the eyes of the same rat contracted the disease. Experiments 1 and 2 yield further evidence in the matter. The spiral microorganism passes through the lacrimal channel into the nasal cavity and thence may enter the mouth though its presence there is not absolutely necessary for transmission through bites. For the upper lip of the rats and guinea pigs is cleft to the nostrils and since the biting animal touches the bitten object with the nose, the organism may enter the wound from this point. I found in three guinea pigs slight changes in the salivary glands, and it is possible, that occasionally a spirochete may enter the mouth by this route.

SUMMARY.

1. Two cases of rat-bite fever with a typical fever course and a maculopapular exanthem came under my observation in Mexico.

2. A spiral organism morphologically identical with one known in Japan as the causative agent of Sodoku was found in a *Mus decumanus* caught in Mexico City.

3. The organism was found to be pathogenic for white rats and guinea pigs, the infection being fatal for guinea pigs.

4. The bite of an infected guinea pig led in one of two instances to infection and death of the animal bitten.

5. The microscopical findings in the guinea pigs infected with this microorganism closely resemble in many respects the findings in Blake's case and in Kaneko and Okuda's first case, the only ones of human rat-bite fever which have been closely studied at post mortem.

6. Eye lesions were found in all the infected guinea pigs and the spiral organisms were demonstrated in the discharge from the eyes and also within the cornea.

7. Similar eye lesions were found in most of the infected rats and the secretion from the eyes of one of them was demonstrated to be infectious for guinea pigs.

8. The eye lesions constitute an evident source for the spiral organisms transmitted by biting, and not improbably the only one.

My experiments may give an explanation for the transmission of some other spirochetal diseases besides rat-bite fever. Cases of Weil's diseases are reported to be caused by the bite of a rat and it is noteworthy that eye lesions occur in spirochætosis icterohæmorrhagica (Manson).

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EXPLANATION OF PLATES.

PLATE 30.

FIG. 1. Guinea pig. 20 days after inoculation with a drop of blood of a white rat. Pronounced keratitis and conjunctivits. Marked hair fall and thickening of the eyelids.

FIG. 2. Same animal. Falling of the hair on the nose.

FIG. 3. Smear of the peripheral blood of an infected guinea pig, showing the organism, Leishman's stain.

PLATE 31.

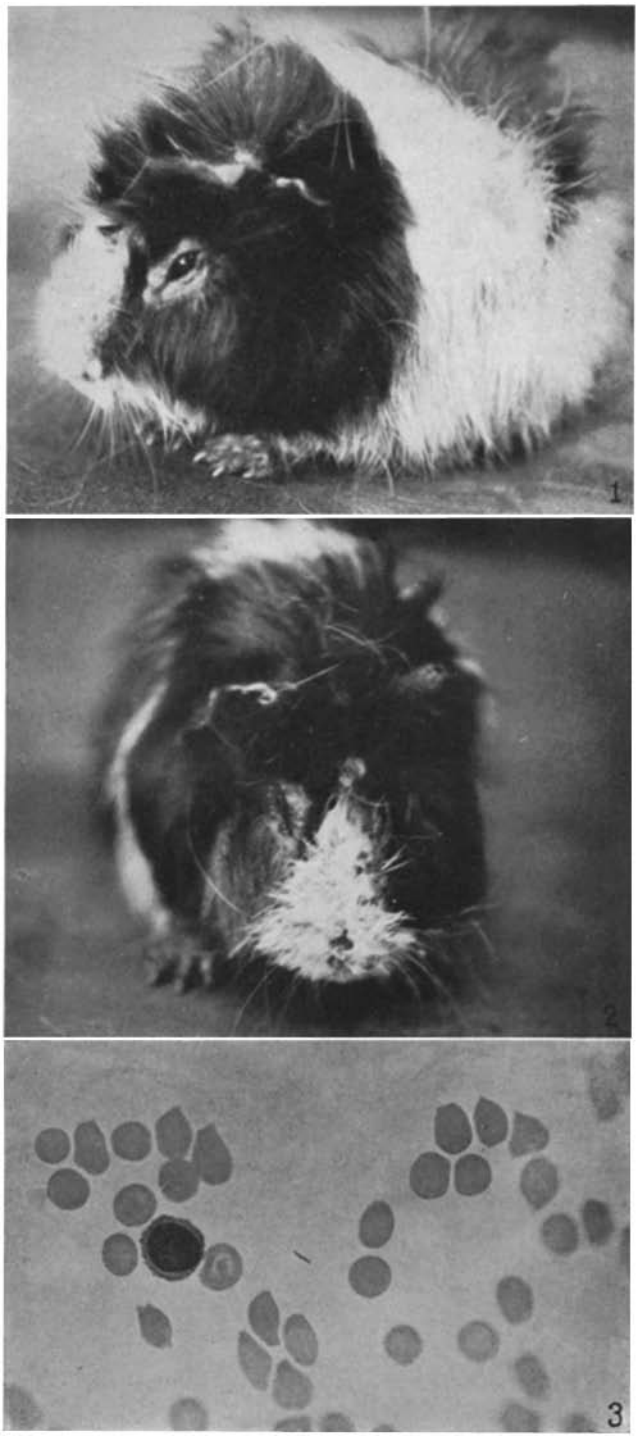
FIG. 4. Section of the cornea of an infected guinea pig. Entering blood vessel surrounded by lymphocytes and plasma cells. Hemalum-eosin, Zeiss obj. D.D.

FIG. 5. Lung thickening of the interstitial tissue, atelectasis, and organization of the alveoli with compensatory emphysema. Hemalum-eosin Zeiss obj. A.

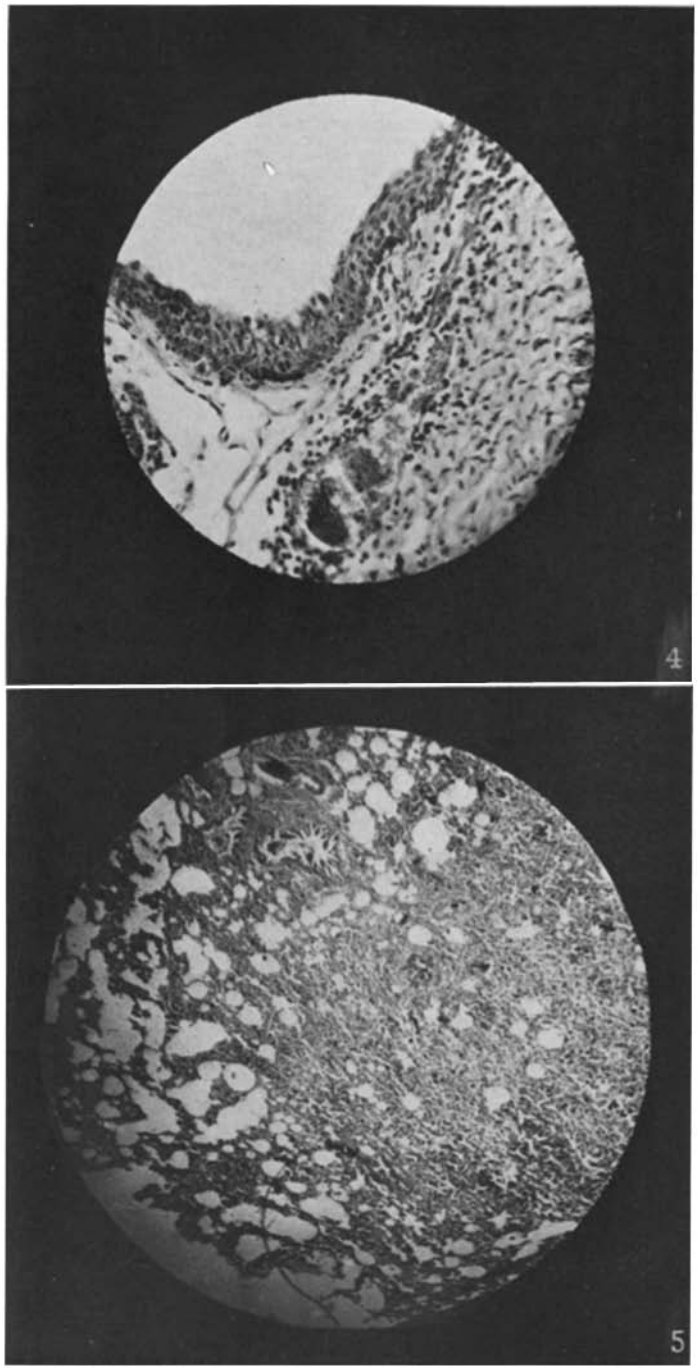
PLATE 32.

FIG. 6. Kidney. Zeiss obj. D. D.

FIG. 7. Brain. Thalamus opticus. Glianodule. Toluidine blue. Zeiss obj. D.D.



(Mooser: Spiral organism in wild rat.)



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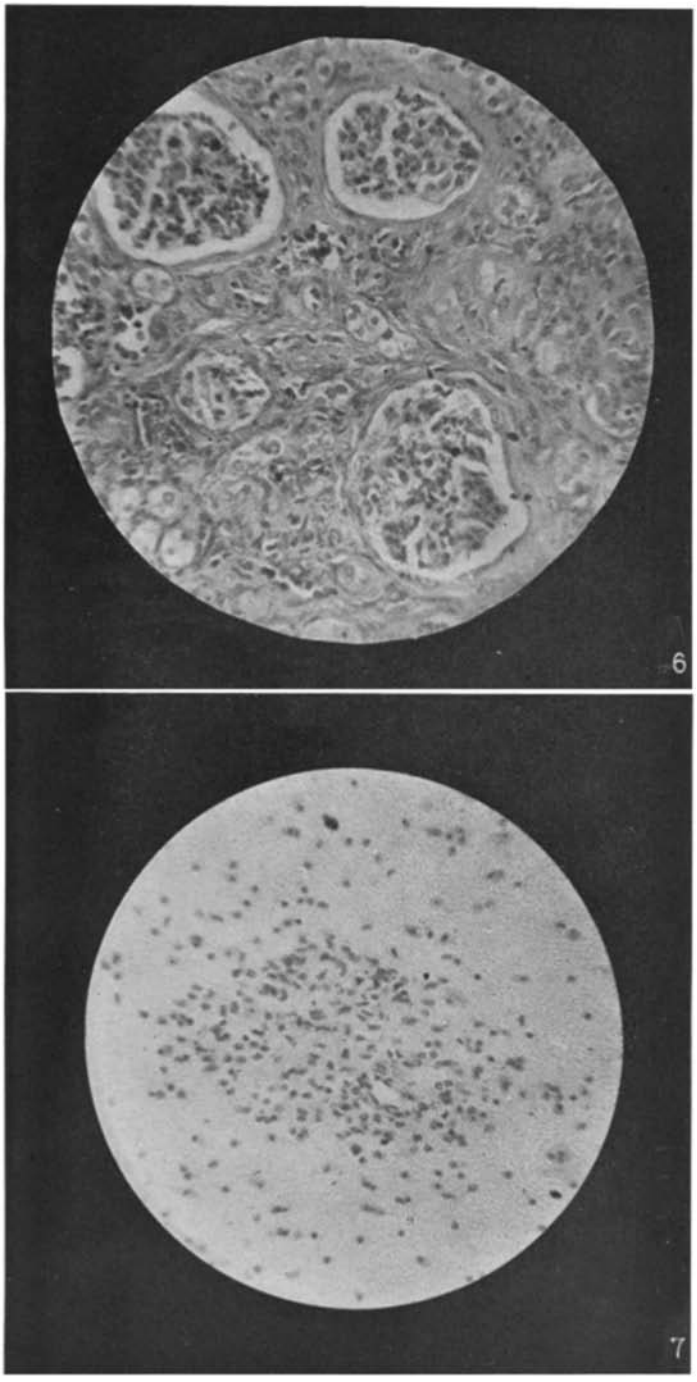

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