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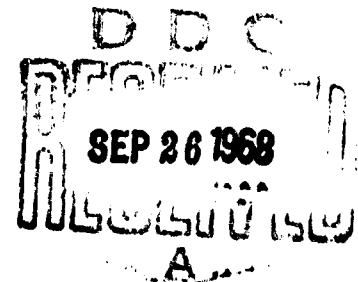
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DEPARTMENT OF THE ARMY  
Fort Detrick  
Frederick, Maryland

Jansen, J. 1941. Todliche Infektionen von Kanichen durch ein filtrierbares Virus. (Fatal infections in rabbits by a filtrable virus). Zentralblatt fur Bakteriologie, Parasitenkunde und Infektionskrankheiten (Central Journal for Bacteriology, Parasitology, and Infectious Diseases) 148: 65-68, 1941

On 13 March, our Institute received for research from another laboratory, the liver of a rabbit, and a rabbit whose abdominal cavity was already opened and was to be macroscopically examined. On 15 March, at our request, an intact animal, which had just died, was sent.

#### CASE REPORT

The report read that on 6 March, ten rabbits were purchased from a dealer. On 8 March, one rabbit died, and on 9 March, two more died. On 13 March, these three arrived (from which we acquired one liver and one opened carcass), on 15 March, the seventh died (the carcass preserved here). Two rabbits, which already had symptoms of illness, were killed for another experiment; the tenth rabbit remained alive. The question concerned an illness with a mortality rate of 70 to 90 %.

The symptoms that were observed were not distinct. The animals were listless one or two days. They sat in a corner staring and did not move around. The feces were too soft. The subsequently examined rabbits should have had no spots on their liver. The dealer reported that he had had no cases of death.

#### INVESTIGATION OF MATERIALS

(a) In the liver are seen considerably irregular, not acute, circumscribed, light-colored spots. In untreated specimens, those from which spots were obtained, no microorganisms were observed under the darkfield microscope. Also, no microorganisms were seen in the bile, and just as

few in stained preparations (methylene blue, gram stain, and Ziehl-Nielson stains). All inoculated cultures (for example, liver broth) remained sterile.

(b) The previously opened carcass showed no other changes than the liver under (a). Also, the results of microscopic and cultural investigations were negative.

(c) The yet unopened, fresh carcass was exhaustively studied bacteriologically. Inoculations were made from the heart, lungs, kidney, spleen, and liver into broth, agar, serum agar, serum broth, and liver broth. After two days under aerobic conditions, the cultures were still sterile. They remained equally sterile under anaerobic conditions. On the basis of these observations, a bacterial infection was considered to be out of the question.

#### EXPERIMENTAL INFECTIONS

From the livers of (a) and (b), a suspension was prepared and was injected subcutaneously into rabbit No. 294. The animal died on the eighth day after inoculation. From the liver and spleen of this animal (c), a suspension was prepared and injected subcutaneously into Rabbit No. 295. This animal also died on the eight day after infection. With Rabbit 294, it was observed that a very large section of the area under the skin going out from the site of infection was uniformly edematous. This edema was colorless and included much moisture. In the liver, the same spots were seen again. The bacteriological investigations gave negative results. Injected with material from these rabbits, rabbit 298 died after seven days (dissection = 294). With the dissection of rabbit 295

No. 295, the following was observed: a somewhat vitreous secretion in the corners of the eyes, a somewhat moist nose and mouth, an anus soiled with soft feces, a vitreous swelling under the skin, hard swollen spleen, a liver with many light-colored spots, lungs somewhat inflated, mucous membranes of the nose red and watery. Bacteriological examinations were negative. Inoculations from the brain, lungs, heart, spleen, kidney, and subcutis were made into agar, broth, serum agar, serum broth, liver broth, and blood agar; all of these media remained sterile. There were now grounds for considering a nonbacterial, contagious disease, probably a filtrable virus.

#### EXPERIMENTS WITH FILTRATE

From Rabbit No. 295, a suspension was prepared from subcutis, lung, liver, heart, spleen, kidney, and brain. After filtration through a Berkefeld filter, a filtrate was obtained that was bacteriologically sterile (controls in serum broth and liver broth). Two rabbits (302 and 303) were injected subcutaneously with this filtrate. Both died after six days. The accompanying chart shows the results of the animal research completed to date.

Since bacteria were not isolated from any of these rabbits and since the clinical picture showed the same changes, it must be assumed that a filtrable pathogenic agent has been the cause of death.

Twelve previously needed experimental rabbits arrived. Of these, four were injected with unfiltered material and eight with filtered material or parts of this material. Of these twelve rabbits, five died on the sixth day, four on the eighth, two on the seventh, and one on the tenth.

#### CLINICAL SYMPTOMS IN THE EXPERIMENTALLY INJECTED ANIMALS

During the first day, one could see no deviation at all. After that, food was suddenly rejected, and after one or two days of loss of energy, the animal died. The impression was obtained that those having the shorter incubation times are visibly ill the shortest time. The animals with longer incubation periods are sick somewhat longer. In agreement herewith are most of the changes in the liver and the spreading of the subcutaneous swelling, both of which are greatest in animals with the longest periods of incubation and sickness.

Concerning the eventual pathogenesis of this "rabbit infecting" virus for other animals and concerning any additional properties, experiments are presently being carried out. The results will be reported later.

#### REFERENCES

In the book by Seidel (1), "Diseases of Rabbits (1935)", no filtrable viruses of rabbits were mentioned at all. In Seifried's "Diseases of Rabbits" (1937) (2), eight filterable virus forms are mentioned, namely: 1) smallpox, 2) infectious papillomatosis, 3) infectious myxomatosis, 4) infectious fibrinomatosis, 5) Conjunctivitis, 6) foot and mouth disease, 7) a virus that generates gangrene of the hind leg, 8) a virus that can be found in healthy rabbits. This list does not cover the virus that we have found.

In the very exhaustive work of Jaffe (3) "Anatomy and Pathology of Spontaneous Diseases of Small Laboratory Animals" (1931), those diseases named under 3, 6, and 8 of Seifried's book were mentioned.

Of the books on filterable virus diseases, the following were examined: "Filterable Viruses" (4) by Rivers (1928) which mentions the so-called Virus III; in the "Handbook of Filterable Viruses" (5) by Fairbanks (1934), no detailed reports on rabbits were found. The "Handbook of Viral Diseases" (6) by Gildemeister, Haagen, and Waldmann (1939) notes the seemingly spontaneous encephalitis virus, the fibriomatosis, myxomatosis, the papillomatosis, and the virus III viruses. The latter was passed by three testicular passages of liquid vaccine material. It followed a course in rabbits almost never fatal and produced no distinct changes. Since the gelatinous aspect of the subcutis somewhat resembled a myxomatosis, which shows a thickening of the outer skin layer and a gelatinous subcutis among other things, rabbit No. 306 was injected intradermally with a Berkefeld filtrate.

When one injects rabbits intracutaneously with myxomatosis material, there develops locally after only three to four days, a thick, solid portion which changes into a tumor. All of the mucous membranes become thickly myxamatosed, especially the area of transition of mucous membranes to skin; the eyelids, nostrils, urogenital openings, and anus are affected. Rabbit No. 306 acquired no tumors at the injection site and the mucous membranes were not thickly myxamatosed. Heavy conjunctivitis, of the type observed in myxomatosis, was likewise never seen with the experimental rabbits, so that an apparent difference exists between this virus and the myxoviruses. (The myxovirus was found and described by Sanarelli (7) in 1898). Hauduroy (8) describes in his book "Les Ultravirus Pathogenesis et Saprophytes" (1934) in addition to the myxovirus and the Virus III,

another virus which concerns hares and was written about by Aoki, Kondo, and Tazawa (9,10). These authors reported in 1927 - 1928 on a virus disease of humans which originates through contact with hares. The virus initially had little virulence for rabbits; through passage, the virulence increased somewhat, but pathologically and anatomically, nothing new was established in the rabbits. In 1938, Kasahara and his associates found a rabbit virus which produced swelling and necrosis of the testicles. The reactions of the eyes corresponded to those associated with variola infections. Also, immunobiologically, this virus is closely related to the poxvirus.

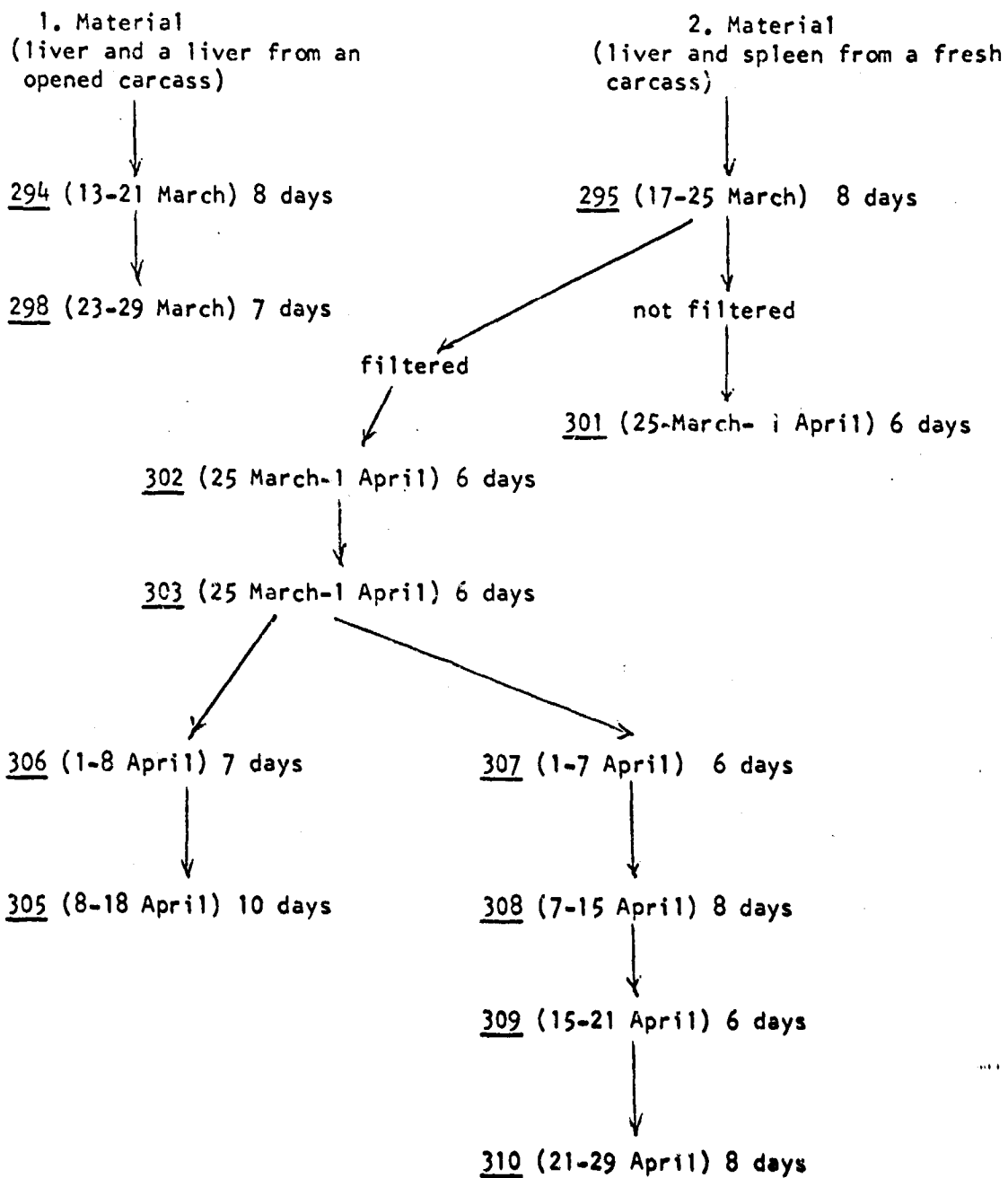
As far as I have been able to see from the literature at my disposal (the newest literature is not very complete), fatal infections of rabbits caused by a filterable virus which I have been able to observe, are still not documented. The research concerning this virus and the pathological-anatomical changes are being carried out further.

#### SUMMARY

A spontaneous, acute, lethal course of disease was observed in ten rabbits, of which only one rabbit liver. The twelve experimental inoculations<sup>10/13</sup> killed all the animals after six to ten days. The causative agent<sup>was</sup> a filterable virus. The symptoms of the spontaneous conditions were 1 to 2 days of no food intake and loss of energy, followed later by death. Upon dissection, small spots on the liver became apparent. The symptoms of the experimental disease were completely normal during the first day, sudden refusal of food, loss of energy, followed by death. Dissection revealed a very moist subcutis, swelling of the spleen and light colored spots on the liver. The intestinal contents were unusually soft.



Fatal Infections of Rabbits by a Filterable Virus



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- (5) Fairbrother, R.W. Handbook of Filterable Viruses, 1934.
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- (8) Hauduroy, P. Les ultravirus pathogenes et saprophytes, 1934.
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- (10) Same authors, Zbl. Bakteriologie. I Orig. 105, 255 (1928).
- (11) Zbl. Bakteriologie. I Ref. 131, 43 (1938).