

## Carrion's Disease. III. Experimental Production in Animals.

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Considerable experimental evidence supports the etiological unity of *verruca peruana* and Oroya fever. In paper IV of this series, a third form of human bartonella infection—the asymptomatic form, detectable only by blood culture—is described. If Oroya fever and *verruca peruana* are caused by a single agent, then virus from either should under suitable conditions, produce both forms of the disease in susceptible animals. The cutaneous form (*verruca peruana*) has been produced in monkeys, directly by the inoculation of verruga nodules<sup>1</sup> and indirectly by the inoculation of cultures of *Bartonella bacilliformis* derived from either form of the disease.<sup>2, 3</sup> The direct inoculation of human Oroya fever material, however, has never, in the past, produced verrugas in monkeys, and the few instances of apparent reproduction of the anemic form (Oroya fever) are not entirely convincing since the possibility of preëxisting bartonella infection was not eliminated. Spontaneous infections of the monkey with Bartonella and related organisms have been reported<sup>4, 5, 6</sup> and the errors which may arise from the use of such animals have been emphasized by Weinman.<sup>7</sup>

Verrugas, identified histologically and by the demonstration of bartonellæ, were produced by the authors in 4 *M. rhesus* monkeys. Lesions developed only in the supra-orbital regions, at the sites of inoculation. In 2 instances the inoculum originated from *verruca peruana* patients (in one case from verruga-tissue; in the other from a positive blood culture). In the other\* 2 instances, the inoculum was an emulsion of lymph nodes containing many bartonella-filled cells, removed postmortem from a fatal case of Oroya fever. Thus, we were able to produce the cutaneous form of the disease in mon-

1 Jadassohn, J., and Seiffert, G., *Z. Hyg. u. Infek.*, 1910, **66**, 247.

2 Noguchi, H., and Battistini, T. S., *J. Exp. Med.*, 1926, **43**, 851.

3 Noguchi, H., *J. Exp. Med.*, 1927, **45**, 175.

4 Pessoa, S. B., and Prado, A., *Rev. Biol. e. Hyg.*, 1927, **1**, 116.

5 Leger, A., *Bull. Soc. Path. Exot.*, 1922, **15**, 679.

6 Malamos, B., *Zbl. f. Bakt.*—I, 1935, **134**, 152.

7 Weinman, D., *Les Parasites Érythrocytaires Révélés par la Splenectomie: Bartonella et Epérythrozoön*, Paris, Amédée Legrand, 1935.

keys by the inoculation of human material both from the cutaneous and from the anemic forms.

The anemic form of the disease was reproduced in one monkey, splenectomized 2 months prior to inoculation, and showing no bartonellæ in blood films during this period of observation. Two cc. of blood from a fatal human case of Oroya fever was injected intravenously and a small amount into the inguinal lymphnodes. Death occurred 26 days after inoculation and was preceded by a severe progressive anemia.

At death, 7% of the red blood corpuscles were infected with bartonellæ, each infected cell presenting one to 12 organisms. Morphologically, these bartonellæ appeared identical with those seen in infected human erythrocytes. The blood of this animal yielded characteristic cultures. Necropsy showed pulmonary tuberculosis and hematophagous nematodes in the intestine, infections which may have played a part in the production of the anemia. The organisms in the erythrocytes, however, were undoubtedly *Bartonella bacilliformis* of human origin.

Finally, in 3 non-splenectomized monkeys, the asymptomatic form of the infection was produced. Blood from a fatal case of Oroya fever was injected intravenously in the first monkey, intravenously and into a lymphnode in the second, and intracutaneously in the third. No clinical evidence of the disease developed, but blood cultures were positive for *Bartonella bacilliformis*.

*Bartonella muris*-free rats, splenectomized or normal, newly weaned and splenectomized adult rabbits, and chickens were not found susceptible to any form of Carrion's disease.

The interpretation of the results of inoculating Peruvian guinea pigs was complicated by the discovery of an undescribed spontaneous bartonella infection in these animals. This problem will be discussed in paper IV.

*Summary.* The 3 types of infection seen in human Carrion's disease have been reproduced in the monkey. The cutaneous form (*verruca peruana*) was produced in monkeys by the inoculation of (a) infected lymph nodes from a patient with the anemic form (Oroya fever), or (b) human verruga tissue, or (c) cultures of *Bartonella bacilliformis* from the blood of human verruga cases. The anemic form (Oroya fever) was reproduced in one splenectomized monkey, free from spontaneous bartonella infection, by the inoculation of blood from an Oroya-fever patient. This animal died showing a multiple infection of his red cells with *Bartonella bacilliformis*. The asymptomatic form was produced in monkeys by the inoculation of blood from Oroya-fever patients.