LEUKAEMIA OF THE FOWL: SPONTANEOUS AND EXPERIMENTAL, NO. VIII

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HARRY C. SCHMEISSER

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I. Review of the Literature.

The first publication was made by Moore[1] in 1895-1896, in which he reported observations upon an epizootic disease of fowls which he designated "infectious leukæmia." His studies were based upon cases obtained from five different outbreaks, and upon those artificially produced by means of the specific organism (Bacterium sanguinarium) isolated from the organs of these fowls. The descriptions of the spontaneous and experimental cases clearly show that he was not dealing with a true leukæmia of the fowl, but rather with an acute infectious disease, characterized by fever, diminution in the number of red blood cells, and increase in number of white blood cells, this increase being "restricted" to the polymorphonuclear leucocyte with the eosin staining spindles, *i. e.*, the phagocyte of the normal fowl's blood.

Butterfield,[2] in 1905, reported three cases of aleukæmic lymphadenoid tumors of the hen. His studies were limited to the livers of these animals. They correspond in every detail, both grossly and microscopically; were uniformly and strikingly enlarged (340, 420, 270 gm. respectively) and of a diffuse, light, cream, yellow color. Histologically, the liver tissue was extensively replaced by large oval or round, sometimes irregular, collections of cells. The intralobular capillaries were filled with the usual nucleated red blood cells. Most of the nodules of tumor cells were thought to be in connection with the portal spaces. The cells resembled in general the "large

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lymphocyte" of the hen's blood.* Allowing for flattening due to pressure, these cells were round or oval, with round or oval nuclei, mostly eccentric. The nuclear chromatin appeared granular or reticular. The nucleus was not infrequently pale and vesicular with one or more bright chromatin bodies. The cytoplasm was present as a narrow rim, non-granular, and basophilic. Mitoses were common. Between these cells was seen a delicate reticulum. In association with these tumor masses were quite large collections of eosinophilic cells, the majority showing a single, pale, round or oval, eccentric nucleus and a relatively abundant cytoplasm, filled with large, round, elongated, or spindle-shaped oxyphilic structures. They varied greatly in size and shape. The lymphocytes and eosinophiles were occasionally seen in the capillaries, but there was "certainly no definite increase within the blood-vessels." From the character of the cells, their relation to the portal spaces and absence of the lymphæmia, the condition was regarded by Butterfield as a proliferation of periportal lymphadenoid tissue, and thought by him to merit the designation "aleukæmic lymphadenoma."

Mohler had under observation five similar cases showing lymphæmia and the same lymphadenoid condition. Mohler's description of two of his cases, as presented by Butterfield, is as follows: The process showed a tendency to involve several organs. In one case the liver and spleen were the principal seats, the lungs and intestine were also involved. The liver was enlarged to twice the normal size, of very light color and mottled. Throughout its surface and within its parenchyma were whitish lymphomatous deposits of varying diameters. A section shows the liver tissue only partly obliterated as a result of a filling up of the interacinous capillaries with leucocytes. The spleen was about the size of an ordinary blue plum. Each lung contained a white spherical area, the size of a pea and composed of hyperplastic lymphoid tissue, infiltrating white cells. In the wall of the large intestine, involving the lymphadenoid tissue, were round, slightly raised nodules. In the second case the changes were most marked in the kidney and spleen. The liver, intestine and heart were also involved. The kidneys were three or four times the normal size and had macroscopically very much the same appearance as the liver in the first case. The myocardium contained some small, whitish

* Obviously the large mononuclear cell of the classification presented in this paper.

areas. Butterfield, in comparing the histological findings in Mohler's cases with his own, finds a convincing similarity between, or identity of, the infiltrating cells. In Mohler's cases, the infiltration was more diffuse and not so regularly arranged about the portal tissue. Above all, the white blood cells were markedly increased in all the blood-vessels, from the intraacinar capillaries to the largest veins. The predominating white cell was indistinguishable from the cells in the tumor masses of both these and Butterfield's cases. From the foregoing, Butterfield felt justified in granting "the existence of a leukæmic and aleukæmic lymphadenoid hyperplasia in hens."

Butterfield and Mohler deserve the credit of showing that leukæmia occurs in the fowl. Their studies were limited to post-mortem findings.

To Warthin,[1] in 1907, we are indebted for the first complete study of this disease in fowls. He had the good fortune to secure a living animal, which he kept under observation for two and a half months before it died. During this time he had an opportunity of carefully studying the clinical course. The blood showed a great reduction in the total number of red blood cells. These varied greatly in size and shape, and contained less hæmoglobin than normal. The total number of white cells was greatly increased. Differential counts showed a striking increase of the "large lymphocyte" at the expense of the other cells of the normal blood. Numerous mononuclear forms of the eosinophiles, cells abnormal to the blood, were seen. From the blood changes Warthin felt justified in making a diagnosis of "lymphatic leukæmia of the large cell type." A careful autopsy revealed the following findings: The liver was greatly increased in size and was pale yellow in color. The spleen and kidneys were also enlarged; both showed numerous yellowish spots from pin-point to pin-head in size. In the hæmolymph nodes small yellowish nodules were found. The bone-marrow appeared as solid plugs, reddish-yellow and friable. The tissue changes were summarized as follows: (1) Tumor-like nodules and infiltrations of lymphoid cells in all the organs, particularly in the liver, spleen, kidneys, bone-marrow and hæmolymph nodes; (2) replacement of the normal white cells of the blood by cells of the large lymphocyte type, more or less atypical in character, but identical with cells in the tumor masses. From the findings, both in the blood and in the tissue, Warthin made the diagnosis of leukæmic lymphocytoma.

He likewise examined the material from two additional cases of lymphadenoid tumors of the fowl. One proved to be of the aleukæmic type, as described by Butterfield; the other was of the leukæmic form, as described above. The histological picture, apart from the increase of white cells in the blood-vessels in the one case, was identical in both cases and also with that in the cases given above (Butterfield's, Mohler's and Warthin's). From these cases Warthin concludes, therefore, that there occurs in the common fowl a condition of disseminated lymphocytoma, sometimes aleukæmic, at other times associated with an increase of the white cells of the blood, this increase consisting in the appearance of great numbers of cells of the large lymphocyte type and apparently identical with the lymphoid cells of the tumor nodules. He also regards the aleukæmic and leukæmic conditions as genetically related, if not actually one and the same process in different stages. Both conditions, he thinks, are in all respects analogous to the similar ones existing in man.

The preceding cases appear to be very similar to those reported by later investigators and designated by them as splenomedullary in type.

Kon[8] in 1907, after the appearance of Warthin's article, reported what he considers a true case of leukæmic disease of the chicken. The gross and microscopical changes, which were studied and reported in great detail, are in general identical with those of the cases above. In addition, he found giant cells, though only a few, in the bone-marrow, and mitoses in the basophiles as well as in the eosinophiles in the kidneys. Because of the lack of smears, he determined the ratio W/R and made differential counts from sectioned blood-vessels of the liver. He found that the white cells, as compared with the reds, were greatly increased and that the large mononuclear was the predominating cell of the whites. Mitoses of this cell were observed. The evidence given, he thinks, is sufficient to consider this a case of true leukæmia. Because of the enormous swelling of the spleen and the plentiful occurrence of the characteristic cell in the pulp of the normal spleen and to a lesser degree in the normal bone-marrow, and in the absence of lymphatic swelling and the occurrence of this cell in the normal lymph tissue, it seems to him most likely that this is a case of true "splenic leukæmia."

Soshestrenski,[9] in May, 1908, reported a case of spontaneous leukæmia of the fowl, very similar to the case described by Kon.

His study was limited to gross and microscopical findings at autopsy. The bone-marrow was omitted. The contents of the blood-vessels of the organs were found to be leukæmic. He designates the case also as "splenic leukæmia," but in so doing he calls attention to the fact that the process involves many of the other organs and appears to be only primary and most marked in the spleen. There was no enlargement of the lymph-glands.

With Ellermann and Bang,[17] in 1908, the subject takes on a different phase. Up to this time, the communications dealt entirely with the recording of spontaneous cases of leukæmia in the fowl. Ellermann and Bang were the first to successfully transmit the disease by experimental inoculations from a spontaneous case to other, healthy, fowls. In fact, they claim to have been the first to successfully produce the disease experimentally in any animal. They report the findings in two typical spontaneous cases giving identical pictures. The blood study during life was found to be practically the same as that of Warthin's case, with the exception that the large mononuclears frequently contained in their cytoplasm many granules, and thus represented cells which are not found in the normal blood—myelocytes. Small granules alternated with very large ones. The autopsy showed an enlarged spleen and liver, the latter with white dots and streaks. The bone-marrow was gray-red. The other organs presented nothing of interest. The microscopical changes were very similar to those of Warthin's case. The experimental leukæmia they transmitted to the third generation, producing a blood picture and organic findings identical with those of the spontaneous cases.

Pseudoleukæmia, which is characterized by the same organic lesions as are found in true leukæmia, but in which the blood picture is normal, they found to occur spontaneously among chickens. They received from the same flock, at the same time, a leukæmic and pseudoleukæmic animal. From the pseudoleukæmic animal, by inoculation, they produced a leukæmic animal, and conclude, therefore, that the leukæmia and pseudoleukæmia of chickens are etiologically identical.

Multiple sarcomatosis of the peritoneum occurs epidemically in the fowl. They consider this a manifestation of leukæmia, because by inoculation from such a case they produced an atypical leukæmia and carried this to the second generation.

They were successful in two out of five inoculations with a filtrate from an emulsion passed through a "Kerze aus Infusorierde" and