ON CERTAIN SPONTANEOUS CHICKEN TUMORS AS MANIFESTATIONS OF A SINGLE DISEASE.

I. SPINDLE-CELLED SARCOMATA RIFTED WITH BLOOD SINUSES.*

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PLATES 69 TO 71.

Recently three transplantable chicken tumors distinct in character have been found to have a filterable cause. The differences between these tumors are traceable to differences in the causative agents. Each agent gives rise in normal fowls to tumors of the sort from which it was isolated by filtration, and to tumors of this sort only. For example, the agent derived from a transplantable osteochondrosarcoma gives rise to sarcomatous tumors in which cartilage and bone are laid down. Certain minor variations, it is true, do occur in each tumor strain as intercurrent phenomena. The cells of the sarcoma known in our laboratory as Chicken Tumor I are, in some chickens, of very attenuated spindle form, again oat-shaped or almost round, again interspersed with sarcomatous giant cells; and the course of the disease varies somewhat in individual fowls. But the growth is always a spindle-celled sarcoma, and its modifications are not greater than those observed in certain rat and mouse tumors propagated only by transplantation and dependent on the survival of a single race of cells. Attempts to bring about variations by injuring the filterable agent have been unsuccessful, as have attempts to make it affect epithelium.

There is good ground to suppose that other tumors of the fowl besides those already studied are caused by filterable agents. The range in structure and behavior among chicken tumors is very wide.

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Even when composed of cells of similar origin they often exhibit, like mammalian growths, a strikingly various structure and course. Must one suppose a distinct causative agent not only for each type of neoplasm as determined morphologically, but for the almost infinite number of variations in structure and behavior of such types? The present article and the one following it deal with this point. Briefly, it has been found that two spontaneous chicken tumors recently transplanted have each given rise to neoplasms identical in composite behavior with a tumor strain already under propagation. As will be shown in the present paper, the spontaneous tumor known as Chicken Tumor 38 of our series, seems to be a manifestation of a disease-complex already reported upon and known as Chicken Tumor 18. This latter growth is a spindle-celled sarcoma, rifted in a characteristic manner with blood sinuses and tending to metastasize to the muscles, especially in the neighborhood of joints.

THE SPONTANEOUS TUMORS.

The spontaneous tumor No. 38 resembled the spontaneous tumor No. 18 only in the fact that it was a growth composed of spindle cells of connective tissue origin. The fowl carrying it was a well grown but emaciated Plymouth Rock hen. It was brought to the laboratory while yet alive. The irregular tumor mass, situated in the subcutaneous tissue between the left leg and the body, measured 10 by 6 by 5 centimeters, was imperfectly encapsulated, attached to the sheath of the thigh muscles, and just beginning to involve the skin. Strands extended between the leg muscles into the drumstick. At the center of the mass was a cavity with ragged walls, containing about forty cubic centimeters of clear, straw-colored fluid. The tumor tissue was finely striated, pinkish white, rather soft, and varied with many irregular, translucent areas of colliquation. There were no metastases. Histologically the growth was composed of strands of attenuated spindle cells with much collagen, sometimes in the form of ribbons (figure 1). A few round cells were scattered here and there in the growth. There was very little resemblance to the spontaneous tumor No. 18. This latter occurred

in the gizzard of a brown Leghorn fowl and metastasized to several points in the skeletal muscles. Both the primary and secondary tumors consisted of a very regular spindle-celled tissue, rifted to an extraordinary degree with blood sinuses into which the growth showed a tendency to extend, with result in an intracanalicicular arrangement.

The fowl carrying Chicken Tumor 38 was killed and bits of the neoplastic tissue were implanted in the breast muscle of two normal Plymouth Rock fowls, in both of which a growth slowly developed. With repeated passage the tumor's rate of growth has increased somewhat, but like No. 18 it is still much less malignant than the simple spindle-celled sarcoma, Nos. 1 and 43. It is now growing in its fourth successive series of hosts. A filterable agent causing it, distinct from the tissue cells, has been demonstrated by three methods; namely, by drying, by glycerination, and by filtration through Berkefeld cylinders impermeable to small bacteria. The findings compared with those in the case of No. 18 are, briefly, as follows:—

**COMPARISON OF THE TUMOR STRAINS.**

Both growths, whether obtained by transplantation or by the action of the filterable agent as such, are, in the gross, solid, pinkish white, unencapsulated, firm, and markedly resistant to the knife. When growing in voluntary muscle they tend to bind the fibers and limit motion, a feature not observed in the case of the simple spindle-celled sarcoma already mentioned. Both growths are composed of attenuated spindle cells arranged, often very regularly, in bundles or strands with much collagen which is usually in the form of bands or ribbons (figure 2). Giant cells are not present. The rifting with blood sinuses, which was so important a feature of the earlier generations of Chicken Tumor 18, is now only occasionally seen in this growth. Absent at first from Chicken Tumor 38, it has recently been met with in several cases (figure 3). Histologically the two growths are at present practically indistinguishable.

Chicken Tumor 18 in its earlier generations showed a notable tendency to metastasize to the skeletal muscles, especially in the neighborhood of joints. The lungs, heart, and liver were affected.
sometimes, though rarely. Among nine fowls which have thus far died of Tumor 38, one had secondary tumors in lung, liver, and gizzard. In three cases there were metastases in the skeletal muscles. The simple, spindle-celled sarcomata, Nos. 1 and 43, have never shown this feature. Of the three instances referred to, one had a nodule in the wing, a second both wing and leg metastases, while in the third the involvement was widespread. A small nodule was present in the lung, larger secondary growths in the muscles of the neck, legs, and hip, and a series of coalescing masses connected the junctions of the sternal and vertebral ribs, forming what may be called a neoplastic rosary (figure 5). The whole condition closely resembled that in a fowl which died of tumors produced by the injection of a filtrate of Chicken Tumor 18.3

Tumor 18, though spontaneous in a brown Leghorn fowl, grows much better in the Plymouth Rock variety, a fact only recently determined and still to be reported upon in full. Chicken Tumor 38 likewise succeeds better in Plymouth Rocks than in brown Leghorns. But the two cases are hardly to be compared, for Tumor 38 occurred spontaneously in a Plymouth Rock fowl, and, from what is known of the laws governing transplantation, might be expected to succeed best in hosts of this sort, as indeed it does. Tumor 18 acts against the rule, growing better in hosts of an alien variety.

THE FILTERABLE AGENTS.

A causative agent for Chicken Tumor 18, as distinct from the cells, has been demonstrated only by filtration experiments. The dried or glycerinated tumor tissue is incapable of causing the growth. Tissue of No. 38, dried or glycerinated, gives rise to the tumor in a considerable percentage of normal fowls injected, and this within a few weeks. The Berkefeld filtrate of an extract of the growth acts almost as quickly. Filtrates derived from No. 18, on the other hand, seldom cause a tumor until several months after the injection. The differences in resistance and activity of the causative agents, as thus indicated, are the only points of dissimilarity between the tumors at present.

3 Rous and Lange, loc. cit.
CHICKEN TUMOR 27.

All in all, the findings give one good reason to suppose that the spontaneous chicken tumors, Nos. 18 and 38, are different manifestations of a single disease-complex. It has seemed possible that other expressions of this complex might be present among our forty-five spontaneous neoplasms of the fowl. A search shows that the growth known as No. 27 is probably such a case. The host, a brown Leghorn hen, had several large lumps in the muscles of the wings and legs which limited motion markedly, a small nodule in the gizzard, and a number of raised, sharply defined, plateau-like masses in the skin, some deeply pitted with feather follicles and one of them ulcerated. It was impossible to say which growth was primary. All consisted of a close textured, finely striated, firm, pink, sarcomatous tissue. At the time, the case appeared unique, and indeed among the spontaneous growths subsequently obtained none has given a similar picture. But among the many fowls dying of transplantation tumors of No. 18,—now in its eleventh successive series of hosts,—a single instance closely resembling that of No. 27 has been met with. The fowl, of the second transplantation generation, is mentioned in a previous article.¹ The discoid masses in the skin consisted, as in the case of Tumor 27, of a sharply defined, nearly homogeneous, spindle-celled, sarcomatous tissue in the looser layers of the corium, the masses in the muscle of the same sarcoma arranged for the most part in the familiar intracanalicular pattern (figure 4). Unfortunately no adequate attempt was made to transplant Tumor 27. The other spontaneous chicken tumors do not suggest, even remotely, the disease-complex of Nos. 18 and 38.

SUMMARY.

Two spontaneous chicken tumors, unlike in several important respects, have given rise on transplantation to neoplasms of identical character. The spontaneous growth, No. 18, situated in the gizzard, was a spindle-celled sarcoma rifted with blood sinuses into which it extended, with result in what may be described as an intra-  

¹ Rous and Lange, loc. cit.
The metastases, which were in the voluntary muscles, showed the same peculiar structure. Tumor 38, occurring in the subcutaneous tissue of the groin, was a solid, spindle-celled sarcoma of rather close texture, with few blood vessels. Here and there were small areas of softening, and at its center was a large degeneration cyst with ragged walls, containing a clear fluid. There were no metastases. The transplantation tumors from both growths have been characterized by slow growth, tendency to metastasize to the skeletal muscles without involvement of the lungs, and a structure which at one time is that of a very regular spindle-celled sarcoma containing many bands and ribbons of collagen, and at another that of a sarcoma rifted with blood sinuses like the spontaneous tumor No. 18. At present the two strains are practically indistinguishable in appearance and general behavior. Both are caused by filterable agents. The agent causing No. 38, unlike that causing No. 18, retains its activity in tumor tissue which has been dried or glycerinated; and in a Berkefeld filtrate it is much the more active in causing tumors. These differences can hardly be thought of as constituting a fundamental distinction between agents which, to judge from their effects, are almost undoubtedly different strains of a single disease cause.

That chicken tumors of markedly different type have different filterable agents as their cause has been proved by experiments already reported. The present findings make it probable that, within certain limits, tumors of rather various character may be dependent upon a single agent. This assumption greatly simplifies the etiological problem. But the truth of the assumption for other instances than those described in the present article can only be determined by the study and comparison in many hosts of the disease-complexes of which each spontaneous chicken tumor is to be considered as an individual expression.
Spontaneous Chicken Tumors.

EXPLANATION OF PLATES.

PLATE 69.

Fig. 1. Section of the spontaneous tumor No. 38. It is composed of spindle cells in strands, with abundant collagen. There is some round-celled infiltration.

Fig. 2. A solid growth of the third generation of transplants. The heavy black spots are artefacts.

PLATE 70.

Fig. 3. Portion of a growth that resulted from the injection into a normal fowl of tumor tissue that had been dried while frozen. The rifting with blood sinuses here shown has been found in several transplantation growths as well.

Fig. 4. Spontaneous Tumor 27. Section of one of the growths in the skeletal muscles.

PLATE 71.

Fig. 5. Secondary growths in a fowl of the first transplantation series of Tumor 38. The primary growths were situated in the pectoral muscles. They have been removed with the sternum except for a small portion of that on the left (A). There are metastases in both legs near the knee (B), in the neck muscles (C), and in the muscles within the bony trunk (D). A number of nodules coalescing into a thick cord (E) connect the junctions of the sternal and vertebral ribs.

The microscopic sections were stained with methylene blue and eosin. The illustrations should be compared with those of Chicken Tumor 18 (Rous and Lange, loc. cit.).
Fig. 3

Fig. 4.
(Rous: Spontaneous Chicken Tumors.)
FIG. 5.

(Rous: Spontaneous Chicken Tumors.)