

MELANOMA (SARCOMA) OF THE EYE IN A SYPHILITIC RABBIT.

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PLATES 29 AND 30.

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Several years ago, we reported the occurrence of a malignant tumor which arose at the site of a syphilitic scar in the scrotum of a rabbit. This tumor was transplanted and subsequently used in an extensive series of investigations dealing with the subjects of tumor growth and malignancy. More recently, we have encountered a tumor of the eye in a rabbit a report of which is given in the present paper on account of the circumstances attending its development and the unusual character of the growth.

History.

The history of the tumor is as follows:

The rabbit was a male of the common grayish brown type, probably about 8 to 10 months old when first placed under observation. At this time, it was noted that the animal was apparently blind in the right eye. The pupil was fixed and irregular, and there was a diffuse opaque white mottling in the pupillary area. An ophthalmoscopic examination was not made.

On January 13, 1921, the animal was inoculated in the right testicle with a strain of *Treponema pallidum* (Strain V of our series) that had been carried in rabbits for 15 months and was of comparatively low virulence. An orchitis developed within 8 to 10 days and the inoculated testicle was removed (under ether anesthesia) on the 15th day after inoculation. A metastatic orchitis of the left testicle developed 40 days after inoculation, and about 2 weeks later there were a few papular lesions in the left scrotum associated with a general enlargement and induration of the inguinal and popliteal lymph nodes. The testicular lesion was comparatively slight and soon healed, leaving the testicle atrophic and fibrous. The papules in the scrotum persisted for several months with varying activity. At times, they almost disappeared, then recurred, and on several occasions showed a tendency to fuse, forming patches of infiltration with a scaly or weeping surface.

There were a few small lesions of similar character on the sheath and about the anus. These may or may not have been syphilitic. No other lesions were noted.

On February 6, 1922, the rabbit was reinoculated in the skin of the sheath with the same strain of *Treponema pallidum* used for the first inoculation, and on March 20, 1922, it was given a third inoculation. In this instance, the organism used was the Nichols strain. The local inflammatory reaction following these two inoculations was comparatively slight. No chancre developed, but on May 4, 45 days after the last inoculation, the right eye showed an intense congestion and edema of the conjunctiva, a diffuse clouding of the cornea with pannus, and small, pale, yellow masses in the upper anterior quadrant of the iris which protruded slightly into the anterior chamber; the bulb was tense and showed several irregular prominences in the region of the sclerocorneal junction. In addition, there was profuse lacrymation and pronounced photophobia. This condition persisted, with some intensification, for 5 or 6 days. The inflammatory reaction then began to subside and by the end of the 8th day the intensely acute manifestations had practically disappeared. The sclera was then of a distinctly yellow color, the bulb less tense and irregular than it had been, but the mass in the iris and ciliary body had extended forward and almost filled the anterior chamber, completely obscuring the greater part of the iris. The animal was in good physical condition and was killed for postmortem examination on the 9th day after the lesion of the eye was first noted.

Postmortem Examination.

The right eye was removed and sectioned horizontally. In the position of the iris and ciliary body there was a mass of tissue measuring 4.0 to 6.0 mm. in thickness which protruded into the anterior chamber (Fig. 1). The mass was semitranslucent and of a pale, yellowish pink color with irregular areas of black pigmentation. Its anterior limits were fairly distinct, but posteriorly it became indistinguishable from the vitreous. At its center, the growth completely surrounded the lens and laterally it fused with the cornea and the choroid. The cornea was thickened and clouded throughout; at the periphery it measured 4.0 mm. in thickness, while toward the center it diminished to 2.0 to 2.5 mm. The lens itself was translucent, but on the inner surface of the capsule there was a thin deposit of chalky white material which covered the pupillary area.

The heart, lungs, and liver were normal. The thymus and spleen were small but otherwise normal. The kidneys showed a moderate scarring. The left testicle was atrophic and its tunics were thickened. The brain and cord were normal. The thyroid was small and of a

yellowish gray color. The parathyroids and the suprarenals were considerably enlarged. The lymph nodes, with the exception of the deep cervicals, were very small and pigmented. The pineal gland was large. The hypophysis was normal. The bones and bone marrow were normal with the exception of an enlargement of the distal end of the right femur and some inflammatory thickening of the tissues about the knee. There was a mucopurulent exudate in the nasal passages and sinuses, and pus in both middle ears.

Demonstration of Treponemata.

Material from the lesion of the right eye was examined for treponemata by dark-field illumination with negative results. An emulsion was then prepared and 0.4 cc. was injected into the right testicle of three rabbits and a small piece of the cornea was implanted in the left scrotum of each of these animals. Two other rabbits were inoculated in the right testicle with an emulsion of a popliteal lymph node.

After a prolonged incubation period, all of these rabbits developed a syphilitic infection in the inoculated testicle which pursued an uneventful course. There was, however, no definite reaction at the site of the corneal implants. In one animal, a small translucent nodule developed and then retrogressed but the nature of the lesion was not determined. The animals were discarded at the end of about 4 months, all lesions having disappeared.

Microscopic Examination.

Microscopic examination of sections from the right eye showed an extensive pigmented growth composed chiefly of spindle cells (Figs. 1 to 7). The iris and ciliary body were virtually replaced by a growth which extended forward into the anterior chamber and the cornea and backward over the posterior surface of the iris, partially surrounding the lens, and into the choroid. The sclera was invaded in several places, but apparently the growth was still confined within the bulb except over a small area on the anterior or nasal side of the eye where it had penetrated into the conjunctival tissues at the sclerocorneal junction (Fig. 1).

The structure of the growth varied in different locations. On the anterior or nasal side, the growth in the ciliary body and adjacent parts

of the iris, the choroid, and the cornea was composed of small spindle cells arranged in irregular compact bundles with a fairly abundant stroma of dense fibrous tissue (Fig. 2). There was little or no pigment in this part of the growth and comparatively few cells showed mitotic division.

The growth in the iris was also composed chiefly of spindle cells, but the cells were much larger and more irregular and were arranged in bundles which showed a tendency to cross at right angles to one another as in the case of the muscle bundles of the iris (Fig. 3). Many of these cells showed mitotic figures.

The growth in the iris also contained more pigment than that elsewhere. The pigment was irregularly distributed but, in general, followed the outlines of what was the posterior surface of the iris and ciliary processes with a finer network extending through all parts of the growth (Fig. 1). It was both free in the tissues and contained in cells, some of which were round or oval, and closely resembled the normal pigment cells of the iris or of the retina, while others were irregular polyhedral or spindle shape (Fig. 3).

The cells composing the growth toward the periphery of the iris and in adjacent parts of the ciliary body were extremely irregular. They varied from a small to a very large spindle and from a small round cell to a large round or polyhedral cell with single or multiple nuclei (Figs. 4 and 5). Another feature of this part of the growth was the presence of numbers of giant cells or irregular protoplasmic masses many of which showed atypical mitotic figures.

In the choroid, large round or oval cells predominated. In fact, this type of cell was most numerous in all of the actively growing parts of the lesion with the exception of the cornea. Here, the growth was composed chiefly of oval and spindle cells (Fig. 6) surrounded by a rich network of coarse, wavy fibrils, and was practically devoid of pigment. The cells showed a remarkable uniformity of arrangement with the formation of a structure which, on section, presented an appearance which might be described as a pennate or even a herring bone arrangement.

There was no unusual development of blood vessels in any part of the growth and no hemorrhage. There were only two extensive areas of necrosis; one of these was situated on the anterior surface of

the iris and the other immediately in front of the lens. Over the posterior surface of the iris and in the region of the ora serrata, in particular, there was some diffuse necrosis, but elsewhere the cells were well preserved and in an active state of division.

There was practically no reaction in the tissues surrounding the growth except in the cornea, which showed a chronic inflammatory reaction (Figs. 6 and 7) identical in all respects with that seen in cases of syphilitic keratitis (Fig. 7). The reaction was most marked at the periphery of the cornea and in the region of the sclerocorneal junction, but, as is usual in such cases, there was a pronounced edema of the entire cornea with a slight cellular infiltration and a diffuse growth of capillary vessels.

DISCUSSION AND CONCLUSIONS.

It is evident from the description that has been given that the growth in the eye of this rabbit was a neoplasm of the type usually designated as a melanoma or sarcoma. Aside from the fact that the tumor appears to be the first of its kind that has been reported in a rabbit, the points of especial interest are its origin at the site of an old lesion of unknown etiology, the sudden assumption of extremely rapid growth, and the relation of the tumor to a syphilitic infection.

The evidence available indicates that the tumor originated in the periphery of the iris or in the ciliary body and that its occurrence was influenced in some way by a preexisting abnormality of a type that is comparatively common among rabbits. The time at which the neoplastic transformation took place is, of course, unknown, but the animals of this group had been examined regularly at least two or three times a week, with especial attention given to the eyes. It is not likely, therefore, that any decided reaction in the eye of this animal could have been overlooked, and it is almost certain that the time between the beginning of active growth and the detection of the lesion was only a few days. In fact, the sudden development of the lesion at an interval of 6 weeks after a superinoculation with a highly virulent strain of *Treponema pallidum*, the appearance of the lesion, and the occurrence of spontaneous retrogression at the end of a week did not suggest tumor growth but a pronounced case of granulomatous

syphilitic iridocyclitis. The condition was unusual, however, in so far as the excessive growth of tissue was concerned, and was of especial interest to us on account of its relation to a superinoculation. At the time, it was thought that the lesion might be an expression of allergy, and the animal was killed in order to obtain material for pathological study and with a view to establishing the supposed syphilitic nature of the affection. The failure to find treponemata by dark-field examination could be satisfactorily explained either on the basis of allergy or as a result of spontaneous resolution. The inoculation of other rabbits showed that treponemata were present, thus confirming the clinical diagnosis of syphilis. There was considerable delay in obtaining sections and the matter was dismissed until very recently when we had occasion to refer to the sections from this autopsy. It was then found that, while there was an unmistakable syphilitic reaction in the cornea, the main lesion was not syphilitic but a definite neoplasm.

These circumstances are related for the purpose of making clear the close association of what was undoubtedly an allergic reaction to syphilis and the sudden development of neoplastic activity. Both of these conditions appear to have been influenced by a preexisting non-specific lesion. Moreover, the occurrence of the two reactions coincided so closely that they appeared to be parts of a single process. This may have been merely a fortuitous coincidence but both conditions are so unusual that we are inclined to regard their simultaneous occurrence as evidence of an etiologic relation. Either condition may have influenced the other, but it seems likely that the original syphilitic infection was the factor which determined the allergic reaction to a subsequent inoculation and was in some way responsible for the sudden development of the tumor.

SUMMARY.

A melanotic tumor developed in a defective eye of a syphilitic rabbit following repeated genital inoculations with *Treponema pallidum*. The appearance of the tumor coincided with the development of a syphilitic lesion in the same eye, suggesting a relation between the occurrence of the two lesions.

EXPLANATION OF PLATES.

PLATE 29.

FIG. 1. Horizontal section through the middle of the eye reconstructed by joining up nasal and temporal portions. The areas designated by letters are those from which Figs. 2 to 7 were taken. $\times 7$.

FIG. 2. Small spindle cell growth from *A*, Fig. 1. $\times 210$.

FIG. 3. Large spindle cell growth from the iris (*B*, Fig. 1). $\times 210$.

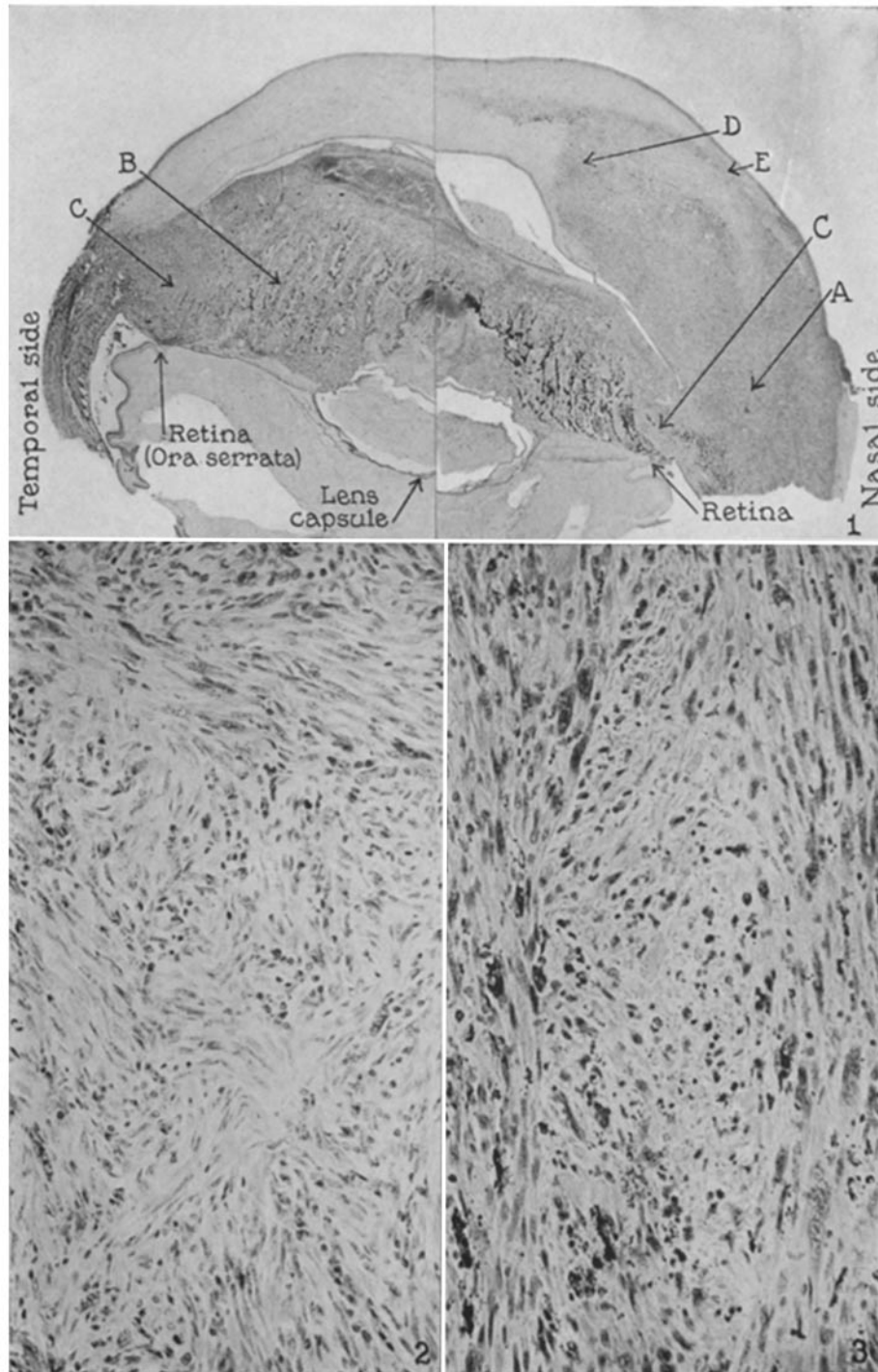
PLATE 30.

FIG. 4. Ciliary body or iris (*C*, Fig. 1). $\times 500$.

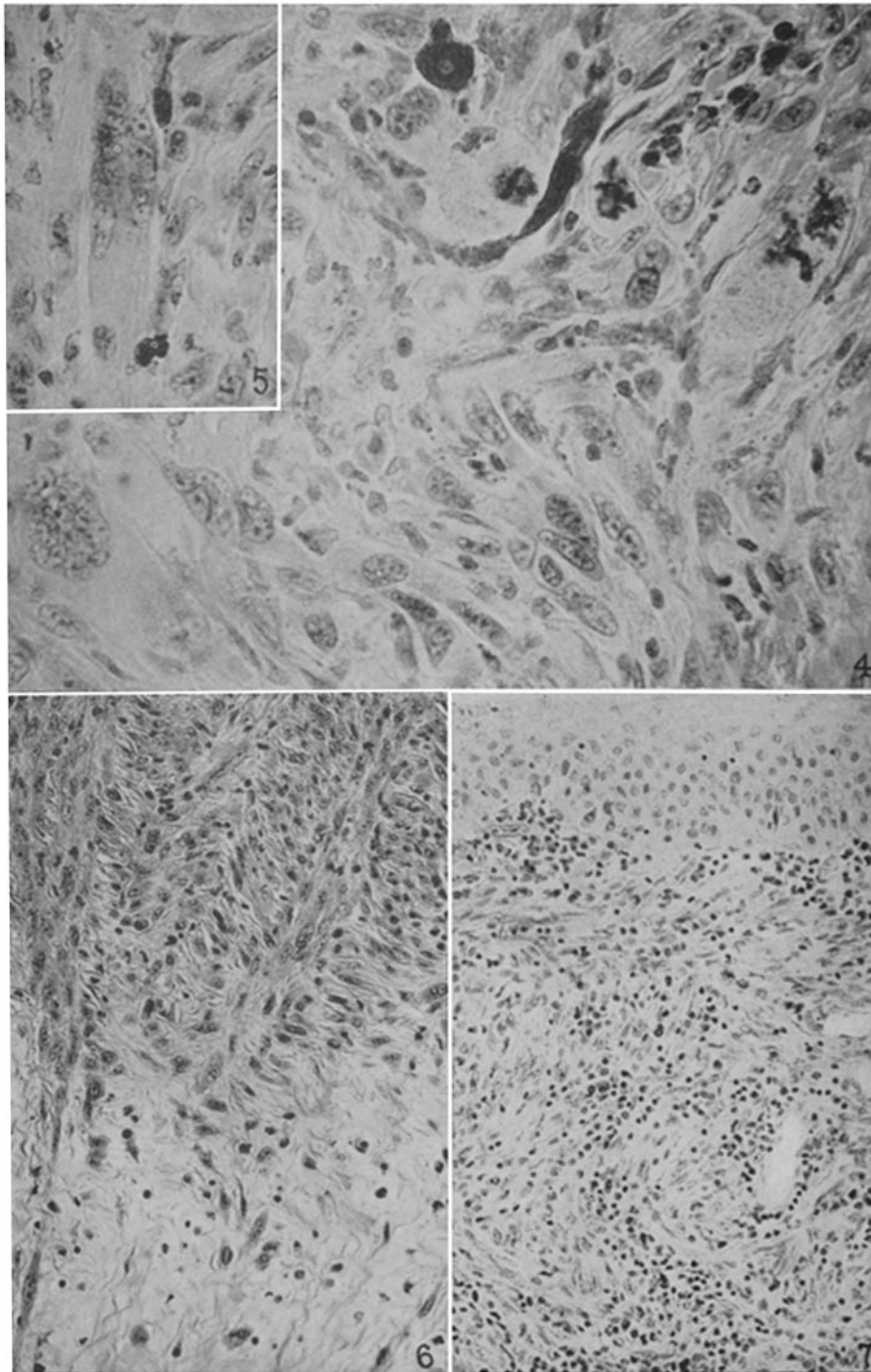
FIG. 5. Same as Fig. 4. $\times 500$.

FIG. 6. The tumor invading the cornea (*D*, Fig. 1). Note character and peculiar arrangement of tumor cells and the reaction in the cornea. $\times 210$.

FIG. 7. Small spindle cell tumor growth with chronic inflammatory reaction (syphilitic) in the peripheral and superficial parts of the cornea (*E*, Fig. 1). $\times 210$.



(Brown and Pearce: Melanoma of eye in syphilitic rabbit.)



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