

## EXPERIMENTAL SYPHILIS IN THE RABBIT.

### VII. AFFECTIONS OF THE EYES.

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PLATES 7 TO 9.

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Infection of the eyes following inoculation of the genitalia was one of the first forms of generalized syphilis to be recognized in the rabbit and has been reported more often than any other metastatic condition. Our knowledge of these affections dates back to 1908-10 when the first cases of metastatic keratitis were reported by Grouven (1-3), Mezincescu (4), Uhlenhuth and Mulzer (5), and Truffi (6). Since that time, several forms of affections have been described. Those most frequently mentioned are conjunctivitis, pericorneal injection, and interstitial keratitis; of these, keratitis is perhaps the only one which possesses a clearly defined status.

In addition to this class of affections, lesions of the eye grounds including choroiditis and chorioretinitis were described by Nichols (7) and by Reasoner (8) working in collaboration with Green. With certain strains of *Treponema pallidum*, these conditions were noted in from 70 to 95 per cent of the animals examined (mode of inoculation not stated) which may indicate that lesions of the eye grounds are more common than those of other structures—at least with some strains of the organism.

Reasoner also reported an instance of cataract of both eyes and a gumma involving the ciliary body, the iris, and the lens.

Our own observations on affections of the eyes were confined to a study of those conditions that could be detected by the unaided eye and included, therefore, affections of only the more superficial structures such as the conjunctiva, the cornea, and the iris. This group of lesions has received more attention than any other class of syphilitic affections but there is still much which may be added to the facts

already recorded. In presenting the results of our observations, we shall not attempt to do more than describe changes which might be recognized by any one familiar with the simpler forms of eye lesions.

The difficulties of their sharp delimitation will doubtless be appreciated, and while the various groups of affections are separated from one another, as a matter of convenience in presentation, it must be understood that combination was one of the most characteristic features of eye involvement.

#### *Pericorneal Injection.*

Pericorneal or ciliary injection is a well recognized condition in rabbits infected with *Treponema pallidum* but in the literature it is practically always referred to in connection with keratitis and apparently no significance has been attached to it apart from this one condition. It is, however, the most frequent sign of infection of the eyes and was often noted in animals where no other gross abnormality could be detected as well as in association with affections of the conjunctiva, the cornea, and the iris.

It occurred in two fairly distinct forms. The one most often seen consisted of a ribbon-shaped band of distended vessels which extended from the fornix to the sclerocorneal margin (Fig. 1) where they spread out and partially encircled the cornea. The usual position of these vessels was the region of the superior rectus muscle but they were also seen in the lower or lateral sectors of the eye.

A second type of pericorneal injection, which is perhaps more analogous to that seen in the human eye, consisted of a series of prominent vessels which encircled the cornea, giving off a few small collaterals which radiated outward as shown in Figs. 2 and 3.

One of these forms appeared to be as characteristic as the other, and in the most pronounced cases, the two were combined in about equal proportion with zonal radiations extending outward from all parts of the cornea. This was the state of the eye in Fig. 1 which was a marked case of pericorneal injection associated with a moderate degree of acute conjunctivitis (shown on the upper lid), but as may be seen, there was no involvement of either the cornea or the iris. This condition lasted for only about 48 hours when the congestion subsided and the eye returned to normal.

Ciliary injection was the first sign of eye infection to appear and the history of a simple injection was usually that of a recurrent affection of short duration. During its early stages and in mild cases, it suggested no more than a vasomotor instability of some particular group of vessels which would suddenly become engorged and return to normal within a very short time, leaving some uncertainty as to whether any abnormality existed. Then a well established injection would take place and subside after a few days or the condition would gradually develop into an outspoken iritis or keratitis.

As yet, no attempt has been made to demonstrate spirochetes in a case of simple ciliary injection. Histologically, however, there were definite pathological changes. These consisted of vascular dilatation and engorgement of the vessels in the episcleral tissue and at the sclerocorneal junction; there were slight edema of these tissues and a moderate polyblastic infiltration which was chiefly perivascular. The identification of this affection as a manifestation of syphilis rests, therefore, upon clinical and histological evidence. A marked ciliary injection presents no difficulties of diagnosis, but unless the milder cases are followed by some more characteristic lesion, they cannot be recognized clinically as more than probable manifestations of syphilitic infection. The significant features are its transient character, the tendency to recurrent attacks, the frequency with which it eventually terminates in iritis or keratitis, and its constant association with these two conditions.

#### *Conjunctivitis.*

Inflammation of the conjunctiva was noted in connection with affections of both the nasolacrimal system and of the eye itself. In the latter instance, it usually preceded or was an accompaniment of other affections of the eye, and it was difficult to determine clinically whether the inflammation of the conjunctiva was the result of a conjunctival infection or only an associated manifestation of an infection centered elsewhere. There were instances, however, in which the conjunctiva appeared to be the chief or sole focus of infection, and, in any case, involvement of the eyes frequently gave rise to marked inflammatory reactions which might affect the entire conjunctiva or only certain limited areas.

An acute diffuse inflammatory reaction was frequently seen in association with a simple ciliary injection or during the early stages of a keratitis or iritis. This form of affection began with reddening and swelling of the margins of the lids and conjunctiva, increased lacrimation, and drooping of the upper lids (Figs. 3, 11, 12, 17, and 19). It progressed rapidly and in some instances resulted in an intense congestion and swelling of the entire membrane with petechial hemorrhages and gray or yellowish gray patches scattered here and there.

In many instances, the inflammatory reaction was confined to a smaller area, the usual seat of such processes being the region of the superior rectus muscle or some part of the palpebral conjunctiva.

The acute manifestations were, as a rule, of short duration and disappeared completely within a few days.

No spirochetes were found in the lacrimal secretion of animals with this type of inflammatory reaction, and no effort was made to demonstrate them in the conjunctiva itself, but sections of the conjunctiva showed a characteristic syphilitic infiltration.

Another form of conjunctival lesion which was frequently seen in rabbits infected with *Treponema pallidum* resembles somewhat the phlyctenular conjunctivitis of man. These lesions were of three types, not all of which could be related to the syphilitic infection. In one group of cases, they appeared as distinct nodules or thickened patches situated at the sclerocorneal margin as in Figs. 4 and 5 or distributed along the course of the vessels in the superior quadrant of the eye (Fig. 6). The nodules were of a pale, opalescent, or yellowish white color and were associated with a well marked ciliary injection as in Fig. 4 or with a vascular reaction which was confined to the affected part of the eye as in Fig. 5.

Usually, the nodules or patches remained comparatively small but in one instance a lesion of this type developed into a mass which practically filled the superior fornix and presented all of the characteristics of a syphilitic granuloma, as may be seen by reference to Fig. 6.

Dark-field examination of the lesions for spirochetes gave inconsistent results. Some of them showed spirochetes in abundance, while in others, no organisms were found. The diagnosis of this group of

conditions was not difficult, however, since they were nearly always followed by or associated with characteristic lesions of the cornea or iris.

A second group of phlyctenular lesions differed from those described chiefly in that they were composed of small, ill defined, gelatinous masses of a pale pink or salmon color. Some of them presented much the same appearance as that in Fig. 5, while others showed no injection of the conjunctiva or episcleral tissues. An example of a lesion of this type is given in Fig. 7.

These affections were at times comparatively common in both infected and uninfected animals. No spirochetes have been found in them, but in some cases, the condition has progressed to a definite keratitis. In the absence of such a history, we know of no clinical means by which the etiology of lesions of this type can be determined.

There is also a third condition, analogous to those just described, which may be referred to briefly. The appearance presented is shown in Fig. 8. There were a series of small discrete nodules of a slightly translucent or opaque white color distributed along the sclerocorneal margin; there was no increased vascularity of the area, and in the few cases seen, the nodules remained essentially as they appear in this photograph. No spirochetes have been demonstrated in lesions of this type, and there is no evidence, either clinical or pathological, to indicate that they are of syphilitic origin, unless it be the fact that they are composed of masses of lymphoid cells which occupy the same position as analogous lesions of established syphilitic origin.

#### *Keratitis.*

Keratitis is the most easily recognized lesion of the eye and (with the possible exception of metastatic lesions of the testicle) has been reported more often than any other manifestation of a generalized infection. It might appear from this that keratitis is the most common of the generalized lesions but such is not necessarily the case; it may be either very common or very rare, depending upon a number of circumstances. As the infection is ordinarily propagated, however, keratitis is of very frequent occurrence with most strains of *Treponema pallidum*.

The form of keratitis usually observed in the rabbit is always preceded by a ciliary injection and frequently by a diffuse inflammatory reaction of the conjunctiva. The lesion described by all writers is an interstitial or parenchymatous keratitis. It is peripheral in origin, and while it may develop from any part of the cornea, or from its entire circumference, the most common location is the superior margin.

The corneal lesions appear either in the form of a delicate fringe of vessels which extend over the edge of the cornea or as a narrow zone of turbidity. As the vascular network spreads, the cornea becomes clouded, or as the zone of infiltration extends centrally, it is followed by the development of a network of vessels so that in either case the lesion produced combines the two elements of corneal infiltration and pannus in a varying degree. There are, therefore, three types of lesions: one, in which infiltration with consequent clouding and thickening of the cornea is especially marked, another in which the the vascular reaction and pannus are the most noticeable features, and a third which combines the two processes in about equal proportion.

Three early cases of the vascular and the infiltrative types of keratitis are illustrated in Figs. 9 to 12. The eye in Fig. 9 shows a well marked ciliary injection with a delicate network of vessels extending over the cornea. The area covered by this pannus was faintly clouded, but outside of this zone it was perfectly clear. Fig. 10 shows a condition of essentially the same character except that in this case the lesion arose from the inferior margin of the corner.

In contrast to these, the eye in Fig. 11 shows a crescent-shaped area of slight opacity with a small opaque dot at its center (descemetitis) which extends from the limbus over the margin of the pupil. At this time, the vessels were just beginning to appear at the corneal margin; 24 hours later (Fig. 12), the infiltration had increased very markedly, forming an opaque, elevated area with a narrow but dense pannus at its outer margin. The relative proportion between the vascular and infiltrative reactions shown in these three cases was maintained throughout their development.

Attention may be called to the ciliary injection and inflammatory reaction in the conjunctiva associated with these, which is well shown in Figs. 11 and 12.

When fully developed, the picture presented in cases of keratitis was very variable. The classical conditions are those presented in Figs. 13 and 14 which show pronounced keratitis involving a large part of the cornea. The first of these (Fig. 13) shows three things: first, a diffuse clouding of the cornea extending well below the pupillary margin; second, dust-like particles of dense opacity which are best seen over the pupil; and third, a very marked and uniform pannus, which extends like a curtain over the upper portion of the cornea.

The second lesion is quite different from this. As in the preceding case, there is a milky clouding of the cornea with granular deposits on the posterior limiting membrane but the noticeable feature of difference is the absence of a well defined pannus or even of a marked pericorneal injection. There were, however, a few vascular filaments in the cornea and a faint pannus can be seen towards the anterior or internal angle of the eye. As seen in these two animals, descemetitis was usually present in cases of marked corneal involvement but was frequently absent in milder ones.

Two older lesions of the cornea which will serve to complete the picture of this condition are reproduced in Figs. 15 and 16. The first of these affections (Fig. 15) was of 6 weeks duration and is given especially to illustrate the deep vascularization of the corneal lesion which frequently occurs during its later stages. The marked interstitial infiltration and descemetitis are quite obvious, and attention may be called also to the granulomatous lesion in the fornix.

The second lesion of this group (Fig. 16) had an unusual history of repeated relapses extending over a period of 27 months and is used to illustrate the formation of the salmon patch which is less constant in cases of keratitis in the rabbit than in man. The irregular area of dense opacity which extends from the upper margin of the cornea across the pupillary area developed 15 months after the first attack of keratitis. It was at first of a reddish gray color, subsequently changing to a pale orange, then yellow and gray. These appearances changed from time to time with the recurrent activity of the eye infection. Eventually the opacity diminished to a considerable extent, but a diffuse haziness of the cornea with a central opacity was still present when the animal was killed 27 months after the lesions first appeared.

Punctate areas of clouding or opacity, unaccompanied by a vascular reaction of any kind, have been observed in the central portion of the cornea in a few instances. We have not been able to investigate these lesions, however, and nothing is known as to their cause or nature.

Briefly, therefore, the only known form of syphilitic keratitis in the rabbit is an interstitial keratitis with pannus which usually arises from the superior margin of the cornea but may develop in other positions or as a circumcorneal affection. Ordinarily only a portion of the cornea is involved and the alterations produced are relatively slight, but in more pronounced cases, the entire cornea may be affected, with the production of deep seated lesions which may persist for months or even years.

The process of resolution of corneal affections was an irregular one. Usually the infiltration was first to disappear, leaving a vascular network as the only mark of the previous lesion. This is well brought out by a comparison of the eyes in Figs. 15 and 6, Fig. 6 representing a period 38 days later than Fig. 15. The aberrant vessels were at times very slow to disappear and have been known to persist almost unchanged for several months. In exceptional instances, the vessels disappeared before the infiltration, or resolution occurred in both directions at about the same rate. As a rule, resolution was complete, leaving no mark of the previous lesion.

#### *Iritis.*

Apparently iritis has not been recognized as a manifestation of generalized syphilis in the rabbit distinct from that of the cornea, except in the one instance recorded by Reasoner of a gumma which involved the ciliary body, the iris, and the lens. Among the animals studied by us, however, it was a very common affection. Case records show a higher incidence of keratitis, but when the nature of the lesions and the relative ease or difficulty of their detection are considered, it appears quite likely that iritis was the more common of the two. The majority of the cases were recorded in albino rabbits, and while we were inclined to attribute this to difficulties of diagnosis interposed by a pigmented iris, it must be recognized that the nature



of the iris may be an important factor in determining the occurrence of these lesions.

The conditions which we have classed as iritis varied from an acute hyperemia of relatively short duration to plastic and granulomatous processes which produced permanent lesions of the iris. While these affections are spoken of as iritis, it must be understood that in many cases the ciliary body as well as the iris was involved, but the exact location of the lesion could not be determined clinically so that the term iritis is used to cover a group of reactions which was characterized chiefly by readily recognizable changes in the iris. Microscopic examination of a number of eyes showed, however, that the lesion was at times practically confined to the base of the ciliary body, while in other cases the ciliary body, the iris, and the choroid were all involved.

The most common form of iritis was an acute diffuse affection which lasted for only a few days. The usual signs in these cases were photophobia and profuse lacrimation with conjunctival and ciliary injection which appeared before any definite alteration could be detected in the iris and lasted until the acute reaction began to abate. The appearance presented in such cases may be seen by comparing Figs. 17 and 18 which show the affected and the normal eyes of an animal at the very beginning of an attack of iritis and Figs. 19 and 20 which show respectively a slightly later stage of iritis and a photograph of the same eye taken 1 week later. (Both eyes of this animal were involved at the same time.)

The changes in the iris itself began with an acute hyperemia. In albino rabbits, the marginal and axial vessels stood out prominently, while the substance of the iris appeared but little altered (Figs. 17 and 21). As the condition progressed, the vessels became less conspicuous while the color of the iris deepened to a dull red, a cyanotic, or rose color (Figs. 17, 19, 21 and 22); occasionally small hemorrhages occurred (Fig. 22) and the structural details of the iris became blurred and indistinct (*cf.* Fig. 18 with Figs. 17 and 19 to 22).

This condition lasted for a very short time, as a rule (24 to 72 hours), the vascular dilatation then subsided, and the diffuse discoloration gradually disappeared, leaving the iris slightly more clouded than normal (*cf.* Figs. 18 and 20).

Meantime, certain alterations in the pupillary reaction were noted. Under the conditions of lighting used, the normal pupil measured from 7 to 9 mm. in diameter; with the development of an acute iritis, the pupil gradually contracted until it measured only 4 to 6 mm. in diameter (*cf.* figures) and reacted very sluggishly to light (flash). The pupil and the pupillary reflexes usually returned to normal as the iritis subsided.

In darkly pigmented irides not all of these changes could be detected. The conditions usually noted were a change in the color of the iris, clouding or opacity, and a narrowing of the pupil. These may be made out by comparing the infected and the normal eyes of the same animal in Figs. 23 and 24 respectively. In this instance, it can be seen that the iris of the infected eye is distinctly mottled and of a lighter color, as well as hazy, and that the pupil is narrower than that of the normal eye; this was the condition usually found in this class of animals.<sup>1</sup>

In the group of cases described, the contents of the anterior chamber were little if at all affected and there was no descemetitis. In a few instances of severe iritis, there were hemorrhages into the anterior chamber (see Fig. 16), or the aqueous was slightly clouded (Fig. 22) and there were granular deposits on the posterior limiting membrane; these are just visible in Fig. 23.

There were also a few cases of plastic iritis. These differed from the condition which has been described in the presence of a slight exudate, which appeared to form on the posterior surface of the iris and protruded beyond the pupillary margin as a grayish white or yellowish white film. In some instances, the pupil was contracted, irregular, and fixed, while in others it retained its normal shape and its accommodation to light was less impaired.

<sup>1</sup>In comparing the pupils and pupillary reactions of rabbits, it should be noted that in the ordinary diffuse light of the laboratory, there is a decided difference in the size and the accommodation to light between an albino rabbit and one with a dark colored iris. The pupil of the albino is relatively smaller and reacts quickly to light (flash), contracting to a very small diameter. The pupil of an animal with a dark colored iris reacts more slowly, and the extent of the contraction is much less—sometimes barely perceptible.

The inflammation in this group of cases also cleared up within a short period of time and the exudate was absorbed without the formation of fibrous synechias.

The diffuse congestive affections of the iris appeared to be referable to a lesion at the base of the ciliary body rather than of the iris itself. It was only in the more pronounced cases and in instances in which hemorrhage or exudative phenomena were present that definite lesions of the iris could be detected, and even in these the ciliary body appeared to be more affected than the iris, but this could not be determined clinically.

Diffuse affections of the iris merged by insensible degrees with another type of affection in which the main lesions were of a focal nature. Fewer of these have been seen and comparatively little is known of them. The most common condition observed was a focal area of congestion or hemorrhage, an example of which is given in Fig. 25. These lesions were single or multiple but produced no alteration in the iris except at the points involved, and symptoms of acute iritis were usually absent.

A second condition, which was more characteristic, is that shown in Fig. 26. These cases presented all of the manifestations of an acute diffuse iritis, but in addition, small granulomatous nodules developed in the substance of the iris, usually near the pupillary border. There was partial or complete fixation of the iris with some irregularity of the pupil.

The pendant nodule seen in Fig. 26 developed in the superior margin of the pupil but in some way became torn loose except at one point, leaving a wedge-shaped defect in the iris which is plainly visible. A second nodule is seen above and to the right of the point of attachment of the first.

As a rule, the granulomatous lesions were comparatively small and tended to resolve without the production of any marked injury to the iris. In one instance, however, a lesion of this type developed into a large granulomatous mass which involved a considerable portion of the iris and filled nearly half of the anterior chamber of the eye. This lesion is shown in Fig. 27.

The formation of posterior synechias resulting in permanent alterations of the pupil was very rare. In one animal of our series, this

condition developed very early and there was marked irregularity and almost complete occlusion of both pupils which lasted up to the time of the death of the animal—a period of nearly 2 years. The right eye of this animal is shown in Fig. 28. The dark area at the center of the eye represents the outline of the original pupil but at the time this photograph was taken, most of this area had been filled in with granulation tissue and the only aperture present was of very small size and can just be seen at the lower and anterior edge of the corneal opacity.

#### *Clinical History.*

*Correlation of Eye Affections.*—The clinical history of the eye affections described as pericorneal injections, conjunctivitis, keratitis, and iritis contains many points of interest. They are so intimately related to one another that they can hardly be considered as entirely distinct forms of infection. One condition may occur without the others but the circumstances were such as to favor a combination of the various affections. Thus, pericorneal injection and conjunctivitis may occur in the absence of any definite lesion of the cornea or iris, but the latter conditions were always preceded or accompanied by pericorneal injection and conjunctivitis. In like manner, iritis and keratitis may occur independently, or they may occur together, or one condition may follow the other. This peculiar association rests upon a simple anatomical basis. Histologically, it was found that these affections could all be traced to a common lesion which was centered about the vessels which encircle the cornea. This lesion first makes its appearance in the wedge-shaped mass of loose connective tissue at the outer side of the sclerocorneal junction (episcleral tissues). The vessels in this area become dilated, the tissue is edematous and infiltrated with polyblasts. If the lesion is confined to this area, it manifests itself in the form of a ciliary injection. The infection tends to spread, however, extending to the conjunctiva, to the substance of the cornea, or inward towards the canal of Schlemm and the spaces of Fontana. This led to the development of lesions in the cornea, the ciliary body, the iris, and occasionally in the choroid, giving rise to clinical signs of infection, the nature of which depended upon the parts thus involved.

When viewed from this standpoint, the eye affections described assume a less complex character.

*Predisposing Factors and the Relation to Other Manifestations of Infection.*—As was mentioned in connection with keratitis, affections of the eyes may be very frequent or very rare with a given strain of *Treponema pallidum*, depending upon a variety of conditions. From an analysis of the circumstances under which eye infections occurred in our series of animals, it was found that in more than 75 per cent of the cases, they were the only generalized lesions which occurred or were the last type of lesion to appear. In other words, eye lesions appeared to occupy a terminal position in the sequence of tissue reactions.

It was also found that experimental conditions could be employed which would emphasize this relation. These cannot be discussed further than to say that in general, circumstances which were unfavorable for the occurrence of other generalized lesions, tended to increase the relative incidence of affections of the eyes and conversely, those conditions which were most favorable for the occurrence of other lesions tended to reduce the relative incidence of eye lesions. Thus, double inoculation and late castration produced a high percentage of eye affections while unilateral inoculation and early castration reduced the incidence of these lesions.

*Occurrence and Duration.*—Considered collectively, eye lesions occurred at about the same interval of time after inoculation as other generalized lesions. The first lesions usually appeared at from 2 to 3 months after inoculation. Pericorneal injection and conjunctivitis were among the early affections, while keratitis and iritis occurred slightly later on the whole and the majority of the cases appeared near the end of the 3 months period. In several instances, eye lesions did not appear for as much as 6 to 8 months after inoculation, and in one animal, the interval was 2 years and 3 months, and in another, approximately 3 years.

One or both eyes might be involved, either simultaneously or in rapid succession. Less often, there was a considerable interval between the appearance of the two lesions. The duration of the affection was very short as a rule; simple pericorneal injections, diffuse conjunctivitis, and iritis frequently lasted for only a few days but

were of longer duration when complicated by lesions of the cornea. Keratitis was the most enduring, but even this rarely lasted longer than 2 to 3 weeks. The most marked corneal lesions lasted for several months, and in the one instance described above the lesions had not cleared up when the animal was killed 33 months after inoculation.

*Recurrence.*—Exacerbation of partially resolved lesions of the eyes or recurrence of completely healed lesions was almost the rule among those animals which were held over long periods of time. Two or three attacks of iritis and especially of keratitis were quite common. In one animal, numerous attacks of keratitis and iritis occurred over a period of approximately 2 years. Actual count of the attacks was lost but the number may be safely placed at more than a dozen. Several additional instances were recorded in which recurrent lesions appeared more than a year after inoculation.

Relapse of partially or completely healed lesions of the eyes occurred more often than in any other class of affections. The tendency to relapse in the case of keratitis has been noted by numerous observers and is the one *redux* phenomenon of the experimental infection which has received general recognition.

The tendency of eye lesions to relapse as well as the peculiar circumstances of their occurrence is probably to be explained by the degree of protection afforded these parts by reactions elsewhere and the feeble protection afforded by the reaction developed in these tissues.

#### SUMMARY AND CONCLUSIONS.

From the study of a number of instances of eye infection in the rabbit, it was found that a variety of affections might occur following scrotal or testicular inoculations of *Treponema pallidum*. Those observed included ciliary injection, conjunctivitis, keratitis, and iritis which might occur separately or in combination with one another, except that keratitis and iritis were always accompanied by a reaction in the ciliary vessels and usually by a conjunctivitis.

Several forms of each of these affections were described, and while some of them were regarded as presenting a very characteristic picture, it was recognized that the conditions present in other cases

were not sufficiently distinctive to permit of a clinical diagnosis. With a few exceptions, however, the pathology of the lesions was sufficient to identify them as processes of a syphilitic nature.

It was also found that this group of lesions usually arose from a common focus of infection which was located in the episcleral tissues immediately surrounding the cornea. From this point, the infection tended to spread to the conjunctiva and the cornea, or toward the canal of Schlemm and the spaces of Fontana and thence to the ciliary body, the iris, and the choroid. The localization of the lesion and the mode of extension were held to be responsible for the combination of manifestations usually observed.

From an analysis of the circumstances under which affections of the eyes occurred, it was found that the great majority of them occupied a definite position in the scheme of tissue reactions, being the only generalized lesions developed or the last type of lesion to appear.

These facts, together with the unusual frequency of relapse in these affections, were believed to indicate that a low degree of protection

~~was conferred upon these tissues by reactions to their local~~  
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## EXPLANATION OF PLATES.

The illustrations are reproductions of photographs which represent the objects at their natural size. Unless otherwise indicated, statements of time are estimated from the date of inoculation.

## PLATE 7.

FIGS. 1 to 8. Ciliary injection, and affections of the conjunctiva and episcleral tissues.

FIG. 1. 61 days. A typical example of ciliary injection with acute conjunctivitis.

FIG. 2. 88 days. Circumcorneal injection (ciliary) with acute conjunctivitis.

FIG. 3. 132 days. Acute diffuse conjunctivitis with pronounced swelling and intense redness of the conjunctiva. There is also a moderate pericorneal injection.

FIG. 4. 54 days. Miliary granulomata of the pericorneal tissues associated with ciliary injection.

FIG. 5. 64 days. A phlyctenular lesion of the conjunctiva and episcleral tissues.

FIG. 6. 156 days. A syphilitic granuloma involving the conjunctiva and episclera. There is also an old lesion of the cornea which is undergoing resolution.

FIG. 7. 45 days. A pericorneal nodule of a type which may or may not be syphilitic. Note the absence of a vascular reaction.

FIG. 8. 49 days. Multiple lymphoid nodules in the pericorneal tissues which apparently are not of syphilitic origin.

## PLATE 8.

FIGS. 9 to 16. Lesions of the cornea.

FIG. 9. 54 days. Interstitial keratitis. Ciliary injection and early vascularization of the cornea.

FIG. 10. 100 days. An early keratitis of the lower margin of the cornea analogous to that in Fig. 9.

FIG. 11. 95 days. An early keratitis of the infiltrative type. There are a well marked pericorneal injection and conjunctivitis with a slight descemetitis.

FIG. 12. 24 hours later. There are an increase in the inflammatory reaction and a well developed pannus at the margin of the cornea.

FIG. 13. 73 days. A typical example of interstitial keratitis with marked pannus.

FIG. 14. 106 days. An example of interstitial keratitis showing marked infiltration of the cornea with comparatively slight vascularization.

FIG. 15. 133 days. Interstitial keratitis involving the entire cornea with deep vascularization.

FIG. 16. 1 year, 8½ months. Keratitis with well marked salmon patch covering large area of cornea. The dark spot in the eye is due to hemorrhage in the iris.



## PLATE 9.

FIGS. 17 to 28. Affections of the iris.

FIG. 17. 94 days. Acute iritis showing drooping of the upper lid, slight lacrimation, and slight contraction of the pupil.

FIG. 18. 94 days. Normal eye of the same animal as that in Fig. 17 given for comparison.

FIG. 19. 70 days. Acute iritis, partial closure of the lids, and lacrimation. Narrowing of the pupil and clouding of the iris.

FIG. 20. 1 week later. Same eye as that in Fig. 19. Photograph shows partial recovery from the iritis. Eye appears normal except for the loss of structure in the iris. *Cf.* with Fig. 18.

FIG. 21. 132 days. An early acute diffuse iritis. There is a well marked pericorneal injection. Vessels of the iris are engorged and its substance is clouded. There is also clouding of the contents of the anterior chamber. The right eye of this animal is shown in Fig. 3.

FIG. 22. 125 days. Acute diffuse iritis, or slightly later stage than that shown in Fig. 21. Vessels are no longer visible but the iris is distinctly clouded and there is a focus of hemorrhage immediately above the pupil.

FIG. 23. 85 days. Acute iritis in an animal with pigmented iris. *Cf.* with Fig. 24. The iris is of a lighter color than normal, somewhat mottled, and the structure indistinct. Pupil is also contracted.

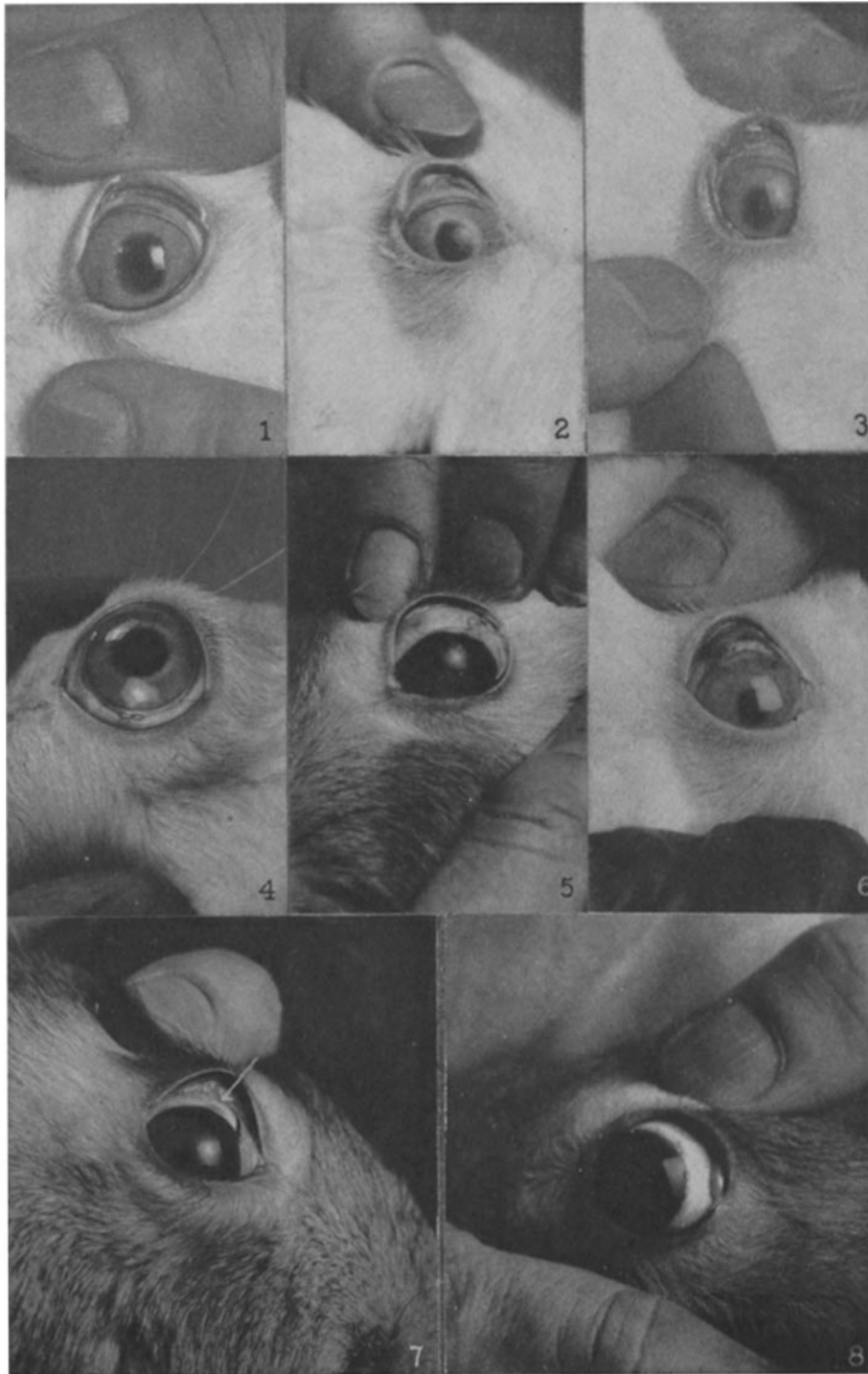
FIG. 24. 85 days. Normal eye of the same animal as that in Fig. 23.

FIG. 25. 95 days. Focal lesion of the iris. Remainder of the iris appears entirely normal.

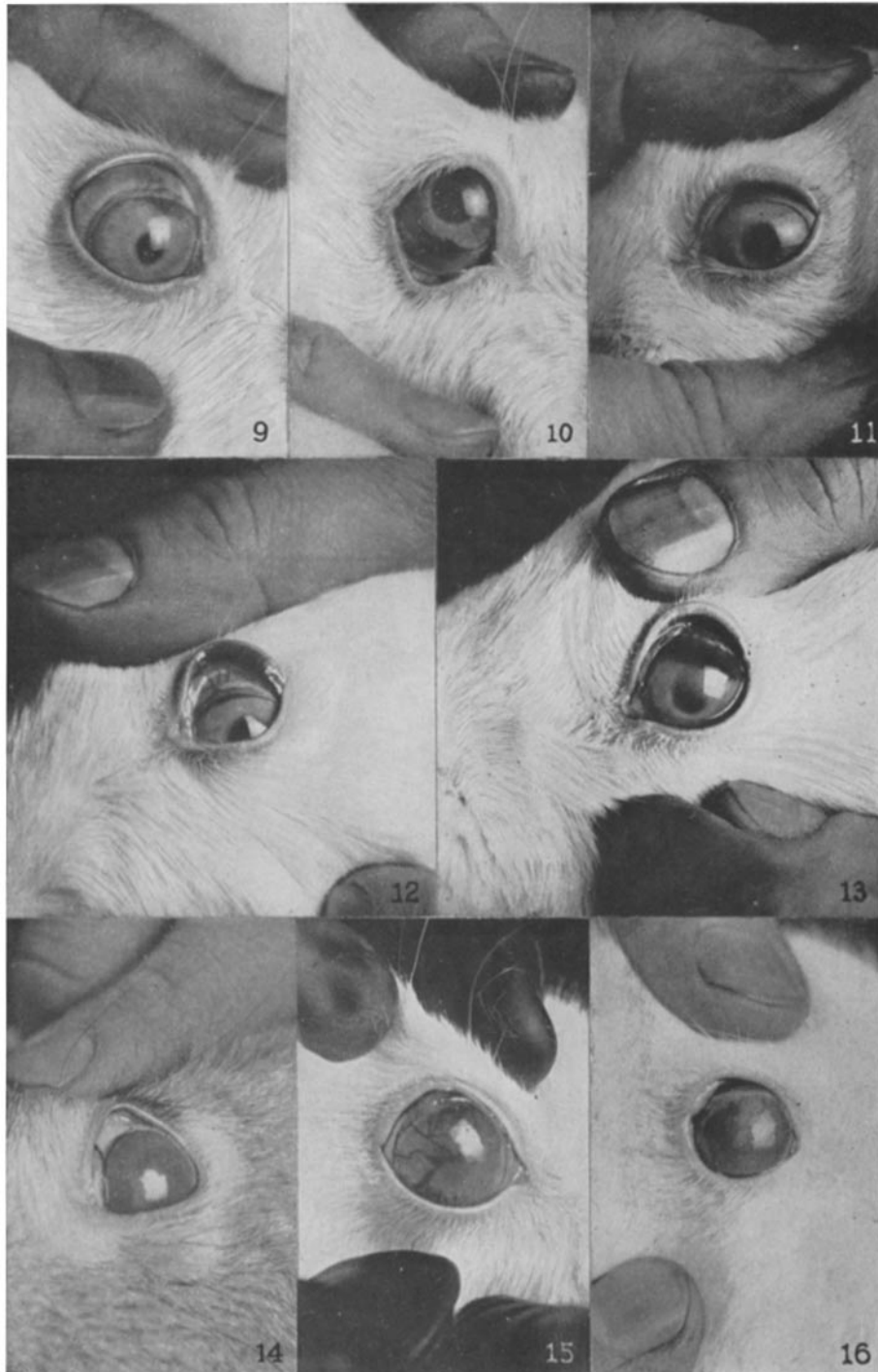
FIG. 26. 82 days. Acute diffuse iritis with a granuloma, superior margin of the pupil. The small nodule seen at the upper margin of the iris has been torn loose from its original position, leaving defect in the margin of the pupil.

FIG. 27. 185 days. Large granulomatous lesion of the iris projecting into the anterior chamber of the eye.

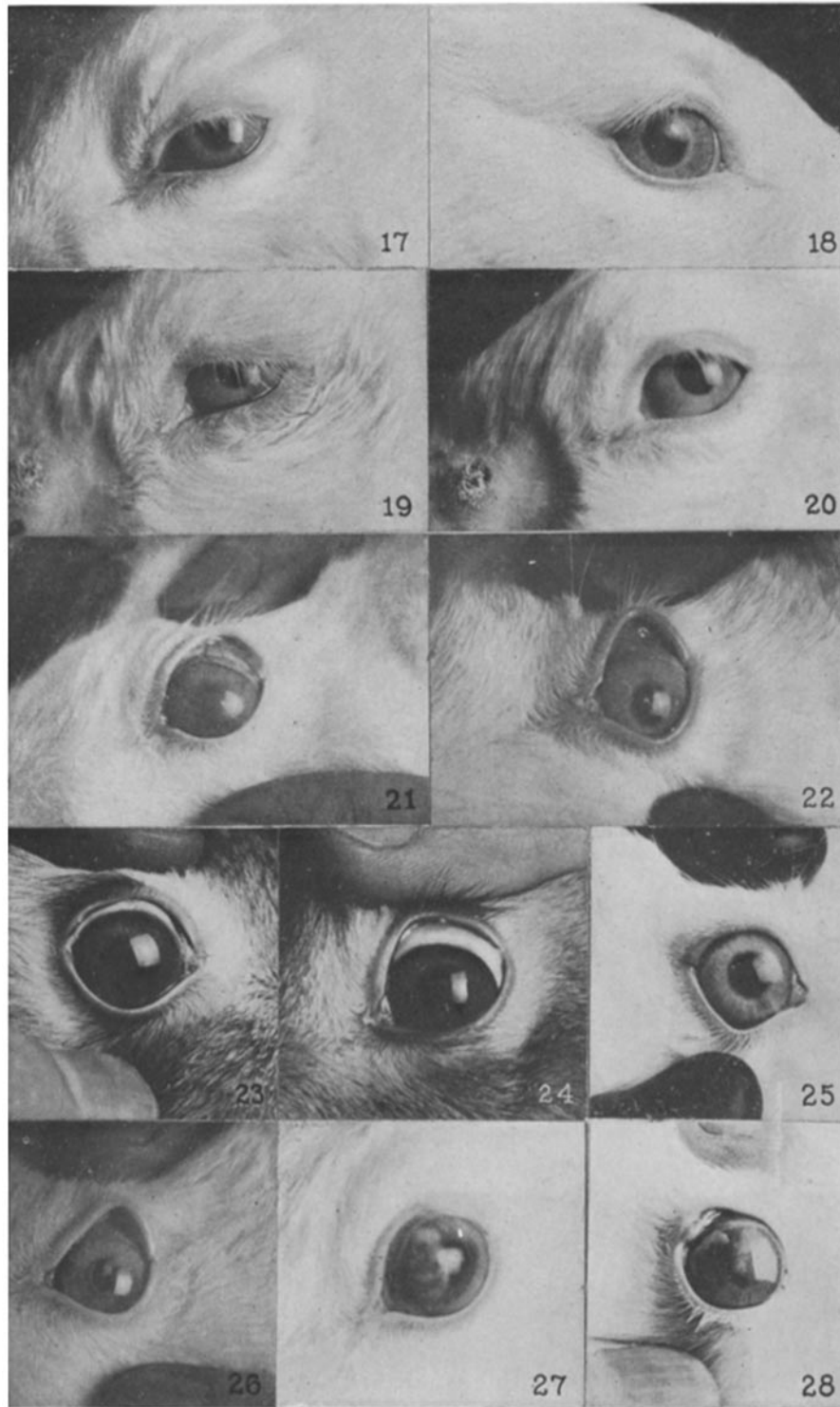
FIG. 28. 1 year, 7 months. Occlusion of the pupil with irregularity and fixation. Permanent lesion.



(Brown and Pearce: Experimental syphilis in the rabbit. VII.)



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