

## EXPERIMENTAL SYPHILIS IN THE RABBIT.

### V. SYPHILITIC AFFECTIONS OF THE MUCOUS MEMBRANES AND MUCOCUTANEOUS BORDERS.

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PLATES 78 TO 83.

(Received for publication, June 14, 1920.)

A study of cutaneous syphilis in the rabbit brought out the fact that although the infecting organisms might be widely distributed through the body, lesions of an easily recognizable character occurred almost exclusively within certain restricted areas while the remainder of the skin surface rarely showed any manifestation of disease (1, 2). In like manner, it has been found that lesions develop with considerable frequency in parts of the body where skin and mucous surfaces join. In some instances, the lesions first appear within the skin area, while in others they develop upon the mucous membrane so that it might be possible to classify most of them as affections of one or the other of these structures. It appears, however, that the transitional area exercises some influence upon the localization of the infection, and since lesions which develop in one tissue usually extend to the other, their classification as affections of mucocutaneous borders seems to be a more logical one.

Syphilitic involvement of the mucous membranes and mucocutaneous borders of the rabbit was first noted by Grouven (3), who described infiltrations of the nasal mucosa and rhagades about the nasal orifices, conjunctivitis, and papular lesions of the anus and sheath. Attention was also called to the presence of a nasal discharge containing spirochetes and to dyspnea presumably resulting from infiltration and swelling of the nasal mucosa. These early observations have been confirmed and amplified to some extent by subsequent observers, but no material additions have been made to the list of conditions originally described by Grouven. Uhlenhuth and Mulzer (4) described tumor-like swellings of the mucous membranes following generalized inoculations, and within recent

years, attention has been directed more particularly to the occurrence of diffuse inflammatory processes of the nose and sheath which show no characteristic lesions but are identified by a mucopurulent discharge which contains spirochetes. These observations constitute the chief contributions which have been made to the study of affections of the mucous membranes and mucocutaneous borders in the rabbit.

Among the animals first studied by us, localized infections of the mucous membranes and mucocutaneous borders were noted in about 20 per cent of the cases but have been less frequent among those studied more recently. The affections seen in these animals were of two general classes, depending upon the type of the lesions present. In one group, the lesions were characterized by diffuse infiltration, surface erosion or ulceration, and the formation of exudates of various types; in the other, there was a greater degree of proliferation and the lesions formed were large granulomatous masses which showed the usual secondary transformations of syphilitic processes. Affections of these two classes were distributed about the nares, the lips, the margins of the lids, the genitalia, and the anus.

*Affections of the Nasolacrimal System and of the Nasolabial Region.*

Infections of the nasolabial region were relatively infrequent, which, as will be explained later, may have been due to the fact that lesions in these areas were of comparatively late development and the animals were not held for a sufficiently long time.

The most common affection seen was a condition which in its earlier stages closely resembled an ordinary case of snuffles. The infection began as a rhinitis with a more or less profuse mucopurulent discharge and apparently extended to the nasolacrimal ducts, producing obstruction and consequent overflow of the lacrimal secretion.

At the onset of the local infection, no characteristic lesions could be detected by ordinary means of examination, but within a short time the discharge from the nose became of a more tenacious character and tended to adhere to the surfaces about the nasal orifices. There was then a noticeable reddening and swelling of the skin and mucous membranes, and removal of the accumulated discharge revealed the presence of minute abrasions as indicated in Fig. 1. An earlier stage of the process may also be seen in Fig. 9 which is a photograph of the same animal as that in Fig. 1, taken 1 month earlier.

As the local infection advanced, the skin areas became denuded of hair; the infiltration of the surrounding tissues was increased, especially along the edges of the alæ nasi, and the nares were obstructed by the presence of accumulated discharges or by thick adherent crusts, the removal of which left numerous raw and bleeding points (Figs. 1 and 2).

Several modifications of this general type of condition were seen. In some animals, the nasal discharge was comparatively slight, and the lesions were of a less diffuse character. Irregular areas of infiltration and rhagades occurred along the margins of the alæ and more especially at the angles of the nares. Occasionally also, simple areas of ulceration or ulcers surrounded by a definite zone of infiltration such as that in Fig. 3 were seen just at the edges of the nasal orifices.

Another very characteristic affection of the nasolabial region is that shown in Fig. 4. The condition as presented by this animal was a marked infiltration of the nasal mucosa and the tissues surrounding the left nasal orifice. The right side of the nose was also affected to a slight extent. The cutaneous portion of the lesion was covered by an accumulation of epithelial scales and crusts, while the mucous surface showed ulcers with a gray necrotic base.

An unusually destructive condition seen in one animal of this group is that shown in Figs. 5 to 8. The usual symptoms of acute rhinitis were absent in this case. When first detected a circumscribed, indurated mass was present in the superior portion of the right nostril and a smaller area in the left (Fig. 5). These lesions increased very rapidly, giving great breadth and prominence to the alæ (Figs. 5, 6, and 10). Depressed ulcers developed upon the mucous surfaces and spread until the skin margins were involved. Heavy reddish brown crusts were then formed and practically occluded the anterior nares on both sides (Fig. 7). The necrosis associated with these lesions was quite marked and led to considerable destruction of the soft tissues and consequent deformity of the nose (Fig. 8). At autopsy, it was found that a large part of the mucous membrane of both nasal passages had become involved and the left chamber was practically obliterated for a distance of about 2 cm. above the anterior orifice. Whether this was due to the *pallidum* infection or was the result of an associated bacterial infection could not be determined.

One other form of lesion was observed at the margins of the nares, and this also was seen in but a single animal. The lesion in this case was a discrete papule about 3 or 4 mm. in diameter situated on the lip near the median line. The tumor-like swellings of the nasal mucosa described by Uhlenhuth and Mulzer (4) were not observed in any of these animals. They have been noted by other observers (5), however, and it is possible that some of the conditions which we have described as infiltrations of the nasal mucosa may represent processes analogous to those referred to as nasal tumors.

Taken as a whole, this group of conditions presented a very characteristic appearance and resembled in many respects the nasal

affections of infants with hereditary syphilis. The essential feature of the lesions was an infiltration of the skin and mucous membranes with irregularly distributed areas of necrosis and ulceration, while the characteristic symptoms were the presence of a mucopurulent discharge, epiphora, or conjunctivitis, and dyspnea, the latter being apparently an obstructive phenomenon.

Lacrimation or lacrimal overflow has been mentioned by different writers as a symptom of infection of the nasal mucosa, and while there was a very constant association of these conditions, the causative connection between the two processes was not entirely certain. During the early stage of the nasal infection, the characteristic condition of the lacrimal system was that shown in Figs. 9 and 10. At this period, the cheeks below the anterior angle of the eye were bathed with a clear lacrimal secretion. The hair was matted together, the skin was slightly inflamed, and usually there was some loss of hair over these parts. The conjunctiva in some instances remained perfectly clear, while in others there were varying degrees of an acute inflammatory reaction. Eventually, the lacrimal secretion was altered, becoming more clouded, or mucopurulent, in character. The conjunctivæ were then dulled, and the secretion accumulated over the cheeks in greater amount as in Fig. 11.

Other workers have reported the presence of spirochetes in the lacrimal secretions, but repeated examination in these cases failed to show them. While this in itself is not conclusive, it suggests that these affections might be referable to occlusion of the nasolacrimal ducts either as a result of involvement of the nasal mucosa or of infection of the ducts themselves rather than to localized infection of the conjunctival sac. Except for its periodicity and its persistence, this feature of the nasal infection differed in no way from a similar condition frequently observed in rabbits from other causes.

*Occurrence and Duration.*—As has been stated, affections of the nasal region were not among the early manifestations of generalized syphilis. The majority of those seen were either late in their development or at least occurred subsequently to other types of lesions. The time at which they were first recognized varied from a minimum of 9 weeks to a maximum of 8 months after inoculation, but there were very few cases in which lesions appeared within the first 4 months.

These statements may give an erroneous impression as to the time at which the infection actually became localized in the mucous membranes of the nose or about the mucocutaneous margins, since the early

symptoms were in most cases but little more than an ordinary rhinitis and specific infection was recognized only after the condition had advanced sufficiently to arouse suspicion as to its etiology. For the same reasons, many cases of nasal infection may have passed unrecognized, since it was not possible to make routine examinations of all nasal discharges.

This group of lesions was not only late in developing but was also of a very enduring character. With a few exceptions, the animals of this group were held for a number of months after the development of the localized infection, and no instance was recorded of complete healing of the lesions during the period of observation. Two of the animals were held for approximately 1 year, and a third was under observation for more than 2 years. In the last animal, there were several periods during which the lesions about the nares underwent almost complete resolution, but each time there was a recurrence. It seems probable, therefore, that this group of conditions may be regarded as among the most persistent of the generalized infections in the rabbit.

#### *Affections of the Lips and Buccal Cavity.*

Syphilitic lesions were occasionally noted upon the mucous surfaces or along the margins of the lips, but the entire buccal cavity of the rabbit is an almost unexplored region. Small papular infiltrations were seen on the skin surfaces or at the mucocutaneous borders of both the upper and lower lips as described in the fourth paper of this series (1, 2), but even these were rare. In addition, lesions were found about the cleft in the upper lip or upon the mucous surfaces of the lips.

The region of the cleft in the upper lip was one of especial interest. Normally, the contact surfaces of this area are covered by a short downy growth of hair which reaches practically to the inner margins as shown in Fig. 12. There were several animals in which an infiltration about the nasal orifices continued downward along the margins of the nasolabial folds, forming a thickened ridge, the surface of which was bare and covered by scales or by gray necrotic patches and small moist areas of erosion. A condition of this kind was present on the left lip of the animal shown in Fig. 4.

In addition to such processes as these, there were a few instances in which independent affections of the cleft were observed. The lesions appeared in the form of small papules or flattened patches of infiltration which tended to spread over the surface of the lips, and the resulting affection presented a very characteristic appearance which is shown in Fig. 13. It will be noted here that the affected portions of the lips are moist and denuded of hair, that there is a distinct thickening of the left lip, and that the surfaces are marked by an irregular network of ridges covered by gray necrotic areas. Eventually small superficial ulcers were formed which bore a striking resemblance to the mucous lesions of man.

Similar affections were also noted on the mucous surfaces of the lips, but, as a rule, these were small erosions of an indifferent character in which no spirochetes could be demonstrated. In a single instance, however, an ulcer with definitely infiltrated margins was found upon the inner surface of the upper lip (Fig. 14).

Another type of condition which was seen in a number of rabbits consisted of small papillomatous growths which were occasionally present on the margins or inner surfaces of the lips, about the gums of the lower incisors, and were especially numerous on the sides and under surface of the tongue. While these affections resembled in some respects certain of the hypertrophic or vegetating lesions of man, we could obtain no proof of a syphilitic origin—either clinical or histological.

*Occurrence and Duration.*—Affections of the lips were in part no more than extensions from those about the nose and were subject to the same general conditions. The independent affections of the lips appeared to be of earlier development and of comparatively short duration. There were very few of these, however, and too much cannot be inferred from such a small group of cases.

#### *Affections of the Eyelids.*

The lesions seen on the eyelids might be separated into two distinct classes according to their location, those which apparently originated in the skin and seemed to bear no particular relation to the marginal area, and those which originated at the mucocutaneous junction of the lid or ultimately involved this area. The first group of conditions was described in the paper dealing with cutaneous lesions. The affections of the mucocutaneous borders proper were also of two general types, first, papular or granulomatous lesions (Figs. 15 and 16), and second, lesions which appeared in the form of ulcers along the margins of the lids (Fig. 17).

The papular and granulomatous lesions presented no essential difference from the skin affections previously described, except as they came to involve the conjunctival surfaces. When this occurred, there was usually a moderate degree of conjunctivitis with reddening and swelling of the conjunctiva and increased lacrimation. These symptoms, however, were only transient, and within a few days, such inflammatory reactions were confined to the immediate area of the lesion (Fig. 16).

Lesions which originated upon the margins of the lids or on the surface of the conjunctiva itself usually produced a greater degree of inflammatory reaction. In most instances, they appeared, as we have said, in the form of small ulcers or abrasions. Occasionally, the initial affection was a minute papule, such as that in Fig. 15, which subsequently underwent ulceration. The appearance presented in these cases depended largely upon the extent of the induration which was associated with the formation of the ulcer. In several instances, lesions of this type developed definite collars of induration such as that shown in Fig. 17. As will be seen from this figure, there was a well marked area of infiltration extending from the margin of the lid back under the surface of the conjunctiva.

*Occurrence and Duration.*—In the few animals which showed lesions upon the margins of the lid, the time of appearance of these lesions varied from about 3 to 11 months after inoculation, but the majority occurred within 4 months. On the whole, they were decidedly less enduring than those about the nose, but in exceptional instances, they lasted for several months with varying periods of activity and quiescence or regression.

#### *Affections of the Penis and Sheath.*

As in the case of localized infections about the nose, it is probable that many cases of specific infection of the penis and sheath occurred which did not lead to the formation of lesions of a sufficiently definite character to attract our attention. Among the animals in this group, there were several in which the diagnosis of the local infection was made prior to the development of any characteristic lesion. These cases were suspected on account of redness and some swelling of the sheath and the presence of a mucopurulent discharge which upon examination was found to contain *Treponema pallidum*. Otherwise the diagnosis was first made on account of the presence of lesions which proved to be syphilitic.

The list of affections which occurred about the penis and sheath included first, cases of a diffuse inflammatory character associated with a mucopurulent exudate, second, circumscribed or diffuse infiltrations which usually led to the formation of papules or ulcers, and third, lesions of a granulomatous type consisting either of circumscribed masses or of more diffuse granulomatous processes.

The acute inflammatory process which marked the beginning of many of these localized infections was a fairly characteristic feature of affections of the moist surfaces or the orifice of the sheath. In one group of cases, there was a diffuse redness and swelling of the parts as in Fig. 18, which lasted for only a short time as a rule and was superseded by a diffuse infiltration (Fig. 19). As the process advanced, erosions or definite ulcers made their appearance in various localities but more especially about the margins of the sheath. Lesions on the skin surface were covered by dry, adherent crusts, while those on the mucous surfaces of the sheath and the shaft of the penis were moist and covered by a gray necrotic exudate. Occasionally small papules or condylomatous growths were also present (Fig. 18).

In another group of cases, the initial lesion was of a more circumscribed character and appeared in the form of a slightly elevated area of a gray, pink, or amber color surrounded by a zone of slight inflammatory reaction (Figs. 20 and 22). Some of these processes tended to spread and formed diffuse areas of infiltration (Figs. 20 and 21), while others developed into circumscribed and indurated nodules as was the case with the lesion shown in Figs. 22 and 23.

When the infection was confined to the skin surface, the acute inflammatory reaction was usually slight and the conditions present were much the same as in the case of other skin lesions. Thus in Fig. 24 there is seen an area of infiltration involving the right side of the sheath which is just beginning to show surface necrosis and eventually developed into the chancre-like mass seen in Fig. 25.

This type of affection was comparatively common and presented numerous variations of the condition illustrated. Two especially marked cases of infection confined to the region of the meatus of the sheath are shown in Figs. 26 and 27. It will be seen that the lesions completely surround the orifice of the sheath and are located practically at the line of junction of the skin and mucous surfaces. In one case (Fig. 26), the necrosis appeared exactly along this line and completely encircled the meatus. In the other (Fig. 27), the necrotic area occupied a similar position, but at the time the photograph was taken, the ulcer was confined to one side.

Another form of unusually marked involvement of the sheath is that shown in Figs. 28 and 29. The condition began with edema and congestion of the sheath, and, as the lesions developed, there was marked enlargement and induration of the sheath extending from meatus to base, associated with a pronounced exfoliation of surface epithelium and the formation of cracks and erosions of the skin



and mucous surfaces (Fig. 28). Eventually, an irregular line of necrosis and ulceration appeared and separated the mucous from the skin surfaces. On the whole, the mucous membrane appeared to be less involved than the skin, and no definite involvement of the penis could be made out.

Involvement of the penis, as has been mentioned, may occur along with that of the mucous surface of the sheath, in which case the lesions seen were of the type of small infiltrations or surface erosions. One other form of lesion may be mentioned which was observed in but one animal. This consisted of an elevated area of infiltration surrounding the urethral orifice as is indistinctly shown in Fig. 30. In addition, it may not be out of place to mention that infection of the mucous membrane of the urethra with the production of lesions has been demonstrated microscopically.

*Occurrence and Duration.*—As might be expected from their proximity to the point of inoculation, lesions of the sheath developed somewhat earlier than those of the other mucocutaneous surfaces. The earliest lesions of this group appeared 26 days after inoculation, in other words, almost as soon as the primary lesion itself. There were two other cases which occurred within 2 months after inoculation, and a number of cases within a period of 3 months, while the latest case of the series was 6 months after inoculation. The subsequent history of lesions of this group was very variable. Some lasted for a comparatively short time, while others endured for many months. For example, the lesions shown in Figs. 28 and 29 were still fairly active when the animal was killed for pathological examination  $5\frac{1}{2}$  months after the lesions first appeared, and in a second animal, the lesions persisted for a little more than a year.

#### *Affections of the Anal Region.*

With a few exceptions, animals which showed specific involvement of the sheath showed lesions of the anus as well, and, conversely, there were only two animals with anal lesions in which corresponding lesions were not present on the sheath. The two groups of conditions, therefore, might almost be considered as one, and apparently the main difference between them was in the character of the lesion which occurs in the two locations, and even this was not great. There were no true exudative affections of the anus. The lesions situated on the cutaneous surfaces were essentially the same in all respects as those

of the sheath. In fact, there was a very striking similarity between the lesions present in the two localities, as may be seen by comparing those shown in Figs. 24 to 29.

The most interesting conditions seen by us in the anal region of the rabbit were lesions which might be classed as condylomata, a typical example of which is given in Fig. 31. These lesions were, as a rule, entirely obscured from observation until the anal ring was distended to a sufficient extent to permit of inspection of the transitional borders. This could be easily done by exerting pressure upon the rectum immediately behind the sphincter.

The first suggestions of the presence of lesions of this character (condylomata) came with slight redness and swelling of the anus, and during the earlier stages of the localized infection, no other alteration might be present. As infection advanced, the reaction became more localized, with the development of areas of infiltration and induration situated in one or more segments of the anal ring immediately along the junction of the skin and the mucous membrane. These were not unlike the patches of infiltration on the mucous surfaces of the sheath. In cases of more pronounced involvement, however, such as that shown in Fig. 31, the entire anal ring was involved, with extension of the process over both the mucous and cutaneous surfaces. The lesion thus formed was a distinctly elevated and indurated mass strikingly like the condyloma latum in man. Judging from our small series of animals, lesions of the condyloma type are more frequent about the anus of the rabbit than on the sheath, and this constituted the chief difference between the lesions of the two localities.

*Occurrence and Duration.*—As regards the time of occurrence and duration of anal lesions, they are again comparable to those of the sheath, but, on the whole, appeared to be slightly more delayed in their development and in a few instances were more enduring. The condyloma shown in Fig. 31 remained active for upwards of 15 months and still showed slight signs of activity when the animal was killed 21 months after inoculation.

#### *Diagnosis of Mucocutaneous Infections.*

Obviously there are many conditions affecting the rabbit which might be difficult to differentiate clinically from some of the affections described above. This is especially true of infections of the nose, eyes, and genitalia, but rare in the case of the anus. A syphilitic rhinitis which is not associated with characteristic lesions presents much the same train of symptoms as the more common condition

known as snuffles. The chief symptomatic difference between the two affections is in the associated involvement of the lacrimal system. As a rule, snuffles is not associated with marked and persistent lacrimal overflow, and when involvement of the lacrimal system does occur, there is usually an acute conjunctivitis. On the other hand, profuse lacrimation without an acute inflammatory reaction is very common even in the early stages of a syphilitic infection. At this stage, however, the distinction between the two processes can be made with certainty only by a demonstration of spirochetes in the nasal discharge or in the mucous membranes themselves.

In cases in which lesions are present, the differentiation of the two conditions presents less difficulty. In the most severe and long standing cases of snuffles, some infiltration and erosion may be present about the nares but they are associated with a greater degree of supuration and could hardly be confused with the conditions described above.

The two main conditions to be considered in connection with the eyelids and conjunctiva are trauma and conjunctivitis of bacterial origin. Slight abrasions of the lids are fairly common among rabbits, especially as a result of scratching, but they usually heal very quickly and should not be confused with syphilitic infiltrations. There is also a parasitic disease of the skin (mange) which occasionally forms small lesions along the margins of the lids, but these are readily identified by the character of the lesion and the presence of a similar affection upon other parts of the body.

Traumatic conjunctivitis and epizootic infections of the conjunctiva must also be distinguished from affections of a syphilitic nature. These conditions, however, have a more immediate connection with affections of the eyes than with those of the present group.

There are several conditions, chiefly infections, which should be mentioned as possible sources of confusion with syphilitic involvement of the penis and sheath. So called gleet is a well known disease of rabbits which affects the genitalia of both males and females and is characterized by an acute inflammatory reaction with a purulent exudate and may lead to necrosis and ulceration. We have seen a few such cases among normal animals but know very little of this condition from personal observation.

Arzt and Kerl (6) have described a similar condition in rabbits due to a spirochete infection which is capable of transmission from one animal to another. It is claimed that the lesions produced by this organism bear some resemblance to syphilitic lesions. We have never encountered infections of this type.

Traumatic and pyogenic infection about the genitalia must also be considered, but as far as we are aware, the only class of syphilitic affections which might be confused with any of the conditions mentioned are those in which no characteristic lesions are present, and in these cases, a diagnosis can be made only by the demonstration of spirochetes.

#### SUMMARY.

In a series of more than 200 rabbits in which generalized lesions were observed following local inoculation with *Treponema pallidum*, there were a number of animals in which characteristic lesions were noted upon mucous membranes or along mucocutaneous borders. These lesions were distributed with about equal frequency between the nose or nasolacrimal system and the eyelids on the one hand, and the genital and anal regions on the other. The lips and buccal mucosa appeared to be less subject to localized infections unless the papillomatous growths noted on the lips and under side of the tongue should prove to be in some way connected with such an infection.

In many instances, the local reaction was initiated by an acute inflammatory process, and in the case of nasal and genital infections, a definite exudate was formed. The succeeding stages of the reaction consisted in an infiltration of the parts involved, together with a variable degree of proliferation of fixed tissue cells, leading eventually to necrosis and ulceration. The resulting lesions differed according to their location and the character of the reaction in the individual case. Localized infections of the nose occurred in several forms, first, as a rather diffuse affection of the nasal mucosa characterized by the presence of a mucopurulent exudate, second, as a more or less circumscribed process of infiltration with an especial predilection for the region of the anterior nares, and third, as a granulomatous process involving the alæ in particular.

Involvement of the nasal mucosa was very commonly associated with lacrimal overflow and with some degree of conjunctivitis.

The lesions of the eyelids were usually small, elevated papules or lesions of an ulcerative character some of which were surrounded by a zone of infiltration. In exceptional instances, large granulomatous lesions occurred along the margins of the lower lids.

Infection of the penis and sheath gave rise to conditions analogous to those of the nose. In one group of animals, there was a diffuse affection characterized by redness and swelling of the parts with a mucopurulent exudate, in another there were circumscribed or diffuse infiltrations, while in a third the lesions formed were indurated granulomatous masses. Secondary necrosis with erosion or ulceration was a common feature of all these conditions.

Localized infections in the region of the anus differed from those in other localities chiefly in the absence of an exudative group of affections and in the frequency with which lesions of a papillomatous type occurred.

Lesions of mucous membranes and mucocutaneous borders developed at periods of time varying from a few weeks to several months after inoculation. Most of them were rather enduring and in several instances persisted in an active condition for considerably more than a year.

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## EXPLANATION OF PLATES.

The illustrations are reproductions of unretouched photographs which, with the exception of Fig. 3, represent the objects at their natural size. Fig. 3 is at a magnification of 1.5. Statements of time are estimated from the date of inoculation unless otherwise indicated.

## PLATE 78.

FIGS. 1 to 4. Syphilitic affections of the nasolabial region.

FIG. 1. 4 months. Syphilitic rhinitis with infiltration about the nares. There is loss of hair over the affected area, with superficial necrosis and ulceration and the formation of adherent crusts.

FIG. 2. 10 months. Marked infiltration of the alæ with necrosis and the formation of ulcers covered by crusts. There were also pronounced lesions at the angles of the nares.

FIG. 3. 68 days. A circumscribed and elevated area of infiltration with central necrosis and ulceration situated in the right nasal orifice. The lip is drawn down to bring the lesion into view.

FIG. 4. 5½ months. A marked diffuse infiltration of the skin and mucous membrane of the left side of the nose and the nasolabial fold with slight involvement on the right. The skin area shows exfoliation of surface epithelium and there were erosions on the mucous membrane.

## PLATE 79.

FIGS. 5 to 8. Stages in the progress of an ulcerating granulomatous lesion of the nose.

FIG. 5. 4½ months. Early granulomatous lesions in the anterior nares with an ulcer on the right. There was no nasal discharge at this time.

FIG. 6. 2 weeks later. A slightly later stage of the affection showing the marked prominence of the alæ and the extension of the necrosis and ulceration, now present on both sides.

FIG. 7. 7 months after the appearance of the lesions. There has been marked destruction of the soft tissues of the nose, and both nostrils are occluded by thick reddish brown crusts.

FIG. 8. The same lesions 1 week later with the crusts removed. There was still slight activity in some parts of the lesions most noticeable on the right. The left nasal orifice was entirely obliterated, and there was only a small opening on the right.

## PLATE 80.

FIGS. 9 to 11. The clinical appearance presented by animals showing a combined nasolacrimal involvement.

FIG. 9. 3 months. The same animal as that in Fig. 1, showing an earlier stage of the affection. Note the characteristic mucopurulent discharge about the nose associated with lacrimal overflow. This condition is not unlike that sometimes seen in snuffles.

FIG. 10. 5 months. The same animal as that in Figs. 5 to 8. A pronounced lacrimal overflow was present in this animal without an associated nasal discharge. Note the swollen condition of the lids and skin at the anterior or internal angle of the eye.

FIG. 11. The same animal at a later period of the infection (1 year after inoculation). Chronic dacryocystitis.

## PLATE 81.

FIGS. 12 to 14. Affections of the labial cleft.

FIG. 12. The appearance of the surface of the labial cleft in a normal rabbit.

FIG. 13. 3 months. A diffuse infiltration of the skin and adjacent mucous surfaces of the labial cleft, more marked on the left than on the right. The skin is denuded of hair on both sides, and the left lip shows a series of irregular ridges covered by gray necrotic epithelium. Mucous patches.

FIG. 14. 3½ months. A sharply circumscribed and indurated ulcer on the inner surface of the left upper lip.

FIGS. 15 to 17. Lesions of the margins of the lids.

FIG. 15. 2½ months. An early papular lesion arising in the margin of the lower lid.

FIG. 16. 3 months. The lower lid everted to show the inflammatory reaction on the conjunctival surface resulting from a syphilitic lesion on the lid.

FIG. 17. 6 months. An indurated ulcer on the upper lid and congestion of the conjunctival vessels.

## PLATE 82.

FIGS. 18 to 25. Affections of the penis, sheath, and anus.

FIG. 18. 4½ months. Diffuse infiltration of the sheath with edema and congestion of both the penis and sheath. There are small papular lesions on the sheath and an area of erosion at the superior margin of the fold in the sheath.

FIG. 19. 145 days. A later stage of the lesions in Fig. 18 showing diffuse infiltration and thickening of the sheath.

FIG. 20. 47 days. A small circumscribed area of infiltration on the mucous surface of the sheath with a diffuse redness and swelling. Sheath retracted.

FIG. 21. 2 weeks later. The same animal. The infiltration has become more pronounced and retraction of the sheath is difficult. Congestion and edema have subsided.

FIG. 22. 2½ months. An early papule situated in the transitional area between the skin and mucous surfaces of the sheath. The papule is surrounded by a slight zone of acute inflammatory reaction.

FIG. 23. 2 weeks later. The same animal. The lesion on the sheath has developed into an indurated nodule with central necrosis and ulceration. The edges of the ulcer are inverted and there are marked vascularization and redness of the tissues at its base (mucous surface).

FIG. 24. 3 months. An irregular area of infiltration in the skin of the sheath. The surface of the lesion shows beginning necrosis at two points. On the dorsal surface of the anus, there is also an indurated granulomatous lesion with a depressed ulcer at the center.

FIG. 25. 1 week later. The same animal. Both lesions have increased somewhat and are now of essentially the same character.

PLATE 83.

FIGS. 26 to 31. Affections of the penis, sheath, and anus.

FIG. 26. 3 months. Syphilitic lesions of the anus and sheath situated at the mucocutaneous borders and completely encircling these parts. The lesions were characterized by an intense induration and the development of a line of necrosis which practically coincided with the transitional area.

FIG. 27. 3 months. A similar group of lesions in another animal. The lesion on the anus, however, was confined to one side.

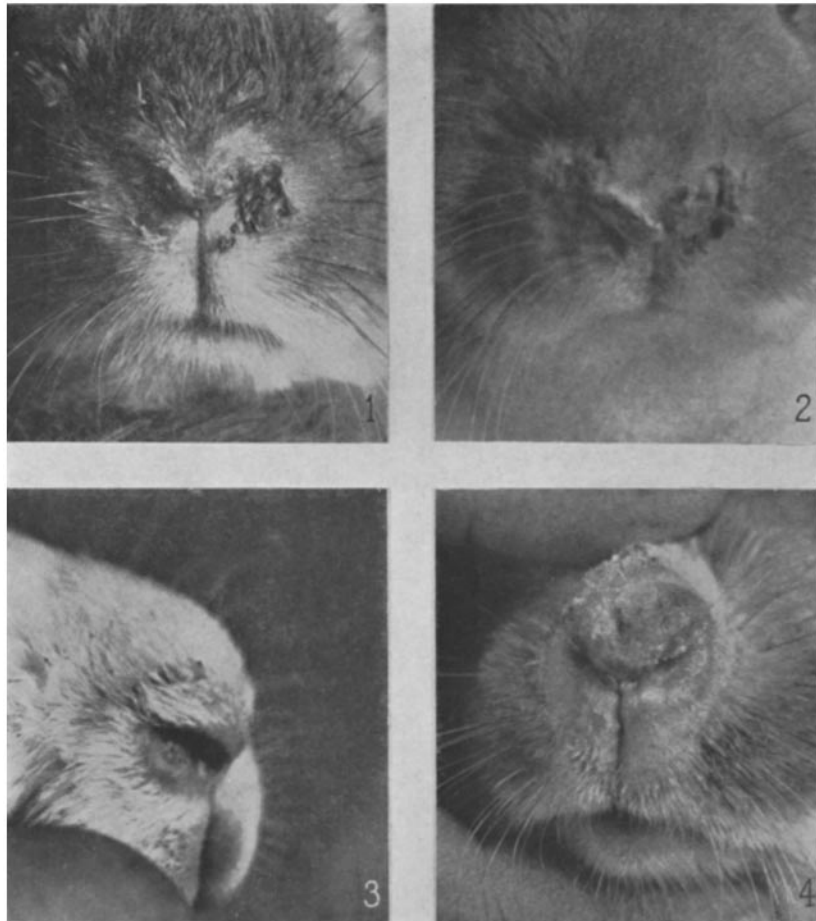
FIG. 28. 3 months. A diffuse infiltrative process involving the entire sheath and anal ring. The surface of the lesion was marked by irregular areas of superficial necrosis and exfoliation; there were also erosions on the mucous membranes.

FIG. 29. 1 month later. The same animal. Note the appearance of a line of necrosis separating the swollen and everted mucous membrane from the skin of the sheath. There was a similar condition of the anal ring.

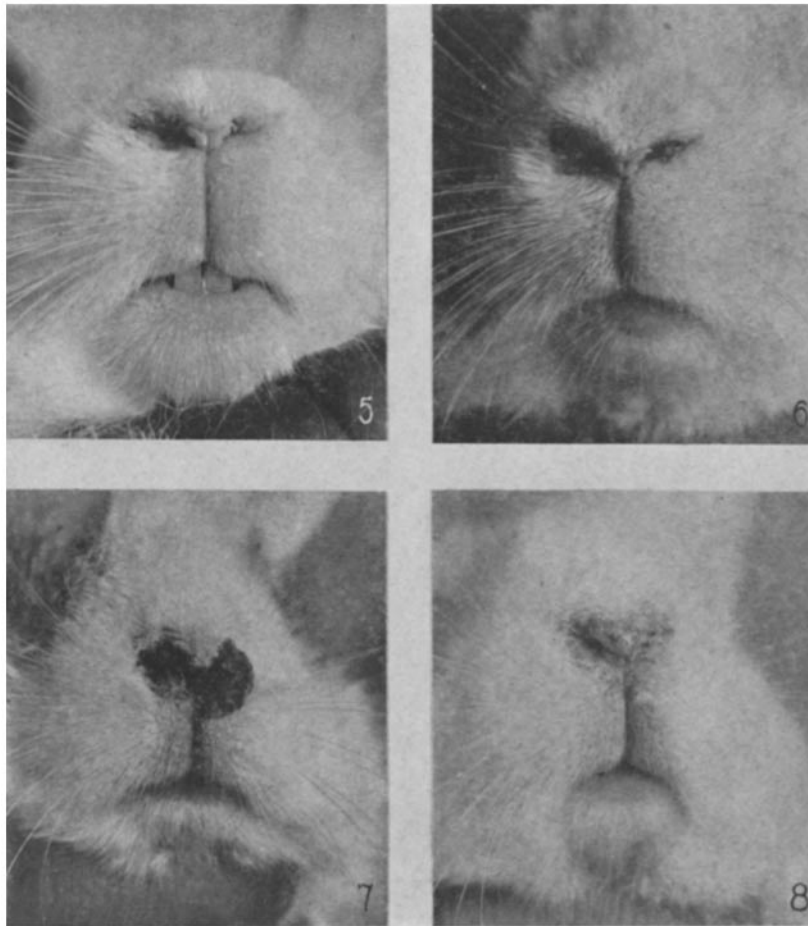
FIG. 30. 2 months. A small mass is seen on the under surface of the penis (marked by an arrow), which was formed by a zone of infiltration surrounding the meatus of the urethra.

FIG. 31. 6 months. Condyloma latum of the anus. The anus is everted.





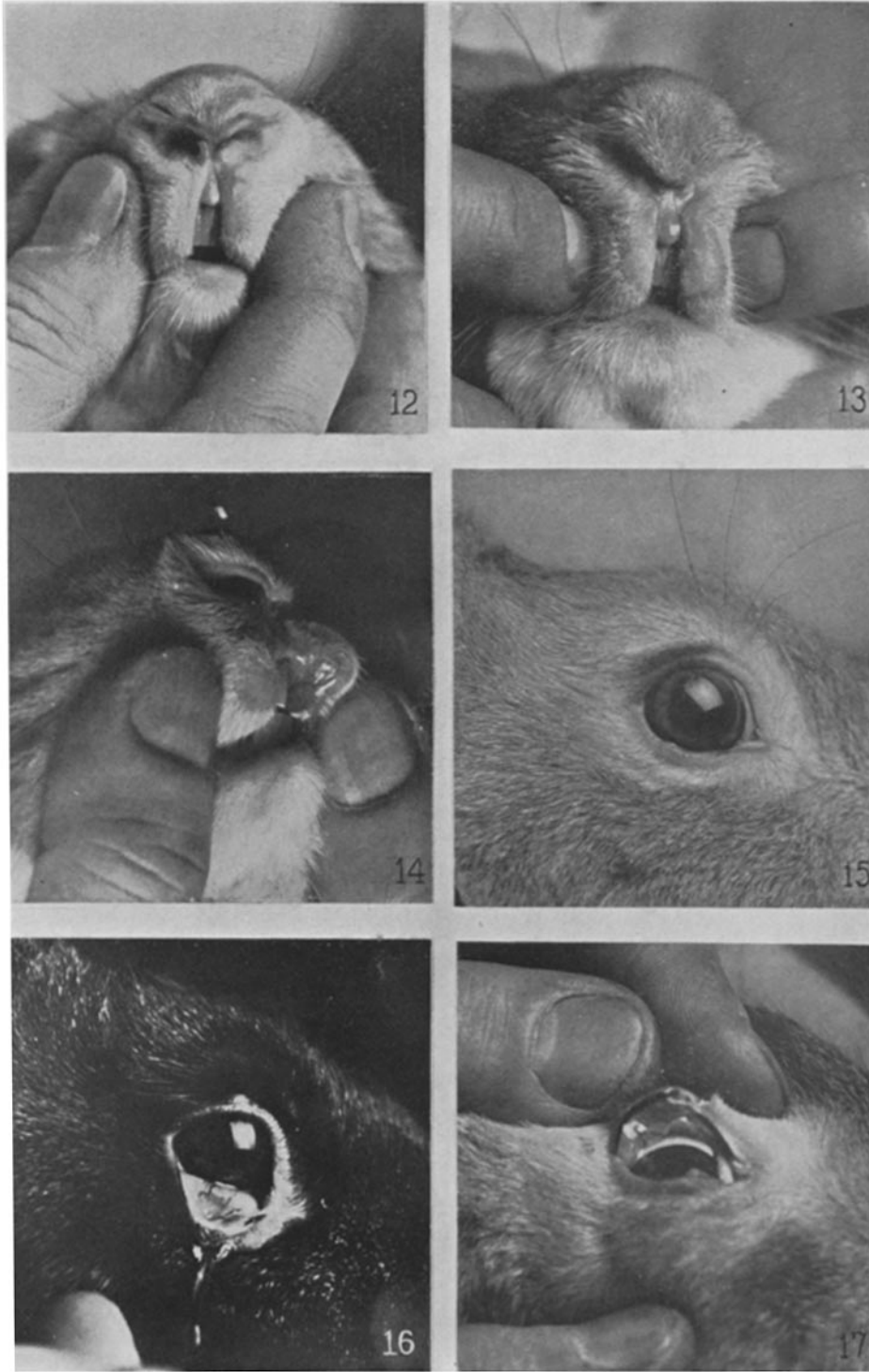
(Brown and Pearce: Experimental syphilis in the rabbit. V.)



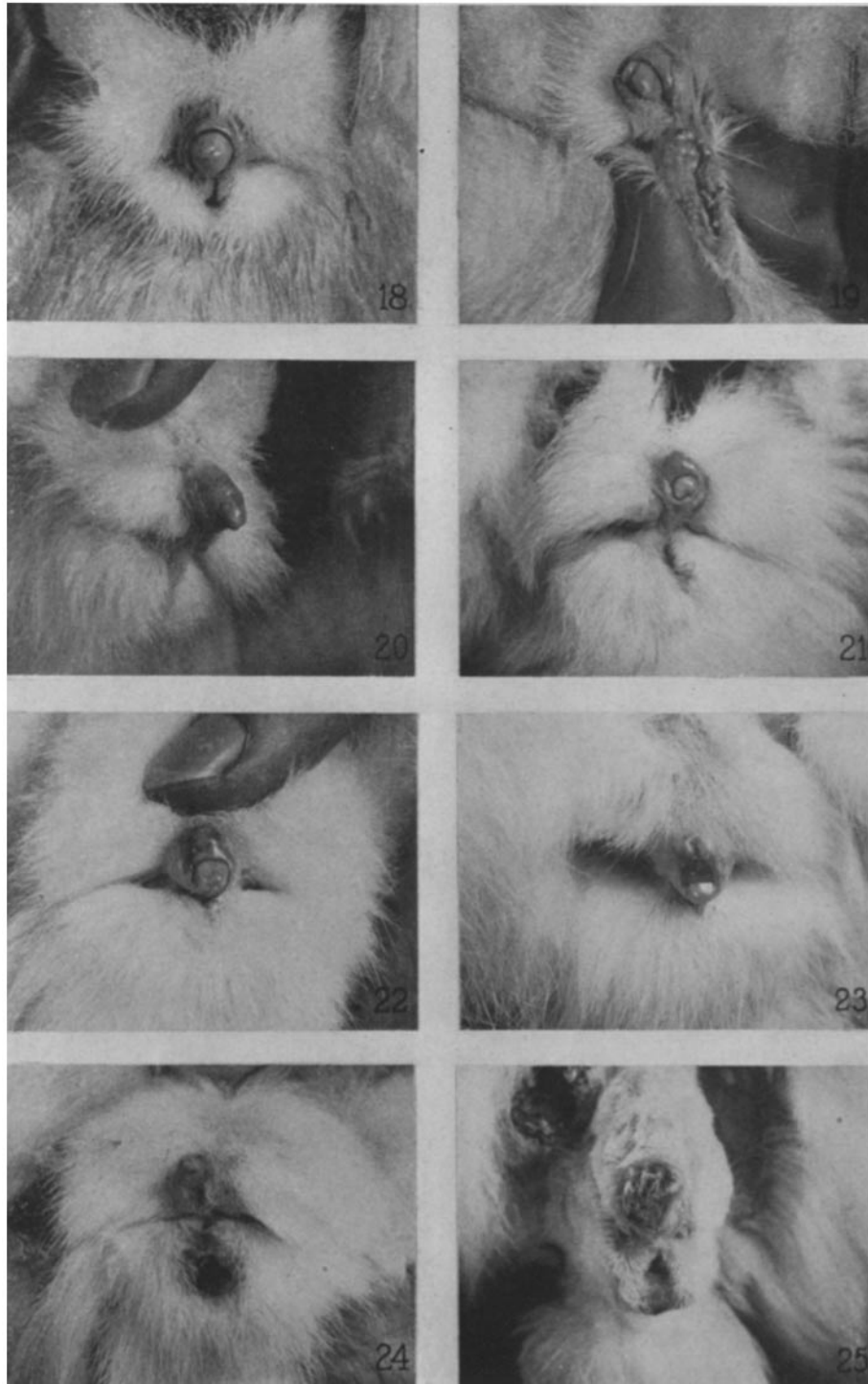
(Brown and Pearce: Experimental syphilis in the rabbit. V.)



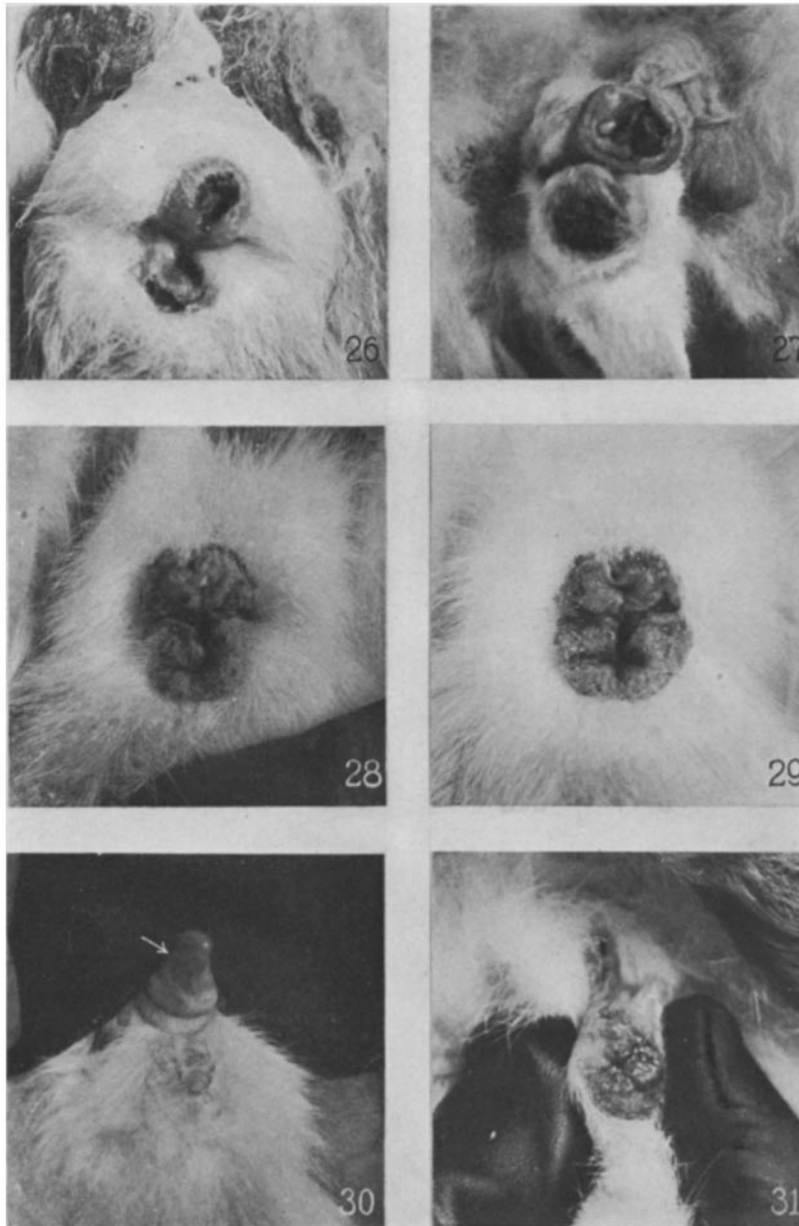
(Brown and Pearce: Experimental syphilis in the rabbit. V.)



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



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



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