EXPERIMENTAL SYPHILIS IN THE RABBIT.

III. Local Dissemination, Local Recurrence, and Involvement of Regional Lymphatics.

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Plates 90 to 97.

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In preceding papers of this series, the testicular and scrotal infections of *Treponema pallidum* were described from the view-point of a progressive local infection, and in following out this mode of presentation, a number of lesions were described as transformations or extensions of the local infection without any attempt to differentiate such lesions from lesions of a similar character which might arise as a result of local dissemination of the infection rather than from direct extension or transformation of primary lesions. It was pointed out, however, that there were many lesions of the testicles and scrotum which occupied a position of uncertainty with reference to the primary infection and that it could not be determined in all cases whether the lesions present represented actual transformations and extensions of a primary infection or had arisen as a result of local dissemination.

In brief, it was recognized that there were two groups of lesions in the testicles and scrotum which could not be clearly separated from one another. One group is composed of modified and persistent forms of primary lesions together with direct extensions and true recurrences, while the other represents lesions which owe their origin to local or regional dissemination of the virus.

These lesions are of especial interest in that they mark a transition between conditions which can be clearly recognized as primary manifestations of infection and conditions which represent true generalized infection. The subjects of chief interest in this connection are those of local spread and local dissemination of the infection, recurrent and

consecutive lesions, and involvement of regional lymphatics. References to this phase of experimental syphilis have been very few and for the most part rather vague.

Attention was called to the phenomenon of local metastasis by Uhlenhuth and Mulzer and by Truffi at about the same time. Truffi (1) reported a case of a granulomatous nodule arising in the epididymis and another of a lesion in the tunics following primary infections of the scrotum. Uhlenhuth and Mulzer (2) reported metastatic infection from one testicle to the other testicle and scrotum and a second case of metastasis to an uninoculated testicle after removal of the inoculated testicle. These observations were made in 1909 and 1910, and since that time, metastases of this kind have frequently been cited as evidence of generalization of the infection in the experimental animal.

Involvement of the inguinal lymph nodes in infected animals has likewise been noted both as an analogy to the human infection and as proof of generalization. This condition was first reported by Ossola (3) (1909) who was able to demonstrate spirochetes in sections of the inguinal nodes of animals inoculated in the scrotum. These findings were confirmed by Truffi (4) and the virulence of the organisms was proven by animal inoculation.

Other than observations of this kind, very little has been recorded concerning this border-line group of syphilitic manifestations.

Local or Regional Dissemination.

In animals infected with *Treponema pallidum*, one must recognize the existence of two opposing influences, the tendency of the organism to spread beyond the local confines of the point of inoculation and the opposing reaction on the part of the animal. Some extension of the infection and of the zone of local reaction occurs in all animals even with the most sharply circumscribed lesions, but the extent of the two processes does not run parallel.

The details of the local changes are either masked in a continuous and widespread reaction or else there are no lesions to mark the extension of the infection beyond the zone of primary reaction. In exceptional instances, however, cases do arise which when linked together furnish some interesting data concerning the spread, or dissemination, of the infection within the regions adjacent to the point of inoculation.

In addition to the widespread reaction commonly observed in the course of development of primary lesions, there were three general

types of local reaction which we were able to make out in connection with the dissemination of the infection in the testicles and scrotum: first, a diffuse reaction with the formation of multiple foci of secondary reaction arising subsequent to the development of the primary lesion; second, a reaction characterized by the formation of lesions having a perivascular arrangement; and third, dissemination of the infection with the production of multiple lesions showing no demonstrable connection with the primary focus of infection. While lesions of these three classes occurred in both the scrotum and testicles, they were most clearly definable in the scrotum, and for that reason, the discussion of the subject will be confined to the scrotal infection.

Diffuse Secondary Reaction with the Formation of Multiple Focal Lesions.—One of the most common forms of local dissemination observed was one which took place with a more or less diffuse reaction about a primary focus of infection and led to the formation of multiple secondary lesions which tended to become fused into a single chancre-like mass. This form of reaction is apt to be confusing and it is only in cases where the successive steps in the process can be followed that the ultimate lesion can be distinguished in any way from a true primary lesion. A typical case of this kind is illustrated in Figs. 1 to 3.

The primary lesions in this animal were small circumscribed chancres of a rather indolent character and for approximately 2 months there was nothing unusual about the local infection. A slight diffuse thickening of the scrotum then developed about these lesions and a number of small thickened plaques were formed here and there in the scrotum. These plaques developed into nodules and the diffuse reaction in the scrotum increased after the manner shown in Fig. 1. At the time this photograph was taken, 85 days after inoculation, the primary lesions themselves (indicated by arrows) had begun to grow actively; the entire scrotum was markedly thickened and slightly reddened, and the focal lesions showed signs of necrosis and ulceration. The development of these lesions continued as indicated by Figs. 2 (91 days after inoculation) and 3 (113 days after inoculation) with the formation of an increasing number of secondary foci which tended to fuse into a single large granulomatous lesion indistinguishable in character from an ordinary chancre.

It should be noted here that the development of this series of lesions in the scrotum, occurring 2 months after inoculation, coincided with the appearance of similar granulomatous lesions on the

feet and legs of this animal and the two sets of lesions ran a parallel course of development.

This is but one of many cases of the kind which have come under our observation but will serve to indicate the possibilities for confusion of primary lesions and lesions which owe their origin to dissemination from a primary focus of infection.

Local Dissemination with the Formation of Perivascular Lesions.— The second form of local dissemination to be considered differed from the first chiefly in that the development of the lesions was less obscured and the lesions themselves were of a very distinctive type.

In taking up this group of lesions, we may refer first to a form of direct extension from the primary lesions which was observed in cases in which the initial lesion was slow in developing or of slight extent and spread of the infection along the perivascular tissues could be detected even before the reaction at the site of inoculation had become well established. The animal shown in Fig. 4 was one of a group inoculated with a virus known to contain large numbers of spirochetes of low vitality. Following inoculation, the implant became soft and cheesy in character and no specific reaction could be detected for about 6 weeks. Finally, a narrow line of induration developed at the outer margin of the implant in the right scrotum and fine thread-like lines of infiltration immediately began to spread along the course of the blood vessels leading away from this area as shown in the photograph (Fig. 4) taken 56 days after inoculation. These lines of infiltration grew until they formed a series of cords about 1 mm. in diameter with node-like thickenings at various points. Later, the intervening sections in the distal portions of the cords disappeared, leaving a series of isolated shotty nodules, while the parts nearest the implant became fused into a single irregular granulomatous mass.

In the left scrotum, a similar type of reaction took place except that the lines of perivascular extension were not so clearly defined. When first discovered, there were numerous isolated points of induration diffusely scattered through the scrotum, many of them occupying a perivascular position. Soon after the appearance of these disseminated lesions in the scrotum, lesions developed upon the sheath and about the anus of this animal.

We have in this animal what appears to be a twofold process, first a gradual but direct extension of the primary reaction along certain definite lines, and second a widespread development of focal lesions resulting from dissemination of spirochetes with which the development of the primary lesion had not kept pace.

A somewhat clearer example of local dissemination with the production of perivascular lesions is to be found in the animal shown in Figs. 5 and 6 which belonged to the same series as that shown in Figs. 1 to 3. The initial lesions were again small ulcerated chancres with slight induration. These lesions were soon transformed into a moderate diffuse thickening of the ventral surface of the scrotum, while the ulcers healed, leaving small puckered scars (Fig. 5). About 6 weeks after inoculation, a series of small shotty nodules was palpable in the dorsal fold of the scrotum. These nodules were just visible as translucent points distributed in chains along the course of the blood vessels extending centrally from the thickened patches in the scrotum. They gradually increased, and at the time the first photograph was taken (Fig. 5, 63 days after inoculation), there were numerous nodules distributed all through the scrotum, including the area beneath the scar, and the course of the blood vessels in the dorsal fold was marked by a series of indurated lines and nodes (Fig. 5). While these lesions are shown on only one side, the condition on the other was exactly the same.

During the next 3 weeks, the character of the lesions changed materially. Many of the papular lesions disappeared, leaving only a few perivascular lesions in the dorsal portion of the scrotum (Fig. 6). The chief seat of the specific reaction shifted back to the ventral surface of the scrotum which showed a heavy shell of doughy thickening with a few large masses of induration. The subsequent changes were much the same as those shown in the first series of photographs (Figs. 1 to 3).

Again we may note that the occurrence of these papular lesions in the scrotum coincided with the development of a periosteal lesion at the distal end of the left ulna.

While lesions of the type described were observed in all parts of the scrotum, the seat of predilection was the lower end of the dorsal fold, and the occurrence of one or more lesions in this location was quite common. When the lesions were multiple or in the form of cords, they frequently followed a definite line of distribution or extension from the point of inoculation or from the primary lesion towards the body axis.

Local Dissemination with the Formation of Multiple Secondary Lesions.—The third group of disseminated lesions to be described differed from the first group only in that they were clearly focalized lesions from the beginning and from those of the second group in that they showed no apparent perivascular relation and no definite connection with the parent lesion. These lesions usually appeared as multiple papules or plaques and tended to develop into multiple lesions of a chancre-like character. Sometimes there were only one

or two such lesions, but at others, there were as many as six or eight. The animal shown in Fig. 7 had six distinct lesions of different sizes and stages of development in each scrotum, among which it would be rather difficult to identify the primary lesion. As in the previous cases, they tended ultimately to diminish in number, and the reaction usually became centered in one or two lesions which developed to a considerable size, overgrowing and fusing with the surrounding lesions.

It is probable that lesions of this class have in general been regarded as multiple primary lesions, but as a rule they do not begin to appear until after a primary lesion of some sort has developed at the immediate point of inoculation or for some 6 weeks or more after inoculation, and while they may become the main lesions present, they are not primary in the sense of lesions developing as a result of simultaneous localization of the infection. This distinction may or may not be of importance according to the significance which may be attached to primary and so called secondary lesions.

Recurrent Lesions.

The lesions which develop in the testicles and scrotum of an infected animal subsequent to the regression or healing of an initial lesion have many points of interest, but their chief importance lies in their bearing upon problems of local dissemination and the persistence of active infection when once the local lesions have completely disappeared. In its application to experimental therapy, there are few subjects of greater importance than this, and while we cannot enter into this phase of the subject with the thoroughness which it demands, the therapeutic importance of recurrent lesions may be kept in mind.

The lesions which develop after spontaneous healing of an initial lesion and those which appear after healing which has been induced by artificial means are identical in all respects. Induced healing, as by the use of therapeutic agents, offers the advantage, however, of clearer definition between the process of healing and recurrence, and for this reason we shall use cases for illustration in which the healing of the original lesion was experimentally induced.

As an introduction to the subject of true recurrence, it may be pointed out that the power of recovery in an early and actively developing scrotal chancre is very great and that regression may be carried almost to the point of complete healing and be followed by prompt regeneration of the lesion. This fact is illustrated in Figs. 8 to 10. Fig. 8 shows two chancres 40 days after inoculation at which time the animal was treated. The lesions regressed rapidly, and 2 weeks later, there was an irregular thickened mass in the right scrotum and only a small ulcer with no induration in the left (Fig. 9). At this point, regeneration set in, and in 2 weeks more, chancres showing the same characteristics as the original lesions were produced (Fig. 10). This is the result usually obtained when regression stopped short of complete healing.

Once complete healing of a lesion was accomplished, it was rare that another lesion developed from exactly the same point. The four most common locations for recurrent lesions were the tissues beneath the scar, the edges of the scar, the dorsal folds of the scrotum, and the testicles. The lesions developing in the scar were usually no more than indurated plaques, although typical chancres were observed which formed upon the basis of an old lesion.

In the tissues beneath the scar, the recurrent lesions usually took the form of indurated nodules, some of which might develop to considerable size and involve the overlying skin with the formation of chancre-like lesions.

A typical example of this form of recurrence is given in Figs. 11 to 13. Fig. 11 is the original chancre 29 days after inoculation, Fig. 12 the healed lesions, and Fig. 13 the multinodular recurrence with an ulcerated chancre-like lesion in the left scrotum 78 days after treatment.

A more common form of deep scrotal recurrence is that shown in Figs. 14 to 16. Recurrence in this animal did not take place until 55 days after treatment, and the lesions formed were small indurated nodules which were at first confined to the subcutaneous tissues. Later, the skin became involved, and a diffuse induration with multiple focal lesions extended over a large portion of the scrotum of both testicles (Fig. 16). During 4 months observation, no typical chancre-like lesion developed.

Another form of recurrence which was frequently seen in the scrotum is that shown in Figs. 17 to 19. This animal was treated 37 days after inoculation and the chancres healed promptly. 55 days after treatment, there were a few small indurated nodules at the outer edges of the scars on both sides. The scars themselves were smooth and thin (Fig. 19, 77 days after treatment). Subsequently other lesions of the same character appeared elsewhere in the scrotum, but they remained for only a short time and none of them developed to a size much larger than that shown in the photograph.

In some instances these recurrent lesions even though they were far removed from the seat of the original chancre showed a form of development identical with that of a chancre. Such a case is illustrated in Figs. 20 to 22. Recurrence took place in this animal 127 days after treatment, and the lesions appeared as single, minute, indurated nodules situated at the lower end of the dorsal fold of the scrotum; they were bilateral and symmetrical. These lesions grew rapidly and assumed the appearance of typical chancres (Fig. 22, 133 days after treatment).

In addition to the various forms of nodular lesions described, diffuse lesions of various types were observed in many animals. A case of this type which combines something of the characteristics of a diffuse and a focal process is shown in Figs. 23 to 25. This animal was treated 48 days after inoculation (Fig. 23). The lesions regressed very rapidly until they had almost healed, when a diffuse infiltration appeared over a large part of the scrotum (Fig. 24). Healing of the initial lesion continued, however, with the formation of an ordinary looking scar, and the thickening of the scrotum diminished (compare Figs. 24 and 25). 28 days after treatment, a series of slightly reddened and translucent points appeared around the margins of the scars (Fig. 25, 35 days after treatment). These spread rapidly, producing a slight diffuse induration in the scrotum with scaly points here and there.

A final form of recurrence to be noted is that which takes place in the testicle following the healing of a scrotal lesion, and it may be mentioned in this connection that such recurrences were quite common as were recurrences of testicular lesions in the scrotum. The most common locations of recurrent lesions in the testicle were the head of the epididymis, the tail of the epididymis, the mediastinum testis, and the tunics, or the same positions in which primary testicular infections tend to become localized.

This form of recurrence is illustrated in Figs. 26 to 28. The chancres in the scrotum of this animal healed completely in 3 weeks. 1 week later, there was a definite swelling of both testicles and indurated nodules were found in the head of the epididymis on both sides (Fig. 28); the scrotum remained normal.

The time of occurrence and the relative frequence of the various types of recurrent lesions will not be entered into. It seems well to mention, however, that the more characteristic lesions usually appeared early after the healing of the original lesion, while the smaller, less easily recognizable ones were more delayed in their development. The time of recurrence in our series of animals varied anywhere from a few days to many months, and so many circumstances enter into

estimations of the possibilities of local or regional recurrence that definite statements as to time limits cannot be made upon the basis of the data at present available.

To emphasize the difficulties attendant upon observations as to recurrence of local infections, the case illustrated in Figs. 29 to 31 may be cited. Following treatment, the chancres in this animal (Fig. 29) healed rather slowly, and healing was not complete at the end of 6 weeks (Fig. 30); however, smooth, thin scars were eventually formed. 63 days after treatment, two small areas of thickening appeared at the edge of the scar in the right scrotum but disappeared within a few days and infection could not be proven. 105 days after treatment, the extremely small nodule shown in Fig. 31 appeared in the left scrotum and proved to be syphilitic. There was a slight local edema associated with this nodule, but the nodule did not increase in size and persisted for only a short time. No other local lesions were found, but the animal developed a specific iritis 192 days after treatment.

A second animal of a similar character which came under our observation was one in which minute points of induration appeared in the dorsal folds of the scrotum 107 days after treatment. These nodules persisted for 8 months with very little change and no other lesions appeared for some time, but eventually a generalized rash developed upon the face and ears.

It will be noted that the lesions described as recurrences are not unlike some of the conditions previously described in connection with transformations of primary lesion and especially like those resulting from local dissemination. In fact, transformation, dissemination, and recurrence are all overlapping processes with no sharp line of separation between them, and each of these phenomena throws some light upon the others.

Involvement of Regional Lymphatics.

Enlargement and induration of the inguinal lymph nodes has been noted by several observers in connection with *pallidum* infections of both the testicles and the scrotum of the rabbit, and organisms have been demonstrated in these nodes in some instances. There is, however, little definite information concerning the relation of lymphadenitis to the experimental infection. The subject is a very broad one in itself and will not be discussed in detail at the present time. This aspect of the problem of experimental syphilis will be taken up in a separate paper, and we shall confine ourselves here to

general statements concerning involvement of the inguinal nodes in primary infections of the testicle and scrotum as a phase of local dissemination.

In normal rabbits, the inguinal glands are small, ovoid, or flattened masses which are barely visible or palpable (Fig. 32). From examination of a large number of rabbits, it was found that enlargement and induration of these nodes was inconstant in testicular infections and depended largely upon the extent of the local infection. In cases in which localized infection was confined to the testicles proper, there was little or no involvement of the inguinal glands, but when the infection extended to the scrotum, these glands became involved just as in cases of primary scrotal infection.

Character of the Involvement.—Localized infection in the scrotum was found to be invariably associated with marked inguinal lymphadenitis. Following inoculation or extension of an infection to the scrotum, pathological changes in the inguinal nodes could be detected almost immediately. The change began as an acute swelling, part of which might have been due to a non-syphilitic reaction but was merged indistinguishably with the syphilitic reaction which progressed rapidly until the affected glands were several times their normal size. During the early stages of the enlargement, the glands remained rather soft but gradually became harder and finally reached a condition of extreme induration. In some instances, the stage of acute swelling was absent; in these cases, the glands first became hard and shotty and then underwent a gradual enlargement.

The exact change which occurred in individual animals was found to be very variable, but a general idea of the inguinal adenopathy may be gained from an examination of the photographs reproduced in Figs. 32 to 43 which represent various forms and degrees of involvement.

As may be seen by reference to Figs. 33 and 34, a well developed adenitis was present in cases of active infection within a few days after inoculation. The 5 day example given in Fig. 33 is a rather pronounced instance of acute bilateral swelling more marked on the right than on the left. In Fig. 34 (7 days after inoculation), the change is not so apparent, especially on the right. Upon close examination, however, it will be seen that there are three nodes in this region, the largest of which is situated immediately over the cord and hence does not stand out so prominently as the one on the left.

The phase of acute swelling as exemplified in these two illustrations frequently reached its height by the end of the 1st or 2nd week after inoculation. The induration, however, continued to increase for some time and was not infrequently associated with a slight temporary decrease in the size of the gland. When fully developed, the inguinal adenopathy presented a variety of appearances. The glands chiefly affected were those immediately adjacent to the inguinal ring. As a rule, the involvement was well marked and of the same character on the two sides but rarely equal (see figures); occasionally the nodes of one side were much more enlarged and indurated than those of the other (Fig. 36). In some instances, the nodes affected were situated higher in the groin (Fig. 37), and even those of the flank might be enlarged and indurated.

Usually there were only one or two nodes involved on each side, and these were of a rounded or oval shape. Sometimes a number of small nodes were grouped together in one mass (Fig. 40); occasionally the nodes were flattened or lay in positions which made it difficult to appreciate the full extent of their enlargement. This may be seen by a comparison of the left inguinals in Figs. 41 and 42, in the latter of which the node has been picked up in order to show its actual size. This photograph also serves to convey some idea of the degree of induration in these nodes which when fully developed were extremely hard and of a semitranslucent appearance.

Significance of Lymphoid Involvement.—As will be noted by a comparison of the various figures, there was no apparent relation between the size of the scrotal lesion and the extent of the lymphadenitis. It frequently happened that the relative involvement of scrotum and nodes was in inverse proportion. The force of this statement is well brought out by Fig. 43 which shows a most pronounced lymphadenitis in an animal with comparatively slight scrotal lesions. Involvement of the inguinal glands appeared to be more an index of the activity of the scrotal infection and of the spread of the infection than of the extent of the local reaction in the scrotum.[1]

[1] In addition to the observations here recorded, this statement is based upon a long series of experiments in which the presence or absence of localized infection in the lymph nodes has been determined at periods of from a few hours after inoculation to more than 2½ years. The details of this work will be reported later. It is sufficient at present to say that enlargement and induration of lymph nodes in the rabbit always signify existent infection of the nodes.

As long as there was active infection in the scrotum, the inguinal nodes were apt to remain enlarged and indurated, but as the scrotal infection subsided, the nodes usually softened and diminished in size. Occasionally these changes occurred even before any very definite change in the scrotal lesions was noted, while in other instances, the adenopathy persisted even though the scrotal lesions showed decided evidence of regression or after they had healed completely.

Enlargement and induration of the inguinal lymph nodes in the rabbit were so constantly associated with scrotal infection that they could be used as diagnostic signs when any doubt existed as to the presence or absence of specific infection in the scrotum; not only this, but these signs could be so used before a scrotal lesion had had an opportunity to develop. The chief interest in involvement of the regional lymphatics, however, is their significance in connection with dissemination or generalization of the infection.

SUMMARY AND CONCLUSIONS.

From a study of the phenomena of the primary infection on the one hand, and the phenomena of local spread, or dissemination, on the other, it is seen that a multiplicity of lesions develops in the testicle and scrotum of the rabbit which have much the same characteristics irrespective of their origin. Some of these lesions are clearly recognizable as primary lesions or parts of a primary reaction to infection, while others are just as clearly the results of dissemination of the virus from a primary focus of infection or correspond with lesions which are commonly spoken of as secondary lesions. The effort to draw a sharp line of distinction between these two groups of lesions or between a primary and a secondary stage of infection in the rabbit, however, would be largely an arbitrary procedure. The fact is that the tissues of the scrotum and testicle of the rabbit constitute favorable surroundings for the localization and development of *pallidum* infections. Under ordinary circumstances, a large part of the reaction to infection which expresses itself in the formation of lesions recognizable by ordinary methods of examination takes place in these tissues. These lesions present certain broad and general characteristics without regard to whether they are primary or secondary in origin; the reaction is merely a reaction to a syphilitic infection which in either case may assume the most diverse character.

Further, it would appear that in rabbits infected with such strains of *Treponema pallidum* as we have used, the virus is never confined to the area occupied by the so called primary lesion, or chancre, but always spreads and always gives rise to a regional adenopathy. There may be no lesions to indicate the progress of this dissemination, but an examination of the inguinal nodes shows that dissemination occurs very soon after inoculation, and a *pallidum* reaction may be detected in these glands even before infection can be recognized in the scrotum. Subsequently lesions develop in all parts of the scrotum and testicle, sometimes involving the entire testicle or scrotum, and at others, forming focalized lesions with an especial predilection for certain locations such as the epididymis, the mediastinum testis, the tunics, and the dorsal folds of the scrotum. In some instances, more or less continuous lesions form along the course of the perivascular lymphatics, suggesting that this is one path taken in the dissemination of the organism. It is probable, however, that lesions of a gross character develop more as a result of accumulation of spirochetes than of mere invasion of the lymphatics since they are not a constant accompaniment of the local infection, while invasion of the lymphatics and extension of the infection to the regional lymph nodes occur in all cases.

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EXPLANATION OF PLATES.

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

PLATE 90.

FIGS. 1 to 6. Lesions resulting from local extension, or local dissemination, in the scrotum.

FIG. 1. 85 days. Diffuse involvement of the scrotum with the formation of multiple focal lesions. The primary lesions are marked by arrows.

FIG. 2. Same animal. 91 days. Subsidence of the diffuse reaction with rapid evolution of the focal lesions.

FIG. 3. Same animal. 113 days. Final stage in the transformation of the disseminated lesions into a chancre-like lesion.

FIG. 4. 56 days. Perivascular lesions extending from the outer edge of an implant about which there has been very slight reaction. The implant is marked by an arrow.

FIG. 5. 63 days. A diffuse thickening of the scrotum with perivascular infiltrations along the vessels of the dorsal fold. The seat of the original chancres is indicated by the tiny crust on the right and the marked depression on the left.

FIG. 6. Same animal. 85 days. A later stage of the same lesions.

PLATE 91.

FIG. 7. 69 days. Multiple focal lesions of the scrotum with tendency to chancre-like transformations.

PLATE 92.

FIGS. 8 to 10. Recovery of incompletely healed chancres after treatment.

FIG. 8. 40 days. The chancres at the time of treatment.

FIG. 9. 2 weeks after treatment, marking the extent of the regression produced.

FIG. 10. 4 weeks after treatment. Compare the regeneration effected with the original lesions and with the extent of the regression produced in the two chancres.

FIGS. 11 to 13. Local recurrence after complete healing of scrotal chancres.

FIG. 11. 29 days. The chancres at the time of treatment.

FIG. 12. 2 weeks after treatment. The right chancre is healed, the left almost healed.

FIG. 13. 78 days after treatment. A recurrence in the form of multiple focal lesions which bear but little resemblance to the original chancres and only one of which could be regarded as a chancre recurrence.

PLATE 93.

FIGS. 14 to 16. Recurrence of focal and diffuse lesions after healing of chancres.

FIG. 14. 43 days. The chancres at the time of treatment.

FIG. 15. 35 days after treatment. The chancres completely healed.

FIG. 16. 64 days after treatment. Recurrence of multiple nodules with diffuse infiltration of the scrotum.

FIGS. 17 to 19. Recurrent papular lesions at the edge of the scar of a healed lesion.

FIG 17. 37 days. The chancres at the time of treatment.

FIG. 18. 21 days after treatment.

FIG. 19. 77 days after treatment. A thin, smooth scar with two small papules at its outer edge.

PLATE 94.

FIGS. 20 to 22. Healing of scrotal chancres with recurrence of chancre-like lesions entirely away from the site of the original lesions.

FIG. 20. 50 days. The original chancres.

FIG. 21. 7 days after treatment. Ulcers healed and chancres rapidly resolving.

FIG. 22. 133 days after treatment. Recurrent chancre-like lesion in the dorsal fold of the scrotum. The testicle is rotated towards the median line.

FIGS. 23 to 25. Transformation of a healing chancre into a diffuse infection of the scrotum followed later by multiple focal lesions of an erythematous character grouped mainly about the edges of the scar.

FIG. 23. 48 days. The time of treatment.

FIG. 24. 21 days after treatment. Chancres almost resolved but replaced by a diffuse infiltration of the scrotum. Note the thickened and refractile fold of the scrotum on the right.

FIG. 25. 35 days after treatment. Multiple focal lesions grouped particularly about the edges of the scars. Slight exfoliation.

PLATE 95.

FIGS. 26 to 28. Healing of scrotal chancres with recurrence in the head of the epididymis.

FIG. 26. 48 days. The chancres.

FIG. 27. 15 days after treatment. The chancres in process of healing.

FIG. 28. 30 days after treatment. The chancres healed; recurrent nodules in the head of the epididymis in both testicles.

FIGS. 29 to 31. Late recurrence of a minute papular lesion.

FIG. 29. 46 days. The chancres.

FIG. 30. 43 days after treatment. The chancres almost healed.

FIG. 31. 105 days after treatment. The recurrence. A minute point of infiltration in the scrotum, marked by the arrow.

PLATE 96.

FIGS. 32 to 37. Inguinal adenopathy associated with scrotal infection.

FIG. 32. Appearance of the inguinal region of a normal rabbit.

FIG. 33. 5 days. Acute swelling of inguinal nodes.

FIG. 34. 7 days. Acute swelling. Left, a single enlarged node; right, a large node situated over the cord and two smaller nodes at the edge of the ring, marked by arrows.

FIG. 35. 18 days. Enlargement with induration. Marked but unequal involvement of the nodes. Chancres small.

FIG. 36. 18 days. Marked lymphadenitis on the left with two small shotty nodes on the right, marked by arrows.

FIG. 37. 82 days. An asymmetrical involvement of the inguinal nodes. The enlarged node on the left is situated high in the groin.

PLATE 97.

FIGS. 38 to 43. Inguinal adenopathy associated with scrotal infection.

FIG. 38. 23 days. Lymphadenitis of moderate degree.

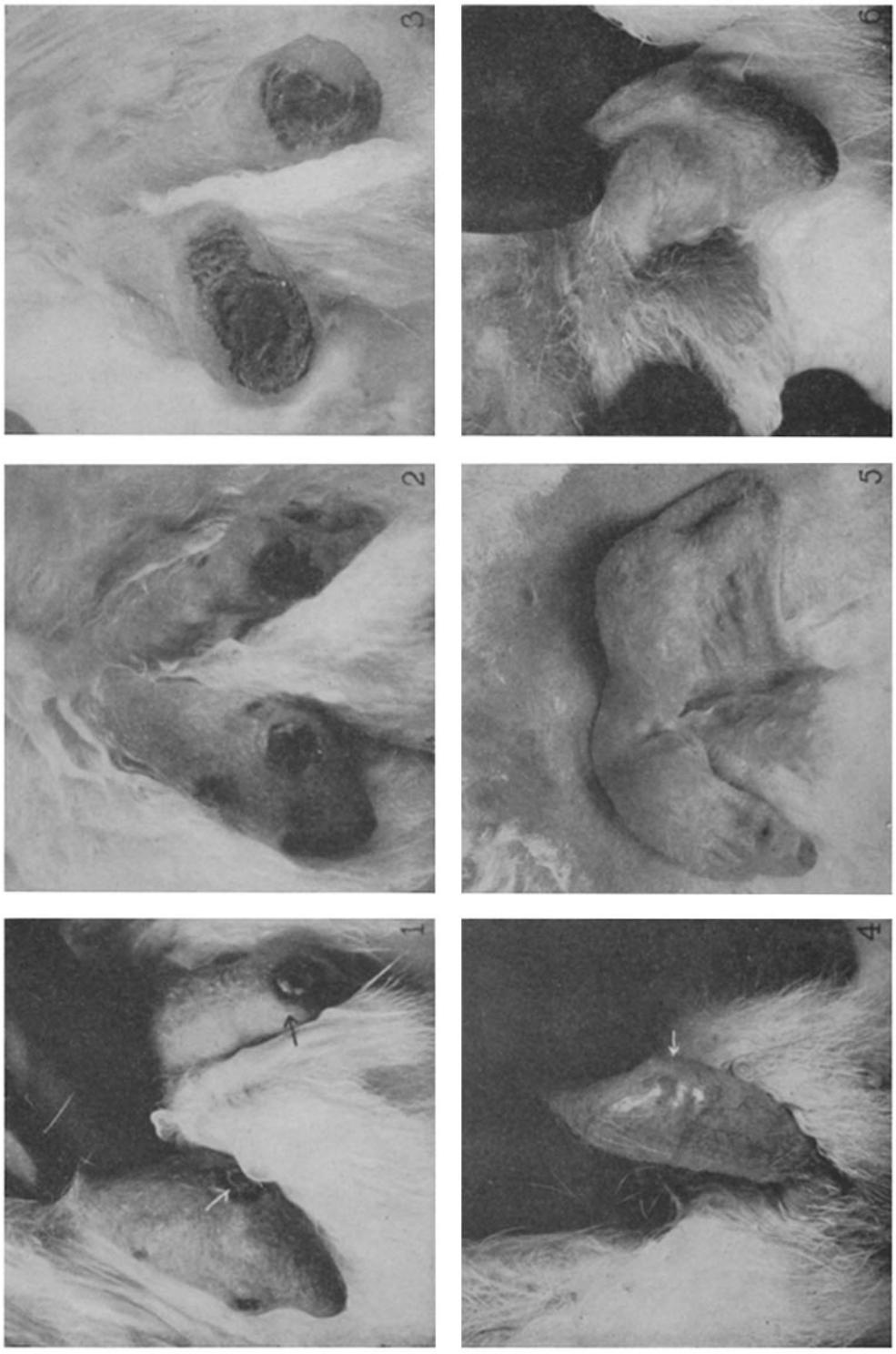
FIG. 39. 28 days. Indurated nodes. Chancres small; nodes large and unequal.

FIG. 40. 64 days. A flattened mass of small nodes on the right with a single rounded node on the left. Chancres large; nodes moderately enlarged but intensely indurated.

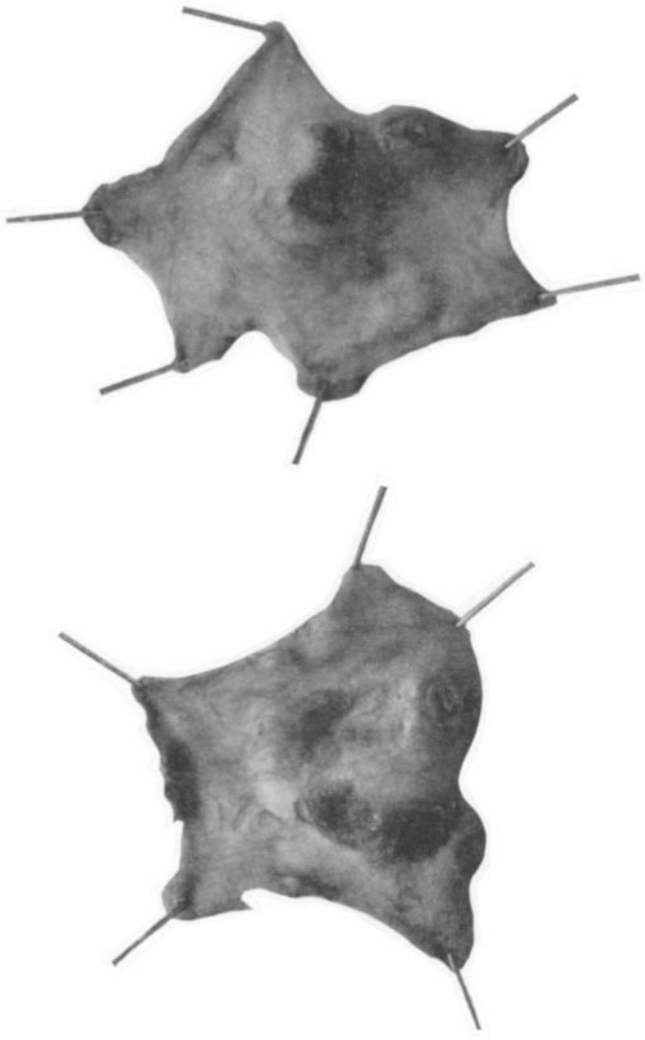
FIG. 41. 60 days. Extremely large chancres with apparently rather small lymph nodes. The nodes are deep, however, and lie directly in the crease of the groin.

FIG. 42. Same as Fig. 41. The left node picked up between the thumb and finger.

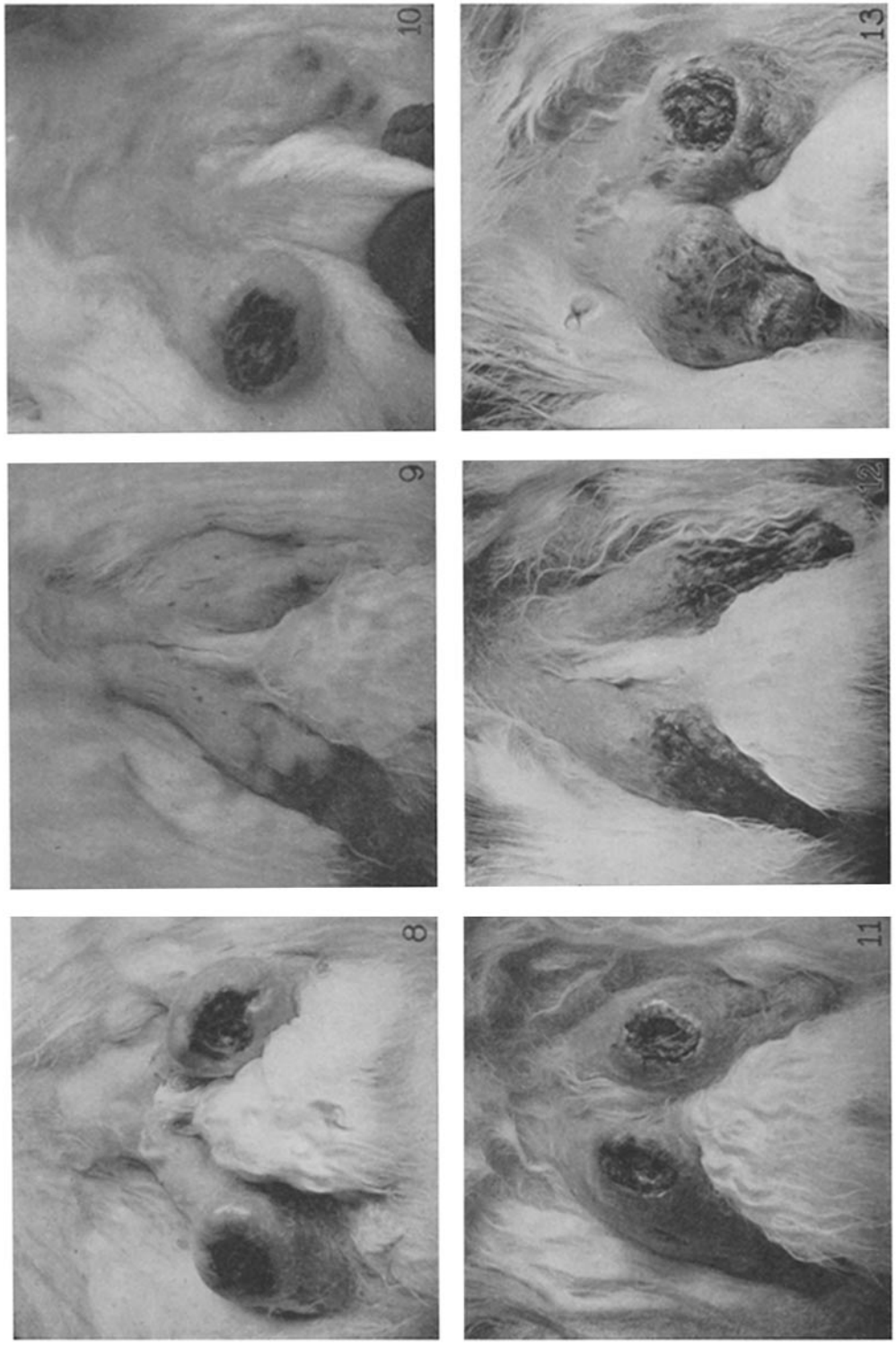
FIG. 43. 63 days. Marked equal and symmetrical lymphadenitis with slight lesions of the scrotum. Same animal as in Fig. 5.



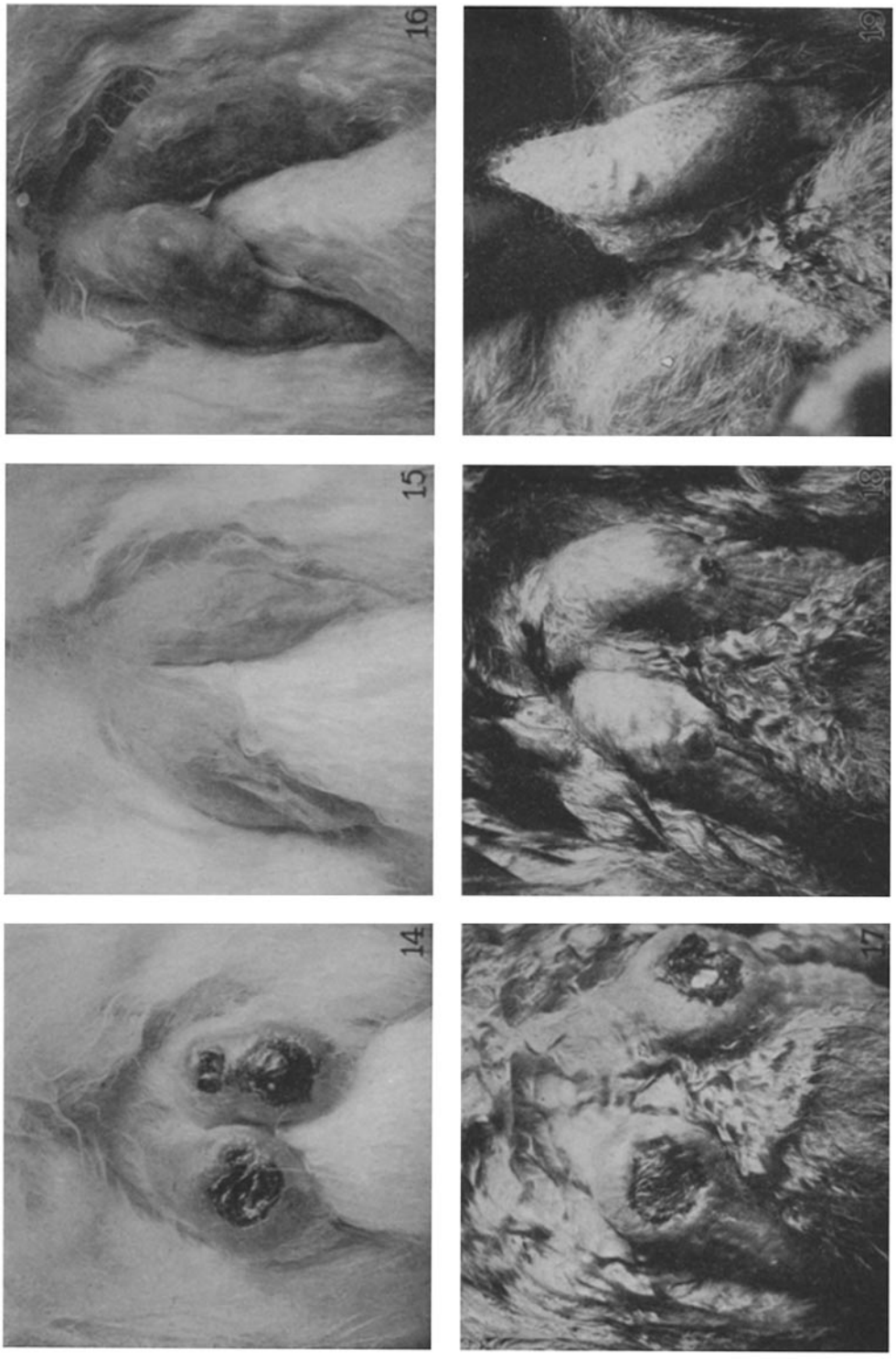
(Brown and Pearce: Experimental syphilis in the rabbit. III.)



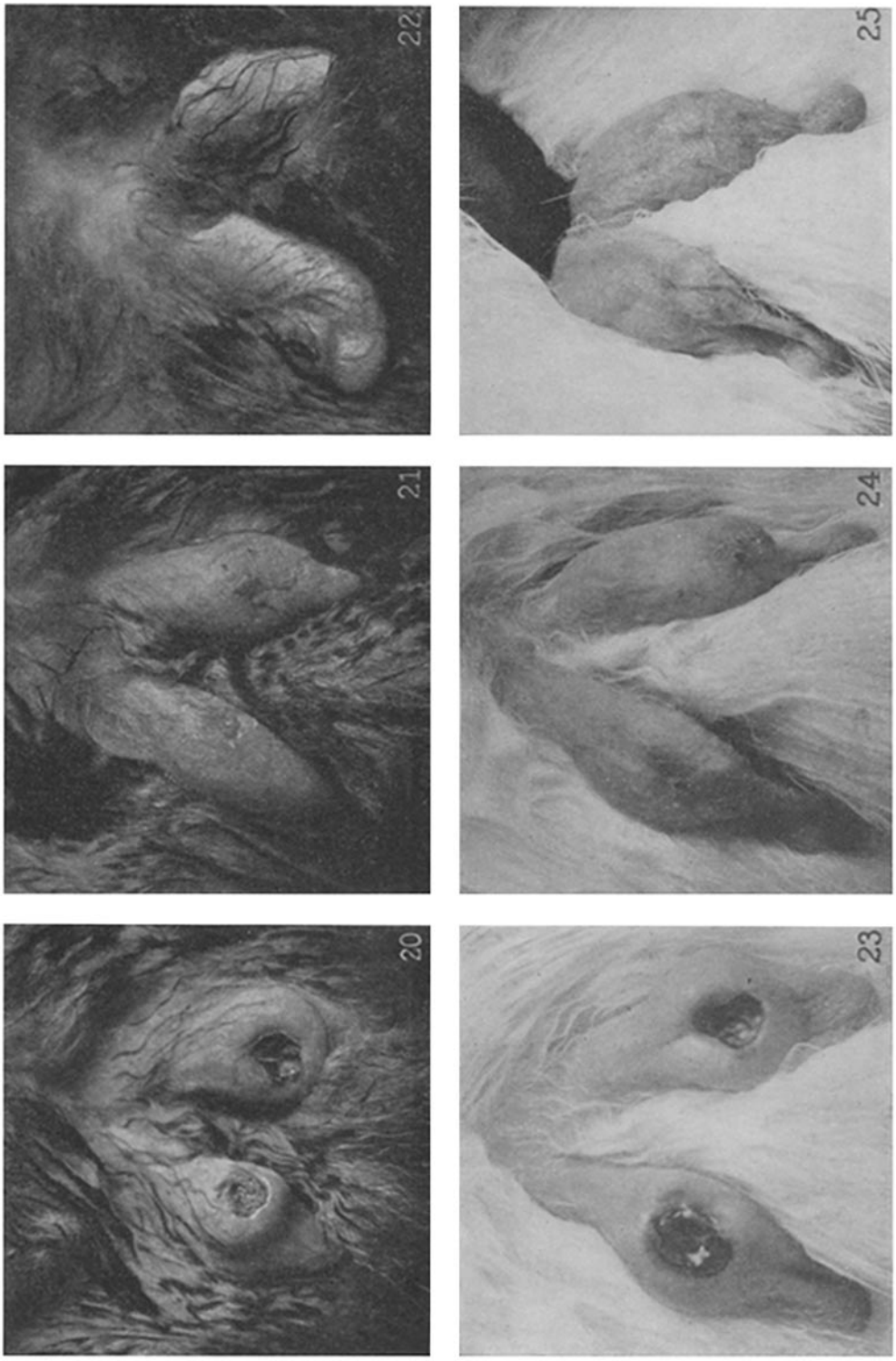
(Brown and Pearce: Experimental syphilis in the rabbit. III.)



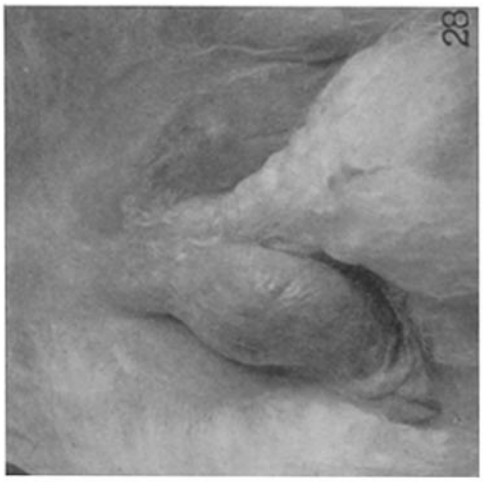
(Brown and Pearce: Experimental syphilis in the rabbit. III.)

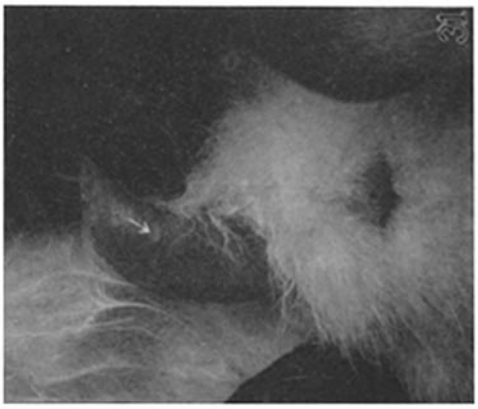


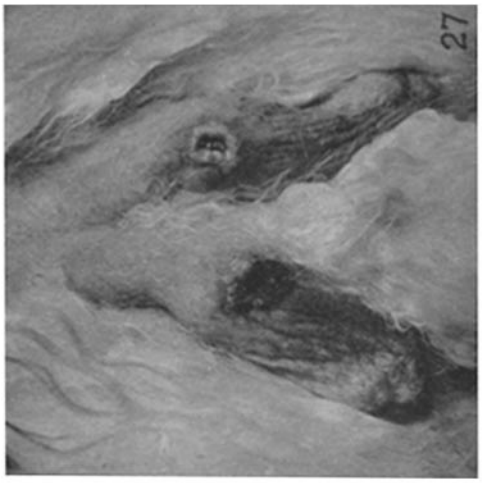
(Brown and Pearce: Experimental syphilis in the rabbit. III.)

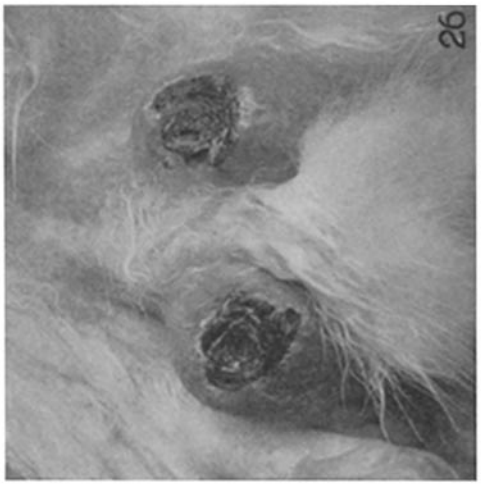


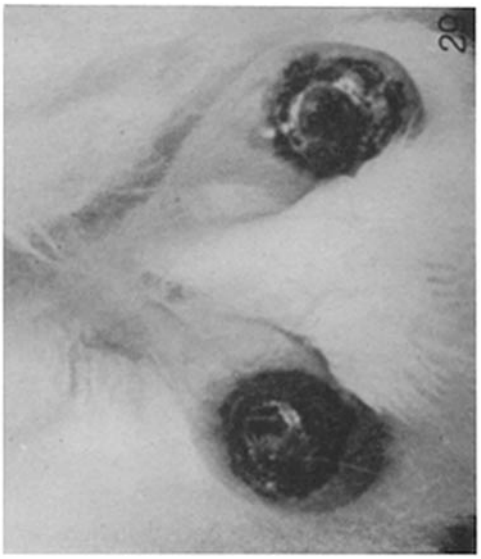
(Brown and Pearce: Experimental syphilis in the rabbit. III.)



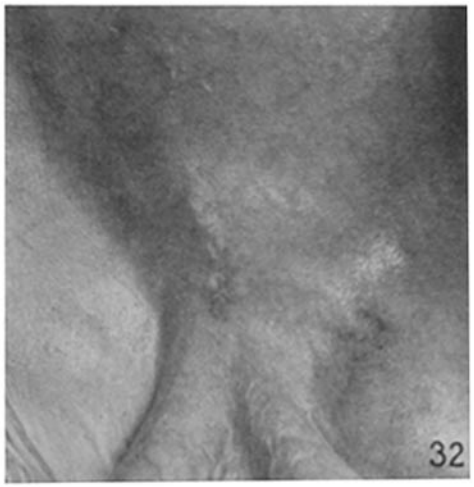


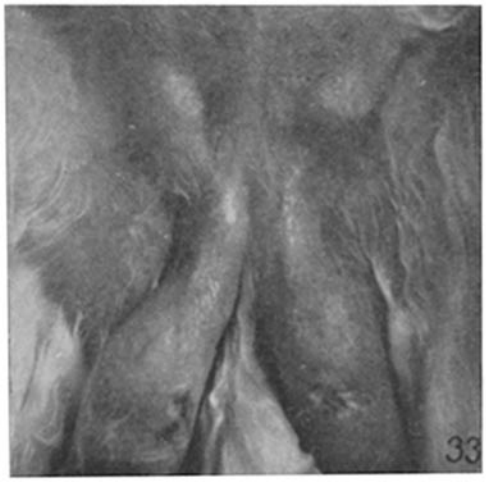


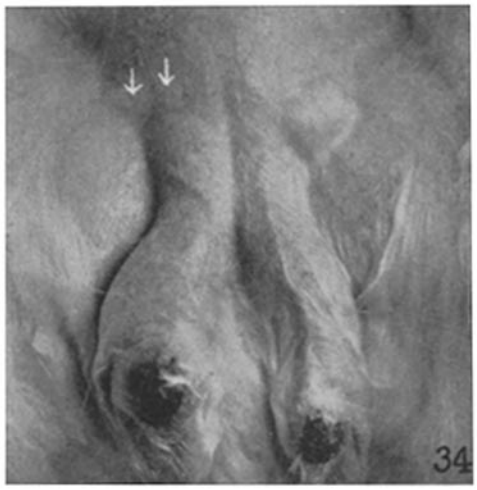


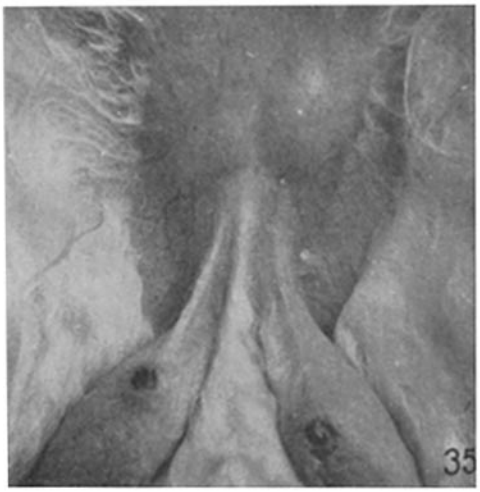


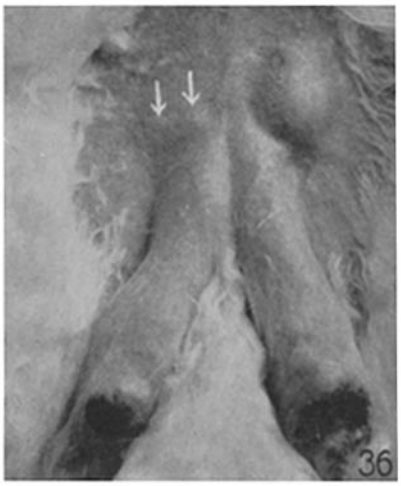
(Brown and Pearce: Experimental syphilis in the rabbit. III.)

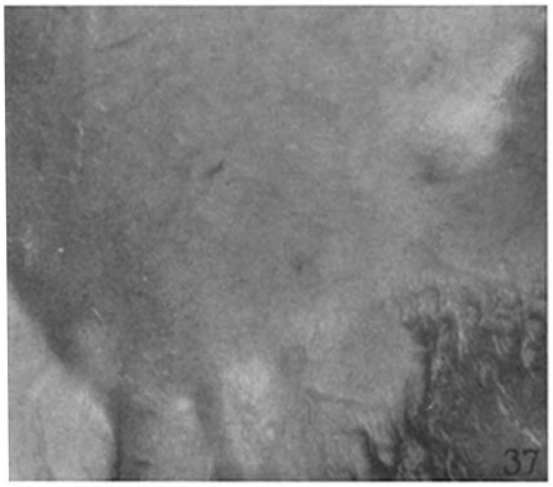




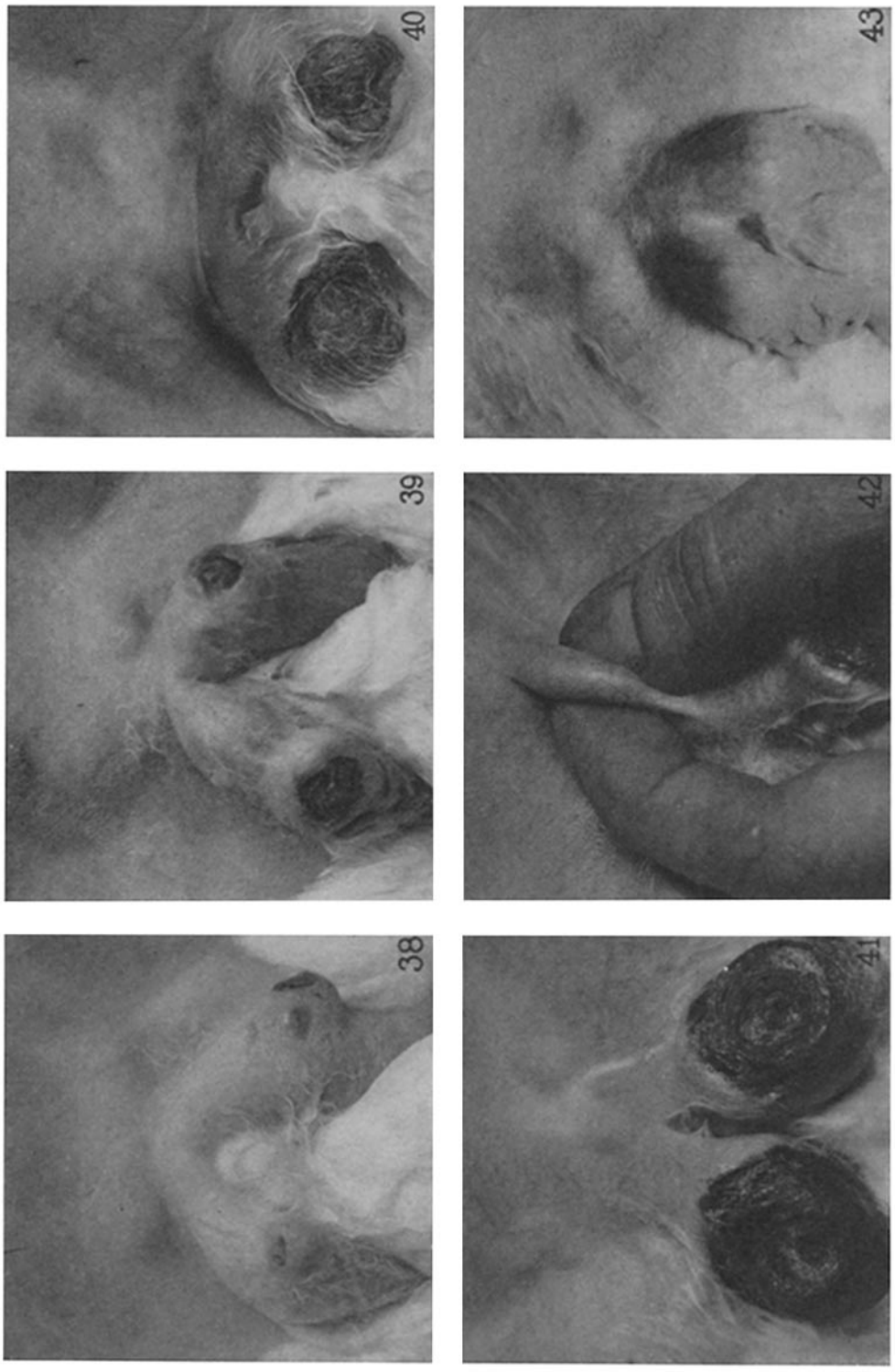








(Brown and Pearce: Experimental syphilis in the rabbit. III.)



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