In Part 1 of this series, the subject of scrotal syphilis in the rabbit was considered from the standpoint of the local reaction to infection. The various elements in this reaction were noted, and the process was traced from the time of inoculation to the development of characteristic skin lesions. Especial attention was called to the multiform character of these reactions and the influence of various elements in the reaction upon the character of the lesion produced, and while cause and effect were not entirely dissociated, the main emphasis was placed upon the process, and no detailed description of the resulting lesions was attempted. This phase of the subject is, however, of great importance in itself, and a more comprehensive view of the scrotal lesions is essential to a correct understanding and use of the experimental infection.

**Primary Lesions of the Scrotum.**

A classification of scrotal lesions which would be acceptable from all standpoints is impossible, but in order to simplify the description of these lesions, they may be separated into several general groups based partly upon fundamental differences in growth tendencies and partly upon structural differences in the lesions themselves, neither of which represent sharply defined or entirely fixed characteristics.
The first division to be made is one which has already been suggested, that of circumscribed and diffuse lesions. The circumscribed chancres include the lesions in which growth takes place from a central focus and tends to be more or less equal in all directions, leading to the development of raised or elevated masses of a circumscribed and indurated character. The diffuse chancres, on the other hand, include lesions which tend to spread laterally and assume a more or less flattened condition. In our experience, chancres of the first group were by far the more common of the two, and since they are more analogous to the classical primary lesions seen in man, they might also be spoken of as typical chancres in contradistinction to the less well defined lesions of a diffuse character.

The variety of primary lesions and the differences which exist between extreme examples of these two groups of lesions are so great that without the intervening links they could hardly be recognized as results of one and the same pathological process. Considerable care has been devoted, therefore, to the mere matter of selection and arrangement of illustrations with a view to giving as accurate an impression of scrotal chancres as possible, both as regards the character of the lesions and the relationship existing between lesions of different types.

_Circumscribed or Typical Scrotal Chancres._

The circumscribed, indurated lesions of the scrotum studied by us were lesions which as a class tended to grow to a very large size—much larger than the primary lesions commonly seen in man. These lesions differed according as they arose from one part of the scrotum or another and according to the mode and rate of their development. Based upon these differences, the typical chancres of the scrotum might be divided into two main groups, the nodular and the lenticular or discoid chancres.

_Nodular Chancres._—The nodular chancres comprise a large group of lesions whose chief characteristics were an irregular spherical form, a relatively small and sharply circumscribed area of superficial necrosis and ulceration, or the absence of any ulceration, and extreme induration. This general class of chancres may be separated into two
divisions, the ulcerated and the unulcerated chancre, characteristic examples of which are given in Figs. 1 to 6 and 7 to 12.

The nodular chancre appeared to develop from the subpapillary layers of the skin, the subcutaneous tissues, or the outer surface of the tunica vaginalis. They began their existence as more or less spherical masses of induration situated in the deeper portions of the scrotum. The growth of the lesions was comparatively rapid, while necrosis took place more slowly and was of relatively slight extent, at least during the period of active development of the lesion. As the overlying skin became involved, therefore, the area of necrosis was small and a sharply circumscribed depressed ulcer was formed, the margins of which were rounded and intensely indurated (Figs. 1 and 2). These lesions were of a dense fibrous structure, and the small area of central necrosis was usually surrounded by a thick wall of well vascularized living tissue.

The chief variations among the chancre of this class appeared to have their origin in the balance existing between the phenomena of growth and necrosis. The typical condition was that shown in Fig. 1. In a second group of cases (Figs. 2 and 3), growth and necrosis were more nearly balanced and a more extensive destruction of the central portion of the lesion took place. This condition, however, appeared to be referable to a corresponding variation in the structure of the surrounding tissue which in these cases was unusually dense or of almost ivory-like hardness. This condition is suggested in Fig. 2.

The chancre reproduced in Figs. 4 and 5 illustrate another modification commonly seen in chancre of this group occurring either during the period of active growth or as a terminal alteration. The condition was no more than a spreading necrosis which in actively growing lesions produced a unilateral flattening due to cessation of growth in the direction of the skin surface. This alteration was especially noticeable with large and rapidly growing lesions such as those in Figs. 4 and 5. It was a common occurrence, however, with all classes of chancre after active growth had slackened or ceased. In these cases, extension of the necrosis due to a continuation of secondary alterations in the granulomatous tissue resulted in a gradual destruction of the blood vessels and shutting off of the blood supply to the chancre.
This secondary necrosis took place in one of two ways which may be suggested by a comparison of the right and left chancres in Figs. 5 and 6. With large lesions showing a unilateral flattening with surface necrosis, there was a tendency for the spreading necrosis to surround the lesion from the outside (Fig. 5), while in lesions with central necrosis and depressed ulcers, the extension of the necrosis took place radially. This latter type of change, as illustrated in Fig. 6, was, of course, not confined to terminal alterations in chancres but occasionally was seen as an early feature of the lesion and is entirely analogous to the condition shown in Fig. 3.

The second division of nodular chancres differed from the first chiefly in respect to necrosis and ulceration. The two groups of lesions had a common origin and a common structure; in one group, surface necrosis and ulceration of moderate degree were characteristic features of the lesions, while in the other, these secondary alterations were of very limited extent or entirely absent. The photographs reproduced in Figs. 7 to 12 have been arranged to show successive gradations in the tendency to skin involvement and ulceration.

It may be of interest to note that all the chancres used for illustration in Figs. 1 to 12 were produced by a common organism—the Zinsser-Hopkins strain of *Treponema pallidum*. Formerly, lesions of the second type were the more common of the two, while at present the order of frequency is reversed.

*Lenticular and Discoid Chancres.*—The lenticular and discoid chancres which form the second main division of typical scrotal chancres differed from the first or nodular chancres in being lesions of a more flattened character, in the occurrence of a more widespread necrosis, and in possessing a lesser degree of induration as a rule. Typical examples of lesions of this class are given in Figs. 13 to 24.

The lenticular and discoid chancres appeared to arise mainly from the papillary layers of the skin, and the chief direction of their growth was in a plane parallel with the skin surface. Some of these chancres showed the thicker center and sloping edges of the lenticular lesion, but more commonly the edges were elevated fully as much or even more than the center, giving to the lesions a discoid rather than a lenticular form.
The growth of these chancres was extremely rapid, as a rule, and was associated with widespread skin involvement. Early in the course of their development, the skin over the central portion of the lesion became necrotic, and the extension of this zone of necrosis tended to keep pace with the growth of the lesion, spreading over the surface of the lesion as well as through its deeper parts. In some instances, the necrotic area softened and sloughed away with the formation of a true ulcer, but in others, the necrotic tissue remained firmly attached to the underlying structures, forming a thick imbricated crust (see figures).

Outside the zone of necrosis, the skin covering these chancres was markedly infiltrated and presented an unusually smooth and translucent appearance—a condition which not infrequently extended entirely to the outer edges of the lesions.

These chancres were as a class less indurated than the nodular chancres. In exceptional instances, however, they showed the same dense, fibrous structure and intense induration as nodular chancres (see Fig. 27), but more commonly they were of a mucoid or cellular character, and while these lesions were indurated, their induration was of an elastic quality, giving the impression of tension rather than of hardness.

Rapid growth and widespread necrosis were such striking characteristics of this group of chancres that two sets of illustrations are given to show the extremes to which these processes may go. Figs. 19 to 21 represent chancres produced by inoculation with a virus emulsion. The original lesions in this animal were excised 20 days after inoculation. There was a prompt recurrence, however, and Fig. 19 shows the lesions present 45 days after inoculation, or 25 days after excision of the lesions. From this point on the evolution of these chancres was extremely rapid. Within 20 days, they increased to the size shown in Fig. 20; during the next 3 weeks, growth continued at a somewhat slower rate with a deepening and extension of the necrosis (Fig. 21). The chancre on the left appears here much smaller than that on the right but was in reality almost as large. The appearance is due to foreshortening as only one chancre could be brought squarely in front of the camera.

The other three figures (Figs. 22 to 24) are from chancres produced by implantation. They show an equally rapid growth with the production of lesions which in this case almost lapped the testicles. The necrosis in these chancres was of the type of a dry gangrene spreading diffusely over the surface without a slough and forming heavy crusts composed of concentric layers and rings of ne-
crotic tissue. The figures represent periods of 39, 46, and 60 days respectively after inoculation.

The entire group of lenticular and discoid chancres thus far presented from Figs. 13 to 24 were produced by the Nichols strain of *Treponema pallidum* and show a certain degree of uniformity in type. Some of the more important variations of this class of chancres are indicated in Figs. 25 to 30.

The first two chancres of this group (Figs. 25 and 26) are of a decidedly mucoid character and the skin over the lesions is quite smooth and translucent. One of these chancres is flat while the other shows a tendency towards a more nodular form. In contrast to these lesions which again were products of the Nichols' organism, the two chancres in Figs. 27 and 28 present a decidedly different appearance. They were older lesions but represented a state of development comparable to that of the other two lesions. These chancres were of a dense fibrous character and were intensely indurated. They were produced by the Zinsser-Hopkins strain of *Treponema pallidum*.

The two remaining photographs of this group (Figs. 29 and 30) are given to illustrate chancres of an indolent type or ones which are less vigorous than most of those previously shown. The first of these chancres showed a normal rate of growth but an irregular growth; the lesions were only moderately indurated and there was but slight skin involvement apart from the area of necrosis. The second set of chancres (Fig. 30) showed a very slow and irregular development, with an undermining necrosis. The skin about the lesions was relaxed and there was the merest shell of living and growing tissue. Lesions such as those in Figs. 29 and 30 are more or less constantly at the border-line of regression and their growth may be interrupted by the slightest of causes.

The chancres thus far described will serve to give a fair impression of the principal chancre types and of the scrotal chancre at its highest state of development. The modifications of these types were so numerous that it would be futile to attempt to describe such a series of lesions. As we pass from these more typical chancres, we come to a group of lesions showing a progressive loss of the characteristics by which we are accustomed to identify primary skin lesions and eventually to lesions which are quite atypical in character. The photographs reproduced in Figs. 31 to 36 are intended to indicate this transition from the typical circumscribed chancres to lesions of a more diffuse and less typical character.

The first three photographs (Figs. 31 to 33) show lesions with all the characteristics of active skin lesions. The chancres in Fig. 31 were virtually thickened plaques with wide shallow ulcers, but the narrow margins as well as the base were markedly indurated. The chancres in Fig. 32 were somewhat less vigorous;
in the right scrotum there was an irregular indurated nodule with a depressed ulcer, and the flattened plaque on the left showed the merest shell of induration. Fig. 33 again shows a nodule or a lenticular thickening in the skin of the right scrotum which fades into the surrounding tissue. On the left, however, there is an extremely small but perfectly characteristic chancre. These photographs represent what was practically the highest point reached in the development of these lesions.

The next three illustrations of this group represent lesions which are decidedly less characteristic. The small ulcer in the right scrotum of the animal shown in Fig. 34 has a definite collar of induration, but on the left, there is little more than a minute sharply defined ulcer with a suggestion of a diffuse thickening in the scrotum. The next lesions (Fig. 35) consisted of irregular areas of thickening with even more irregular areas of ulceration. These lesions represented the height of the local reaction in this animal, and it may be of interest to note that generalized lesions appeared elsewhere just at this time (58 days after inoculation). The final photograph of the series (Fig. 36) shows small nodular lesions in the scrotum of both testicles which persisted for months with almost no change from the condition here shown.

Atypical and Diffuse Lesions of the Scrotum.

The lesions classed as atypical and diffuse include conditions varying from chronic ulcers and nodular thickenings in the scrotum to various inflammatory processes of an ill defined character. As a class, these lesions persist for a long time, and while there is usually no considerable difficulty in demonstrating the specific nature of the lesions, they are subject to frequent transformations which make it very difficult to say whether they should be regarded as primary or as secondary manifestations of infection, or where the line of separation between the two should be placed. At all events, the lesions are the same in either case, and since one group cannot be clearly differentiated from the other, they must be considered here without reference to their primary or secondary character.

Several groups of lesions belonging to this class have already been described and illustrated in Part 1 of this paper. These descriptions of atypical and diffuse scrotal lesions may be supplemented by further examples of lesions of a somewhat different type.

The photographs reproduced in Figs. 37 and 38 represent forms of primary scrotal lesions which were very commonly seen and frequently were the starting points for lesions such as those in Figs. 39 to 42. The first of these photographs
(Fig. 37) was taken 43 days after inoculation and shows a small indurated nodule with an apical ulcer in the right scrotum and an area of diffuse infiltration in the left. The skin in this area showed a loss of papillae and increased translucency together with the formation of yellowish white scales over its central portion. The second photograph (Fig. 38) shows changes of an analogous character but somewhat more pronounced. The infiltration of the scrotum was more marked on both sides, and on the right there were definite areas of superficial necrosis and exfoliation. This photograph was taken 77 days after inoculation, and just at this time, patches closely resembling those in the right scrotum made their appearance upon the skin at the base of the ears. While neither set of the scrotal lesions shown (Figs. 37 and 38) might conform to the usual conception of a chancre, they were nevertheless the primary lesions of these animals and are just as characteristic of *pallidum* infection in the rabbit as any of the lesions previously described.

Fig. 39 represents another form of scrotal syphilide which occurred either as the starting point of an infection (primary lesion) or as a transformation of other types of lesions. This animal was kept under observation for 29 months after inoculation and never developed lesions more analogous to the ordinary chancre than those shown in Fig. 39, the photograph of which was taken 136 days after inoculation. Altogether, these lesions persisted in essentially the form represented for about 18 months and this animal showed a most marked generalized infection.

The lesions shown in Fig. 40 (190 days after inoculation) are a somewhat different form of the same process as that in Fig. 39. In this animal, there was a diffuse thickening of the scrotum of both testicles, most marked in the dependent portions. On both sides, there was a curved ridge (shown in the photograph only on the right) extending downward and spreading out into a flattened head at the lower end of the scrotum. This ridge and portions of its terminal expansion were profusely covered with scales and thin crusts with erosions here and there.

Finally, there are two illustrations (Figs. 41 and 42) of lesions which in their later transformations tended to revert to a form more like an ordinary chancre. The initial lesions of the animal shown in Fig. 41 were circumscribed nodular lesions with marked congestion and edema of the scrotum. These lesions were of short duration, and by the end of the 5th week after inoculation, they had almost disappeared, leaving a diffuse thickening of the scrotum analogous to that shown in Fig. 37 or 38. 94 days after inoculation (Fig. 41) there was involvement of both testicles (orchitis), diffuse thickening of the scrotum with the formation of fine bran-like scales (shown fairly well on the left), and indolent ulcers on both sides with thickening but no induration about them. These lesions persisted with some further transformations of an equally atypical character up to the time the animal was discarded 11 months after inoculation.

The last photograph of the series (Fig. 42) represents the lesions present in the scrotum of a rabbit 316 days after inoculation. The infection in this animal
began with the formation of lesions almost identical with those shown in Fig. 35 and remained a diffuse infiltrative and exfoliative type of process for upwards of 9 months. It was not until during the 10th month after inoculation that circumscribed lesions of the character shown in Fig. 42 began to appear. On the right, the lesions became confined almost entirely to the nodular mass at the lower end of the scrotum, but at least two-thirds of the left scrotum was the seat of a diffuse infiltration and at times showed a tendency to the formation of scattered exfoliative lesions. (Note the dark colored spots on the scrotum which represent areas of recent exfoliation.) In the midst of this diffuse process, the chancre-like lesion shown in the photograph was formed.

From the standpoint of the human infection, this group of atypical and diffuse lesions of the scrotum is of the utmost importance. They are in many instances lesions which at first glance do not suggest syphilis or at least primary syphilis. They have doubtless been noted by many observers, but very little attention has been paid to them, possibly for the reason that they were interpreted as evidences of a low grade or slight infection which is not necessarily the case.

We have had many rabbits with lesions of this type, a large proportion of which came from the Zinsser-Hopkins strain of *Treponema pallidum*. These animals were of no particular use for therapeutic experiments, and consequently only a comparatively small number of them was kept under observation for any considerable period of time. Those kept were held partly with the hope that they might eventually develop lesions which could be used and partly for the purpose of studying this particular class of infections. It was in this way that we learned what we have about them.

As a class, these atypical and diffuse lesions persisted fully as long or longer than any other class of primary lesions; they contained actively motile spirochetes in abundance, and these organisms were highly virulent which has been demonstrated in two ways, first by the fact that rabbits in which these lesions occurred were frequently the subjects of severe generalized infections, and next that organisms taken from such lesions also produced high grade infections when inoculated into other animals.
Judged upon the basis of the changes which took place in the lesions or by the reaction in the scrotum, the course of the scrotal infection appeared to be fundamentally the same as that in the testicle, modified undoubtedly by differences in the character of the tissue within which or from which the lesions developed. In the scrotum, as in the testicle, there were evidences of periodic changes, but the specific reaction in the scrotum was more stable than that in the testicle and less subject to marked or rapid changes in one direction or another. While one could distinguish between lesions or processes which were diffuse and those which were circumscribed, it was more difficult to draw a sharp line of demarcation between processes which were acute or exudative and those which were proliferative in character.

In general, the initial reaction in the scrotum usually progressed without interruption until a well defined lesion had been produced or for some 2 or 3 weeks at the least. The reaction then assumed an irregular character with periods of growth interrupted by longer or shorter intervals during which little or no change could be detected in the lesions, or during which the lesions appeared to regress. As long as the lesion was merely quiescent or inactive, it retained its appearance unaltered, but when regression set in, the skin about the lesion became relaxed and wrinkled, the induration softened, or the lesion diminished in size. At times, the entire lesion was affected by these changes, while at others, only certain parts of the lesion were affected, or, as in the case of the testicular infection, one portion of the lesion might be actively developing while another was rapidly regressing.

The time element in these changes was most uncertain—some lesions lay dormant over long periods of time (several months) and then grew actively, while others grew steadily for a long time before showing any sign of cessation of activity. Again one group of lesions would develop by more or less regular periods of growth interrupted by short intervals of inaction, while another would show the greatest degree of irregularity. As a rule, a period of growth lasted for a week or more before it was interrupted by an interval of inactivity.
The extent of the change which took place during one of these periods of growth or regression was also a matter of great variation. Growth might be rapid or extremely slow, so rapid that a chancre measuring 2 or more cm. in diameter would develop within as many weeks from the commencement of the reaction, or so slow that no change could be detected from week to week and growth was recognizable only by the change which took place from month to month. Conversely, the phase of regression might be limited to inaction only or might go so far as almost to obliterate the lesion which had been developed and still be followed by an active renewal of growth. However, marked changes in one direction followed by marked changes in the other were extremely uncommon except in cases in which the complete life cycle of the lesion consisted of one such series of changes or was the terminal change in the local infection.

While the extent of the cyclic change was usually limited to a moderate reaction in one direction or the other, the number of such cycles was at times very great, especially in lesions which developed slowly and persisted over long periods of time. As a rule, however, the complete series of such cycles did not exceed three or four and not infrequently was limited to a single cycle.

The duration of the infection in the scrotum as a local or primary focus of infection may be variously stated as from 1 to 18 months. In a limited number of cases the infection developed quickly and subsided with equal rapidity or there was but slight local reaction and this soon subsided. At the other extreme, there were infections which remained firmly established for more than a year, but the average duration of the scrotal chancre was hardly more than 4 to 6 months.

In the majority of instances, the infection terminated by degrees. Development gradually ceased and after remaining in a more or less stationary condition for a time, the lesion gradually underwent resolution or healing with the production of a scar, the process consuming on an average from 4 to 6 weeks.
Spirochete Content of Scrotal Chancres.

To demonstrate the presence of spirochetes by the aspiration of fluid from scrotal lesions is usually a very simple operation, but owing to differences in the character and structure of the lesions, comparisons of the numbers of spirochetes in different examples or in different portions of the same lesion are always open to some question. Thus spirochetes are obtained with comparative ease from lesions of a cellular or mucoid character but are more difficult to obtain from fibrous lesions. Again, calculations may be considerably upset by the simple element of dilution which becomes of especial importance where edema exists, and in any case, a negative examination has only a relative significance.

It seems well to emphasize the importance of these points, since in therapeutic experiments, so much stress has been laid upon the number of spirochetes present in lesions at the time of treatment and upon the relative reduction in the number of spirochetes produced by different therapeutic agents. From a wide experience, we realize that no small part of such differences may be traceable to just such factors as those which have been enumerated. This is especially applicable to effects attributed to drugs which produce a marked increase in the fluid content of lesions as a characteristic feature of their action, and, we may add, there are many such drugs, and these are the ones which, as a rule, produce the most striking apparent reductions in the number of spirochetes present.

With these facts in mind, it may be said that during the early period of chancre growth and as long as a uniform and continuous growth was maintained, actively motile spirochetes could be found in abundance throughout the lesion. Eventually the spirochete content became variable as in other primary lesions. They were numerous and actively motile during periods of active growth or even quiescence, but decreased or even disappeared temporarily from the aspirated fluid during periods of actual regression.

Spirochetes varied likewise with developmental processes or with pathological alterations taking place in different portions of the lesion. As central necrosis developed, they became less numerous towards the center of the lesion or less active and tended to accumu-
late in greatest numbers towards the outer or growing edge. In well
developed lesions with necrotic but firm fibrous centers, spirochetes
were obtained with difficulty from the central zone and might be
obtained only from the outer shell of living tissue. However, in
chancres which underwent central softening following necrosis, spi-
rochetes were at times quite numerous in the necrotic debris.

With the progress of the infection and the appearance of irregu-
larly distributed areas of growth and of necrosis, the distribution
of spirochetes became likewise irregular; they tended to be numer-
ous and actively motile in regions of most active growth, less numer-
ous and less active in portions of the lesion which were inactive or
regressing.

The relation of the spirochete to the size and character of the lesion
was less definite. Spirochetes were as abundant and as actively
motile in some of the smallest and most insignificant lesions as in the
largest and most typical lesion. As a rule, spirochetes were obtained
in greater numbers by aspiration of cellular and mucoid lesions or
portions of lesions than from fibrous lesions or areas, but, as previ-
ously stated, this does not necessarily represent actual differences in
the spirochetal content of the respective lesions.

Results Obtained from Scrotal Inoculation.

Before concluding the subject of the scrotal infection in the rabbit,
it seems well to refer briefly to the results which one may obtain from
scrotal inoculations with Treponema pallidum and certain factors
which influence these results.

As has already been indicated, there is no particular difficulty in
obtaining an infection with organisms which have been thoroughly
adapted to the rabbit. With such organisms as we have used, 100
per cent of takes can be obtained with perfect regularity provided
one observes a few simple precautions which concern chiefly the
state of the virus, the animals used, and the technique of inoculation.
As regards the character of the local infection, or more properly the
local reaction, uniformity is more difficult to attain, but this also is
influenced to a considerable extent by the same factors.
It has been found that the first essential to success is the use of a suitable virus. As far as mere infection is concerned, material taken from any lesion containing a fair number of actively motile spirochetes will produce infection, but the character of the infection will vary according to the state of the lesion or of the spirochetes in the lesion. Other conditions being equal, the local reaction will take place more promptly and large actively growing chancres will be produced with greater regularity when the material for inoculation is taken from a fresh actively growing lesion, preferably before the height of the first cycle of reaction has been reached. Material taken from lesions during the ascending phase of the second cycle of an orchitis or of later cycles in the case of skin lesions will sometimes give good results, but at other times, the results are apt to be irregular and less satisfactory as far as the production of chancres is concerned.\footnote{It is not to be inferred that the extent of the local reaction in the scrotum is an index of the severity of the infection as a whole, for, as has been pointed out, some of the most severe generalized infections follow the most insignificant local reactions. Further, there is evidence to the effect that in general a pronounced local reaction in the testicles or scrotum of the rabbit inhibits the development of other focal infections. This subject will be dealt with in detail in a subsequent paper.}

In addition, it should be noted that certain strains of Treponema pallidum will give results which are more constant and more satisfactory than the results obtained with other organisms.

The second factor in the production of scrotal chancres is the character of the animal used. The proverbial large rabbit or rabbit with large testicles which is usually interpreted as an old rabbit with a more or less ample or redundant scrotum is a poor subject for the production of scrotal chancres. The best animals are those just approaching full maturity with well developed but not necessarily large testicles and a thin delicate scrotum. It is also desirable that the rabbits used be well nourished and free from disease.

Among the various breeds of rabbits, there are great differences in the scrotal reaction to pallidum infections. The Belgian and Flemish giants in particular give poor results, while the small albinos, grays, browns, and Dutch belts on the whole give results of the most satisfactory character.
Technique is another factor which plays some part in the success of scrotal inoculations, and the chief element here is simplicity. No antisepsis is necessary, and the use of strong antiseptics is distinctly contraindicated both on account of irritant action upon the scrotum and the possible effect of these substances upon the spirochetes themselves. Many failures in scrotal inoculations have been directly attributable to unnecessary precautions in this direction. Cleanliness, careful operation, and avoidance of undue trauma are the three essentials.

With the use of a suitable virus, good animals, and proper technique, one may attain a high degree of uniformity from scrotal inoculations in as far as the percentage of takes and the production of typical scrotal chancres is concerned. Large indurated chancres were frequently obtained by us in from 75 to 100 per cent of the animals inoculated, but as a rule such lesions were produced in not more than 50 to 75 per cent of the animals. The factor of individuality in the reaction to infection cannot be entirely overcome in _pallidum_ inoculations. Just as the typical chancres in a given series of animals will differ from one another, so also one may expect to obtain all degrees of variations in the response of individual animals to a constant set of conditions of inoculation, and irregularities will appear in the results in spite of all that can be done to prevent them.

CONCLUSIONS.

A study of the local infections produced by _Treponema pallidum_ in the testicles and in the scrotum of the rabbit leads to the conclusion that the phenomena of infection in the two cases are essentially the same and that such differences as do exist are attributable to differences in the character of the two organs. Upon the basis of these studies, it is possible, therefore, to extend the conclusions which have already been reached in regard to the nature of the local or primary reaction to infection with _Treponema pallidum_.

One is accustomed to think of this reaction as essentially a process of infiltration and proliferation and of the chancre as a circumscribed, indurated, granulomatous lesion. From a consideration of the facts derived from a study of the local infection in both the testicles and the
EXPERIMENTAL SYPHILIS IN THE RABBIT. II

scrotum, it is apparent, however, that in the rabbit at least, this conception of the syphilitic infection is true only in part and that it is derived more from a study of a condition accomplished than from the process concerned in the production of this condition.

It would seem that there are concerned in the local reaction to infection an element of toxic injury with subsequent degeneration and necrosis which affects especially the lymph and blood vascular systems, a process of exudation and infiltration, and finally proliferation and a mass necrosis due to a progressive destruction of the vessels supplying the affected area. While infiltration, proliferation, and necrosis are the most noticeable features of the local reaction in the usual case of infection, they are, however, no more characteristic than the other processes mentioned and appear to be phenomena of secondary character and importance.

None of these changes bears a fixed relation to the infection, but they are subject to the widest possible variations and in consequence give rise to lesions of the most diverse character in all of which evidences of the same fundamental processes are to be seen. As one feature or another of the reaction becomes more marked, the character of the lesion changes accordingly. Thus the lesion produced in different animals or in the same animal at different periods of the infection may range from lesions in which congestion, edema, and even hemorrhage are the most prominent characteristics to massive granulomatous lesions on the one hand, and from diffuse or ill defined patches of infiltration with desquamation or exfoliation of the surface epithelium to the most sharply circumscribed and intensely indurated nodules on the other.

Finally, it may be said that there is nothing so far as we have been able to discover which clearly differentiates the local reaction at the primary focus of infection from localized reactions to a generalized infection, unless it is the one element of the intensity of the reaction. In many instances, even this distinction is lost, and, as will be brought out in subsequent papers, one reaction is but a repetition of the other, modified to a greater or less extent by the general reaction opposed to the infection and the character of the tissues within which the reaction takes place.
SUMMARY.

From a study of the reaction to scrotal inoculation with *Treponema pallidum* in a large series of rabbits, it was found that the specific reaction presented the following characteristics.

In general, the reaction in the scrotum became apparent within 7 to 14 days after inoculation but was subject to considerable variation. The early reaction took the form of an edematous swelling and congestion associated with a new growth of vessels or of an infiltration with more or less proliferation of fixed tissue cells. These reactions were either confined to a small circumscribed area of the scrotum or were of a diffusely spreading character, and as the infection advanced, the infiltration and proliferation together with such secondary changes as exfoliation, necrosis, and ulceration became the most conspicuous features of the reaction.

The course of the reaction in the scrotum was essentially the same as that in the testicle; that is, it was periodic in character and was marked by a phase of active progression followed by quiescence or regression and renewed activity.

The scrotal reaction resembled that in the testicle also in the varying character of the reaction, appearing at times as a circumscribed focus of reaction and later becoming diffuse, or first as a diffuse reaction which subsequently became more localized.

The lesions produced in consequence of this reaction were of two general types—one a circumscribed indurated granulomatous lesion closely resembling the human chancre, the other a diffuse infiltration more analogous to the secondary skin lesions of man. Both groups of lesions presented the greatest degree of individual variations and possessed no fixed status but were subject to frequent and marked transformations. After a period of from a few weeks to many months, the lesions in the scrotum disappeared spontaneously.
EXPLANATION OF PLATES.

All the illustrations are reproductions of untouched photographs which represent the objects at their natural size. The statements of time given are estimated from the date of inoculation except where otherwise stated.

PLATE 83.

Figs. 1 to 6. Typical nodular chancres of the scrotum.

Fig. 1. 49 days. Characteristic multinodular chancres with small depressed ulcers.

Fig. 2. 41 days. Intensely indurated chancres with marked central necrosis. Edema and congestion of the scrotum with focal hemorrhages on the left.

Fig. 3. 44 days. Nodular chancres with unusually marked central necrosis and only a comparatively thin shell of living tissue. These features were developmental characteristics.

Fig. 4. 44 days. Large nodular chancres with unilateral flattening. Growing surfaces slightly mucoid in character. Edema of the scrotum.

Fig. 5. 44 days. Large nodular chancres with marked surface flattening of the right chancre due to spreading necrosis.

Fig. 6. 70 days. A vigorous nodular chancre on the left with marked central necrosis of the chancre on the right—a phenomenon of decadence.

PLATE 84.

Figs. 7 to 12. Nodular chancres of a more spherical type with a lessened tendency to necrosis and ulceration.

Fig. 7. 43 days. Spherical chancres. Spreading surface necrosis on the right, slight necrosis on the left.

Fig. 8. 46 days. Spherical chancres ulcerated and unulcerated.

Fig. 9. 60 days. Spherical chancres. The skin surface on the left still uninvolved.

Fig. 10. 90 days. Irregular nodular chancres with small areas of skin necrosis.

Fig. 11. 89 days. Spherical chancres in the subcutaneous tissues of the scrotum, with no sign of surface necrosis. Diffuse infiltration of the lower end of the scrotum on the left.

Fig. 12. 112 days. Spherical chancres in the deeper layers of the skin with infiltration of the papillary layers but no necrosis.

PLATE 85.

Figs. 13 to 18. Typical lenticular and discoid chancres of the scrotum.

Fig. 13. 28 days. Rapidly growing lenticular chancres with spreading necrosis of the skin surface. Thick acuminate crusts.

Fig. 14. 28 days. Discoid chancres with deep necrosis and ulceration on the right.
Fig. 15. 38 days. Discoid chancres with deep ulceration and thick, dry crusts. Marked edema of the scrotum.

Fig. 16. 45 days. Typical mucoid chancre with extensive ulceration and infiltration of the skin.

Fig. 17. 39 days. Discoid chancre of more fibrous type.

Fig. 18. 46 days. Discoid chancres with spreading necrosis and thick imbricated crusts.

**Plate 86.**

Figs. 19 to 21. Growth and necrosis of mucoid chancre.

Fig. 19. 45 days.

Fig. 20. 65 days.

Fig. 21. 86 days.

Figs. 22 to 24. Evolution of a more spherical mucoid chancre.

Fig. 22. 39 days.

Fig. 23. 46 days. Necrosis beginning to spread.

Fig. 24. 60 days. Spreading necrosis with thick imbricated crusts.

**Plate 87.**

Figs. 25 to 30. Modified types of lenticular and discoid chancres.

Fig. 25. 35 days. Lenticular mucoid chancres.

Fig. 26. 40 days. Mucoid chancres tending towards a spherical form.

Fig. 27. 61 days. Lenticular chancres of dense fibrous structure.

Fig. 28. 65 days. Lenticular chancres of dense fibrous structure showing marked necrosis and thick adherent crusts.

Fig. 29. 37 days. Mucoid chancres with moderate induration, slight skin involvement, and undermining necrosis (right).

Fig. 30. 97 days. Old fibrous chancres with undermining necrosis and relaxed skin covering. Inactive.

**Plate 88.**

Figs. 31 to 36. Transitional types of chancre reactions.

Fig. 31. 84 days. Right, a flattened plaque of induration with ulceration extending practically to its edges. Left, an irregular area of induration, necrosis, and ulceration. Both chancres still quite active.

Fig. 32. 73 days. An irregular ulcerated nodule on the right and a small flattened chancre on the left.

Fig. 33. 55 days. Irregular mass of induration on the right and a very small but typical lenticular chancre on the left.

Fig. 34. 36 days. Small lenticular chancre on the right and a small patch of necrosis in the skin on the left.

Fig. 35. 58 days. Irregular patches of necrosis and ulceration with slight infiltration of the surrounding tissues.

Fig. 36. 29 days. Small nodules of induration.
PLATE 89.

Fig. 37 to 42. Atypical scrotal lesions (chancres (?)).

Fig. 37. 43 days. Right, a small indurated papule with central ulcer. Left, an area of diffuse infiltration and slight desquamation of epithelium.

Fig. 38. 77 days. Diffuse infiltration with superficial necrosis and exfoliation.

Fig. 39. 136 days. Marked infiltration of certain areas of the scrotum with focalized areas of necrosis and ulceration and extensive exfoliation.

Fig. 40. 190 days. Diffuse infiltration of the scrotum with marked exfoliation in certain areas.

Fig. 41. 94 days. Diffuse infiltration of the scrotum, secondary ulceration with slight induration, and double orchitis.

Fig. 42. 316 days. A late reversion of a diffuse scrotal syphilis to lesions of a circumscribed type.
(Brown and Pearce: Experimental syphilis in the rabbit. II.)
(Brown and Pearce: Experimental syphilis in the rabbit. II.)
(Brown and Pearce: Experimental syphilis in the rabbit. II.)
Brown and Pearce: Experimental syphilis in the rabbit. II.