EXPERIMENTAL HERPES ZOSTER *

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PART I

EXPERIMENTAL HERPES ZOSTER

In a previous communication ¹ we have reported the production of an experimental disease in guinea pigs and rabbits with the virus of herpes febrilis or simplex, which clinically and pathologically is quite analogous to the human disease herpes zoster. Painting the skin of these animals with coal-tar a few times at three- or four-day intervals renders the epidermis more susceptible to a local inoculation with the virus; and shortly following an initial "take," there appears a band-like eruption of vesicles, discrete or confluent, in a zone extending in some experiments from the mid-dorsal to the mid-ventral line corresponding to the distribution of the spinal nerve supplying the inoculated spot. Details of these experiments will be presented in this paper. In the second part of the paper a consideration of the relationship of herpes zoster and herpes simplex is presented, with experiments dealing with a strain of virus from a case of supra-orbital herpes.

While it is probable that any strain of the virus from herpes simplex would be readily inoculable upon the cornea of a rabbit with the production of an acute purulent keratitis and conjunctivitis, affinity for the epidermis as well as for the nervous tissue is a more variable property. Of two strains studied by us and designated virus "F" and virus "M," the former exhibited no tendency to invade the central nervous system, while the latter regularly caused a fatal encephalitis following inoculation upon the rabbit's cornea, though they produced an equally

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intense keratitis. Inoculation after scarification upon the untreated skin of rabbits and guinea pigs rarely resulted in a local "take," and that microscopic in size. Levaditi,² however, using a herpetic virus that had been passed from rabbit to rabbit many times, produced vesicles in the skin of rabbits at the site of inoculation; and Lipschütz,³ reinoculating the skin of the thigh of a patient with the virus of herpes genitalis from vesicles on the female genitalia, observed the appearance of a group of herpetic vesicles at the site of inoculation.

In an endeavor to render the skin of experimental animals more susceptible to the virus of herpes febrilis, it occurred to us that by the preliminary application of coal-tar an active hyperplasia of the epithelium could be produced, which might afford the conditions we desired, inasmuch as actively growing tumor cells have been found to be particularly susceptible to some of the filtrable viruses, including, according to Levaditi, the virus of herpes. This proved to be true; not only did typical vesicles develop at the site of inoculation of the herpes virus, but groups of vesicles appeared later in the tarred area along the distribution of the spinal nerve supplying the area of skin inoculated.

For these experiments our strain, virus "M," from a herpetic lesion of the lip of a patient with lobar pneumonia was used. We have shown in an accompanying paper⁴ how great an affinity for nervous tissue this strain possesses and the readiness with which it traverses nerves.

As a preliminary to inoculation the hair was clipped in a band 3 to 5 centimeters wide about midway of the body on one side, extending a short distance beyond the dorsal and ventral midlines, and upon this area crude coal-tar was applied. The application of tar was repeated two or three times at intervals of three or four days. The skin of guinea pigs withstands the irritant action of the tar better than that of rabbits, and greater care is necessary with the latter to prevent encrustation of the surface from serous exudate after the tar is finally removed. Three or four days after the final application the remaining tar is peeled off with forceps, and by this time there is depilation, leaving a smooth, slightly thickened epidermis. For the inoculation, virus contained in twenty-four to forty-eight hour ex-

udate from an infected eye of a rabbit inoculated with herpes virus was rubbed into superficial scarifications in an area about one-half centimeter square usually situated about midway of the tarred band. At times the exudate was introduced into the skin by puncture with a syringe needle. Usually, twenty-four hours later, this area was lightly rescarified and reinoculated. A local "take" was indicated in the succeeding seventy-two hours by elevation, induration, and reddening of the inoculated spot, and finally by the appearance of one or more small white or yellow vesicles surrounded by a red halo within the areola. Often, within twenty-four hours after these appeared, a zonal eruption was evidenced by the outcropping of vesicles, at first usually ventrally to the site of inoculation, later dorsally. Vesicles never appeared beyond the midlines, although the tarred area extended to either side.

The vesicles appear as whitish points surrounded by a red halo. As they increase in size, the red halos of neighboring vesicles may coalesce and the vesicles become more or less flattened pustules measuring from 1 to 3 millimeters in diameter. There is a striking resemblance to the herpetic lesions of man. The pustules were shown to be due to the virus of herpes, by the following experiments. The contents of a pustule were inoculated on the scarified cornea of the right eye of a rabbit. A keratitis and purulent conjunctivitis resulted, and the rabbit's head showed the typical turning toward the right side on the fifth day. In another experiment an eye inoculated with the content of a vesicle was removed after twenty-four hours, and microscopically showed vesicles on the cornea, and typical intranuclear bodies in epithelial cells.

In another instance the three spinal ganglions on the side of the site of inoculation, which innervated the area of inoculation and eruption, were ground up in saline solution and inoculated into the brain of a normal rabbit. This rabbit in a few days developed an encephalitis, and the nuclear inclusion-bodies characteristic of an herpetic lesion were found in sections of the brain. It seems, therefore, that, when herpetic vesicles appear along the distribution of a spinal nerve on the skin of a rabbit that had been subjected to a preliminary treatment with coal-

tar, the herpes virus is present in the corresponding spinal ganglion.

The following are typical protocols of these experiments.

Experiment 1

Guinea pig 421. Wt. 205 gms. (Plate XL)

- 5/30/23 — Hair clipped with scissors in a band on right side. Tar applied over the band.
- 6/ 2/23 — Tar applied on right side.
- 6/ 6/23 — Tar applied on right side.
- 6/ 9/23 — Small portion of tar and hair removed from right side. Exposed skin scarified and inoculated with pus (24 hours) from the right eye of R. 439 (virus "M").
- 6/10/23 — Reinoculated at same spot with 48-hour pus from R. 439.
- 6/11/23 — Tar with hair removed, and skin cleaned with soap and water.
- 6/12/23 — A distinct "take" at the site of inoculation, with three vesicles or pustules at the margin of this local lesion. In late afternoon other vesicles began to appear. Tarred area shaved.
- 6/13/23 — Eruption started late yesterday afternoon and is out full this morning. Band of vesicles, square cut at mid-dorsal line; last vesicle exactly in mid-ventral line. The tarred area extended 1 cm. or more beyond each of these lines.
- 6/14/23 — Found dead.

Experiment 2

Guinea pig 457. (Plate XII, fig. 1.)

- Tar applied to right side of body from mid-dorsal nearly to mid-ventral line on June 13, 17, and 20.
- 6/22/23 — Inoculated by means of one needle puncture entirely through the skin and out again at another point, with 48-hour virus from the eye of R. 405 (virus "M"), at about the middle of the tarred area after removing the tar locally.
- 6/24/23 — Weight 170 gms. Guinea pig is losing weight. Skin still covered with tar except at the site of inoculation. No "take."
- 6/26/23 — A "take" at the site of inoculation, consisting of two very small ulcers surrounded by a well-marked red halo. Tar with attached hairs peeled off from skin.
- 6/27/23 — Weight 160 gms. One vesicle appeared about $\frac{1}{2}$ cm. ventral to the site of inoculation.
- 6/28/23 — During the course of the day five more vesicles appeared, forming with the preceding one a single line of vesicles extending along the course of a spinal nerve.
- 6/29/23 — Found dead this morning.

Experiment 3

Guinea pig 479. Wt. 250 gms. (Plate XII, fig. 2.)

- 6/27/23 — Hair clipped with scissors over a band across right side of body. Tar applied.
6/30/23 — Tar applied to same area.
7/ 4/23 — Tar applied to a third time to same area.
7/ 7/23 — Spot near centre of tarred area inoculated with herpes virus "M."
7/ 8/23 — Same area vigorously reinoculated with 48-hour pus from eye of R. 489.
7/10/23 — Good "take." Scab elevated and has surrounding red halo.
7/11/23 — Eruption this morning consisting of a single line of vesicles about ten in number, extending from mid-dorsal to mid-ventral line. Died 10 P.M.

Experiment 4

Guinea pig 324. Wt. 220 gms.

- 4/21/23 — Tar applied over large area of left side.
4/24/23 — Tar applied as before.
4/27/23 — Tar applied as before.
4/30/23 — 9.30 A.M. Inoculated on small spot on left side with three-day pus from eye of R. 334, after removing tar and scarifying lightly. 3 P.M. same spot reinoculated.
5/ 2/23 — Small scab at one point of inoculated area.
5/ 4/23 — Red V-shaped scab, sides 3 mm. at site of original inoculation. Caudad there are two distinct vesicles, 1 mm., with faint pink areola, one situated 5 mm., the other 1 cm. from the margin of V-shaped scab. There is an areola (1 mm.), and a corresponding area of induration about the V-shaped scab. These vesicles are probably included in the area of inoculation. In a line almost perpendicular to the spinal column there is situated, $2\frac{1}{2}$ cm. from the original site of inoculation and $\frac{1}{2}$ cm. from the mid-dorsal line on the same side, a red area 1 mm. in diameter, which appears to be a vesicle with a small yellowish-gray cap.
5/ 5/23 — During the day two groups of vesicles appeared ventral to the site of inoculation, and a second one dorsally.
5/ 6/23 — 6 P.M. Pustules with their halos form almost a continuous red band from the dorsal to the mid-ventral line, somewhat paler this afternoon than this morning. No evidence of paralysis. General condition of guinea pig good. Wt. 235 gms.
5/ 7/23 — Eruption much paler.
5/ 8/23 — Eruption has almost faded out. No paralysis. No zone of anaesthesia determined.
5/17/23 — Has fully recovered.
6/ 2/23 — Tar applied to see if a return of the eruption could be called forth. No eruption appeared.

Experiment 5

Guinea pig 463. Wt. 235 gms. (Control. No tarring.)

- 6/20/23 — Hair of right side clipped with scissors and shaved. Centre of shaved area inoculated with pus (48 hours) from eye of R. 460.
6/21/23 — Reinoculated with 24-hour pus from R. 460, at same spot.
6/23/23 — Scab $1\frac{1}{2} \times 3$ mm. surrounded by reddish halo 1 mm. broad. No eruption. Shaved on right side to detect eruption.
6/24/23 — Local "take" as yesterday, but possibly a little paler. Guinea pig lively. No eruption.
6/29/23 — Local lesion has faded. There is a small scab. No eruption.
7/ 6/23 — Completely healed. Guinea pig in good condition.

Experiment 6

Rabbit 235.

- 5/22/23 — Tar applied in band on right side and at one spot on left side.
5/29/23 — Tar applied as before.
5/31/23 — One spot in each tarred area inoculated with 48-hour virus from eye of R. 416.
6/ 3/23 — Slight redness at both sites of inoculation.
6/ 4/23 — A "take" at both sites of inoculation. No eruption. General condition good.
6/ 7/23 — A group of flat vesicles dorsal to the site of inoculation, and another ventral, both surrounded by an area of reddened skin which is continuous, including both groups of vesicles and the local lesion at the site of inoculation. Another group of vesicles in line with the above, about $1\frac{1}{2}$ cm. from the mid-ventral line. Two large vesicles about half way from the local lesion to mid-ventral line, also directly in line. All vesicles in tarred area. On left side there is a group of four small vesicles dorsal to tarred area. Hind legs weak.
6/ 8/23 — Complete paralysis below line of inoculation. Eruption not so distinct as yesterday. Killed with ether. The corresponding spinal ganglia ground in a mortar with saline and injected into brain of R. 440, on this date. R. 440. Temperatures as follows: 6/11/23 — 104.6° ; 6/12/23 — 106.8° ; 6/13/23 — 110° F. Died. Pieces of brain fixed and stained showed typical herpetic encephalitis with abundant intranuclear inclusion bodies.

Experiment 7

Rabbit 224.

- 5/22/23 — Tar applied to right side in band and to one spot on left.
5/29/23 — Tar applied as before.
6/ 6/23 — Tar removed. Skin inoculated at centre of tarred area on right side, and in tarred spot on left, with 48-hour pus from eye of R. 427.

- 6/ 8/23 — Both sites of inoculation show a "take" with reddish halo.
6/ 9/23 — Both sites of inoculation show ulceration with dry scab.
6/12/23 — Rear half of body paralyzed. There is an extensive band-like eruption of pustules in tarred area on right. All the pustules are in the tarred area and none passes the mid-dorsal or mid-ventral line, although the tarred area extends about 2 cm. beyond the mid-dorsal line and 1 cm. beyond the mid-ventral line. The pustules near the site of inoculation are large and become confluent at places. They are broader and flatter than in the guinea pig.
6/13/23 — Moribund. Killed with ether.

As is illustrated in the foregoing experiments, many of our animals died shortly after the appearance of the secondary herpetic eruption. This was true especially of younger guinea pigs. Others became paralyzed from invasion of the spinal cord with the production of herpetic myelitis, an invariable complication in rabbits, which are particularly susceptible to this highly neurotropic strain of virus. In other instances, in older guinea pigs, a typical zonal eruption appeared, from which the animals completely recovered without untoward sequelae.

Coal-tar applied to large surfaces is quite toxic for younger guinea pigs and rabbits. Following its application, the animals rapidly lose weight until they become greatly emaciated, and a herpetic infection superimposed is sufficient to kill them. A large part of the toxic effect no doubt is due to absorption of poisons through the skin, although a certain amount may be due to ingestion of tar in attempts to remove this irritant.

In our experience with the one strain of herpetic virus, the condition of irritation of the skin effected by the applications of tar is necessary for the appearance of a zoster-like eruption, although a local "take" may be induced in an untreated skin. Following two or three applications of tar as practised in the above experiments, there is produced a mild degree of inflammation of the skin characterized by slight edema and congestion. The epidermis becomes thickened through hyperplasia of the Malpighian layer, which in microscopic sections shows numerous mitotic figures. It seems probable that it is this active growth of epithelial cells, with many resulting young undifferentiated cells, which rendered the skin more susceptible to a local infection with the herpes virus, and prepared the way

for a secondary extension of the infection from the site of inoculation along the course of the nerves to other points on the skin correspondingly innervated.

The lesion of the skin which follows the initial inoculation is due to proliferation of herpes virus locally. Microscopically there is a central area of ulceration, the base of which and the surrounding corium are infiltrated with polymorphonuclear and endothelial leucocytes. In the epithelial margins one finds numbers of epithelial cells, especially in the Malpighian layers, containing within their nuclei typical eosin-staining inclusion-bodies such as are found in the epithelium about the vesicles of human herpes zoster. Sections of corresponding posterior root ganglions show a mononuclear cellular reaction and degenerative changes in the ganglion cells, such as shrinking of the entire cell and of nuclei, increased affinity for acid dyes, and chromatolysis — lesions which are quite comparable to those found in human ganglions innervating the area of the zonal eruption.⁵ That these lesions in our experimental animals are due to the virus of herpes is indicated by the proof of the local presence of the virus by inoculating the ganglions into the brain of a normal rabbit, which later succumbed to herpetic encephalitis. Additional evidence is the fact that in many cases, especially in rabbits, the virus does not stop at the posterior root ganglions, but passes into the spinal cord by way of the dorsal roots, producing a unilateral dorsal myelitis on the inoculated side, which may spread within the cord, causing a more extensive lesion. Associated with the myelitis is also an acute meningitis with cellular and fibrinous exudate.

Herpes zoster in man also is sometimes associated with paralyses;⁶ and an increase in mononuclear cells of the spinal fluid indicates an inflammation of the meninges.

The vesicles of the secondary eruption in point of distribution and gross characteristics are as nearly identical with those in human herpes zoster as one might hope to reproduce in experimental animals. Histologically they are vesicles or pustules filled with necrotic epithelial cells and sero-purulent exudate. The surrounding corium is infiltrated with both polymorphonuclear and mononuclear leucocytes. The vesicles rapidly

ulcerate as they extend entirely through the epidermis. Epithelial cells about the vesicles, as in the original lesion, show the typical intranuclear inclusion bodies, but fewer in number. The presence of herpetic virus in the vesicular contents has been proved by inoculations upon the rabbit's cornea, with the production of herpetic keratitis containing typical intranuclear bodies in epithelial cells, and followed by the unilateral herpetic encephalitis so characteristically produced by the virus which we have used.

In these experiments it appears that the herpes virus first multiplies at the site of inoculation in the skin and passes up the corresponding spinal nerve to its spinal ganglion; the virus then seems to pass centrifugally along the nerve and its branches to the skin, where, owing to the increased susceptibility produced by the application of tar, it multiplies rapidly and gives rise to characteristic herpetic vesicles.

Another possibility is that the virus may travel from the site of inoculation to the main nerve-trunk, and then centrifugally along other branches of the nerve, without first reaching and multiplying in the spinal ganglion. We feel certain that the secondary vesicles did not arise through accidental contamination of the surface of the skin with the virus, or through transfer of the virus by way of the lymphatic vessels of the skin and subcutaneous tissue, or by way of the blood-stream. The distribution of the vesicles forces one to conclude that the virus passes along the course of the nerves to the skin, as in herpes zoster.

PART II

THE RELATIONSHIP OF HERPES ZOSTER AND
HERPES SIMPLEX

In the preceding experiments the virus from a human vesicle of herpes simplex on the lip of a patient with lobar pneumonia was inoculated into rabbits and guinea pigs, and with it an experimental disease was produced analogous in its clinical course and pathological anatomy to human herpes zoster. Since no one has as yet confirmed the claim of Lipschütz that the virus of herpes zoster can be successfully inoculated upon the rabbit's cornea, our results do not mean that the human disease herpes zoster has been reproduced in animals or that it is caused by the same virus which we employed experimentally. The analogy, however, is obvious, and we feel that there is a very close relationship between the experimental and the human disease, and between the virus of herpes simplex and that which causes the human zona, even to the extent that they may be the same virus differing only in virulence. A comparison of the clinical features of these two diseases, and certain experimental evidences which we shall present, strengthen this assumption.

Herpes zoster usually presents a clinical picture quite different from that of herpes simplex. It occurs on the trunk, where herpes simplex is not seen; or the eruption may consist of large vesicles or bullae, whereas the vesicles of herpes simplex are always small. It is almost always unilateral; herpes simplex is almost always bilateral. It is usually associated with more or less sharp neuralgic pains, which do not accompany herpes simplex. Its eruption is distributed along the course of sensory nerves, while herpes simplex arises at the muco-cutaneous borders of the mouth or nostrils. It occurs only once in the same person, while herpes simplex very commonly recurs.

Paralleling this contrast in the clinical pictures, the viruses from the two conditions behave differently when inoculated upon the scarified cornea of the rabbit. Material from the vesicles of herpes simplex usually calls forth a keratitis and purulent conjunctivitis, which may be transferred from rabbit to

rabbit. Material from the zoster vesicles has, in the hands of nearly all workers, yielded entirely negative results.

These striking contrasts would tempt one to conclude that the two conditions are entirely unrelated. A careful consideration of the known facts, together with the experimental evidence to be presented in this paper, shows, we think, that such a conclusion is unwarranted. The most striking and apparently most fundamental difference between the two conditions is the close association of the virus of herpes zoster with a posterior spinal root ganglion and its passage along the corresponding peripheral nerves, causing a band-like distribution of the eruption around one half of the body; whereas such association with nerves appears to be entirely lacking so far as the eruption of herpes simplex is concerned. We have demonstrated most conclusively in a preceding paper, however, that the virus of the strain of herpes simplex with which we were working, regularly travels along nerves in experimentally inoculated rabbits, and enters the brain or spinal cord with the nerve, causing an encephalitis. Furthermore, Howard,⁷ demonstrated at autopsy lesions of the Gasserian ganglion in cases of herpes simplex in man. Finally, we have shown in the preceding experiments that under certain conditions the virus of herpes simplex, inoculated at one spot into the skin of a rabbit or guinea pig, calls forth a vesicular eruption distributed in a band-like manner across one side of the animal, exactly as is the eruption of herpes zoster in man.

The clinical differences in the two conditions cited above, while true of the majority of cases, are by no means true of all. There are borderland cases in which it is impossible to say whether they are herpes zoster or herpes simplex. We shall present such a case below and describe the behavior of the virus obtained from it when inoculated into rabbits.

There is a great variation in the virulence of different strains of herpes simplex for rabbits, and B. Lipschütz has shown that the virus of herpes zoster can produce lesions in the rabbit's cornea.

Finally, acidophilic intranuclear inclusion-bodies similar in character have been demonstrated in the lesions in man of both

herpes simplex and herpes zoster, as well as in the cornea of rabbits inoculated with both of these viruses.

It seems to us, therefore, that the evidence at present available indicates that herpes zoster and herpes simplex are caused by strains of the same virus of varying degrees of virulence, or else by closely related viruses.

The following case is presented in illustration of a borderline infection typical of neither herpes simplex nor herpes zoster, but a herpetic infection neural in distribution.

Patient P. Q., a man about forty-five years old, was admitted to the Allegheny General Hospital in the service of Dr. McKelvy on July 6, 1923, at 3 P.M. Six days previously, while swinging a sledge-hammer in work on a railroad, a severe pain in his right shoulder compelled him to stop working. July 1 he was confined to bed with a stiff, painful shoulder. July 2 he reported for work, but quit after two hours, and was given a night job flagging at a railroad crossing. In the afternoon the pain left the shoulder and the patient states that he had a cold and fever. He worked during the nights of July 2 and 3, but felt miserable. Was unable to work on July 4 because of pain in the legs.

When seen on July 6, patient had a herpetic eruption on the forehead over the right eye, the distribution of which is shown in the accompanying photograph. The vesicles were small and situated upon a hyperaemic and slightly raised base. There were perhaps twenty or thirty of the vesicles in all, most of them being contained in four or five more or less distinct groups. All the vesicles, together with the hyperaemic base, formed a band about one and a half centimeters broad and about five centimeters long, lying directly over the course of the right supra-orbital nerve. The patient said that he had some pain in the right side of his head and none on the left. The chief pain of which he complained, however, was in both legs. The patient was an Italian, who spoke very broken English, and the history obtained was not very reliable. He could not say when the eruption had appeared on his forehead. But since the vesicles had not ruptured and the base was hyperaemic, it could not have been more than two or three days old. On the morn-

ing of July 7 a lumbar puncture was made, and a clear fluid showing a normal cell count was obtained. The vesicles on the forehead were scraped with the point of a sterilized knife, and the tops of the vesicles and their contents were taken up in a small amount of sterile kaolin. Both the spinal fluid and the material from the vesicles were inoculated into rabbits.

On July 7 and 8 the patient no longer complained of any pain in the head, and during the following days the pain in the legs also disappeared. The eruption began to dry up on July 7, and soon disappeared. The spinal fluid and material from the vesicles was carried at once to the laboratory and inoculated into rabbits.

Experimental. A portion of the scrapings from the vesicles was inoculated directly upon the scarified skin of a rabbit which had been previously tarred, and a typical experimental zona was produced.

Rabbit 490.

- 7/ 7/23 — Band on right side overlapping mid-dorsal line shaved, and a thin layer of tar applied.
- 7/10/23 — Tar removed with xylol and alcohol. Skin scarified in two places and inoculated with scrapings from herpetic vesicles on forehead of P. Q.
- 7/15/23 — Local "take" at site of inoculation.
- 7/18/23 — Group of vesicles appeared near mid-ventral line.
- 7/20/23 — Good eruption. Several groups of confluent whitish vesicles with red halos. One group dorsal and five groups ventral to original site of inoculation.
- 7/21/23 — Eruption has faded. Ulceration at site of inoculation.
- 7/26/23 — Eruption has almost healed.

A second portion of material from the vesicles was immediately inoculated upon the scarified cornea of a normal rabbit, and produced a typical herpetic kerato-conjunctivitis, from which the animal recovered without symptoms of encephalitis. The virus from the infected eye was transplanted to normal rabbits' eyes in series. The animals receiving the first two transplants developed herpetic keratitis but no symptoms of encephalitis; the third, however, showed turning of the head toward the inoculated side and died of herpetic encephalitis, and the virus continued to invade the brain in several succeed-

ing transfers. In the following experiment an experimental zona was produced in a rabbit with this virus derived from the eye of the animal receiving the second transplant.

Rabbit 61. Wt. 2210 gms.

7/13/23 — Tar applied to right side.

7/23/23 — Skin inoculated with 3-day virus from R. 8. Skin cleaned with ether, and a small amount of tar applied.

7/24/23 — Skin reinoculated at same spot with 24-hour virus from opposite eye of R. 8.

7/28/23 — Shows a mild "take." No eruption. Piece excised for section.

7/29/23 — Skin cleansed with soap and water.

7/30/23 — Good eruption this morning. Drawing made. Vesicle excised for section.

7/31/23 — The halo around vesicles is brighter red in color. A new group of vesicles has appeared, in line with the others and quite near the mid-ventral line.

8/ 1/23 — Eruption fading. Two vesicles scraped off with a knife and inoculated upon the cornea of R. 33.

8/ 2/23 — Posterior half of body paralyzed. Rabbit is able to move legs slightly. Abdominal muscles flaccid.

8/ 4/23 — Rabbit killed. Central nervous system saved for section.

Microscopic sections of the original site of inoculation show an ulcer of the skin, the base of which is infiltrated with polymorphonuclear and endothelial leucocytes. At the margins of the ulcer, epithelial cells contain eosin-staining intranuclear bodies, and there are present multinucleated epithelial cells, each nucleus of which contains a similar inclusion.

Sections of secondary lesions show pustules involving the entire epidermis. These contain debris of necrotic epithelial cells and polymorphonuclear leucocytes. At the margins there are a few epithelial cells containing acidophilic intranuclear inclusions, and there are also multinucleated giant epithelial cells. The corium beneath the pustule is infiltrated with polymorphonuclear and endothelial leucocytes.

The posterior root ganglions innervating the area of skin involved show in sections a dense infiltration with mononuclear leucocytes and degenerative changes in several of the ganglion cells. These show increased density, an acidophilic staining property, shrinking, and chromatolysis.

The corresponding portion of the spinal cord shows an acute dorsal myelitis involving the right dorsal horn. Here there is extensive destruction of nerve fibres, necrosis, hemorrhage and mononuclear cell infiltration. There are also small hemorrhages in the corresponding ventral horn.

Sections of the cornea of R. 33, inoculated twenty-four hours before removal with scrapings from a vesicle on the skin of R. 61, show typical vesicles, the epithelial cells of which contain the intranuclear inclusions typical of herpes.

The above case illustrates a herpetic infection in man, with a typical vesicular eruption undoubtedly neural in distribution along terminals of the supra-orbital nerve, and produced by a virus which is pathogenic for rabbits, capable of producing on primary inoculation into the tarred skin a herpetic eruption in the distribution of the corresponding sensory nerve, and causing lesions in the posterior root ganglions, comparable to those in human herpes zoster. Clinically the human disease was typical neither of zona nor of herpes simplex, and constitutes an example of an intermediate infection produced by a strain of virus which exhibits pathogenicity for rabbits.

While undoubtedly the virus of most cases of typical herpes zoster is not easily inoculable into rabbits, such intermediate infections as that presented strongly suggest that the virus of herpes zoster is also closely allied to the virus which causes herpes simplex, possibly differing only in virulence.

CONCLUSIONS

1. An experimental disease has been produced in guinea pigs and rabbits, analogous clinically and pathologically to herpes zoster in man, by inoculating the tarred skin with the virus of herpes simplex.
2. There are intermediate forms of herpes in man, the eruption of which is definitely neural in distribution, caused by a virus strongly pathogenic for rabbits. The virus from such a case has produced, on primary inoculation into the tarred skin, a typical experimental herpes zoster.

3. The opinion is expressed that herpes zoster in man is produced by a strain of virus differing from the virus of herpes simplex only in virulence, or by a virus closely related to that of herpes simplex.

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DESCRIPTION OF PLATES XI-XIV

PLATE XI

G. P. 421. Experimental herpetic eruption extending half around the body. The dark ulcerated area represents the site of inoculation.

PLATE XII

Fig. 1. G. P. 457. Herpetic eruption, with single line of vesicles after inoculating small area by puncturing skin.

Fig. 2. G. P. 479. Herpetic eruption extending half around body after small local inoculation.

PLATE XIII

R. 61. Herpetic zonal eruption following inoculation with virus from case of supra-orbital herpes.

PLATE XIV

Fig. 1. Patient P. Q. showing supra-orbital herpes with neural distribution. Virus from these vesicles was virulent for rabbits and caused a zonal herpetic eruption, as in R. 61.

Fig. 2. Secondary herpetic lesion from skin of R. 61.

Fig. 3. Section from epithelial margin at site of inoculation in R. 61, showing multinucleated giant cell containing intranuclear bodies.

Fig. 4. Posterior root ganglion innervating area of eruption in R. 61, showing cellular infiltration and degenerative changes in ganglion cells.

Teague and Goodpasture

Herpes Zoster

1

2

Teague and Goodpasture

Herpes Zoster

Teague and Goodpasture

Herpes Zoster

1

2

3

4

Teague and Goodpasture

Herpes Zoster