THE HISTOLOGY OF EQUINE ENCEPHALOMYELITIS

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The severe epidemic of equine encephalomyelitis raging along the Atlantic seaboard in August and September, 1933, afforded an opportunity of studying the histology of the naturally occurring malady, the causative virus of which appeared to be serologically distinct from that responsible for the rather similar disease in California (TenBroeck and Merrill, 1933). At that time an experimental study of the western type of encephalomyelitis was under way, the histological features having been only cursorily dealt with by Meyer and his colleagues (1932). The opportunity is now taken of comparing the lesions of the two infections.

Histological Findings in Horses

(a) Equine Encephalomyelitis in New Jersey and Virginia

The organs of eight field cases were examined histologically; all the animals were killed by bleeding or anesthesia, and the tissues deposited in fixatives within half an hour or so of death. The duration of nervous symptoms varied from a few hours to several days. Macroscopically the nervous system was congested and often somewhat edematous. The microscopical lesions, of identical nature in all eight cases, were of the same general type as those in monkey poliomyelitis, though their distribution was vastly different. In view of their character it is perhaps necessary to emphasize the statement that on culture the majority of the brains were sterile.

Most prominent in the nervous system with the low power of the microscope was the cellular infiltration (Fig. 1). In many regions polymorphonuclear leucocytes, distributed diffusely and in small or large foci, swarmed in the tissues (Fig.

2); with these was associated very early microglial proliferation giving rise to many rod cells. In rare foci composed almost wholly of polymorphonuclear leucocytes the tissues appeared on the verge of actual softening. In other areas microglial elements predominated, though nearly always leucocytes were present and were often numerous. In either case perivascular infiltration might be inconspicuous; commonly, however, cuffs one to many cells deep surrounded the local vessels (Fig. 1). They consisted almost wholly of neutrophil leucocytes, many karyorrhectic, or of small and large lymphocytes associated with a variable number of neutrophils and rare eosinophils. Polymorphonuclear leucocytes often overflowed into the adjacent nervous tissues, while among the lymphocytes mitoses were numerous. The meninges overlying areas of intense change were often infiltrated to a marked degree with similar cells; on the other hand, over many areas similarly affected, and over those showing slighter changes, meningeal infiltration was wholly wanting. Only occasionally was infiltration noted in the choroid plexuses.

When resort was not had to bleeding, vascular congestion was pronounced and small perivascular hemorrhages not infrequent. In the congested state of the vessels the latter observation probably has little significance, as hemorrhage might well be produced by trauma during removal of the brain. Signs of reaction indicating extravasations of some standing were never seen.

The essential lesion, and one occurring in a few places in the absence (as yet) of any marked cellular reaction, was acute necrosis of nerve cells, which appeared as shrunken eosinophilic structures devoid of nucleus or showing pyknotic nuclear remains (Fig. 2). In severely affected cortical areas cellular architecture was partly disorganized. Often the necrotic cells were in process of lysis by neutrophils plastered on their surfaces (Figs. 3 and 4). In other instances, more frequently perhaps in brain stem and cord, neuronophagia by microglial cells was observed. Less severe degenerative changes in the neurons included vacuolation of the cytoplasm and invasion of the vacuoles by neutrophils, occasionally in the presence of almost normal Nissl substance. Simple chromatolysis and nuclear eccentricity commonly affected cells of the cranial nerve nuclei and anterior horns of the spinal cord. In most of the affected areas, whatever their site, many of the neurons appeared normal. Nuclear inclusions (Fig. 9), much less numerous than in the guinea pig but of the same type and distribution, will be described in connection with the changes in that animal, in which fuller study was made; they bore considerable resemblance to those associated with Borna disease.

Neuroglial nuclei were often greatly swollen and very pale; no inclusions were detected therein or in mesodermal elements.

The foregoing alterations were most pronounced in the cerebral cortex. Although many unaffected areas existed side by side with zones of severe destruction, and in individual cases the anterior frontal or occipital regions or the cornu Ammonis might be relatively lightly involved, no major subdivision was immune from attack or was consistently more affected than another. The lesions mani-

fested no predilection for a particular cortical layer. The cornu Ammonis and rhinencephalic cortex never showed the massive necrosis to be described in the guinea pig, etc. The olfactory bulb was not affected with exceptional severity. In the subcortical white matter foci of neutrophil infiltration or microglial increase occurred much more rarely than in the grey matter, though more frequently than in most virus diseases. Here, sometimes, massed polymorphonuclear leucocytes collected in the nervous tissues around part of the circumference of an artery not itself infiltrated; occasionally the impression of incipient softening was given. The caudate and lenticular nuclei usually showed less severe changes than did the cortex; the optic thalamus and hypothalamic regions were fully as badly damaged. In two instances the fiber bundles entering the putamen were packed with leucocytes, while the grey matter of the nucleus had largely escaped involvement (Fig. 6). In five cases the brain stem and cervical cord were definitely less affected than the higher centers; the intensity of the changes often varied greatly at different levels and attained a maximum in the grey matter around the ventricular system, in the pontile nuclei, and in the olives. At some levels the lesions appeared to be very early and consisted mainly in nerve cell degeneration and stuffing of the capillaries with polymorphonuclears, which could be seen passing through their walls into surrounding structures. In the cord both anterior and posterior horns were involved, but nerve cell destruction took place chiefly in the former. Only mild changes were present in the cerebellar cortex, and in two animals no lesions were detected here; the cerebellar nuclei usually suffered more severely. In all the horses the Gasserian ganglia were normal.

No significant abnormality was detected in the lungs, liver, spleen, kidneys, adrenals, salivary glands or lymph nodes. In one advanced case the centers of the liver lobules appeared to be in the preliminary stages of acute necrosis; the liver cells were shrunken and eosinophilic with pyknotic nuclei, the Kupffer cells greatly enlarged and increased in number, and numerous neutrophils occupied the sinuses and central veins. At the margins of these areas some fatty infiltration was apparent and the liver cell nuclei were often greatly enlarged. No virus was present in the organ, nor were bacteria demonstrable in sections. It does not appear probable that the changes were the direct result of virus activity. In several instances the cervical lymph nodes were greatly congested but showed no other abnormality.

To summarize, the eastern type of equine encephalomyelitis is characterized histologically by an unusually diffuse and intense acute inflammation affecting most territories of the central nervous system but more particularly the grey masses. Nerve and neuroglial cell degeneration is undoubtedly primary, though accompanied or speedily followed by heavy tissue infiltration with polymorphonuclear leucocytes and reactive changes in the microglia. In the nerve cells

nuclear inclusions occur rather similar to those in Borna disease. Perivascular infiltration may be predominantly polymorphonuclear or wholly mononuclear. Meningeal infiltration is clearly secondary to changes in the underlying nervous substance. No significant changes are consistently present in organs other than the nervous system.

The foregoing picture was accurately reproduced in a horse inoculated intracutaneously (in the dorsal region) with the brain of a field case.

(*b*) *Lesions in a Horse Infected with the Western Virus*

This horse, inoculated intranasally and intracutaneously (in the area of supply of the fifth cranial nerve) by Dr. Erich Traub, was killed on the 12th day, after having exhibited nervous symptoms for 3 days. It presented lesions which individually could not be distinguished from those described above. They were, however, far less numerous and intense. But few areas of the cerebral cortex were involved; the chief sites of injury were the olfactory bulbs, the optic thalamus and hypothalamic region, and the brain stem. Only a few nerve cells were acutely necrotic and undergoing neuronophagia; in the areas named, polymorphonuclear tissue infiltration, microglial proliferation and mononuclear infiltration were less intense than in the eastern cases. In this horse the Gasserian ganglion showed mononuclear interstitial infiltration.

Histological Findings in the Calf, Sheep and Dog

These animals were inoculated intracerebrally with the eastern virus by Dr. C. TenBroeck. The calf developed pronounced symptoms and was killed 72 hours after inoculation. The sheep died 117, and the dog 84 hours after injection. In all, the microscopical picture was essentially that depicted above; the minor differences observed necessitate only brief mention.

In the calf, changes in the cerebral cortex were in places even more intense than in horses, with acute necrosis of a larger proportion of neurons. In parts of the cortex, basal ganglia, brain stem and anterior horns of the spinal cord small foci of softening crammed with polymorphonuclear leucocytes might be discerned. In most regions, however, lesions were less severe. Perivascular cuffing was

everywhere mainly or exclusively mononuclear. The cerebellum was unaffected. Meningeal infiltration, though marked over some regions of the cerebral hemispheres, may have been due in part to the introduction of foreign nervous tissue, since over severely affected parts of the brain stem and cord it was often wholly wanting.

Lesions in the sheep were rather less severe than in the calf and, probably as a result of greater duration of the inflammatory process, the infiltrating polymorphonuclear leucocytes were highly karyorrhectic. Necrotic nerve cells were frequent in parts of the cortex and in the anterior horns of the cord. Perivascular cuffs were solely mononuclear. Mild lesions obtained in the cerebellar cortex and more marked lesions in the dentate nucleus, etc. Meningeal infiltration was in most areas inconspicuous.

Changes in the dog resembled those in the sheep except that at only a few levels of the brain stem and cord did marked lesions prevail. The cerebellum was unaffected.

Histological Findings in the Guinea Pig

The guinea pig is the laboratory animal of choice for the study of equine encephalomyelitis. Lesions were substantially the same whether the virus was introduced intracerebrally, intramuscularly, subcutaneously or intradermally, and whether the eastern or the western virus was employed. Any differences apparent in infections with the two viruses could well be ascribed to greater virulence of the one and the lesser virulence of the other. It happened that more intense lesions were present in guinea pigs inoculated peripherally than in those inoculated intracerebrally; probably the longer incubation in the former allowed wider dissemination and greater multiplication of the virus. On the whole the lesions produced by intracerebral inoculation of the western strain were comparable with those following peripheral inoculation of the eastern organism. The more or less uniform symptomatology was little indication of the degree of microscopic abnormality, which increased with longer duration of the developed disease. At the time when nervous symptoms were first manifest only early degeneration of those nerve cells later most severely affected was present: vascular and interstitial inflammation were absent or at a minimum. It was at this stage that many of the animals inoculated intracerebrally with the eastern virus died.

In the fully developed disease, lesions in the cerebrum were of fairly uniform distribution, with a decided tendency to greater intensity in the cornu Ammonis

and rhinencephalic cortex. In less severe and acute cases (histologically), perivascular infiltration with small and large lymphocytes affected a variable number of vessels; in their vicinity and elsewhere in the nervous substance microglial proliferation obtained (Fig. 7). In more acute cases polymorphonuclear leucocytes, many karyorrhectic, appeared in the perivascular infiltrate and constituted an overwhelming majority of the tissue infiltrate Some proliferation of vascular adventitial cells occurred. In several cases massive acute necrosis involved large parts of the cornu Ammonis or rhinencephalic cortex, or both regions, and vast numbers of polymorphonuclear leucocytes congregated around the destroyed neurons (Fig. 8). Meningeal infiltration rarely amounted to more than the presence of a few mononuclear cells, with some polymorphonuclears, in the depths of the fissures; occasionally it was marked over an area of cortex showing very intense changes.

Lesions in the brain stem and spinal cord were variable in degree and were not necessarily most evident in animals inoculated peripherally. Acute necrosis often struck cells of the cranial nerve nuclei, olivary bodies and anterior horns; in the cerebellum Purkinje cells suffered with much less frequency. Cellular infiltration as in the cerebrum, and sometimes neuronophagia followed; in the cord the former was limited usually to the grey matter, but occasionally a focus of proliferated microglial cells lay in the white matter. Less severe nerve cell degeneration taking the form of tigrolysis and nuclear eccentricity was common. The Gasserian and spinal ganglia were normal in all cases inoculated intracerebrally; after intramuscular inoculation only some mononuclear infiltration with a few polymorphonuclears was noted in the nerve roots.

Careful search invariably demonstrated nuclear inclusions in nerve cells, neuroglial cells, mesothelial cells of the pia-arachnoid and adventitial cells of the vessel walls, in this order of frequency. In the nerve cells of the brain stem, single or multiple bodies were relatively frequent at an early stage preceding marked tissue and perivascular infiltration (Figs. 10–12); six or seven cells containing inclusions might be seen in a single section. In other neurons they were more seldom found either then or later; in the cornu Ammonis they were not more numerous than in the general cortex, and in both situations definitely less common than in the brain stem. Affected nerve cells usually showed other signs of degeneration, if only incipient, but inclusions were not detectable in dead or moribund elements. The round or slightly oval, strongly oxyphilic bodies of sharp contour bore considerable resemblance to those in Borna disease; they were, however, often rather larger, less often showed a center paler than the periphery or a central vacuole-like structure, and possessed perhaps slightly less sharp contours. Normal weakly oxyphilic nuclear material was often diminished in amount or absent, and the inclusions were differentiated from the feebly oxyphilic masses normally present (nucleonephelium of Saguchi, 1930) by greater regularity and definition of outline and deeper coloration with the acid dye. The sharpness of definition of the bodies was greater in cases with a longer incubation period, and was less with virus strains producing symptoms within a short time of inoculation.

Nuclear inclusions in the other elements mentioned took the form of very tiny, less strongly oxyphilic spherules. In glial cells swelling and pallor of the nucleus and margination of basophilic chromatin often coexisted, especially in areas where marked changes were present. The tiny bodies were difficult to demonstrate, and but for the presence of definite bodies in the nerve cells would have been disregarded. Similar granules did not occur in normal animals and it seemed legitimate to accept them as analogous to the abnormal nuclear products met with in the neurons; they bore roughly the same dimensional relation to the enclosing nuclei as did the larger bodies to the nerve cell nuclei.

The lungs frequently showed pathological changes. Macroscopically one or more lobes appeared solid and plum-colored; or the organs were deeply congested with darker plum-colored areas of serpiginous outline indicated on the pleural surface. Edema and petechial hemorrhages might be present. Histologically, large areas of collapse existed and enclosed bronchopneumonic areas; the latter also occurred independently of atelectasis. In the bronchial exudate of such cases a great variety of bacteria might commonly be demonstrated. A second type of pulmonary change took the form of partial atelectasis with pronounced interstitial change and no exudate in the bronchi or alveoli. The alveolar walls were thickened by a mononuclear infiltrate containing scanty neutrophils, and intense perivascular and peribronchial infiltration with similar cells was evident. Small foci of proliferation and desquamation of the alveolar epithelium occurred. In some cases both types of pulmonary change coexisted.

In two animals necrosis of isolated liver cells with some polymorphonuclear infiltration existed in the apparent absence of any excitant other than the infecting agent employed. In one case moderate interstitial mononuclear infiltration was present in the salivary glands. The sinuses of the spleen usually contained an excessive number of neutrophil leucocytes. In two guinea pigs isolated cells of the adrenal cortex were necrotic.

In the guinea pig, then, the virus of equine encephalomyelitis (eastern or western strains) produces a histological picture fairly comparable with that in horses, except that the maximum injury in the cerebrum is inflicted upon the cornu Ammonis and rhinencephalic cortex. Nuclear inclusions of the type encountered in Borna disease occur chiefly in the brain stem, and, as is not the case in the horse, tiny oxyphilic bodies of apparently similar nature are less frequently observed in glial and mesodermal elements. Unlike the horse, this animal commonly presents pneumonic lesions in the lungs, sometimes those of a secondary bronchopneumonia, sometimes of the type which is now recognized as typical of virus infections. Minor changes less certainly due to virus action are sometimes found in other organs.

Histological Findings in Rabbits and Mice

The virus of equine encephalomyelitis is less pathogenic for the rabbit than for the guinea pig; this is more especially true of the western strains which even on intracerebral inoculation rarely produce more than a temporary illness. The histological picture, though essentially the same as in guinea pigs, is correspondingly less acute. Polymorphonuclear leucocytes are but rarely present in the tissues, where more advanced metamorphosis in the direction of granular corpuscles is permitted in the microglia. Meningeal infiltration is more marked than in the guinea pig and almost wholly mononuclear, as are the perivascular cuffs. Massive acute necrosis is rarely seen in the cornu Ammonis, where, however, long stretches of nerve cells of the pyramidal layer often undergo severe degeneration and exhibit swollen cell bodies completely devoid of Nissl substance; nuclear inclusions here may be particularly large and numerous. Inclusions are seen only in nerve cells.

On intracerebral inoculation the eastern virus produces in mice a very rapidly fatal disease, often killing the animal in 50–60 hours. The scanty lesions are similar in nature and distribution to those of the more rapidly fatal disease in guinea pigs. Massive necrosis may be seen in the cornu Ammonis and rhinencephalic cortex. Inclusions are present only in nerve cells.

Histological Findings in Rabbits Infected with the Virus of Borna Disease

In the brains of three rabbits, lesions similar to those described by Zwick, Seifried and Witte (1927) were much less acute than in infections due to the virus of equine encephalomyelitis.

No polymorphonuclear leucocytes were present in the tissues, though occasionally lymphocytes overflowed from the perivascular cuffs. The latter were composed wholly of mononuclear elements and included a number of plasma cells; the cells of the adventitia sometimes showed active proliferation. Mononuclear meningitis was marked in places, and often accompanied in the subjacent zone by infiltration with round cells and microglial cells and definite enlargement of the subpial glial cells. Active diffuse and focal microglial proliferation in the cortex was associated with marked satellitosis of neurons and sometimes neuronophagia. The rhinencephalic cortex, cornu Ammonis, lateral cortex and region of the third ventricle were particularly affected; in the first, acute necrosis of nerve cells was

noted. In the brain stem small microglial foci and marked perivascular infiltration obtained, together with degenerative changes of moderate severity in some of the nerve cells. Nuclear inclusions were rather smaller than in equine encephalomyelitis, but had a more "solid" appearance and rather sharper contours; they more frequently showed paler central "vacuoles" and indications of a not absolutely homogeneous structure. Only sparse lesions were evident in the cerebellum. The Gasserian ganglia were the seat of marked infiltration, nerve cell degeneration with the formation of nuclear inclusions, and around some neurons multiplication of capsule cells. Typical changes as described by Nicolau, Nicolau and Galloway (1929), and by Zwick, Seifried and Witte (1929) were present in the peripheral nervous system.

COMMENT

The lesions in naturally occurring cases of equine encephalomyelitis are thus typical of acute neurotropic virus diseases, and in nature, though not in distribution, are comparable with those of poliomyelitis in the monkey. Their greater acuity provides a criterion of value in differentiating them from the changes in Borna disease; on the other hand, they are not of the hyperacute type seen in pseudorabies of the rabbit (Hurst, 1933), where death occurs too soon to permit appreciable cellular reaction.

The present study throws little light on possible routes of entry of the virus under natural conditions. Although one horse was killed in the first few hours of nervous manifestations, alterations were already widespread, though at some levels of the brain stem they were at a very early stage. Of the whole series of field cases, not one showed lesions in the olfactory bulbs as marked as did the experimental animal inoculated intranasally and intradermally (in the area of supply of the fifth cranial nerve) with western virus; yet lesions elsewhere in this brain were much less severe than in the eastern cases. It has also been remarked that the distribution of changes seen in field cases in the eastern outbreak was accurately reproduced in a horse inoculated intracutaneously in the dorsal region with eastern virus. These observations, if repeated, might possibly suggest search in the natural disease for a portal of entry other than the nose.

Experimentally, with the eastern strains of virus, the essential histological features of the naturally occurring disease can be reproduced in a number of domestic and laboratory animals. With both eastern and western viruses in the guinea pig and rabbit, and with

the former in the mouse, the chief difference apparent from the histological picture in the higher mammals is the tendency to massive acute necrosis in certain olfactory centers; *viz.*, in the rhinencephalic cortex ventral to the fissura rhinica and in the cornu Ammonis, where, irrespective of whether the virus be introduced intracerebrally or peripherally, whole stretches of pyramidal cells may be destroyed *en masse.* It does not appear to be generally recognized that, wherever else necrosis of neurons may occur, massive necrosis in these situations is of extremely frequent occurrence in the brains of these lower mammals infected with any one of a whole range of neurotropic viruses. In the corresponding diseases of higher animals, although foci of nerve cell destruction may be observed here, massive necrosis is not present. In the case of rabies in the rabbit, Lentz (1909) described the resulting eosinophilic structures containing pyknotic nuclear remains as "*passagewutkörperchen,*" though they are also found in rabbits infected with street virus (Hurst, 1932); I have not seen them in rabies in the cow, dog or monkey. Similar appearances obtain in mice with louping ill (Hurst, 1931 *a*), but not nearly to the same extent in the monkey. I have since seen massive necrosis in the cornu Ammonis of the rabbit with herpetic encephalitis, and in the mouse with yellow fever, while at a recent meeting of the Society of American Bacteriologists (Philadelphia, December, 1933) Dr. L. T. Webster exhibited a lantern slide showing this lesion in a mouse infected with the virus of the St. Louis outbreak of encephalitis. Rivers and Stewart (1928) described similar appearances in Virus III infection in the rabbit. Evidently the lesion is one characteristic of a certain type of animal host, rather than of the action of a particular virus. Now in all these small mammals the olfactory brain is relatively better developed than in higher forms, and is presumably relatively more abundantly supplied with fiber connections. If, therefore, the neurotropic viruses spread by the axis cylinders, for which there is evidence in poliomyelitis, rabies and herpes, we might proffer an explanation of these observations in terms of the probable amount of virus reaching a given locality.

The inclusion bodies present in the nerve cells in equine encephalomyelitis bear considerable resemblance to those described in Borna disease (Joest and Degen, 1909, and others) and in poliomyelitis

(Covell, 1929; Hurst, 1931 *b*). In view of the recent criticisms of Wolf and Orton (1932) regarding this type of inclusion, particular attention was devoted to the nuclear structure of normal nerve cells. As various observers, including myself, have pointed out, bodies somewhat resembling these inclusions are often present in the normal nerve cell nucleus. (Incidentally fixatives containing osmic acid render closer the resemblance; in the present investigation, however, Zenker fixation was employed.) Wolf and Orton reproduce a number of photographs of these normally occurring bodies as proof that structures indistinguishable from the inclusions of poliomyelitis occur in other pathological conditions in man; since the appearances depicted by them can be seen equally well in normal nerve cells, it is not necessary to resort to pathological human material, necessarily inferior to fresh tissue, to determine the point at issue, whether these normal structures can or cannot be differentiated from the alleged inclusions.

Four photographs showing the inclusions of equine encephalomyelitis (Figs. 9–12) are offered for comparison with those of four normal nerve cells (Figs. 13–16). In all except Fig. 16 the magnification is the same. The photographer was instructed to obtain the sharpest picture possible of the intranuclear masses, but was uninformed of the question in dispute. The pictures in monochrome do not, unfortunately, adequately suggest the deeper and brighter color, in preparations fixed and stained strictly comparably, of the bodies in the cases of encephalomyelitis, but there is obviously a difference between the two groups. Comparison with Wolf and Orton's photographs shows that the structures in Figs. 13–16 possibly more nearly resemble the inclusions in Figs. 9–12 than do those chosen by the authors named to illustrate their inability to draw a distinction.

The bodies present in normal cells are usually smaller and less acidophilic. They have less sharp and distinct contours, often appearing rather fluffy in outline, and having a less solid appearance. They frequently show little projections uniting them to the general, weakly acidophilic, nuclear reticulum. They never show evidence of internal heterogeneity, as do frequently the bodies described as nuclear inclusions. Moreover in addition to the greater individuality of the bodies in poliomyelitis, equine encephalomyelitis, etc., the nuclei containing them exhibit a definite tendency to disappearance of

acidophilic material other than that in the inclusions, and a margination of the scanty basichromatin on the nuclear membrane; it is difficult to show all this in a photograph focussing only one plane, yet the general nuclear reticulum in Figs. 9–12 is obviously less in amount than that in Figs. 13–16. This clearing of the nucleus is well shown in the plate previously published to illustrate the similar bodies in poliomyelitis. The appearance of these inclusion bodies represents, therefore, a departure from the normal nuclear structure and is characteristic of certain virus diseases. It is not suggested that the inclusions are necessarily wholly new-formed structures; indeed, in the more acute cases of equine encephalomyelitis in the guinea pig, the appearances suggest that they may be derived from the normal nodal masses which become enlarged, more acidophilic, and freed from the disappearing oxyphilic reticulum. Nor are the bodies considered of greater significance than as indicating in these virus diseases abnormal physicochemical conditions in the nucleus, analogous in a way to those evidenced by solution under various circumstances of the tigroid substance. But it is maintained that these bodies can be distinguished from those occurring in the normal condition and in pathological conditions not due to virus action, when as far as the oxyphilic nuclear components are concerned the normal state is maintained.

SUMMARY

The virus of equine encephalomyelitis (eastern strain) evokes in the horse, calf, sheep and dog an unusually intense encephalomyelitis characterized by acute primary degeneration of nerve cells, the appearance in neurons of the brain stem and elsewhere of nuclear inclusions resembling those in Borna disease and poliomyelitis, polymorphonuclear infiltration in the nervous tissues with early microglial proliferation, and perivascular cuffing with mononuclears and polymorphonuclears in varying proportions. The grey matter is affected more than the white. Lesions may be less marked in the striatum, brain stem and cord than in the cerebral cortex, thalamus and hypothalamic region, and are always of low grade in the cerebellum. Meningeal infiltration is secondary.

Similar changes produced in the horse by the western strain of virus are less intense and extensive.

In the guinea pig, rabbit and mouse, the eastern virus causes an acute encephalomyelitis which, as is usual in neurotropic virus diseases of these lowly species, has a special tendency to affect the higher olfactory centers. In addition to inclusions in the nerve cells, tiny oxyphilic bodies occur with less frequency in the glial and mesodermal nuclei of the guinea pig. In this animal, too, interstitial or bronchopneumonia may complicate the picture.

In the guinea pig the disease resulting from infection with the western virus may be indistinguishable from that due to the eastern.

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EXPLANATION OF PLATES

PLATE 36

FIG. 1. Eastern type of encephalomyelitis in the horse. Enormously increased cellularity of the tissues due largely to focal and diffuse polymorphonuclear infiltration. An artery shows pronounced perivascular cuffing. Iron alum hematoxylin and Van Gieson. × 71.

FIG. 2. Eastern type of encephalomyelitis in the horse. Comparatively mild polymorphonuclear tissue infiltration in the cerebral cortex. Necrosis of a nerve cell indicated by the arrow. Iron alum hematoxylin and eosin. × 337.

FIG. 3. Eastern type of encephalomyelitis in the horse. Acute necrosis of a nerve cell of the pons. The cytoplasm is markedly eosinophilic, the nucleus absent (in serial section). A polymorphonuclear leucocyte occupies a vacuole in the cell

body, and a second is applied to the surface of the cell. Microglial satellites are also in evidence. Iron alum hematoxylin and eosin. × 1259.

FIG. 4. Eastern type of encephalomyelitis in the horse. Approaching necrosis of a nerve cell of the brain stem. Polymorphonuclear leucocytes have invaded a large vacuole in the cytoplasm; the cell is surrounded by polymorphonuclear and microglial elements. Iron alum hematoxylin and eosin. × 718.

PLATE 37

FIG. 5. Eastern type of encephalomyelitis in the horse. This artery in the lenticular nucleus shows little infiltration in the perivascular space but many polymorphonuclear leucocytes are collected in the nervous tissues immediately adjacent. Iron alum hematoxylin and eosin. × 385.

FIG. 6. Eastern type of encephalomyelitis in the horse. Polymorphonuclear infiltration of a fiber bundle entering the putamen; the surrounding grey matter is almost free from infiltration. Iron alum hematoxylin and eosin. × 310.

FIG. 7. Equine encephalomyelitis (western strain) in the guinea pig. Mononuclear perivascular sheathing and microglial proliferation in the cerebral cortex. Intracerebral inoculation. Iron alum hematoxylin and eosin. × 292.

FIG. 8. Equine encephalomyelitis (western strain) in the guinea pig. Massive necrosis in the cornu Ammonis with intense polymorphonuclear infiltration in a bacteriologically sterile brain following intramuscular inoculation. Iron alum hematoxylin and eosin. × 244.

PLATE 38

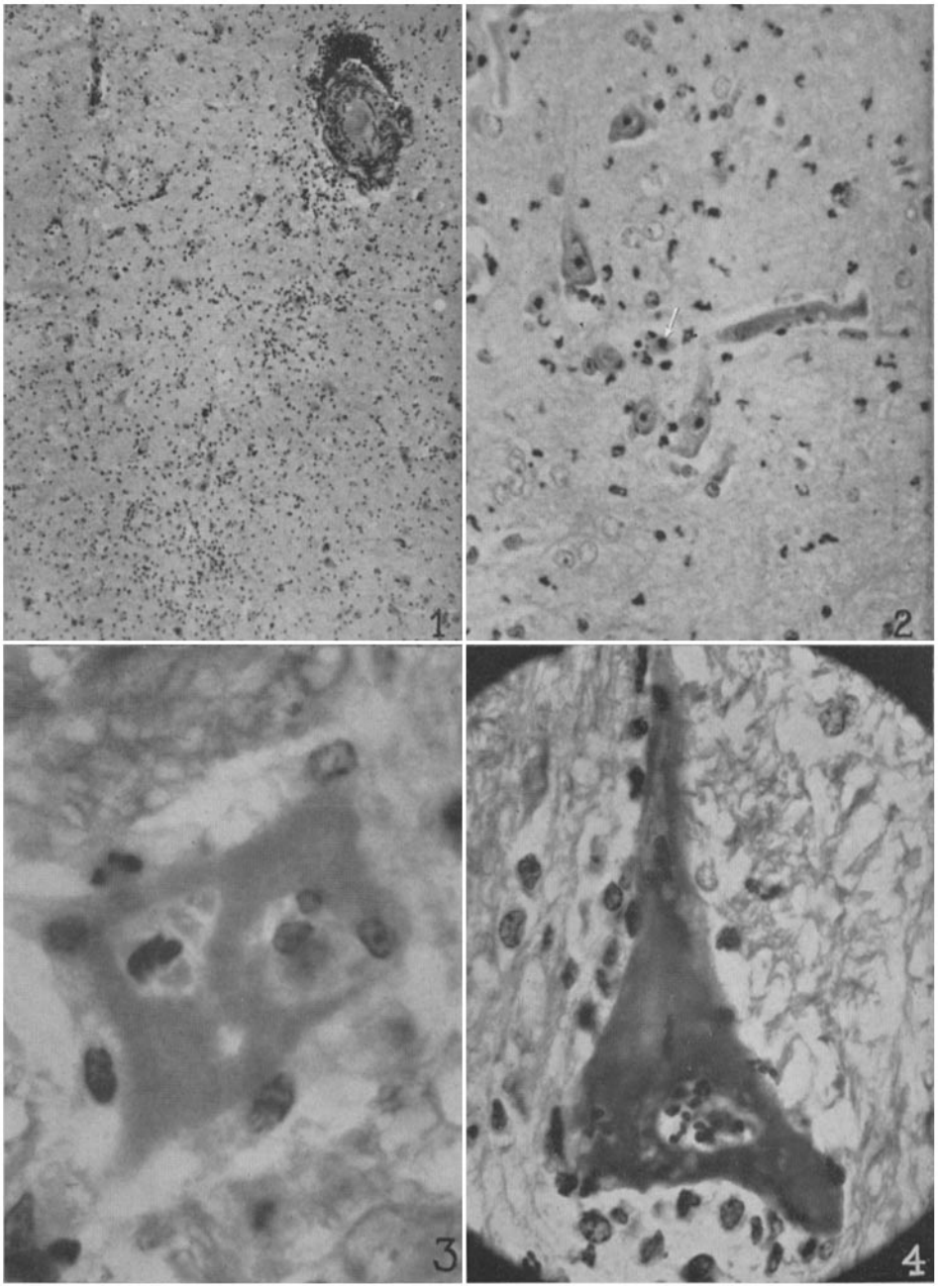
FIG. 9. Eastern type of encephalomyelitis in the horse. Intranuclear inclusion in a nerve cell of the brain stem. Near the cell is an infiltrating polymorphonuclear leucocyte. Phloxin-methylene blue. × 1888.

FIGS. 10–12. Equine encephalomyelitis in the guinea pig. Nuclear inclusions in neurons of the brain stem. Fig. 10, infection with eastern virus; Figs. 11 and 12, with western virus. Phloxin-methylene blue. × 1888.

PLATE 39

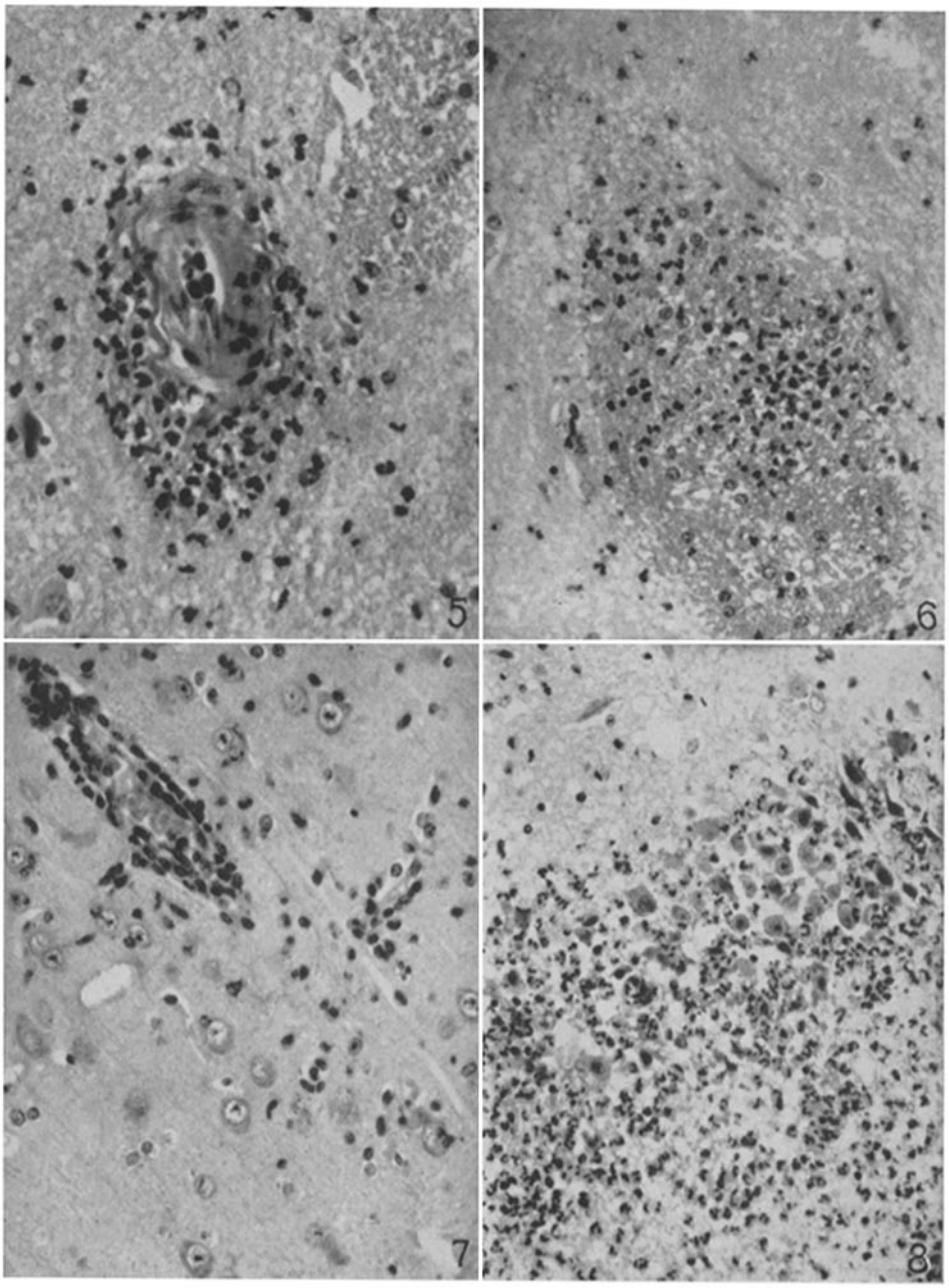
FIGS. 13–15. Nerve cells in brain stem of healthy guinea pigs to show acidophilic nuclear bodies normally present. Phloxin-methylene blue. × 1888.

FIG. 16. Normal nerve cell from spinal ganglion of pig. Phloxin-methylene blue. × 851.



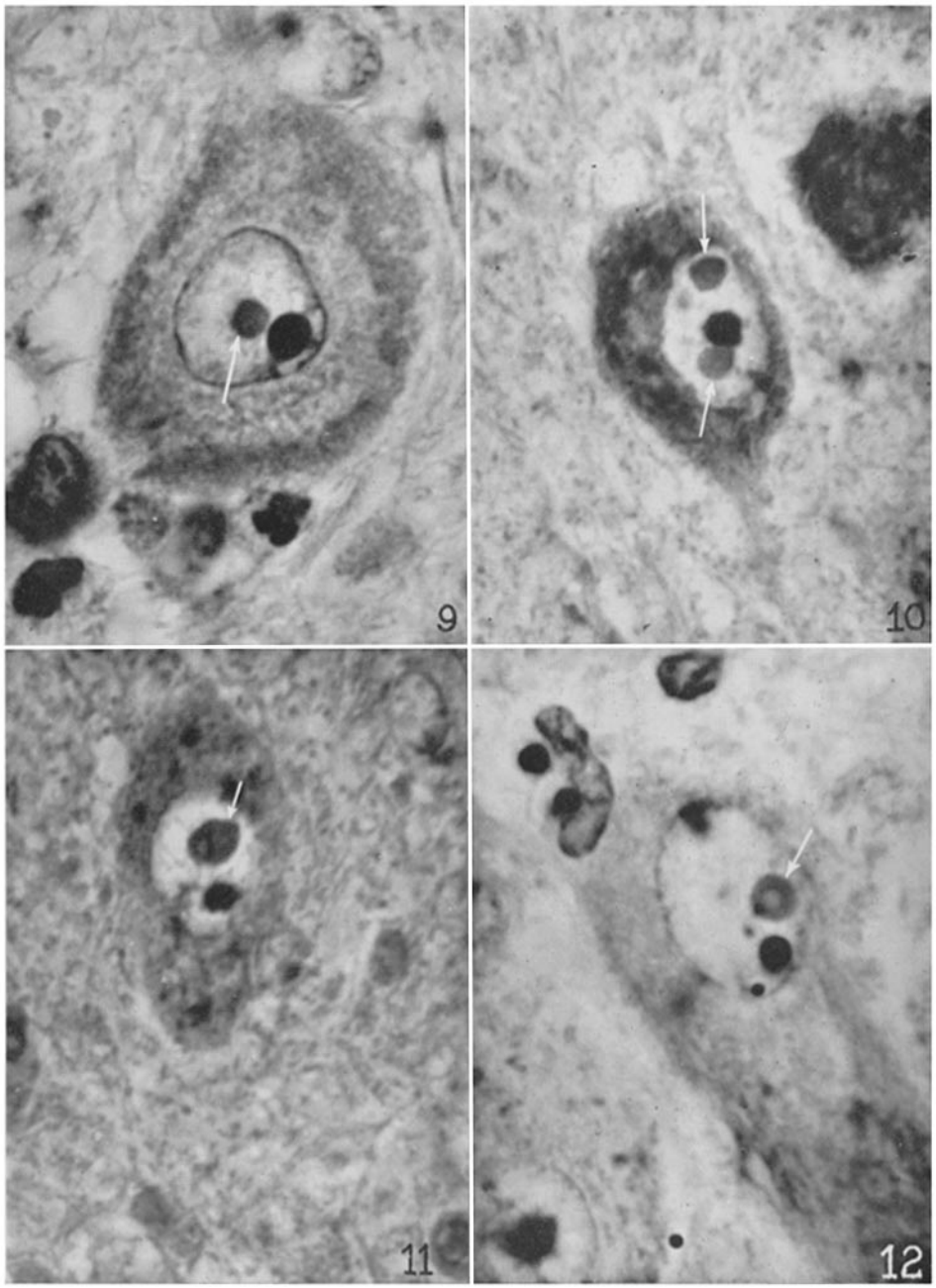
Photographed by J. A. Carlile

(Hurst: Histology of equine encephalomyelitis)



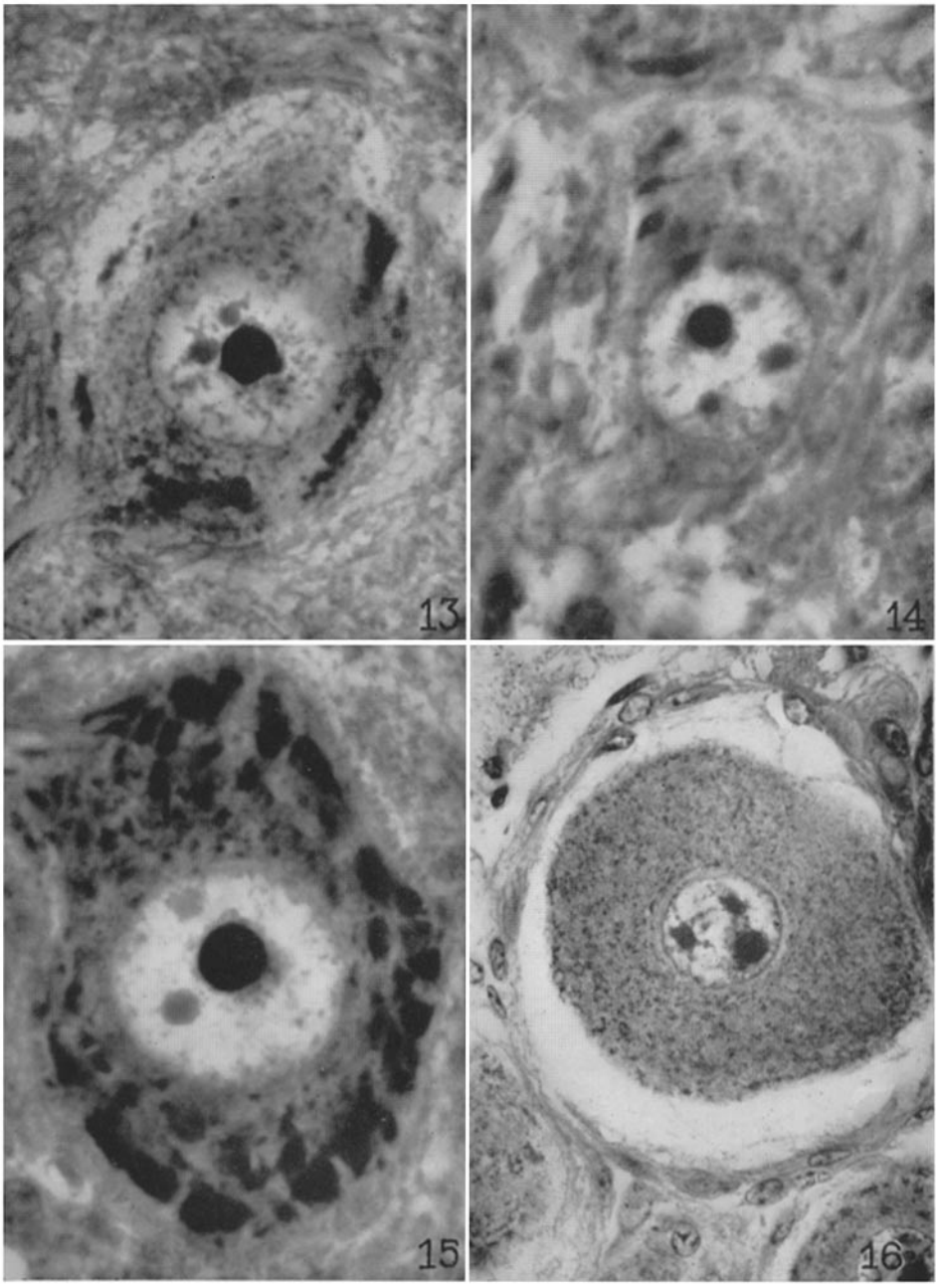
Photographed by J. A. Carlile

(Hurst: Histology of equine encephalomyelitis)



Photographed by J. A. Carlile

(Hurst: Histology of equine encephalomyelitis)



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