COMPARATIVE PATHOLOGICAL INVESTIGATION ON ENCEPHALITIS OF DOMESTIC ANIMALS; ESPECIALLY ON THE EOSINOPHILIC ENCEPHALITIS OF SWINE AND DISTEMPER ENCEPHALITIS II.

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Localization and Distribution of Encephalitic Lesions It is not possible to discuss the encephalitic lesions without regard to the changes of nerve cells. To cite an example, there is an encephalitic disease such as field cases of fowl plague which shows so-called "neuronopathia" even if it has few reactive changes in which the degeneration of nerve cells plays a leading role. However, the appearance of the changes of nerve cells in various encephalitides of domestic animals is different depending on the cases. The present author can hardly find any constant tendency either in his own observations or in those reported by other workers. It can be said without doubt that one often encounters degenerated nerve cells in the tissue which shows a reactive change, however, there are many exceptions where such cells do not appear. From the various known factors, the author considers that such non-constant appearance may be attributed to the close relation between the indication of degenerated nerve cells and the course of the disease. This point can be explained by considering that the changes of nerve cells are observed only in the first stage of the affection different to the few reactive changes and that along with the course of the disease, the appearance of the change becomes irregular especially in an affected animal which is getting over the disease. The writer is convinced that he has found several cases in the brains of rabies and Japanese equine encephalitis cases which are enough to support his above-stated opinions.

It does not apply, at least in the encephalitis of domestic animals, that "specific vulnerability" can be obtained in a special layer of the cerebral cortex as O. VOGT suggests.

Pertaining to the localization and distribution of reactive change, a strict constancy cannot always be found, but the gray matter played an active part in most of the cases of encephalitis observed in domestic animals. This finding is

Continued from p. 72.

not new; it is almost in agreement with that of many other investigators in the past. With regard to methods for indicating the characteristic of virus, the author would like to express his opposition to the tendency to classify en bloc as neurotropic the virus of encephalitis of which gray matter is affected by lesion, because many exceptions can be pointed out in the localization and distribution of reactive change. Furthermore, the observations on the brains of rabies cases clearly indicate that the appearance of reactive change is not due only to the causal agent since the lesion has been observed only in the temporal lobe and unilateral tissue of the *medulla oblongata*. TAJIMA, in his study on Japanese equine encephalitis, has encountered a similar fact; he states that importance should be attached to the patients' condition. The present author would like to call attention to the theory that motor nerve cell in the gray matter is selected as an object for the challenge by virus. This is the very case of anterior poliomyelitis as shown in the previous figure. In this case, it is emphasized that the lesion most actively attacks the anterior horns of the spinal cord as indicated in the name of the disease. With regard to this point, SPIELMEYER, however, is decisively opposed to these views, presenting the following evidences:

1) That he could not admit a special relation between motor nerve cell and the polio virus even though his co-workers had found that that lesion could also be found in *gyrus centralis anterior* which had never been noticed previously in this disease.

2) That the portion in which the lesion occurs in the spinal cord is not limited only to the anterior horn but is found in two-thirds of the anterior part of gray matter of the spinal cord (the ventral portion in animal).

Among the encephalitides of domestic animals it is rarely observed that those of hog cholera and rinderpest are accompanied by the phenomenon above noted, that is by frequent occurrence of lesion in white matter. This fact has been observed in hog cholera by many other investigators as well as by the present author. As for the encephalitis of rinderpest, adequate observation cannot be made on the localization and distribution of lesion due to the slightness of the reactive change and to few observations which have been made. This remark is likewise pertinent to the present author's rabies cases except the field cases.

There is another standpoint for the observation on the localization and distribution of encephalitic lesions, namely the entrance of the causal agent into the brain and its diffusion after entrance. The author, however, would like to emphasize, probably other workers would agree, that giving a definite diagnosis to the entrance route of causal agent into brain tissue based on the morphological changes alone must be realized to surpass the morphologist's ability. It is beyond question in respect to this statement that one is likely to fall into some arbitrary

decision if he tries to base his discussion upon the encephalitic changes because of the many routes connecting the cerebral tissue and possible other entrance points in other portions of the body. The author would like to introduce into his comment some mention of SPATZ's theory. Based on the observation of brains obtained from the Borna disease and rabies, SPATZ pointed out that the interior and exterior layers are the most often found locality for lesion; he used the phrase "von Liquor aus" regarding the entrance of causal agent into brain tissue. In connection with the Borna disease, there is nothing to say. As far as rabies and Japanese equine encephalitis are concerned, the author has observed many cases with frequent occurrence of lesion along the internal wall of the ventricle of the brain stem. However, it is true that a case is often observed without such distribution of lesion; the author has experienced the same indication in each fowl plague and Newcastle disease. He would not dare to agree to SPATZ's views despite many exceptions. The explanation of the above-stated variation may depend upon further investigations but the author, along with many other workers, is of opinion that attention should continue to be directed to the fact that encephalitic lesions often occur in the gray matter particularly in the internal wall of the ventricle and the nuclei of the forebrain.

Listeriosis encephalitis is very interesting. According to TAJIMA, excepting one or two cases, lesion is found only in the *pons* and *medulla oblongata* in most cases. In conformity with the experimental results and the findings on the naturally affected ovine cases obtained by ASAHI et al.[35] and TAJIMA et al. respectively, it has become easy to derive an explanation for the specificity of localization of lesions from the fact that purulent inflammation proceeds centripetally,— the causal bacilli of that invasion begins from the external surface of the head. Since the facts that many routes exist in invasion from various portions of the body and that listeriosis is accompanied by the occurrence of septicemia, have been previously noted by some investigators, the author merely considers that there is a room left for investigation concerning this peculiar "vulnerability". In other words, it seems that there may be a real possibility that the change in brain stem precedes morphologically, and secondly that purulent inflammation disseminates centrifugally into peripheral parts. Anyway, it is true fact that the localization of encephalitic lesions of listeriosis is characterized by its peculiarity in comparison to other diversified encephalitic lesions.

Classification of Encephalitis of Domestic Animals The author, as above mentioned, has referred to the kind, localization and distribution of reactive changes in the encephalitis of domestic animals alluding to the degenerative and necrotic changes in non-encephalitic diseases. The selected encephalitic diseases were limited only to the ones with obvious etiological agent of diseases. The author

is well aware that various names have been given to known encephalitic diseases according to certain aspects in encephalitic changes, but the following described classification is proposed from the pure morphological standpoint.

As for the standard of classification, the author followed SPIELMEYER's formula accepting the arrangement in which he placed the names of the diseases on two sides respectively characterized mainly by glia cell reaction and by mesodermal reaction; cases showing both reactions were placed in the center.

The writer wishes again to say that he recognizes the opinions of other investigators who have carried on research on the etiological or clinical peculiarities as to the quality, localization and distribution of lesions. However simple and direct such classification of encephalitic diseases may be, the author cannot simply accept the majority of so-called specificities of each encephalitic type in the classification. He is, therefore, reluctant to use the classification for fear of unconsciously influencing decisions in the wrong direction in the future study on the unknown-cause diseases.

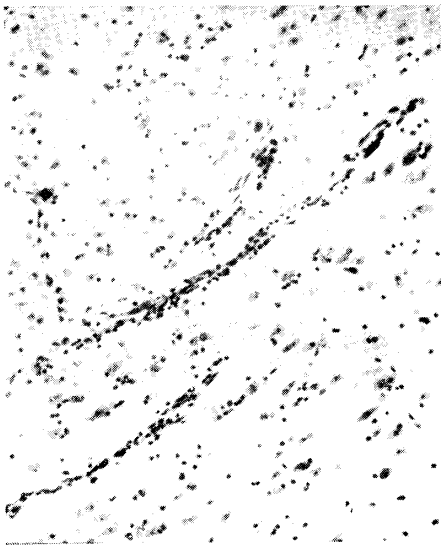
Fowl plague encephalitis and rabies encephalitis caused by passage viruses can be designated amongst those to be placed on the left side with the encephalitic diseases of domestic animals. On the right side, there are the encephalitides of the field cases of fowl plague, Newcastle disease caused by passage virus, hog cholera, rinderpest and listeriosis. Rabies encephalitis of field cases and Japanese equine encephalitis fall in the center.

The author, in regard to the classification of encephalitic diseases of domestic animals, would like to say a word about non-encephalitic diseases which cause focal necrosis in the central nervous system. The diseases are, as has been repeatedly explained, not rare in the field of veterinary medicine. The reason why they are watched by the author with keen interest is that focal necrosis, especially that which originated in the local functional disturbance of blood circulation, is also observed in the encephalitic diseases together with epileptic fit and other peculiar clinical symptoms. In connection with the cause of these non-encephalitic diseases, the majority still remain amongst the diseases of unknown origin. The author accordingly would like to be deliberate in the future study on the unknown-cause diseases of the central nervous system lest he should impatiently deny the occurrence of the encephalitic diseases by the mere reason of the non-indication of inflammatory changes derived from the examinations on a few cases or on some limited portion of the nervous system. The author would like to refer to the appearance of an opinion that *encephalitis disseminata acuta* can be the acute stage of multiple sclerosis proposed at a discussion as to whether or not multiple sclerosis is an encephalitic disease in human medicine.

The author considers that he has presented a sufficient number of the

encephalitic diseases of known cause in domestic animals as above. He has made a classification of the encephalitic diseases of domestic animals broadly from the viewpoint of comparative pathology in the last portion of this report. However, it should be stressed that the above-discussed findings are concerned with the characteristics of morphological changes and that the diseases should not be or cannot be decided only by histological findings in the practical field. In this regard, the author would like to present a simple explanation of three cases of encephalitic diseases in cattle. These cases were obtained at Wangyehmiao, Manchuria (Case No. 1), Minamishiribetsu, Hokkaido (Case No. 2) and Darahan, Inner Mongolia (Case No. 3). They were microscopically suspected as rinderpest encephalitis, Japanese B encephalitis and rabies respectively in order. The detailed explanation is not given presently. However, according to the nature of histological changes, case No. 1 was placed in the right in our classification and cases No. 2 and 3 in the middle from their quality, localization and distribution of lesions (Figs. 67, 63 & 69). However, it should be repeated that this judgment is based on pathological findings only. As for case No. 3, fortunately it did not come to a question because rabies was proved etiologically. Case No. 1 did not provide any additional information except it died of encephalitic symptoms, therefore, it was not possible to decide the disease—however, encephalitic disease was confirmed only by examination of brain preparations. Based upon the

FIG. 67. *Bovine Encephalitis (Rinderpest Encephalitis ?)*

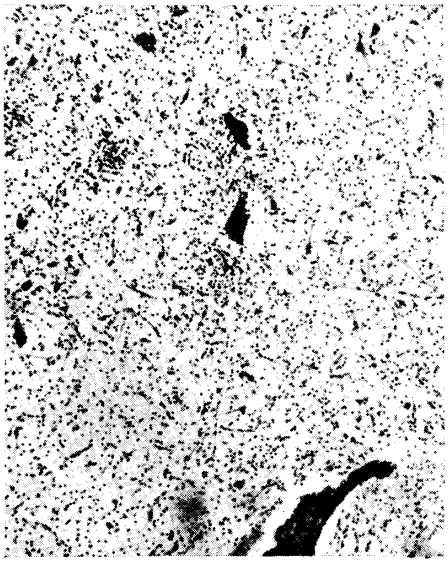


Vascular cell accumulation. Slight infiltration seen in two fine blood vessels. Wangyehmiao/No. 8. NISSL.

FIG. 68. *Bovine Encephalitis (Japanese B Encephalitis ?)*

Vascular cell infiltration and patchy glia cell foci. E. 36. NISSL.

FIG. 69. *Rabies Encephalitis* (Cattle)



Glia cell nodules and vascular cell infiltration. Darahan/No. 1. NISSL.

characteristic of the encephalitic picture, the author did suspect whether it was rinderpest. Case No. 2 did provide sufficient histological evidence to be suspected as Japanese B encephalitis and rabies. It presented clinically obvious encephalitic indication and was slaughtered after one week's observation. An etiological study was not made because the examination was requested on only fixation materials. It should be also taken into consideration, as a reference in diagnosis, that this case occurred not only in the autumn of 1948 when Japanese B encephalitis was epidemic but also it was in Shiribeshi sub-prefectural area which has never failed to show the occurrence of the disease in epidemic season in Hokkaido. Even though the above histological findings are lacking in material for a study of causal agent but they do play an active part in deciding the name of disease.

II.

The author would like to enter into a consideration pertaining to the eosinophilic encephalitis of swine, *encephalitis eosinophilica suis*,[26] which belongs to the category of unknown cause without anything similar to it being discussed in literature and to distemper encephalitis which is believed still to have left diversified problems despite its having been studied by foreign and Japanese investigators for more than one hundred years.

Eosinophilic Encephalitis of Swine In conjunction with the dissemination of Japanese B encephalitis in Japan a few years ago, the swine encephalitic disease came into limelight. So far as the present author and his co-workers are concerned, even though one of 2 cases reported by TAJIMA and TSUBAKI was Japanese B encephalitis the other one of their 2 cases, 2 by the present author et al. and 2 by UEDA were all diagnosed as encephalitic diseases of unknown cause. As the author and co-workers have obtained 14 additional swine brains with histological changes which belong to the same category in Hokkaido up to date, he would like to discuss briefly these 19 cases in this report. It is expected they will be reported in detail in the near future by SATOH of this laboratory.

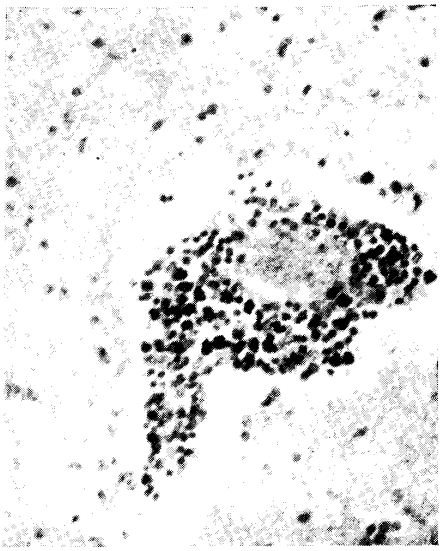
The most characteristic histological feature may be the predominant parti-

cipation of eosinophilic leucocytes in cellular vascular and tissue infiltration (Fig. 70). In the first place it has been explained on the mesodermal reaction observed in the already known encephalitic diseases of domestic animals that cellular infiltration plays an active part in the histological changes of encephalitic lesions but that eosinophilic leucocytes do not create a problem as an infiltrated cell element. However, in the present cases of swine brains, eosinophilic leucocytes are generally playing an overwhelming role in the histological picture as indicated in the figure. Blood vessels which indicate the infiltration are of medium and smaller diameter for the most part and show different quantitative balance with those which form thick cellular sheaths and those in which a few infiltrated cells are recognized in the perivascular lymph space (Fig. 71).

FIG. 70. *Encephalitis eosinophilica suis*

Eosinophilic leucocyte infiltrations on the meninges of parietal lobe and cortical blood vessels with diffused emigration into nerve tissue. E. 711. H.-E.

FIG. 71. *Encephalitis eosinophilica suis*



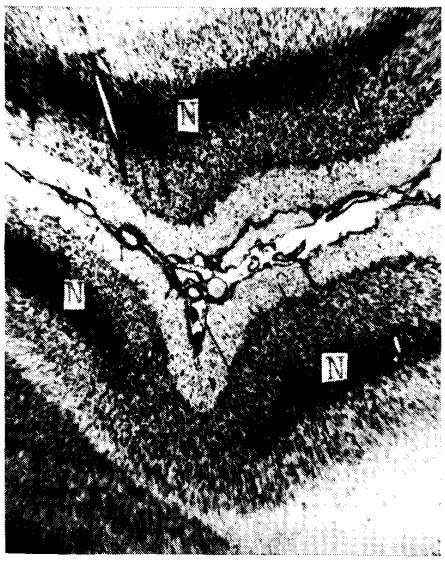
Vascular and tissue infiltration of eosinophilic leucocytes in cerebral cortex. Hokken/Swine-No. 2. H.-E.

Some cases reveal the infiltration diffusely into perivascular tissue depending upon the case or the localization. Mainly the telencephalic cortex presents the area for this reaction, but cerebral nuclei such as *thalamus opticus*, *nucleus caudatus*, etc., sometimes afford the place. The *mesencephalon*, *rhombencephalon* and spinal cord are usually not accompanied by this reaction. Even though emigration of eosinophiles is often observed in the *pia mater* of the base of the brain, etc., it is limited only to the *pia mater* which covers the endbrain especially in the portion of severe lesion and is not of great significance as compared to the remarkable infiltration picture.

What can be listed as a secondary characteristic of this swine encephalitis is the appearance of focal necrosis principally

observed in the cerebral cortex. However, no additional detailed explanations to the character and substance of these focal necroses are given here because they are the same as those explained previously in connection with encephalomalacia. Cases of focal necrosis have often been encountered in which the majority of the circumscribed foci are to be seen in the middle layer of the cerebral cortex as well as those which have come to indicate glio-mesodermal reaction rather than the fresh focal pallidness (Erbleichung SPIELMEYER's) (Fig. 72). In this point, attention should be directed to the fact that the eosinophilic perivascular and tissue infiltration occur inside the foci with a few exceptions. This feature indicates outstanding difference to those discussed in the foregoing description of sheep and horse brain, etc. Focal necroses, which pseudo-laminarly appear in the portion of gyral leg and bottom of sulcus, are likely to draw attention by the size of the foci, development of changes, etc.; a few of them located in another portion, however, are recognized as a small focus which shows obscure boundary and indefinite shape.

FIG. 72. *Encephalitis eosinophilica suis*



Pseudolaminar necrosis (N) at the median layer of occipital cortex. Remarkable glio-mesodermal reaction has already occurred. Pr. 3085. NISSL.

In addition to this, the significance in the whole histological pictures of swine brain of this kind is the poverty of glia cell reaction. In other words, only nodular foci or diffused proliferation of rod cell were detected in a mere few out of the 19 cases although many preparations were subjected to microscopical observation. However, such observations were naturally made on the changes other than the secondary glia cell reaction in the foci of focal necrosis.

The author has diagnosed these swine encephalitic lesions as the eosinophilic encephalitis of swine based on the above-described characteristics. In this regard, it may well be that other findings have been made differing from the author's, for example, glia cell reaction may not always be found in all cases in the histological diagnosis of encephalitis or, eosinophilic cell infiltration may be limited to the *telencephalon* and no final decision can be reached on the non-relationship between focal necrosis and eosinophilic infiltration. However, the author has handled these cases as an independent unique encephalitic disease attaching

importance to the fact (1) that an independency and originality are observed in the cell infiltration of which the major portion is composed of eosinophiles as a sort of mesodermal reaction and (2) that the degeneration and necrosis of nerve cells are also confirmed in portions other than those of focal necrosis throughout the brain tissue. The author accordingly would like to interpret the focal necrosis with a characterized appearance in all cases as one caused by local functional disturbance of blood circulation from the viewpoint of its histogenesis and to understand that the focal necrosis has a secondary significance.

What sets a problem is as to whether or not this encephalitic disease is nosologically independent. The writer considers that defining it as a sort of infectious encephalitic disease can be permitted at present though a detail consideration will follow in a later report. The encephalitic disease in piglet is just such a case. The reasons are as follows:

1) The majority of such cases are 2~3 months old with three exceptions.

2) Clinically, pyrexia is observed and all show nervous symptoms without exception. However, convulsive and epileptic symptoms which are believed to have close relations with morphological change, so-called focal necrosis of cerebral cortex, play an active part, and in some cases, manic or melancholic symptoms are noted. The course was recorded for 2~3 days in the majority of cases many of which resulted in death.

3) According to the data made by the concerns who presented the materials, the endemic occurrence is usually observed in the prison, in a pig raising farm and in the area where pigs are collectively raised.

4) Etiological study was made only on a couple of cases but the virus of Japanese B encephalitis was detected in TAJIMA and TSUBAKI's case. In their neurohistological findings, many cases had common points with those in Japanese equine encephalitis as to their character, localization and distribution. MOCHIZUKI et al.[27] and ISHII et al.[28] paid remarkable attention to neutrophilia as hematological changes and typical non-purulent encephalitis in their reports but did not give any description on eosinophilic cell infiltration or focal necrosis.

The author concludes on the basis of characteristic findings obtained histopathologically from swine brains: The author picked representing cases of eosinophilic encephalitis as temporarily named:

1) Encephalitic change which has its center in eosinophilic vascular and tissue infiltration is to be regarded as the major change of this disease (Fig. 73).

2) Secondary significance is to be attached to focal necrosis. The focal necrosis is observed in comparing with encephalitic lesions of human and domestic animals as previously explained.

FIG. 73. *Encephalitis eosinophilica suis*

Remarkable vascular infiltration of eosinophilic leucocytes in frontal lobe. No focal necrosis, but obvious meningitis. Pr. 2900. NISSL.

Distemper Encephalitis There is a disease, so-called distemper, which prefers to attack young dogs, takes in most cases acute and subacute courses and is often considered as a nervous trouble handled under the name of "nervous form". Many investigators have presented reports on the pathological changes in the brain in such cases. The writer, with G. PETERS of Munich, once presented a discussion from the viewpoint of pathology on an encephalitic disease which can be diagnosed as distemper encephalitis. Since that time, investigations by the writer and co-workers have been continued on nearly 200 cases which are diagnosed as distemper in Hokkaido. Detailed report on them is to be made by OHBAYASHI of this laboratory before long.

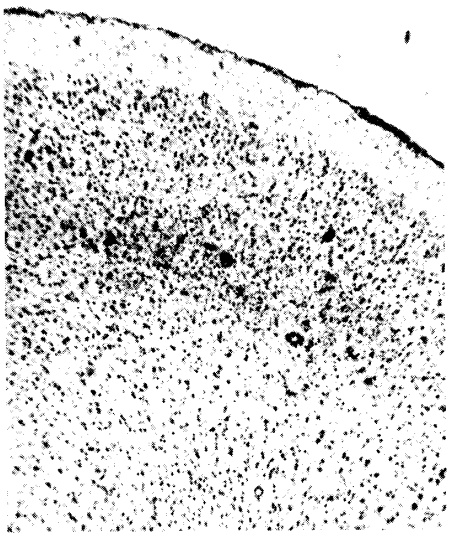
The relation between distemper encephalitis and its causal agent has recently been painstakingly reported by European and American veterinarians. It is true that CARRÉ virus has been regarded as a causal agent for the disease called distemper. However the author finds extreme differences between the reports by DUNKIN & LAIDLAW (1926),[29] MACINTYRE et al. (1948)[30] and SULMAN (1951)[31] to the effect that no relationship exists between the contraction of CARRÉ virus and encephalitic disease and the reports that HURST et al. (1943),[32] KOPROWSKI et al. (1950)[33] and WINQVIST (1950)[34] have proved encephalitic changes. In addition, MACINTYRE et al. and SULMAN, according to themselves, have proven a new virus other than that of CARRÉ for the causal agent of distemper encephalitis and have named this encephalitic disease "hard pad disease" or "paradistemper". Furthermore, GREEN et al.[35] are attaching importance to the detection of intracellular inclusion bodies in the epithelia of respiratory and urinary tracts as a pathological finding closely related with the contraction of CARRÉ virus.

What does the histological picture of distemper encephalitis, as obtained by the writer, look ? Comment centering on his findings starting with glia cell reaction follows :

The proliferation of rod cells was observed as shown in fig. 2 in the previous contribution, but the frequency of appearance of this change is very low. It

often shows pseudolaminal proliferation in cerebral cortex. What is most commonly observed as glia cell reaction is a sort of focal proliferation. As its characteristic, the contour of the focus is lacking in distinctness and the increase of glia cells is not remarkable. It can safely be said that few cases show perivascular proliferation but there are some cases in which those rounded glia cells or compound granular corpuscles fill in the focus, depending on the foci or cases. Increase of protoplasmic macroglia cells is usually observed in the foci and some cases show an outstanding increase of plump astrocytes and astrocytes. In other words, it cannot be said that glia cell reaction is not active in respect to its quantity. Of course some of them show an external appearance similar to the nodular focus observed in rabies encephalitis (Figs. 74, 75 & 76).

FIG. 74. *Distemper Encephalitis*

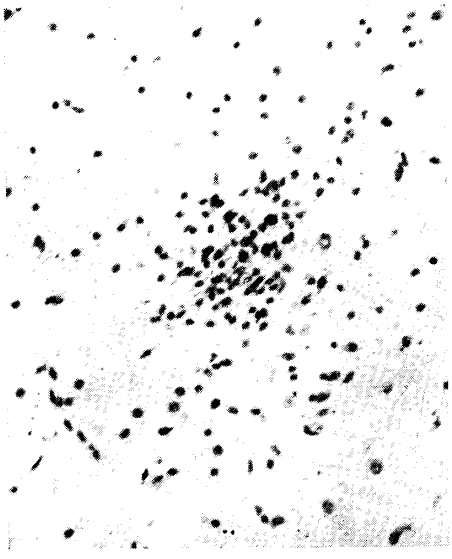


Pseudolaminal glia cell proliferation on the deep layer of cerbral cotex. 198/35 (Forschungsanstalt für Psychiatrie). NISSL.

FIG. 75. *Distemper Encephalitis*

Focal necrosis in cerebellar lamella. Compound granular corpuscles and neuroglia cells within the focus. 108/35 (Forschungsanstalt für Psychiatrie). NISSL.

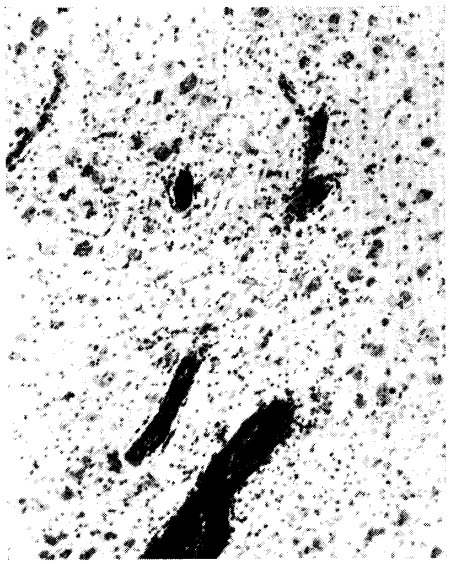
FIG. 76. *Distemper Encephalitis*



Nodular glia cell proliferation on the molecular layer of *cerebellum*. 18/29 (Forschungsanstalt für Psychiatrie). NISSL.

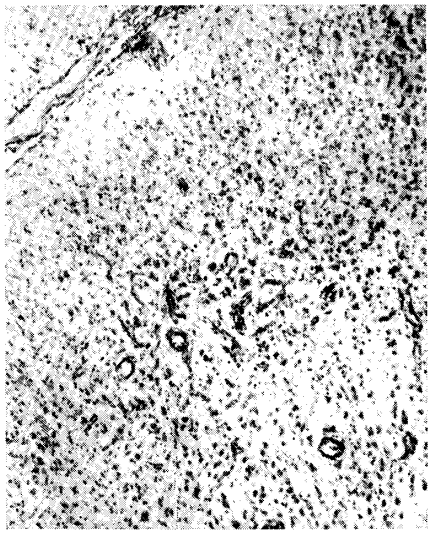
The next point is as to mesodermal reaction. — This also shows small activity. Such reaction comprises principally vascular cell infiltration and focal vascularization by blood capillaries which can be observed together with increase of cells in the wall of small blood vessels. The vascular cell infiltration is normally observed with glia cell reaction and it is very rare that lesions appear independently. Blood vessels with cell infiltration appear inside of glia cell focus and its surroundings; mononuclear round cells which contain lymphocyte are the infiltrated cell element. They are very few in quantity. In many cases, cell infiltration is observed simultaneously in the *pia mater* close to the portion of lesion. Focus formation of new blood capillaries is usually observed as a solitary appearance in the cerebral cortex and sometimes in the white matter even though the cases actually observed by the author are very few (Figs. 77 & 78).

FIG. 77. *Distemper Encephalitis*



Vascular cell infiltration in thalamic gray matter. With glia cell proliferation. 50/31 (Forschungsanstalt für Psychiatrie). NISSL.

FIG. 78. *Distemper Encephalitis*



Increase of wall cell of blood capillaries and newly formed blood vessels. 118/35 (Forschungsanstalt für Psychiatrie). NISSL.

As for the localization and distribution of inflammatory changes, the following characteristics can be presented:

In section preparations, such changes show as (1) a narrow belt-like focus of much regularity along the internal and external surfaces of brain stem and *medulla oblongata* and, (2) a hill-like focus with its low peak facing the center. Besides, the entire surfaces are also observed as the location of foci on the preparation. Cerebellar white matter, especially medullary lamellae, are often subject to the

location inside the parenchyma, and in this case an inflammatory change often invades the neighbouring granular layer showing extreme diffuseness. The *telencephalon* also presents a site for the lesion and its white matter is favorably localized.

The author has described the appearance of cells as above; he is also able to present the picture of parenchymatous destruction in diversified degree in the focus of glia cell reaction as one of the findings concerning the preparations of myelin sheath, axis cylinder and fat. However it should be noted that such diversified degree destruction remains in the purview of necrobiosis. In other words, even in those cases accompanied by malactic focus on the routine preparation, the persistence of degenerated axis cylinder and myelin sheath are recognized in various degrees and fatty destruction is not remarkable by the special staining methods. In the indistinctly demarcated focal lesions, an obvious shady portion, consequently, does not appear on the preparation and the degeneration of parenchymatous tissue is confirmed only by large amplification (Fig. 79). Based on the above, the statement that gliosis is found in HOLZER-preparations cannot be credited.

FIG. 79. *Distemper Encephalitis*

Focal necrosis (N) in cerebellar lamella. 108/35 (Forschungsanstalt für Psychiatrie). SPIELMEYER.

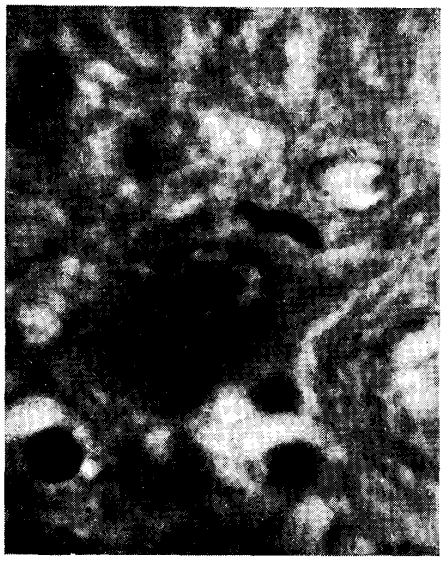
The above described are the pathological changes appearing in the brains which have been handled as cases of distemper encephalitis. All of the materials examined by the author and his co-workers are those clinically diagnosed as, or probably, distemper with the exception of the endemic cases obtained in Hiyama area. However there will naturally be room for discussion in opposition to the observation made on all materials en bloc as in the encephalitic diseases of which the characteristics are already known because epidemiological and etiological studies have not been made. With respect to a few cases in which solitary vascular cell infiltration is observed, it may be proper to leave them for future study, and yet, so far as the other cases are concerned, it is not meaningless to classify them under distemper-encephalitis for the time being, from the morphological point of view.

It can be said that descriptions and discussions which have been reporting distemper encephalitis in the literature since CERLETTI, etc. have great significance in the study of so-called distemper. SCHERER (1944) once called distemper "Multiple

Sklerose der Hunde". INNES has also showed interest in "multiple sclerosis" in his recent report concerning the relation between the distemper infection and canine encephalitis; he mentioned it together with sway-back in his discussion of "demyelinating diseases of animals" as well as of his so-called canine encephalitis and the present writer's distemper encephalitis. The present author in a joint work with PETERS has reported a comparison of distemper encephalitis with the disease in human multiple sclerosis. On these points, that close relation can be clearly explained from the viewpoint of comparative pathology, does not mean at all that the author intends to alter his inclination to give more importance to *encephalitis non-purulenta disseminata*, so-called "acute multiple sclerosis", rather than to multiple sclerosis. The above fact consists in the difference between the characteristics of the inflammatory focus of distemper encephalitis and that of multiple sclerosis and in the certain clinicopathological similarities between the distemper and so-called acute multiple sclerosis. The present author consequently finds his view opposed to that of INNES in respect to the latter's comparison of the encephalitic changes of the distemper with those of multiple sclerosis. Frankly speaking, the degenerative phenomenon in inflammatory focus of distemper encephalitis can be regarded as a phenomenon subordinate to those of glia cell and mesodermal reactions.

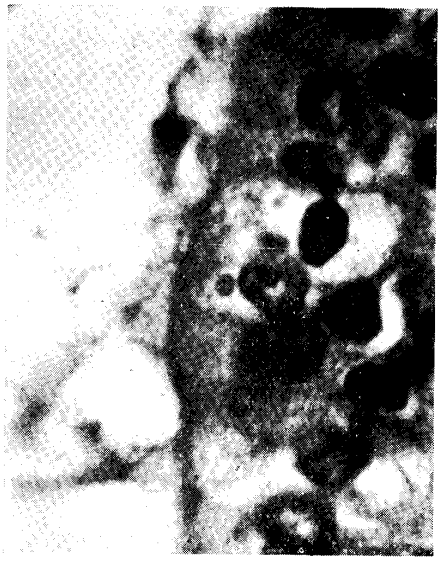
To this end, the author would like to discuss simply the inclusion body (Figs. 80~82). The following table indicates the appearance of the inclusion body

FIG. 80. *Distemper Encephalitis*



Nuclear inclusion body in nerve cell. E. 1396. H.-E.

FIG. 81. *Distemper Encephalitis*



Cytoplasmic inclusion bodies in bronchial epithelia. Pr. 3377. H.-E.

among the cases examined by OHBAYASHI of this laboratory (Table 1).

Though the table suggests various points, the author would like to stress that approximately two-thirds of distemper encephalitis cases reveal the inclusion bodies in negative. The author has described in this report that GREEN et al. attach importance to the appearance of the inclusion bodies in distemper cases. In consequence, the above interpretation suggests that there may be some encephalitides which consist in the affection by CARRÉ virus and some which do not fall under distemper encephalitis as defined by the present author. In this regard, no conclusion can be reached since no etiological experiments have been made on the present materials. Judging from the results obtained by KOPROWSKI et al., the present author's so-called distemper encephalitis, regardless of the appearance of the inclusion bodies, can be said to originate in the classical distemper virus. It also can be said that the negative cases of the inclusion bodies which form the majority of cases examined are attributed to some other etiological agent according to the idea of MACINTYRE et al. The present author has made reference to the findings on the inclusion bodies at this time, but what can be pointed out is nothing but the fact that the pathological changes which appear in distemper encephalitis were observed very distinctly. The author himself realizes that he

FIG. 82. *Distemper Encephalitis*

Cytoplasmic inclusion bodies in bladder epithelia. E. 691. H.-E.

TABLE 1. *Incidence of Inclusion Bodies in Examined Cases*

DIAGNOSIS	NUMBER OF CASES WITHOUT INCLUSION BODIES	NUMBER OF CASES WITH INCLUSION BODIES IN		
		Central Nervous System Only	Central Nervous System & Viscera	Viscera Only
Distemper Encephalitis	46	7	4	14
Non-Encephalitis	27	0	0	11

In making researches on the inclusion bodies, OHBAYASHI attached importance to the appearance of inclusion bodies in glia cell in the central nervous system and as for the viscera in the epithelial cells of the respiratory and urinary tracts.

is not in position to give a complete description of the relation existing between the character of changes and the two or three viruses described in the literature.

The author has, above, offered various comments on matters connected with eosinophilic encephalitis of swine and distemper encephalitis starting from known encephalitic diseases of domestic animals. The author feels his discussion in this report may not give satisfaction to others but he, on the other hand, is of opinion that the foregoing findings may have reached the maximum possible in morphological observations. It is due to the architectural and functional specificities of central nervous system that an arbitrary opinion is apt to enter into the worker's interpretation of changes. Accordingly it is most desirable that the discussions on the encephalitides of domestic animals to be made in moderation, which may naturally cause others to hold obstinately to their own opinions even in respect to classification. Despite the above considerations, the author is confident in reporting the following observations which were made centering around the known encephalitic diseases of domestic animals: They are, the cases traceable to the same infection show differences in pathological changes dependent upon the strains of causal agent; there is an obvious transition in tissue reaction during the course of the disease; the examination concerning the localization and distribution of lesions should never be neglected. In regard to the encephalitic diseases of domestic animals which are of unknown cause or which require etiological solution, the author also is convinced that comparative pathology could, in advance of etiological research, make clarification of characteristics of diseases which appear in histological changes. So far as the above role is limited to the characteristics and an absolute specificity can never be derived from the cell and tissue reaction, attention should again be called to the fact that etiology is the very study which will give a conclusive solution to the etiological problems in the investigation of encephalitic diseases of domestic animals. It should naturally be stressed among the etiologists that the dominant performer in the whole picture of encephalitis of domestic animals is not only the causal agent but also the local or general readiness (Bereitschaften) of patient for direct and indirect injurious action brought about by infectious diseases.

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Erratum for Vol. 3, No. 2

Page 68, 12th line, for granule read granular.