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HISTOLOGICAL CHANGES IN THE CENTRAL NERVOUS SYSTEM OF SWINE INOCULATED WITH SOME ENTEROVIRUSES[1)]

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The Teschen virus strains, which belong to the enteroviruses, are known since long to cause polioencephalomyelitis in pigs. All Teschen strains comprise one serotype, which according to *Mayr* (8) can be divided into two sub-types. The causative agent of the Talfan disease in England (5) and possibly also the benign enzootic paresis in Denmark (14) are Teschen viruses (2). The histological changes in the CNS at Teschen disease have been described in detail (4, 7, 14).

Investigations on swine enteroviruses, which do not cross-neutralize with the Teschen strains but show similar clinical and morphological pictures in experimental pigs, have been reported by *Betts & Jennings* (1), *Sibalin & Lannek* (10), and *Izawa et al.* (6).

This report deals with histological changes observed in the CNS of colostrum-deprived piglets used in pathogenicity tests of enteroviruses isolated in Sweden (10, 12, 13).

MATERIAL AND METHODS

1. *Virus strains.* The viruses used in the experimental work have been described and characterized as enteroviruses (10, 11, 12, 13). All strains, except S180/4 and U6, are shown in Table 1.

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Table 1. Degree and localization of the histologic changes in the CNS.

Piglets No.	Inoculum: Strain	Inoculum: t. c. passage	Inoculum: neg. $\log_{10}$ TCD_{50}/ml.	Volume and route (ml.)	Age at inoculation (days)	First symptoms observed (days)	Age at killing (days)	Lumbar cord	Thoracic cord	Cervical cord	Medulla oblongata	Cerebellum	Rhombencephalon	Cerebrum I	Cerebrum II	Cerebrum III	Cerebrum IV
HE-26/1	S159	18	6.1	2p/o	1	—	30	(+)	—	(+)	(+)	(+)	(+)	(+)	(+)	+	(+)
HE-26/2	S159	18	6.1	2p/o	1	12	30	+	(+)	(+)	+	(+)	+	+	—	—	—
HE-26/3	N7	6	6.5	2p/o	1	9	12	++	(+)	++	+	+	+	+	—	+	(+)
HE-26/4	N7	6	6.5	2p/o	1	11	30	+	(+)	+	++	+	+	—	—	+	+
HE-26/5	N7	6	6.5	2p/o	1	9	17	++	(+)	++	++	+	+	+	++	(+)	(+)
HE-26/6	V4	6	6.5	2p/o	1	16	28	+	(+)	+	+	++	+	(+)	+	—	(+)
HE-26/7	V4	6	6.5	2p/o	1	10	28	+	(+)	+	(+)	(+)	(+)	(+)	(+)	—	—
HE-26/8	V4	6	6.5	2p/o	1	—	28	+	(+)	+	—	(+)	+	(+)	—	—	—
HE-26/9	U1	6	6.1	2p/o	1	14	29	+	(+)	+	++	+	++	+	+	(+)	+
HE-26/10	U1	6	6.1	2p/o	1	8	13	+	(+)	+	++	+	++	+	++	+	(+)
HE-26/11	U1	6	6.1	2p/o	1	16	29	(+)	(+)	+	+	+	++	+	(+)	—	(+)
HE-26/12	not inoculated				—	—	30	—	—	—	—	—	—	—	—	—	—
HE-26/13	not inoculated				—	—	30	—	—	—	—	—	—	—	—	—	—
HE-27/1	N11	6	5.7	2p/o	3	—	31	+	(+)	+	(+)	—	—	—	—	—	—
HE-27/2	N11	6	5.7	2p/o	3	10	31	(+)	(+)	+	(+)	—	—	—	(+)	—	—
HE-27/3	U10	6	5.9	2p/o	3	8	32	+	(+)	+	+	(+)	(+)	—	—	—	—
HE-27/4	U10	6	5.9	2p/o	3	—	32	(+)	(+)	(+)	+	+	+	(+)	—	—	—
HE-27/5	not inoculated				—	—	33	—	—	—	—	—	—	—	—	—	—

— = Negative; (+) = not well defined changes; + = well defined changes; ++ = marked changes.

2. *Experimental pigs.* The raising of colostrum-deprived piglets, which were obtained by hysterectomy, has been described elsewhere (13). Altogether 26 inoculated and 10 non-inoculated piglets as shown below, were examined.

Virus strain	Number of piglets		c. f. reference no.
	inoculated	non-inoculated	
S 180/4	9	5	10
U 6	3	2	12
Others (see Table 1)	14	3	13 (Table 4)

The pigs were bled to death under ethyl-ether narcosis.

3. *Histological examination.* The following specimens were taken for histological examination (see Fig. 1).

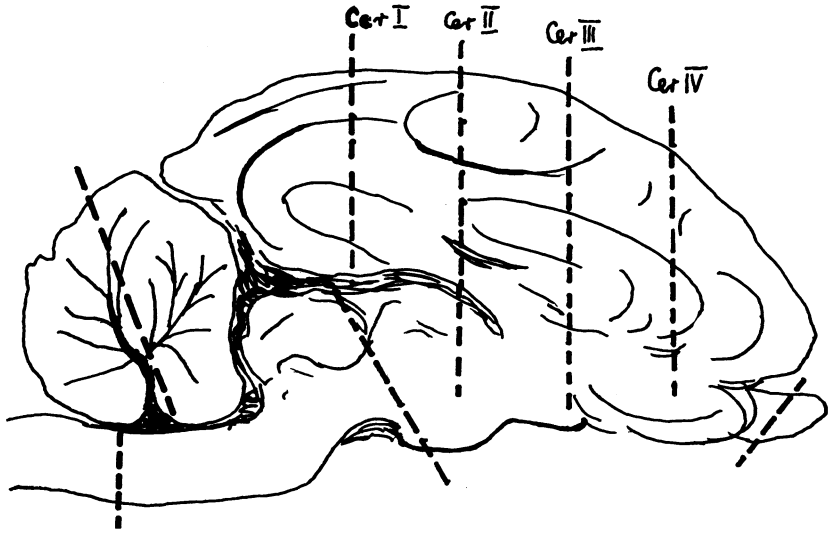

Fig. 1. Localization of (transversal) sections of the brain.

Part of CNS	Number of specimens
Brain hemispheres and adjacent parts	4
Brain stem	1
Bulbus olfactorius	1
Cerebellum	1
Medulla oblongata	1
Spinal cord, cervical	1
„ „ , thoracic	1
„ „ , lumbar	1

Specimens were also taken from the nasal turbinates, lungs, liver, spleen, kidneys, heart, and gluteal musculature. Tissues were fixed in 10 per cent formalin and embedded in paraffin. The sections were stained with haematoxylin and eosin.

RESULTS

The lesions of the CNS can be characterized as a non-purulent meningitis and encephalomyelitis, the latter principally affec-

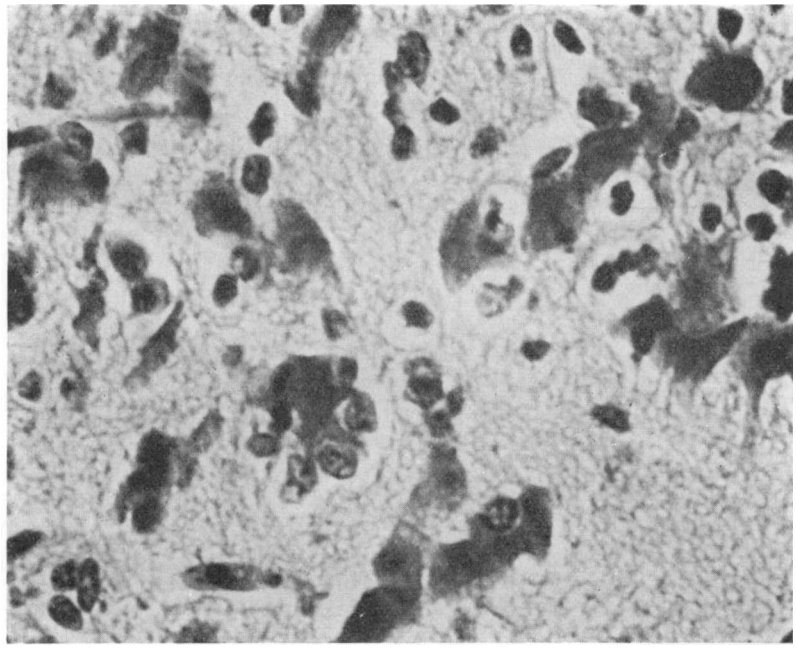

Fig. 2. Increase of glia cells and neuronophagia in the superficial layer of pyramidal cells of the cerabral cortex. Exp. inf. with strain V26. Magnif. 830 ×.

ting the grey matter. The changes consisted of perivascular round cell cuffs and gliosis as well as hyperaemia and haemorrhages in various parts of the brain and spinal cord. Some areas showed changes more frequently than others and the lesions within a certain area usually showed about the same picture from case to case. For this reason the description will be confined to such areas and the changes more or less typical thereof.

In the cerebral cortex there were foci of gliosis superficially in the layer of small pyramidal cells. The nerve cells often

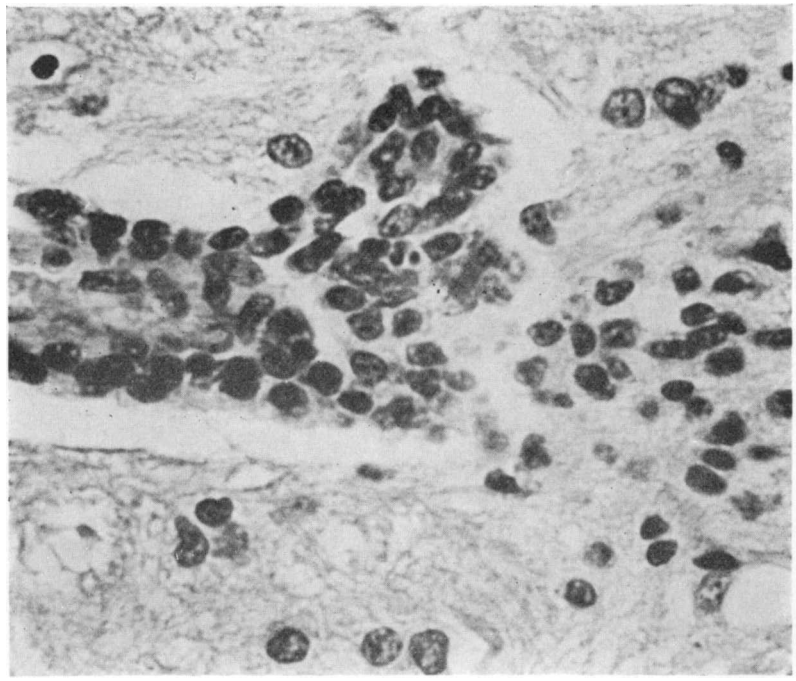

Fig. 3. Perivascular cuffing and glia reaction outside the vessel. Medulla oblongata. Exp. inf. with strain N7. Magnif. 830 ×.

appeared shrunken and signs of neuronophagia were not rare (Fig. 2). In some foci there ware no pyramidal cells left between the glial elements. Perivascular cuffs also occurred in the cerebral cortex but were less common than in the deeper parts of the brain *e. g.* corpus striatum and the diencephalon. They had the usual appearance of lymphoid cells within the perivascular space. In some instances there was a glial reaction outside that space. The olfactory bulb appeared normal in most cases.

In the diencephalon and mesencephalon changes were not common. Perivascular cuffs were occasionally observed, mainly in the basal parts. Degeneration of nerve cells and accompanying gliosis were comparatievly rare findings.

The rhombencephalon was affected in many cases. Perivascular cuffs were more frequent in the pons than in the cerebellum while gliosis was prevalent in the latter. A typical site was the layer of Purkinje cells. These cells were shrunken and the molecular layer immediately above showed rarefication and considerable accumulations of glia cells. In a few cases there was some

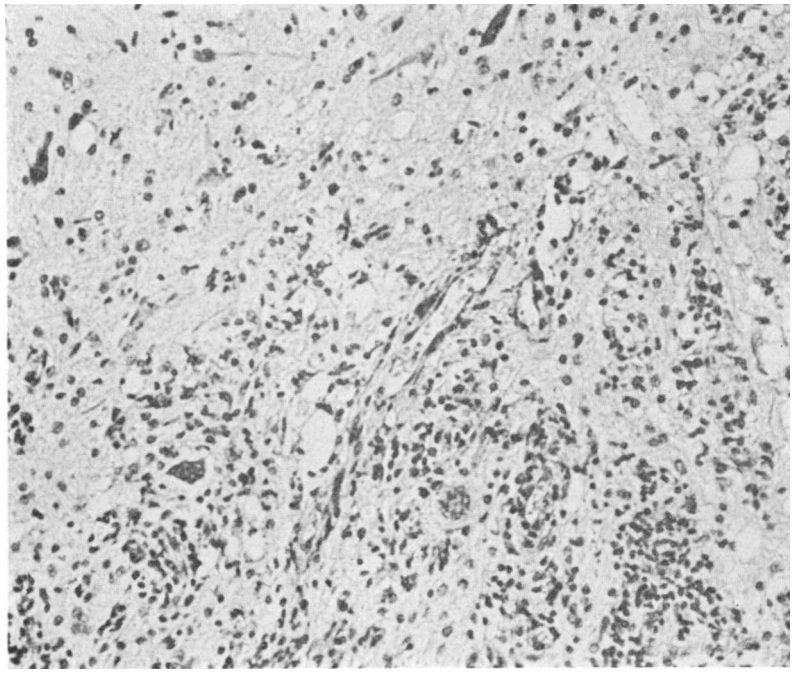

Fig. 4. Glial and vascular reaction in ventral grey column and adjacent white matter of cervical spinal cord. Exp. inf. with strain N7. Magnif. 207 ×.

demyelinization of the medullary lamellas and a proliferation of neuroglia as well as a moderate mesenchymal reaction.

The medulla oblongata was frequently the site of perivascular cuffs mainly in the marginal parts (Fig. 3), and glial reactions in the central and dorsal parts. Degeneration of nerve cells and neuronophagia were encountered within some glial foci.

Changes in the spinal cord were quite common and all parts could be affected with only a slight prevalence for the lumbar region. The characteristic lesion was a destruction of nerve cells in the pars intermedia of the grey matter and down into the ventral grey column with accompanying proliferation of glia cells, and a more or less marked mesenchymal reaction (Fig. 4), sometimes with perivascular cuffs. The white matter was affected only in spinal cords that also showed changes in the grey matter. The lesions appeared as glial foci and perivascular cuffs. In a few cases the spinal cord lesions were severe with a malacia-like

picture in the grey matter and demyelinization and micro- and macrogliosis in the adjacent part of the white matter.

There was no substantial difference regarding the changes in the CNS of pigs infected with different virus strains, with the possible exception of the pigs infected with strain S 159. Here the changes were less severe than in the other experiments.

Only a few of the experimental pigs exhibited signs of a non-purulent leptomenigitis with slight infiltration of lymphoid cells.

Except for the pneumonitis, which was described in piglets inoculated with S 180/4 (10), no significent changes were observed in other tissues than CNS.

DISCUSSION

The changes of the CNS observed in the present material have much in common with those caused by various strains of Teschen virus and by other enteroviruses, which are distinct from the Teschen virus. The CNS changes at Teschen disease (4, 7) can be summarized as a diffuse, nonsuppurative encephalomyelitis. The lesions are most frequent in the grey matter and are marked in the cerebellum.

At Talfan disease similar changes were observed (5) but here numerous lesions in the white matter were also present. This was supposed to indicate a separate etiology but later work (3) showed Talfan disease to be a mild form of Teschen disease. The identity of the diseases was demonstrated serologically (2). Similarly, because CNS lesions of the benign enzootic paresis in Denmark were found to be less extensive and massive than those of Teschen disease, it was concluded that the diseases had a different etiology (14). However, the identity between the benign enzootic paresis and Teschen-Talfan disease can be accepted as very probable (2).

The lesions caused by enteroviruses, which are serologically separate from Teschen virus, in similarity to Teschen disease are characterized by a polioencephalomyelitis with peri- and extravascular infiltrations of monoclear cells, degeneration of the ganglions, and gliosis. These changes were obtained in colostrum-deprived piglets. *Betts* (1) concluded that the entero-virus strains T 80 and T 52A did not involve the cerebellum as severly as the agents of the Teschen-Talfan disease.

Although we saw less changes in the olfactory bulb and more changes in the cerebral cortex than some other investigators, there is little reason to believe that this difference should be of diagnostic value. One should be very cautious in attributing the variation of the histopathological picture to strain specificity, since many other factors, *e. g.* immunological conditions and the intensity and duration of the infection may play a major role.

The conformity in the changes of pigs infected with the Teschen strain and of those infected with other strains in the present study would rather support the view that many strains of porcine enterovirus are able to cause an unspecific nonpurulent encephalomyelitis. The observation that apparently healthy pigs may exhibit signs of a nonpurulent encephalomyelitis supports the view that the disease like other viral infections may have a subclinical course.

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SUMMARY

The histopathological changes of the central nervous system in experimental infection of colostrum-deprived piglets with porcine enteroviruses, isolated in Sweden, are described. There was no marked difference in the type of nonpurulent encephalomyelitis caused by a Teschen strain and other strains of porcine enterovirus. A slight affection of the central nervous system may be present without causing clinical symptoms.

ZUSAMMENFASSUNG

Histologische Veränderungen im zentralen Nervensystem der Schweine geimpft mit einige Enteroviren.

Die histopatologischen Veränderungen im zentralen Nervensystem bei experimentell geimpften, ohne Kolostrum aufgezogenen Ferkeln mit in Schweden isolierten Schweineenteroviren wurden beschrieben. Es wurde kein ausgeprägter Unterschied zwischen der nicht-eitrigen Encephalomyelitis verursacht durch einen Teschen-Stam und anderen Schweineenterovirusstämme, beobachtet. Eine leichte Affektion kann in dem zentralen Nervensystem ohne klinische Symptome vorliegen.

SAMMANFATTNING

Histologiska förändringar i centrala nervsystemet hos grisar inokulerade med några enterovirus.

De histopatologiska förändringarna i centrala nervsystemet vid experimentell infektion med svineenterovirus, isolerade i Sverige har beskrivits. Försöksdjur var smågrisar uppfödda utan kolostrum. Någon påtaglig skillnad i typen av nonpurulent encephalomyelit orsakad av en Teschen-stam och andra enterovirusstammar kunde ej iakttagas. En lätt affektion av centrala nervsystemet kan föreligga utan kliniska symtom.

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