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CONGENITAL INTERNAL HYDROCEPHALUS
AND HYDRANENCEPHALY
IN CATTLE

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ABSTRACT

INTRODUCTION

Congenital defects are abnormalities of structure or function present at birth. Most are characterized by death, disfigurement or impaired vitality at birth; some are manifested in later life. Defective genes and adverse environmental factors affecting the fetus during critical periods of development may induce congenital malformations.

The early history of the study and elucidation of congenital defects' etiologies (teratology) in man was recently reviewed by Woollam (1978). The inherent mystery of human congenital defects has prompted intense research and the development of a highly specialized field of medicine. For several reasons, a comparable field in veterinary medicine has suffered an agonizingly slow course. This complex animal science necessitates a thorough knowledge of comparative embryology, neonatal pathology, teratology, and genetics of numerous species. Much of the early work has been published in a variety of European journals, and until recently, studies written in English were minimal. Periodicals, such as the Bibliography on Spontaneous Defects in Mammals (WHO 1973-1979) and the Bibliography of Comparative Neuropathology (WHO 1966-1979), have provided monumental assistance. Nevertheless, Leipold et al (1972) pointed out major deficiencies in reports of bovine congenital defects: (1) inadequate information, ie. too few cases reported; (2) inadequate pathological investigations and descriptions by husbandry specialists and geneticists; (3) inadequate and inappropriate genetic analysis by veterinarians and pathologists; and (4) failure to integrate findings contributing to an understanding of the underlying basic processes of embryology, pathology, and genetics.

Genetic congenital diseases in animals suffer reduced priority compared to those of infectious origin. Leipold (1978a) pointed out that while direct losses to congenital defects are fewer than losses to nutritional or infectious disease, defects may cause considerable economic loss when they are realized in repeated generations. Reduced parentage value of purebred stock carrying defective genes has prompted most breed associations to develop guidelines for reporting defects, and testing sires with defective progeny.

Compared to other body systems, little is known about congenital defects of the central nervous system (CNS) of domestic animals. Early work by Dobberstein (1938), Frauchiger and Fankhauser (1957), Innes and Saunders (1957, 1962), and Koch et al (1957) and a review of the literature through 1965 by Kalter (1968) provide a sound base for expansion. As with all congenital defects, those of the CNS may occur singularly, or in combination with other body system defects (Herzog 1971; Cravero et al 1976; Cho et al 1978).

Causes of congenital defects of the CNS are poorly understood. An excellent overview of intrinsic and extrinsic components and their interrelationships in various species was compiled by Done (1975). Intrinsic components (hereditary factors) are determined by mutant genes, chromosomal aberrations, and improper gene dosage. Extrinsic components (environmental factors) include: infectious agents, toxins, maternal hyperthermia, ionizing radiation, nutritional imbalances, trauma, and hormones (Gruenwald 1947; Kalter and Warkany 1959; Willier et al 1955). Of this group, infectious agents, principally viruses, were most frequently documented: blue-tongue (Osburn et al 1971a,b), Akabane (Inaba et al 1975), bovine

virus diarrhea-mucosal disease (Scott et al 1973) and border disease (Terlecki 1977).

An exhaustive review of bovine CNS congenital defects was published by Cho and Leipold (1977b) covering the literature through 1976. Known hereditary defects are few. Most are simple autosomal recessives. A checklist of hereditary defects of the CNS in various species was compiled by Saunders (1952). General considerations and specific examples of genetic defects in cattle were presented by Herschler et al (1962), Leipold et al (1972), Jolly and Leipold (1973), Jolly and Thompson (1976), Leipold and Schalles (1977), and Leipold (1978a).

The frequency of bovine congenital defects varies with breed, herd, geographic location, year, and sampling technique (Priester et al 1970; Leipold et al 1972). The National Academy of Science Subcommittee on Prenatal and Postnatal Mortality in Cattle records annual losses of 14-36% from all causes of neonatal mortality. In a review of 7 studies. Cho and Leipold (1977b) reported that 0.2-0.36% of all newborn calves have congenital defects. CNS malformations accounted for 12.1% of 1,275 congenitally defective calves in Kansas (Cho and Leipold 1977b) and 21.6% of 2,293 defective calves in Germany (Finger et al, 1970).

No satisfactory classification has been established for congenital diseases of the CNS. A combination of anatomical and pathological criteria were utilized by Cho and Leipold (1977b), in their review of bovine congenital CNS diseases. Genetic diseases where the modes of inheritance are unknown and morphologic studies are inadequate are nearly impossible to classify. Similarities between genetic and environmentally-induced defects present additional classification problems (Leipold 1978b). When primary defects are known, eg. achondroplasia,

classification according to resultant secondary defects, eg. hydrocephalus, must be avoided.

The objectives of this study were to:

1. Study field cases of suspected hereditary hydrocephalus in Horned Hereford cattle and categorize pathologic alterations for use as diagnostic criteria.

2. Study and characterize the morphologic aspects of field cases of congenital hydrocephalus and hydranencephaly in cattle.

I. REVIEW OF THE LITERATURE

A. HYDROCEPHALUS

Hydrocephalus is defined as excessive fluid accumulation within the cranial cavity. It is present at birth or as a consequence of other abnormalities present at birth in the congenital form or may be acquired in later life. Accumulation of fluid may occur within the subarachnoid space (external hydrocephalus); within the ventricular system (internal hydrocephalus, non-communicating, or obstructive hydrocephalus); or in both locations (communicating hydrocephalus).

According to Russell (1949) Vesalius appears to have given the first clear account of internal hydrocephalus in man in 1514 followed by Morgagni's confirmation that fluid accumulates within the ventricles, some 200 years later. Today bovine hydrocephalus occurs widely and is the most common and best documented central nervous system (CNS) defect in cattle (Leech et al 1978). Virtually all major beef and dairy breeds are affected.

Primary hereditary hydrocephalic conditions occur in several breeds, generally as simple autosomal recessive traits and secondary to other inherited disorders (Table I). Abnormal karyotypes in calves with hydrocephalus and other syndromes in which hydrocephalus was a component indicate chromosomal aberrations may be responsible in some cases (Table II).

In Hereford cattle internal hydrocephalus occurs as an autosomal recessive (Blackwell et al 1959; Baker et al 1960, 1961; Hadlow 1962; Rhodes et al 1962; Belling and Holland 1962; Urman and Grace 1964; Cho and Leipold 1977b). Calves were dead at birth or born weak and died shortly thereafter. Weak calves were said to elicit a characteristic bawl, hence the term "bawlers" applied by stockmen. Calves were

TABLE I

Congenital hydrocephalus as an apparent primary, familial
anomaly or secondary to other familial anomalies

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
(ANGUS (SECONDARY))					
2 days		Obstruction 4th ventricular lateral aperture	1	Internal hydrocephalus associated with cystic, "jelly-like" masses occluding the 4th ventricular lateral aperture and chondrodystrophy	Greene <u>et al</u> (1974a)
5 months 7 months	M		2	Internal hydrocephalus, moderate and severe, associated with mannosidosis. Hereditary, single autosomal recessive	Leipold <u>et al</u> (1979)
AYRSHIRE (PRIMARY)					
Fetus 240 days or term calves				Internal hydrocephalus associated with calvarial enlargement at birth and ab- normalities of the cerebellum and corpora quadrigemina. Simple autosomal recessive inheritance hypothesized	Huston <u>et al</u> (1961)
ARYSHIRE (SECONDARY)					
			2	Internal hydrocephalus associated with enlarged cranium and high levels of cop- per and atypical proteins in various tis- sues. Hereditary, complex-multiple gene sites	Nuss <u>et al</u> (1967)
CHAROLAIS (PRIMARY)					
10 hours 12 hours 6 hours		Aqueduct stenosis	3	Internal hydrocephalus associated with aqueduct stenosis and patent ductus arteriosus in the 1st calf, aqueduct stenosis and enteritis in the 2nd calf and stenotic 3rd ventricle in the 3rd calf. Familial pattern	Greene <u>et al</u> (1974a)
CHAROLAIS (SECONDARY)					
11 days	M		1	Internal hydrocephalus associated with slight anterior bimalic arthrogryposis	Leipold <u>et al</u> (1969)
			1	Internal hydrocephalus associated with tetramelic arthrogryposis, hypermobility of the carpalphalangeal and metatarsophal- geal joints and palatoschisis	Leipold <u>et al</u> (1973)
DANISH (SDM) (SECONDARY)					
			1	Internal hydrocephalus associated with acortieriasis	Hansen (1974)
DEXTER (SECONDARY)					
Fetus 6-7 months			1	Internal hydrocephalus associated with achondroplasia, hydroamnios and fetal anasarca	Craw (1923-24)
FRIESIAN (PRIMARY)					
New born			6	(Holstein) Internal hydrocephalus assoc- iated with dilated lateral ventricle communication through the septum palluci- dum, normal 3rd ventricle and normal calvaria except in one calf	Gilman (1956)

TABLE I CONT'D

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
FRIESIAN (SECONDARY)					
New born	M/F		5	(Holstein) Internal hydrocephalus associated with enlarged calvaria, dysplasia of the foramen magnum, shortened humeri and femurs, tetramelic arthrogryposis and papilledema. Hereditary, autosomal recessive	Cole and Moors (1942)
Fetus 346 days gestation	M		1	(Holstein) Internal hydrocephalus associated with enlarged calvarium, meningocele, hypoplastic pituitary, small immature thyroids and prolonged gestation	Huston and Gier (1958)
Fetus 8 months	F	Aqueduct forking	1	(Black Pied) Internal hydrocephalus associated with forking of the aqueduct and acroteriasis	Herzog (1971)
Fetus 8 months	M	Aqueduct stenosis	1	(Black Pied) Internal hydrocephalus associated with agenesis of the corpus callosum, stenosis of the aqueduct and acroteriasis	" "
New born	F	Aqueduct forking	1	(Black Pied) Internal hydrocephalus associated with forking of the aqueduct and acroteriasis	" "
			14	(Black Pied) Internal hydrocephalus associated with chondrodysplasia	Tücking (1976)
			5	(Red Pied) Internal hydrocephalus associated with chondrodysplasia	" "
GALLOWAY (SECONDARY)					
New born	F-3 M-2	Prolapsed Cerebellar vermis	5	Internal hydrocephalus associated with prolapse of the cerebellar vermis, cranioschisis and meningocele, non-fusion of the Mullerian ducts in females and bilateral cryptorchidism in males, and agenesis or shortening of the tibia. Hereditary, simple autosomal recessive	Ojo <u>et al</u> (1974)
GUERNSEY (SECONDARY)					
Fetus			14	Internal hydrocephalus associated with hypotrichosis, adeno-hypophyseal aplasia and prolonged gestation. Hereditary, simple autosomal recessive	Kennedy <u>et al</u> (1957)
HEREFORD (PRIMARY)					
Dead at birth or shortly thereafter	M/F		19	Internal hydrocephalus associated with small body size, calvarial enlargement, incompletely developed teeth, partial occlusion of supraoptic foramina with a number of small ones and occasionally excessive amniotic fluid.	Blackwell <u>et al</u> (1959)
Dead at birth or shortly thereafter	M/F		73	Internal hydrocephalus associated with calvarial enlargement, enlargement of the choroid plexus, microphthalmia, light lower jaw tapering to a narrow muzzle, light birth weight and inability to stand. Hereditary, autosomal recessive	Baker <u>et al</u> (1960) " " (1961)

TABLE I CONT'D

AGE	SEX	ETIOLOGY	NUMBER	DESCRIPTION	REFERENCE
HEREFORD (PRIMARY) CONT'D					
Dead at birth or shortly thereafter				Internal hydrocephalus associated with dilatation of the lateral and 3rd ventricles, patent fontanelle and enlarged calvaria	Belling and Holland (1962)
Dead at birth or shortly thereafter		Mesencephalon malformation	12	Internal hydrocephalus associated with calvarial enlargement, narrowing of the aqueduct of Sylvius due to deformation of the mesencephalon, cerebellar hypoplasia, microphthalmia and generalized primary muscular dystrophy	Urman and Grace (1964)
Dead at birth or within 5 days			21	Hereford Syndrome I - (2) calves internal hydrocephalus associated with domed calvaria, microphthalmia, cerebellar hypoplasia and myopathy; (5) calves internal hydrocephalus associated with domed calvaria, microphthalmia and cerebellar hypoplasia, (patent ductus arteriosus in 1 calf); (1) calf internal hydrocephalus associated with domed calvarium, microphthalmia and myopathy; (2) calves internal hydrocephalus associated with domed calvaria, cerebellar hypoplasia and myopathy; (3) calves internal hydrocephalus associated with domed calvaria and microphthalmia, (bilateral cryptorchidism and patent foramen ovale observed in 1 calf and patent ductus arteriosus in another); (3) calves internal hydrocephalus associated with domed calvaria and cerebellar hypoplasia, (tetralogy of Fallot observed in 1 calf)	Greene <i>et al</i> (1974a)
Dead at birth or within 48 hours except one which lived for 11 months		Aqueduct stenosis	11	Hereford Syndrome II - (8) calves internal hydrocephalus associated with normal calvaria, dorsal kinking of the mesencephalon, aqueduct stenosis and cerebellar hypoplasia, (cystic optic nerves, suppurative meningitis and patent ductus arteriosus were observed in 3 calves); (3) calves internal hydrocephalus associated with dorsal kinking of the mesencephalon, mild cerebellar hypoplasia and microphthalmia	" " "
HEREFORD (SECONDARY)					
10 days			1	Internal hydrocephalus associated with chondrodystrophy and arthrogryposis	Johnson <i>et al</i> (1950)
5 days or less			4	Internal hydrocephalus of varying degrees associated with chondrodystrophy	Pahnish <i>et al</i> (1955)
				Internal hydrocephalus associated with short headed (snorter) dwarfism	Julian <i>et al</i> (1959)
Born dead			2	Internal hydrocephalus associated with domed calvaria and chondrodystrophy	Greene <i>et al</i> (1974a)
			1	Internal hydrocephalus associated with chondrodystrophy, polysyndactyly and metaphyseal dysplasia	" " "

TABLE I CONT'D

AGE	SEX	ETIOLOGY	NUMBER	DESCRIPTION	REFERENCE
HEREFORD (SECONDARY) CONT'D					
Born dead			1	Internal hydrocephalus associated with domed calvarium, chondrodystrophy, partial cyclops, right macrophthalmia, left microphthalmia, aprosopia, cheiloschisis and protruding tongue	Greene <u>et al</u> (1974a)
Fetus (term)			1	Internal hydrocephalus associated with proportional dwarfism (wt 4 kg), thoracic kyphosis, tetramelic arthrogryposis, cardiac septal defect and generalizing myopathy	" " "
Adult	F		3	Internal hydrocephalus associated with incomplete albinism and coloboma	" " "
JERSEY (SECONDARY)					
Fetus (term)	M		1	Internal hydrocephalus associated with agnathia	Ely <u>et al</u> (1939)
LIMOUSINE (PRIMARY)					
				Internal hydrocephalus associated with cardiopathy	Lauvergne and Pavaux (1969)
MAINE-ANJOU (SECONDARY)					
6 months			1	Internal hydrocephalus associated with proportional dwarfism	Greene <u>et al</u> (1974a)
MARCHE (PRIMARY)					
New born	M/F		18	Internal hydrocephalus associated with enlarged calvaria and limb malformation in (9) calves. Hereditary, autosomal recessive	Giannocci (1952) Polidori (1952)
RUSSIAN SWAN CATTLE (PRIMARY)					
New born	M/F		27	Internal hydrocephalus	Makaryan (1977)
SHORTHORN (PRIMARY)					
5 months 6 months	M(c) F	Aqueduct stenosis	1	Internal hydrocephalus associated with dilation of the lateral and 3rd ventricles and Sylvian aqueduct, perivascular lymphocytic cuffing around the aqueduct, multiple ocular lesions, normal calvaria and white coat color	Leipold <u>et al</u> (1971)
Born dead to 6 months	M F	Aqueduct stenosis	4 2	Internal hydrocephalus associated with aqueduct stenosis, retinal dysplasia, microphthalmia and white coat color	Green and Leipold (1974)
Calves adult	F	Aqueduct stenosis	10 1	Internal hydrocephalus associated with stenosis of the aqueduct, microphthalmia, retinal dysplasia and white coat color	Greene <u>et al</u> (1974a)
2 days	F		1	Internal hydrocephalus associated with dilation of the lateral 3rd and 4th ventricles and the Sylvian aqueduct, normal calvarium, multiple ocular defects and white coat color	Leipold <u>et al</u> (1974)

TABLE I CONT'D

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
SHORTHORN (PRIMARY) CONT'D					
5 years	F	Aqueduct	2	Internal hydrocephalus associated with	Greene <u>et al</u> (1978)
5 years	M	stenosis	1	dilation of the lateral and 3rd ventricles, stenosis of the Sylvian aqueduct, microphthalmia, retinal dysplasia, normal calvaria and white coat color	
SIMMENTAL (SECONDARY)					
Born dead	F	Aqueduct obstruction (septum)	1	Internal hydrocephalus associated with subdivision of the aqueduct and dolichostenomelia	Herzog (1971)
			10	Internal hydrocephalus associated with chondrodystrophy	Tücking (1976)
UNSTATED BREED (SECONDARY)					
Born dead			1	Hydrocephalus associated with a "bulldog" head and platoschisis	Brüggermann (1951)
			1	(Crossbred) Internal hydrocephalus associated with chondrodysplasia	Tücking (1976)
3 days			1	Internal hydrocephalus associated with prolonged gestation (354 days), enlarged calvarium, diaphragmatic hernia and hypophyseal aplasia	Leroy (1977)

TABLE II

Congenital hydrocephalus associated with chromosomal abnormalities

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
FRIESIAN					
			1	(Black Pied) Internal hydrocephalus associated with anophthalmia and ditetraploid mosaicism	Herzog and Höhn (1971)
			1	(Black Pied) Internal hydrocephalus associated with hydromyelia and ditetraploid mosaicism	" "
			1	(Black Pied) Internal hydrocephalus associated with exophthalmia and ditetraploid mosaicism	" "
			1	(Black Pied) Internal hydrocephalus associated with optic nerve dysplasia, brachyuria and ditetraploid mosaicism	" "
			1	(Black Pied) Internal hydrocephalus associated with dwarfism, heart defect and trisomy 17	Rieck <i>et al</i> (1979)

TABLE II CONT'D

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
				GERMAN RED	
			1	Internal hydrocephalus associated with atresia ani and anuria and ditetraploid mosaicism	Herzog and Höhn (1971)
				SIMMENTAL	
			1	Internal hydrocephalus associated with Arnold-Chiari malformation and ditetra- ploid mosaicism	Herzog and Höhn (1971)

frequently premature and undersized with enlarged craniums, although not always.

Excessive amniotic fluid was occasionally observed. Eyes and orbits were reduced in size and retinas were dysplastic. Generalized myodysplasia was present that frequently could be detected grossly as pale watery musculature, especially the quadriceps. There was dilation of lateral and 3rd ventricles and elongation and compression of the mesencephalon with dorsal kinking at the corpora quadrigemina. The aqueduct was stenotic and forking occurred. Cerebellums were hypoplastic and occasionally compressed. Studies indicated patent aqueducts, normal cerebral spinal fluid (CSF) pressure, and more than 30-fold elevation of serum enzymes (SGOT, SGPT, LDH, MDH and aldolase) in hydrocephalic calves. Greene et al (1974a) described two conditions in Hereford cattle designated "Syndromes 1 and 2". Syndrome 1 was characterized by stillbirth or death within 5 days of age. Calves were weak, could not stand and had deformed heads. There was moderate to marked internal hydrocephalus with no observed obstruction to CSF flow. Cerebellar hypoplasia, microphthalmia and myopathy characterized by pale skeletal muscles were present in various combinations. Eleven calves with Syndrome 2 were stillborn or died during the first 48 hours of life. However, one calf lived 11 months. A single calf bawled continuously while others were dumb. Syndrome 2 calves had normal craniums, dorsal kinking of the mesencephalon causing aqueduct stenosis and cerebellar hypoplasia. Microphthalmia was occasionally observed but not myopathy. Hereford Syndromes 1 and 2 had genetic implications. Syndrome 1 had all the features of the autosomal recessive trait reported by Blackwell et al

(1959) and morphologically resembled the autosomal recessive trait described by Baker et al (1960, 1961) and Urman and Grace (1964).

Internal hydrocephalus associated with or secondary to other known and suspected hereditary conditions in Herefords include: three incomplete-albino cows with moderate hydrocephalus and coloboma (Greene et al 1974a); internal hydrocephalus associated with chondrodystrophy and arthrogryposis (Johnson et al 1950); hydrocephalus of varying degrees associated with chondrodystrophy in four Hereford calves (Pahnish et al 1955); internal hydrocephalus associated with short headed (snorter) dwarfism (Julian et al 1959); internal hydrocephalus associated with domed cranium and chondrodystrophy (Greene et al 1974a); internal hydrocephalus associated with domed cranium chondrodystrophy, partial cyclops, right macrophthalmia, left microphthalmia, aprosopia, cheiloschisis and protruding tongue (Greene et al 1974a); and internal hydrocephalus associated with proportional dwarfism (4 kg), thoracic kypypsis, tetramelic arthrogryposis, cardiac septal defect and generalized myopathy (Greene et al 1974a). Albinism was reported to occur in association with dwarfism in Herefords with cranial conformations suggestive of hydrocephalus, although no necropsy was performed (Hafez et al 1958).

Hereditary hydrocephalus occurred in Shorthorn cattle in association with white coat color (Leipold et al 1971; Leipold et al 1974; Greene et al 1974a; Greene and Leipold 1974; Greene et al 1978). From breeding trial results, a simple autosomal recessive trait was determined to be the cause. Adult cattle and resulting progeny had normal craniums, moderate internal hydrocephalus, aqueduct stenosis, and retinal dysplasia often in conjunction with microphthalmia. Chronic non-progressive hydrocephalus was

present in older cattle. Hydrocephalic to hydrocephalic matings produced some lethal calves. Karyotypes were normal although methods employed were not capable of detecting single abnormal genes.

Primary internal hydrocephalus has been described by Gilman (1956) in six Holstein-Friesian calves attributed to a simple autosomal recessive gene. The condition was lethal shortly after birth. Craniums were normal in all calves, except one with markedly dilated lateral ventricles with communication through the septum pellicidum. Dilation of the third ventricle was not noted.

Hydrocephalus secondary to chondrodysplasia was reported in Friesian breeds (Tücking 1976). Hydrocephalus secondary to acroteriasis congenita in three German black pied calves was observed by Herzog (1971). Abortion at 8 months gestation or stillbirth occurred in all cases. Internal hydrocephalus was associated with forking of the aqueduct and, in a single calf, agenesis of the corpus callosum. Cole and Moore (1942) reported lethal internal hydrocephalus associated with enlarged craniums, shortened humeri and femurs, tetramelic arthrogryposis, and dysplasia of the foramen magnum. This condition was thought to be due to a simple autosomal recessive gene for bony abnormalities with hydrocephalus the result of partial or complete blockage of the foramens of Magendie and Luschka.

Primary genetic hydrocephalus has not been reported in Angus calves. Ojo et al (1975) reported hydrocephalus in Angus calves with a facial-digital syndrome. Internal hydrocephalus has been found associated with mannosidosis (Leipold et al 1979).

Greene et al (1974a) reported three cases of internal hydrocephalus in Charolais cattle with a familial pattern of occurrence. Hydrocephalus

was due to stenosis of the aqueduct. Hydrocephalus has also occasionally been noted secondary to the arthrogryposis, cleft palate, and spinal dysraphism complex in the Charolais breed, inherited as a incomplete dominant (Leipold et al 1969, 1973).

Hereditary hydrocephalus as a primary condition has not been reported in Jerseys. Ely et al (1939) reported a single case of mild internal hydrocephalus in a group of four agnathic calves.

Makaryan (1977) reported 27 cases of hereditary hydrocephalus in Russian Swan cattle. Calves were usually born alive and survived only a few days. One calf lived 105 days.

In the Ayrshire breed, Nuss et al (1967) described inherited hydrocephalus in calves with copper and free radical accumulation in various tissue, resembling Wilson's disease in man. Hydrocephalus was observed in association with cardiopathy in Limousine cattle as a heritable defect (Lauvergne and Pavaux 1969). In Galloway cattle hydrocephalus was observed associated with tibial hemimelia, prolapse of the cerebellar vermis, cranioschisis, and meningocele (Ojo et al 1974, Leipold et al 1978).

In Maine-Anjou cattle hydrocephalus was observed in a proportional dwarf (Greene et al 1974a). Hydrocephalus in Marche cattle was reported by Giannotti (1952), presumably due to a simple recessive gene. Hydrocephalus in association with dolichostenomelia and chondrodysplasia has been recorded in Simmental cattle (Herzog 1971; Tücking 1976).

The influence of environmental factors in hydrocephalus and other malformations is difficult to ascertain and poorly understood. Several infectious agents, nutritional deficiencies and excesses, and other chemicals and physical factors have been reported to cause hydrocephalus in animals (Gruenwald 1947; Willier et al 1955; Kalter and Warkany 1959;

Elizan and Fabiyi 1970; Catalano and Sever 1971; Sever 1971; Done 1975, 1978). Most reports involved laboratory animals. Extrapolation of these findings to man and other species, while useful in elucidating specific etiologies, is not without its hazards (Barry and Barlow 1976). Interspecies differences in metabolism (ruminant vs carnivore) and relative differences in maturation of specific organ systems, provide sources of error. Table III summarizes reported cases of hydrocephalus in cattle of environmental and unknown causes.

Viral agents as the cause of hydrocephalus in cattle are largely undocumented with exception of bovine viral diarrhea - mucosal disease virus (BVD-MD) (Horvath 1976; Allen 1977). Consistent findings in the two reports were hydrocephalus and cerebellar hypoplasia, usually without malformation of the cranium. The teratogenic effect of BVD-MD in the bovine fetus are multiple, with a predilection for the CNS (Brown et al (1975).

Infectious agents have been found to cause ependymal damage and aqueduct stenosis leading to hydrocephalus. Experimental congenital hydrocephalus produced in monkeys (London et al 1979) and hamsters (Kilham and Margolis 1975) with mumps virus; in hamsters with parainfluenza type 2 virus (Margolis and Kilham 1977); and mice, ferrets, hamsters and rats with reovirus type 1 (Masters et al 1977; Margolis and Kilham 1969 suggested damage to the ependyma and subsequent stenosis of the aqueduct underwent repair to such a degree that histological evidence was completely lacking. Similar observations have been made in neonatal laboratory animals with mycoplasma (Kohn et al 1977), mumps virus (Johnson et al 1967), influenza A virus (Johnson and Johnson 1969), reovirus (Nielsen

TABLE III

Congenital hydrocephalus due to
environmental and unknown causes

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
ANGUS					
6 weeks	M	Medulloblastoma	1	Internal hydrocephalus (mild) associated with medulloblastoma continuous with the anterior portion of the cerebellum causing distortion of the brainstem and partial displacement of the cerebellum into the foramen magnum	Jolly and Alley (1969)
8 days		Aqueduct obstruction	1	Internal hydrocephalus associated with obstruction of the aqueduct	Greene <i>et al</i> (1974a)
		Intracranial cyst	1	Internal hydrocephalus associated with a meningeal cyst filling the caudal fossa and cerebellar aplasia	" " "
			5	Internal hydrocephalus (miscellaneous types). One calf had a meningocele, purulent meningitis, extreme microphthalmia and patent ductus arteriosus and another had cystic optic nerves, retinal dysplasia, high ventricular septal defect, dextro-position of the aorta, wry tail and melanosis of the rumenal serosal surface	" " "
			1	Internal hydrocephalus associated with spina bifida and syringomyelia	Cho and Leipold (1977b)
			6	Communicating internal hydrocephalus	Cho <i>et al</i> (1978)
AYRSHIRE					
Fetus (term)	F		1	Internal hydrocephalus associated with hydromyelia and scoliosis	Hughes (1952)
	M	Mesencephalon malformation, aqueduct stenosis	15	Internal hydrocephalus associated with lateral compression of the mesencephalon, vascular proliferation, overlying of the colliculi, aqueduct stenosis, cranial enlargement and exophthalmus	Barlow and Donald (1963)
	F		11	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with palatoschisis	Oksanen (1972)
			3	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with cardiac septal defect	" "
			7	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with brachygnathia inferior	" "
			2	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with brachygnathia superior	" "
			8	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with schistosomus reflexus	" "
	M		7	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with cryptorchidism	" "

TABLE III CONT'D

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
AYRSHIRE CONT'D					
			3	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with subcutaneous edema	Oksanen (1972)
			8	(Ayrshire or Finnish, breed distribution not stated). Hydrocephalus associated with scoliosis, kyphosis and lordosis	" "
BRAHMA					
1 year		Meningitis	1	(Brahma cross) Internal hydrocephalus with chronic, calcifying meningitis	Greene <u>et al</u> (1974a)
DURHAM					
8 weeks		Massa intermedia malformation	1	($\frac{1}{2}$ Durham, $\frac{1}{4}$ Jersey, $\frac{1}{4}$ Hereford) Internal hydrocephalus associated with fused thalami, absence of the pineal body, adenomatous overgrowth of eosinophils of the hypophysis, enlarged cranium and evidence of acromegaly. Note: Sire of the calf had wide spaced horns suggestive of hydrocephalus	Houck (1930)
FRIESIAN					
7 months	F		1	(Holstein) Internal hydrocephalus (unilateral, left) associated with deformation of the cranium and blindness	Sholl (1931)
Born dead	F		1	(Holstein) external hydrocephalus associated with meningoencephalocele and palatoschisis	Williams and Frost (1938)
1 day			1	(Holstein) Internal hydrocephalus associated with enlarged cranium and anophthalmia	Julian <u>et al</u> (1960)
3 months 8 months		4th ventricular lateral aperture obstruction (intracranial cyst)	2	(Holstein) Internal hydrocephalus associated with cystic dilation of the roof of the 3rd ventricle compressing the cerebellum and obstructing the lateral 4th ventricular aperture	Greene <u>et al</u> (1974a)
			6	(Holstein) Internal hydrocephalus (miscellaneous types) associated with marked cerebellar hypoplasia in two calves and microcystic degeneration of the cerebral cortex in a third calf	" " "
6 months		Meningitis	1	(Holstein) Internal hydrocephalus associated with focal chronic fibrosing meningitis	" " "
5 days		Meningitis	1	(Holstein) Internal hydrocephalus associated with suppurative meningitis and ependymitis, severe in the 4th ventricle	" " "
		Meningitis (Experimental kaolin induced)	5	(Holstein) Internal hydrocephalus associated with dilation of the entire ventricular system and meningitis. Additionally syringomyelia in two calves	Greene <u>et al</u> (1974b)

TABLE III CONT'D

AGE	SEX	ETIOLOGY	NUMBER	DESCRIPTION	REFERENCE
FRIESIAN CONT'D					
2 months			1	(Holstein) Internal hydrocephalus associated with meningocele, bilateral divergent strabismus and interventricular septal defect in the heart	Julian (1975)
4 days	F		1	(Holstein) Internal hydrocephalus (normotensive) associated with asymmetrical cranial enlargement, foramen magnum dysplasia and high ventricular septal defect with partially overriding aorta	Nelson <i>et al</i> (1976)
			2	(Holstein) Internal hydrocephalus associated with Arnold-Chiari malformation, spina bifida, syringomyelia and arthrogryposis. Additionally hydromyelia in one calf	Cho and Leipold (1977a)
			1	(Holstein) Internal hydrocephalus	Cho <i>et al</i> (1978)
Born dead	F	Aqueduct forking	1	(Black Pied) Internal hydrocephalus associated with forking of the aqueduct, palatoschisis and brachyuria	Herzog (1971)
2 days	M	Aqueduct forking	1	(Black Pied) Internal hydrocephalus associated with forking of the aqueduct, micropolygryria, microtia (unilateral) and campylognathia	" "
30 days	F	Aqueduct forking	1	(Black Pied) Internal hydrocephalus (unilateral, left) associated with an aqueduct forked into two small channels and thin cranial bone	" "
Born dead	M	Aqueduct malformation	1	(Black Pied) Internal hydrocephalus associated with doubling of the aqueduct (one on top of the other) and brachygnathia superior	" "
Born dead	F	Aqueduct stenosis	1	(Black Pied) Internal hydrocephalus associated with a small, folded aqueduct	" "
3 days	F	Aqueduct stenosis	1	(Black Pied) Internal hydrocephalus associated with narrowing of the aqueduct and abnormal gyri	" "
Born dead	M	Aqueduct stenosis	1	(Black Pied) Internal hydrocephalus associated with narrowing of the aqueduct, hydromyelia, neuromyodysplasia and arthrogryposis	" "
1 day	M	Aqueduct obstruction (septum)	1	(Black Pied) Internal hydrocephalus associated with subdivision of the aqueduct by loosely knit neuroglia, anophthalmia, persistent foramen ovale, atresia ani and anuria	" "
2 hours	F	Choroid plexus papilloma	1	(Black Pied) Communicating hydrocephalus associated with choroid plexus papilloma, polydactyly (right hind limb), patent foramen ovale, uterus didelphys and inguinal hernia	" "
13 days	M		1	(Black Pied) Internal hydrocephalus associated with cerebellar dysplasia, microphthalmia and unilateral microtia	" "

TABLE III CONT'D

AGE	SEX	ETIOLOGY	NUMBER	DESCRIPTION	REFERENCE
FRIESIAN CONT'D					
			3	(Black Pied) Internal hydrocephalus	Rieck <u>et al</u> (1979)
Born dead			1	(Red Pied) Hydrocephalus	Faix (1950)
Born dead	M	Aqueduct obstruction (vessel)	1	(Red Pied) Internal hydrocephalus (unilateral, right) associated with narrowed aqueduct by a vessel in the lumen, spina bifida, neuromyodysplasia, arthrogryposis and atresia ani	Herzog (1971)
1 day	F	Aqueduct forking	1	(Red Pied) Internal hydrocephalus associated with forking of the aqueduct, palatoschisis and brachyuria	" "
Born dead	F	Aqueduct forking	1	(Red Pied) Internal hydrocephalus associated with dorsal forking of the aqueduct and high ventricular septal defect (heart)	" "
			4	(Red Pied) Internal hydrocephalus	Rieck <u>et al</u> (1979)
GERMAN RED					
Born dead	M	Aqueduct forking	1	Internal hydrocephalus associated with forking of the aqueduct, palatoschisis and brachygnathia superior	Herzog (1971)
GUERNSEY					
			1	Internal hydrocephalus (Miscellaneous type)	Greene <u>et al</u> (1974a)
HEREFORD					
1 year	Mc	Medulloblastoma	1	Internal hydrocephalus associated with medulloblastoma which occupied much of the 3rd and 4th ventricles and aqueduct	Cordy (1953)
			1	Internal hydrocephalus associated with normal conformation, i.e. not chondrodysplastic	Pahnish <u>et al</u> (1955)
		Aqueduct forking	1	Internal hydrocephalus associated with forking (obstruction) of the aqueduct	Greene <u>et al</u> (1974a)
1 day		Aqueduct forking	1	Internal hydrocephalus associated with forking (obstruction) of the aqueduct, thoracic limb arthrogryposis, and myopathy	" " "
1 year		Aqueduct forking	1	Internal hydrocephalus associated with forking (obstruction) of the aqueduct, retinal dysplasia and retinitis pigmentosa	" " "
48 hours		Aqueduct stenosis	1	(Hereford crossbred) Internal hydrocephalus associated with stenotic aqueduct, arthrogryposis and microphthalmia	" " "
		Aqueduct stenosis	1	Internal hydrocephalus associated with stenosis of the aqueduct and moderate cerebellar hypoplasia (gross)	" " "

TABLE III CONT'D

AGE	SEX	ETIOLOGY	NUMBER	DESCRIPTION	REFERENCE
HEREFORD CONT'D					
Fetus (term)		Aqueduct stenosis	1	Internal hydrocephalus associated with stenosis of the aqueduct and myopathy	Greene <u>et al</u> (1974a)
1 hour		Aqueduct stenosis	1	Internal hydrocephalus associated with stenosis of the aqueduct, kyphoscoliosis, tetramelic arthrogryposis and myopathy	" " "
1 day		Aqueduct obstruction	1	Internal hydrocephalus associated with obstruction of the aqueduct	" " "
1 year		Aqueduct obstruction	1	Internal hydrocephalus associated with obstruction of the aqueduct, retinal dysplasia and retinitis pigmentosa	" " "
			1	Internal hydrocephalus associated with patent ductus arteriosus, palatoschisis and foreign body pneumonia	" " "
2 weeks		Meningitis	1	Internal hydrocephalus associated with subacute, diffuse meningitis	" " "
2 days			1	Internal hydrocephalus associated with bilateral glaucoma, exophthalmous, iridocyclitis and enlarged orbits	" " "
			5	Internal hydrocephalus associated with tetramelic arthrogryposis and myopathy	" " "
			10	Internal hydrocephalus (miscellaneous types)	" " "
			1	Internal hydrocephalus associated with spina bifida and syringomyelia	Cho and Leipold (1977a)
			1	Internal hydrocephalus associated with Arnold-Chiari malformation, spina bifida, syringomyelia, hydromyelia, diastematomyelia and arthrogryposis	" " "
			58	Internal hydrocephalus	Cho <u>et al</u> (1978)
	Mc	Glial hamartoma	1	Internal hydrocephalus associated with glial hamartoma of the aqueduct, high dombed skull and dysconjugate eye movements	Leech <u>et al</u> (1978)
JERSEY					
7 days			2	Internal hydrocephalus associated with lateral and 3rd ventricular dilation enlarged cranium, optic nerve degeneration, corneal opacity and enlarged thyroids. Both calves born premature to dams on experimental, low carotene ration	Bone (1953)
			1	Internal hydrocephalus (miscellaneous type)	Greene <u>et al</u> (1974a)
1 day	M	Aqueduct obstruction	1	Internal hydrocephalus associated with dorso-ventral compression of the cerebellum and brainstem and enlarged cranium	Chandna <u>et al</u> (1976)
1 week		Viral, BVD-MD suspected	8	Hydrocephalus associated with cerebellar hypoplasia	Allen (1977)

TABLE III CONT'D

<u>AGE</u>	<u>SEX</u>	<u>ETIOLOGY</u>	<u>NUMBER</u>	<u>DESCRIPTION</u>	<u>REFERENCE</u>
LINCOLN RED					
20 months	M	Aqueduct obstruction	1	Internal hydrocephalus associated with a parasitic cyst (<i>Coenurus cerebralis</i>) obstructing the aqueduct	Clegg and Bayliss (1958)
MURRAY GREY					
			1	Internal hydrocephalus (miscellaneous type)	Greene <u>et al</u> (1974a)
SHORTHORN					
96 hours		Aqueduct stenosis	1	Internal hydrocephalus associated with stenosis of the aqueduct	Greene <u>et al</u> (1974a)
1 day		Aqueduct obstruction	1	Internal hydrocephalus associated with a misshapen and obstructed aqueduct and retinitis pigmentosa	" " "
			1	Internal hydrocephalus associated with Arnold-Chiari malformation, spina bifida occulta, hydromyelia, syringomyelia and arthrogryposis	Cho and Leipold (1977a)
SIMMENTAL					
1 day	F	Aqueduct forking	1	Internal hydrocephalus associated with forking of the aqueduct and abdominal fissure	Herzog (1971)
2 months	M	Aqueduct obstruction	1	Internal hydrocephalus associated with blocked aqueduct and bilateral microphthalmia	" "
Born dead	F	Aqueduct obstruction (septum)	1	Internal hydrocephalus associated with sub division of the aqueduct with neuroglial tissue	" "
			1	Internal hydrocephalus (miscellaneous type)	Greene <u>et al</u> (1974a)
			3	Internal hydrocephalus	Rieck <u>et al</u> (1979)
UNSTATED BREEDS					
Born dead			1	Hydrocephalus associated with anencephalocoele, campylognathia, acheilia superior and sarcodontia	Crocker (1919)
Fetus (term)			1	Internal hydrocephalus associated with dilation of the ventricles and aqueduct, bulging cranium and club foot	Williams (1931)
Fetus (term)			1	Internal hydrocephalus associated with bulging cranium, small body size, multiple rigid joints including the spine and brachygnathia inferior	" "
Fetus 8 months		Lymphoma	1	Hydroencephalocoele associated with multiple lymphomatous nodules in the brain	Hatzioles (1960)
		Aqueduct stenosis and forking	1	Internal hydrocephalus associated with forking and stenosis of the aqueduct	Greene <u>et al</u> (1974a)

TABLE III CONT'D

AGE	SEX	ETIOLOGY	NUMBER	DESCRIPTION	REFERENCE
UNSTATED BREEDS CONT'D					
		Aqueduct obstruction	1	Internal hydrocephalus associated with obstruction of the aqueduct	Greene <u>et al</u> (1974a)
		Meningitis (infectious)	1	Internal hydrocephalus associated with meningitis and abscesses around the 4th ventricle	" " "
			11	Internal hydrocephalus (miscellaneous types)	" " "
3 weeks	M		1	Internal hydrocephalus associated with cerebellar hypoplasia, optic nerve hypoplasia and keratitis	Cravero <u>et al</u> (1976)
1 day	F		1	Internal hydrocephalus associated with large, open fontanelles	" " "
6 months			1	Internal hydrocephalus associated with ankylosis of the 2nd and 3rd cervical vertebrae and malacia of the cord	" " "
Fetus 9 months	F		1	Communicating internal hydrocephalus associated with cerebellar hypoplasia, patent aqueduct, alopecia, palatoschisis and anophthalmia	" " "
		Viral (BVD-MD)		Internal hydrocephalus associated with cerebellar hypoplasia	Horvath (1976)
New born		Viral (Akabane)	53	Hydrocephalus and hydranencephaly associated with cavitation of the brain and spinal cord, subepithelial gliosis and edema, perivascular cuffing and dilation of the spinal canal	Mayer (1976)
			2	Communicating hydrocephalus associated with fluid distension of the ventricles and arachnoid space and agenesis of the cerebellum	Guarda <u>et al</u> (1977)
			2	Internal hydrocephalus associated with cerebellar hypoplasia in one calf	" " "
			13	(One crossbred and 13 unstated breeds) Internal hydrocephalus	Cho <u>et al</u> (1978)
			1	(Crossbred) Internal hydrocephalus	Rieck <u>et al</u> (1979)

and Baringer 1972; Phillips et al 1970), parainfluenza type 2 virus (Friedman et al 1975), adenovirus type 12 (Huebner et al 1962), polyoma virus (Holtz et al 1966), and Newcastle vaccine virus (Chew-Lim and Webb 1976). Many of these and similar agents are ubiquitous in the bovine environment.

Experimental vitamin deficiencies notably vitamin A, have resulted in hydrocephalus in rabbits (Millen et al 1953, 1954), pigs (Palludan 1961, 1966) and rats (Rokkones 1955). Rise in CSF pressure, bony abnormalities, and aqueduct stenosis were common factors leading to hydrocephalus. Although not demonstrated to cause hydrocephalus, vitamin A deficiency has been associated with increased CSF pressure, cranial bone abnormalities, and cerebellar prolapse in cattle (Blakemore and Ottaway 1957). Similar findings were observed in rats on diets deficient in vitamin B₁₂ and folic acid (Overholser et al 1954), and zinc (Warkany and Petering 1973). Numerous compounds had been reported to produce hydrocephalus experimentally in laboratory animals, although the applicability is doubtful. Hydrocephalus associated with maternal ingestion of blighted potatoes in monkeys could be applicable (Allen et al 1976). While there is no evidence that hyperthermia causes bovine hydrocephalus, Edwards (1978) reviewed the effects in other species. Trauma and its relationship to ventricular hemorrhage and hydrocephalus were discussed by Herzog (1971).

Hydrocephalus is the most frequent CNS defect in cattle (Cho and Leipold 1977b). The incidence was given as 15.4 per 10,000 (Priester et al 1970) comparable to 14 to 17 per 10,000 births in man (Haynes et al 1974). One-third to one-half of the human cases were associated with

spina bifida. Greene et al (1973) reported 12.1% of 1,275 congenital defects from 588 herds in Kansas over a 2-year period involved the CNS; 63% were hydrocephalic. Most cases were in Herefords. In man there is a preponderance of hydrocephalus in males presumably due to the X-linked recessive form (Myrianthopoulos and Kurland 1961). No sex distribution is known to occur in cattle, although a combination of relative numbers and the presence of hereditary forms in Herefords probably account for the high incidence in this breed.

Hypothetically, hydrocephalus may result from oversecretion of CSF, obstruction to CSF flow, and impaired venous absorption; however, there is no firm evidence. With few exceptions, the pathogenesis may be regarded as a disturbance of CSF flow by obstruction at genetically susceptible sites (Milhorat 1972).

Most reports of bovine hydrocephalus involve calves and are sporadic. With few exceptions adequate pathological examination was lacking and the basic lesions obstructing the flow of CSF were not determined. As a consequence no satisfactory classification system exists (Greene et al 1974a). Milhorat's modification of Russell's classification subdivides noncommunicating and communicating types into congenital and acquired (Russell 1949; Milhorat 1972). The differentiation of communicating and noncommunicating types from a pathologist's point of view is difficult; however, the system is a basis for discussion. With few exceptions only congenital lesions will be considered. Aqueductal obstruction (stenosis) accounts for two out of three cases of congenital, noncommunicating hydrocephalus in man. Gliosis and forking are the 2 most common causes (Milhorat 1972). In the case of gliosis, ependymal damage due to a variety

of environmental factors seems to be the underlying cause (Russell 1949). The entire aqueduct may be involved; however, the superior and inferior colliculi are the most common sites. In cattle, the 3rd and 4th ventricles and the aqueduct are long and narrow compared to other species (Fitzgerald 1961) providing genetically predisposed sites for obstruction.

Forking of the aqueduct in man, unlike gliosis, is frequently associated with other congenital lesions e.g. spina bifida, meningocele, Arnold-Chiari malformation and fusion of the corpora quadrigemina (Milhorat 1972). The etiology is somewhat controversial although Russell (1949) maintained it is always congenital. Specific references to gliosis are few in cattle and are usually lumped into the general category of stenosis. Herzog (1971) and Greene et al (1974a) studied the basic pathologic lesions obstructing the flow of CSF in hydrocephalic calves and used them to classify the various types. Multiple defects were associated with forking of the aqueduct in 8 cases (Herzog 1971), while those reported as stenosis consisted of principally single defects. In the second study most cases were associated with other defects. True narrowing of the aqueduct characterized by a small, histologically normal passage is rare in man (Milhorat 1972); it occurs in association with spina bifida, meningocele and the Arnold-Chiari malformation.

Two examples of aqueduct septal obstruction were reported by Herzog (1971). The term was developed by Russell (1949) and its existence is controversial. Milhorat (1972) surmised it to be a variety of gliosis. Glial reactions were noted in Herzog's cases.

Histologic classification of aqueductal malformations based on the

presence of gliosis, forking, stenosis or a septum, while attractive, is not clear-cut (Drachman and Richardson 1961). Mixed and intermediate cases occur and congenital and acquired lesions may not be clearly separable. Furthermore, aqueduct stenosis may be the result of hydrocephalus in some cases (Williams 1973).

Atresia of the foramen of Lusk and Magendie (Dandy-Walker Syndrome) is characterized by panventricular dilation, agenesis or hypoplasia of the cerebellar vermis, and atresia of the posterior foramina. Whether the atresia is primary or secondary is debatable (Milhorat 1972). Although not the same syndrome, congenital dysplasia of foramen magnum in Holstein cattle (Cole and Moore 1942) had the same effect.

A third cause of congenital noncommunicating hydrocephalus are masses obstructing CSF flow. Benign intracranial cysts are most commonly arachnoid, ependymal, and porencephalic cysts. Greene et al (1974a) reported 3 such cases; one a meningeal cyst in an Angus calf, and two cases of cystic dilation of the third ventricle in Holstein calves. Although of doubtful congenital origin, a parasitic cyst (Coenurus cerebralis) was the cause of aqueduct obstruction in a Lincoln Red calf (Clegg and Bayliss 1958). A single case of vascular occlusion (vascular malformation) of the aqueduct was reported by Herzog (1971) in a Red Pied calf. Tumors occasionally obstruct CSF flow. Medulloblastoma of the cerebellum has been reported associated with hydrocephalus (Cordy 1953; Jolly and Alley 1969). Hatzios (1960) reported a case of meningoencephalocele in a calf with lymphoma of the brain. Leech et al (1978) reported a case of glial hamartoma obstructing the aqueduct.

Congenital communicating hydrocephalus in man is usually associated

with encephalocele, the Arnold-Chiari malformation, and rarely leptomeningitis. Encephaloceles usually do not cause hydrocephalus unless located in the occipital or suboccipital areas in association with malformation of the tentorium (Milhorat 1972). Communicating hydrocephalus is rarely reported in cattle. Two cases were reported (Cravero et al 1976; Guarda et al 1977) in association with cerebellar hypoplasia. Cho and Leipold (1977a) reported communicating hydrocephalus associated with spina bifida and the Arnold-Chiari malformation.

Hydrocephalus secondary to chronic leptomeningitis in older calves, perhaps of doubtful congenital origin, is likely communicating although not reported as such.

B. HYDRANENCEPHALY

Hydranencephaly is defined as complete or almost complete absence of cerebral hemispheres in a cranium of normal conformation, with the space filled with CSF surrounded by a thin membranous cerebral tissue (Kalter 1968; Jubb and Kennedy 1970). The term includes a group of disorders that vary widely in time of onset, mechanism of pathogenesis, CNS region of involvement, and anatomic organization of the brain remnant (Halsey et al 1971).

The earliest recognizable description in man appeared in case material of Amroise Paré (Hamby 1960) followed by systematic description of the disorder by Cruveilhier (1829-42, 1856) who used the term "anencéphalic hydrocéphalique" to describe its essential features (Halsey et al 1977). The term "hydranencephaly" was introduced by Spielmeyer (1904-1905).

In 1956, Blood and 1957 Whitem in Australia published the first clinical and pathologic description of a congenital arthrogryposis-hydranencephaly complex that occurred as a sporadic condition since 1945 with periodic increases in incidence in 1951 and 1955.

No classification of hydranencephalic lesions in domestic animals is available. Halsey et al (1977) have established 5 morphogenic classifications of cerebral defects in human infants occurring in relatively normal sized transilluminable craniums. Most cases of hydranencephaly were considered to occur between the 3rd and 5th months of gestation characterized by lissencephaly and schizencephaly. Destructive processes occurring after the 5th month of gestation were characterized by bilateral porencephaly, multiple cystic encephalomalacia and periventricular necrosis. Developmental abnormalities occurring during the first trimester were anencephaly, cyclopia and holotelencephaly and resulted in major craniofacial defects. External hydrocephalus with trivial or extensive cerebral destruction and obstructive and communicating hydrocephalus accounted for the terminal points of the spectrum. The differentiation between hydrocephalus and hydranencephaly is sometimes difficult since hydrocephalus is frequently present and probably often plays an accessory role in the morphogenesis of hydranencephaly (Halsey et al 1977). Although normal cranial conformation is usually considered characteristic by definition, rapid enlargement may occur following birth (Halsey et al 1977). This feature poses a problem peculiar to domestic animals and in particular, cattle, in that neonates are frequently not observed at birth.

The frequency of hydranencephaly in man is given as 1 per 500 new-

born and infant autopsies in university referral centers where there are active neurosurgical practices (Halsey et al 1977). Furthermore, 1% of cases thought clinically to be hydrocephalus are found to be hydranencephaly. Comparable data are not available for cattle; however, Christoferson et al (1977) reported 5 cases of hydranencephaly among 26 cases of bovine hydrocephalus.

Most reports of bovine hydranencephaly have been epizootics of the arthrogryposis-hydranencephaly (AG/HE) syndrome with epizootiological, serological and pathological findings indicating environmental factors as the cause, especially viral agents (Cho and Leipold 1977b).

In Australia, Blood (1956) and Whittem (1957) found AG/HE occurred independently or as a complex and postulated that the two were different manifestations of the same condition. Arthrogryposis-hydranencephaly affected all breeds of cattle and the age of dams appeared to have little effect on the occurrence of abnormalities although no cow was known to produce more than one affected calf. Arthrogryposis was characterized by absence or reduction of ventral horn cells in the spinal cord resulting in neurogenic muscular atrophy. Hydranencephalic calves were generally regarded as blind and ataxic with normal craniums except for occasional slight enlargement with cerebral hemispheres replaced by fluid filled sacs. The rhinencephalons were considered normal. Both conditions were thought to be due to degeneration of normally developed nervous tissue. Lordosis, kyphosis, torticollis and spina bifida were occasionally associated with AG/HE. Subsequently similar outbreaks of AG/HE were reported in cattle and sheep from Australia (Bonner et al 1961; Hartley and Wanner 1974; Hartley and Haughey 1974a). Attempted trans-

mission of AG/HE utilizing emulsions of cerebrum and spleen in newborn lambs failed (Hartley and Haughey 1974b). Concurrently in Japan (Tajima et al 1951; Sugawa et al 1951; Sugiura and Fujio 1961; Inui and Maruyama 1967; Hataya 1973) and in Israel (Markusfeld and Mayer 1971; Nobel et al 1971) reported outbreaks of AG/HE in cattle, sheep and goats. Abortion, premature births and stillbirths characterized by encephalomyelitis preceded most outbreaks. Arthrogryposis was characterized by small calves and dystocia and hydranencephaly, generally observed as the epizootics waned, was characterized by corneal opacity and inflammatory ocular changes, ataxia, hemiplegia or paraplegia, dysphagia, regurgitation and stertorous breathing in addition to previously noted abnormalities. Although hydranencephaly was the principal cerebral defect, anencephaly, micrencephaly and hydrocephalus were occasionally observed. Cerebellar hypoplasia occurred sporadically and spina bifida and the Arnold-Chiari malformation were rarely noted.

Young (1969) in Australia, studying the relationship between the enzootic ephemeral fever virus and AG/HE, concluded from a serological survey that ephemeral fever virus was probably not the cause of AG/HE. Oya et al (1961) in Japan and later Doherty et al (1972) and St. George et al (1978) in Australia and Metselaar and Robin (1976) in Kenya isolated Akabane virus from mosquitoes and Culicoides brevitarsis in areas where AG/HE had occurred and demonstrated serological evidence of the virus in cattle, horses and sheep. Wanner and Husband (1974) found serums and CSF serologically negative for bovine viral diarrhea, infectious bovine rhinotracheitis, parainfluenza and ephemeral fever viruses in 2 hereford calves from an outbreak of AG/HE in Australia in 1973. Serum IgM levels

were elevated in affected calves and they concluded that hydranencephaly may result from a specific infectious or toxic agent operating at a critical stage of gestation. Trainin and Meirum (1973) in Israel similarly noted increased immunoglobulins in serums of calves with AG/HE.

Serum neutralizing antibody as evidence for Akabane virus as the cause of AG/HE in fetuses and in calves without colostrum has been found in Japan (Miura et al 1974; Kurogi et al 1975; Shiraishi et al 1977), in Australia (Hartley et al 1975; Hartley et al 1977; Cybinski et al 1978; Coverdale et al 1978), in Israel (Kalmer et al 1975; Mayer 1976), and in South Africa (Barnard 1977; Zumpt et al 1978). "Akabane" disease and "Abortion-Arthrogryposis-Hydranencephaly" syndrome have been proposed as names for the AG/HE condition (Inaba et al 1975; Hataya et al 1976).

Isolation of Akabane virus from natural occurring cases of AG/HE was first reported by Kurogi et al (1976) in Japan and later St. George et al (1978) in Australia. The condition has been reproduced experimentally in calves, lambs and kids (Inaba 1975; Parsonson et al 1975; Kurogi et al 1976, 1977) with pathological findings similar to those reported previously from natural outbreaks (Konno et al 1975; Moriguchi et al 1976).

Hartley et al (1977), Shepherd et al (1978) and Della-Porta et al (1976) in an extensive epizootiological, serological, and pathological study of 130 calves from an AG/HE epizootic in Australia identified five groups of the condition based on pathological findings and time of occurrence. Group 1 calves were incoordinate or unable to stand with no gross abnormalities and histologic evidence of nonsuppurative encephalitis in the mid and posterior brain stem; group 2 calves exhibited incoordination, flaccid paralysis or mild arthrogryposis, mild nonsuppurative encephalomyelitis, Wallerian degeneration of lateral and ventral funiculi in the

spinal cord and loss of ventral horn cells; group 3 calves had severe arthrogryposis, marked depletion of myelin in lateral and ventral funiculi of the spinal cord, loss of ventral horn cells and moderate to severe atrophy of skeletal muscles; group 4 calves were characterized by blindness, slight cranial doming, hydranencephaly, porencephalic cavi- tations of the cerebrum occasionally associated with arthrogryposis, normal myelination and mild to moderate perivascular cuffing; and group 5 calves had a variety of defects. Common to most were thickened cranial bones, micrencephaly or porencephalic cavitation and small cerebellums. Groups 1-3 were thought to represent infection during the last 1-3 months of gestation with good serological correlation in group 3. Group 4 represented infection during mid gestation with excellent serological correlation. Group 5 was interpreted as the result of infection during early gestation with only 50% of serums positive for Akabane neutralizing antibodies.

In the United States, Anderson and Campbell (1978) demonstrated placental transfer of Akabane virus in the hamster.

Several causes of hydranencephaly in ruminants have been identified or incriminated including ephemeral fever virus (Young 1969), hyperthermia (Hartley et al 1974), Japanese encephalitis virus (Tajima et al 1951), bluetongue virus (Young and Cordy 1964; McKercher et al 1970; Richards et al 1971; Osburn et al 1971a,b; Osburn and Silverstein 1972; Barnard and Pienaar 1976), Akabane virus (Inaba 1975; Parsonson et al 1975; Kurogi et al 1976, 1977) Wesselsbron disease and Rift Valley fever viruses (Coetzer and Barnard 1977), aino virus (Coverdale et al 1978) and BVD-MD virus, (Markson et al 1976;). Recently hydranencephaly was reported from

Canada (Greene 1978) although no specific cause was determined; environmental factors were implicated.

The pathogenesis of hydranencephaly is, for the most part, obscure although destructive and maldevelopmental mechanisms appear to be essential features (Halsey et al 1977).

Vascular lesions, in particular those of the internal carotid arteries, have been suggested as a mechanism in the destruction of cerebral tissue (Urich 1976). Although previous cases are rare, experimental occlusion of the carotid arteries in dogs (Becker 1949) and monkeys (Meyers 1969) successfully produced the condition. Destructive processes characterized by multiple cystic encephalomalacic and porencephalic lesions have been experimentally reproduced in sheep via in utero infection with bluetongue vaccine virus (Osburn et al 1971a,b; Osburn and Silverstein 1972). The important aspects appeared to be selective vulnerability of undifferentiated nerve cells to bluetongue virus and late development of immunologic competence. Recently Akabane virus has been found to produce similar destructive lesions although the mechanism was not determined (Kurogi et al 1977).

Schizencephaly and lissencephaly, failure of neuroblast proliferation and migration, appear to make up the second maldevelopment component (Halsey et al 1977). The mechanism involved is obscure. Hartley et al (1977) in an extensive study of Akabane virus-induced malformations in cattle observed a spectrum of hydranencephalic lesions with hydro-micrencephalic or lissencephalic-like forms occurring in cases believed to result from fetal infection early in gestation that suggested a possible common relationship between apparent destructive

and maldevelopmental forms based on the time of fetal disruptive event.

C. ARNOLD-CHIARI MALFORMATION

The Arnold-Chiari Malformation (ACM) is defined as herniation of a tongue-like process of cerebellar tissue through the foramen magnum into the anterior cervical spinal canal with simultaneous caudal displacement and elongation of the medulla oblongata, pons and 4th ventricle (Urich 1976). The term was coined by two of Arnold's students (Schwalbe and Gredig 1907), to emphasize the occurrence of hindbrain malformations with spina bifida described by Chiari (1891) as Type II in his initial observations of herniation of the cerebellum as a result of hydrocephalus, and the description by Arnold (1894) of an infant with spina bifida, that he termed myelocyst, and prolongation of the cerebellum over the roof of the 4th ventricle. With the current definition, hydrocephalus spina bifida and/or meningocele may or may not be present.

The integral association of ACM with spina bifida and hydrocephalus warrants a few comments related to the history of these defects and their association. The early reports of hydrocephalus have been reviewed (vide supra). Brocklehurst (1971), in his excellent review of spina bifida, noted that Nicolai Tulp (1652) first described the condition as "spina dorsa bifida". Morgagni (1761) was the first to note the relationship of spina bifida to hydrocephalus. Cleland (1883) described a brain stem deformity that later became known as the Arnold-Chiari Malformation in addition to his classical description of spina bifida and its components and a deformity of the corpora quadrigemina now known as

"tectal beaking".

In his original description, Chiari (1891) described three types of hindbrain malformation associated with hydrocephalus; a fourth type was added later (Chiari 1895). Type I consisted of prolongation of the cerebellar tonsils and the medial portion of the inferior lobe with herniation through the foramen magnum, "cerebellar coning". Of the 14 cases described only one had spina bifida. Type II was characterized by herniation of the cerebellar vermis and fourth ventricle into the cervical spinal canal and kinking of the medulla oblongata. Of the seven cases all had spina bifida and the defect was considered a more severe form of Type I. Type III deformity was more severe with the fourth ventricle and cerebellum located within a cervical encephalocele. Cerebellar hypoplasia was the outstanding feature of Type IV; spina bifida was not a component. Chiari concluded all these conditions were the result of hydrocephalus.

The incidence of ACM in man has been given as 1 per 1,000 births by Matson (1969) who further stated that the condition was probably present in all patients with myelomeningocele and hydrocephalus. The condition was also found in absence of spina bifida at an incidence of about 1 per 25,000 births (Myrianthopoulos 1977). Laurence (1959) noted that ACM in man with or without spina bifida, aqueduct stenosis, and gliosis accounted for 60% of all hydrocephalus and 80% of hydrocephalus in neonates in England.

The condition is allegedly not rare in animals (Frauchiger and Fankhauser 1952). However, few cases have been reported in cattle (Cho and Leipold 1977c). In his reporting of ACM in a dicephalic

calf Gruys (1973) reviewed the literature and noted that all cases described in animals had spina bifida. Frauchiger and Fankhauser (1952) were the first to describe the condition in a calf with spina bifida and moderate dilation of the lateral ventricles. Since that time field cases have been reported by Akker (1962) Herzog (1971) Herzog and Höhn (1971); Gruys (1973) Hartley and Wanner (1974) Gruys and Bethlehem (1976) and Cho and Leipold (1977 a,c).

In man, ACM is nearly always associated with other malformations: hydrocephalus with aqueduct gliosis or forking, spina bifida and meningo-myelocoele, hydromyelia, syringomyelia, diplomyelia, polymicrogyria, craniolacunia, heterotopic grey matter along the walls of the lateral ventricles, "beak-like" deformity of the quadrigeminal plate in which the colliculi may be fused into a single mass that points dorsally and caudally and bony malformations in the area of the foramen magnum; basilar impression, platybasia, and Klippel-Feil deformity (Milhorat 1972). Similar findings have been noted in cattle (Gruys 1973; Gruys and Bethlehem 1976; Cho and Leipold 1977 a,c).

To date there are five theories to explain the pathogenesis of the ACM. Hydrocephalus with posterior displacement of the rhombencephalon was thought to be the cause (Chiari 1891, 1895; Gardner and Goodall 1950; Gardner 1959; Masters et al 1977). This explanation does not account for cases occurring without hydrocephalus (Schwalbe and Gredig 1907), nor does it account for the common association with spina bifida in the Type II defect. Fankhauser (1959) noted that more CSF is resorbed in the spinal subarachnoid space as a possible explanation why hydrocephalus is absent or only slightly developed in animals as opposed to 3/4 to 4/5 of CSF resorption by the brain surface in man (Russell and

Donald 1935). Margolis and Kilkam (1969a,b) noted ACM in suckling hamsters with reovirus type I induced hydrocephalus and concluded that the experiment supported Chairi's original theory that hydrocephalus was the cause and Types I and II were different grades of the same lesion although no spina bifida occurred in their hamsters.

Traction due to fixation of the spinal cord as a result of spina bifida or meningomyelocele at an early embryonic stage when the ascensus medullae takes place has been offered as a second explanation (Lichtenstein 1949). ACM and spina bifida has been produced in newborn rats with trypan blue (Gunberg 1956; Vickers 1961; Kalter 1968). Gunberg (1956) noted deviated spinal nerves in his study and concluded that traction was the cause. Barry et al (1957) and Akker (1962) were unable to substantiate spinal nerve deviations in human fetuses and lambs, respectively, and the condition occurred in animals where only slight ascensus takes place (Fankhauser 1959). Goldstein and Kepes (1966) were unable to produce ACM by ligating the lumbar spinal cord of newborn rats and opossum fetuses. Sacral myelocele also occurs in man in the absence of ACM (Cameron 1957).

Overgrowth of the central nervous system in relation to the skull is a third possible factor. Regional differentiation of the brain and spinal cord may be accompanied by overgrowth and involve different areas to different degrees (Barry et al 1957; Akker 1962). Overgrowth in the lumbosacral area would prevent closure of the vertebral arches and larger cerebral hemispheres may displace the tentorium cerebelli caudally resulting in protrusion of the medulla oblongata and caudal parts of the cerebellum into the cervical spinal canal. Protrusion of the cerebellum

occurred with vitamin A deficiency in rats (Wallach and Bessy 1941), dogs (Mellanby 1944), rabbits (Millen and Woollam 1958), piglets (Palludan 1961, 1966; Gilter 1962), and in cattle (Blakemore and Ottaway 1957). Reduction in the cranial cavity due to thickening of the cranial bone was thought to be the cause except in rabbits where the defect was considered to be caused by hydrocephalus.

Pressure disturbances resulting from loss of CSF from the spina bifida is a fourth alternative (Cameron 1957; White et al 1979). This, however, does not account for cases of ACM without spina bifida (Peach 1965; Teng and Papatheodorou 1965; Gruys 1973).

Finally, ACM has been suggested as a congenital malformation of unknown morphogenesis (List 1941; Russell 1949; Feigin 1956; Kalter 1968).

No single hypothesis can account for all varieties of the ACM. Various factors may interact in the pathogenesis and the pathogenesis may be different in each case, or the various forms of the malformation may be a variation or different manifestations of the same defect (Cho and Leipold 1977c).

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II. HEREDITARY INTERNAL HYDROCEPHALUS OF HORNED HEREFORD CATTLE

INTRODUCTION

Hydrocephalus is a congenital defect of man and a variety of domestic animals. While most reports of bovine hydrocephalus describe sporadic cases in calves, a number of heritable syndromes have been documented in the major beef and dairy breeds¹.

Hereditary internal hydrocephalus in Hereford cattle was first described as a lethal defect in the New Mexico Agricultural Experiment Station experimental herd in 1959². The condition appeared in progeny of an outcross in a previously closed herd. The incidence and sex distribution led to the hypothesis of inheritance by a single autosomal recessive gene; subsequent breeding trials have supported this^{3,4,a}. Although the breed involved was not published, test animals were confirmed to be horned Herefords by the cattleman who provided them^b.

The condition is widespread in the horned Hereford breed, occurring in both purebred and commercial herds. Selective breeding, or indirect genetic engineering⁵, provided herds with the genetic predisposition for substantial losses when carrier cattle are inadvertently introduced. The net effect is an increased frequency of superior and undesirable genes. Losses from 2 to 10 percent have been recorded for individual herds; an estimated 20% to 44% of the females were heterozygous for the hydrocephalic trait^{4,b}. Individual calf losses are minor compared to the loss of parentage incurred when undesirable genes enter and persist in

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reputable purebred herds.

Most studies have dealt with the genetic and gross pathologic aspects^{2-4,6,7}. Three hydrocephalic syndromes identified in Hereford cattle had implied genetic causes¹. Clinical and pathologic features resembled previously described syndromes.

The purpose of this investigation was to study field cases of suspected hereditary hydrocephalus in horned Hereford cattle and to categorize pathologic alterations for use as diagnostic criteria.

MATERIALS AND METHODS

Calves and Tissues - Tissues from 11 horned Hereford calves and near-term aborted fetuses with clinical histories suggestive of hydrocephalus were submitted to the Kansas State University over a 18-month period from January 1978 to July 1979. Six were intact calves from Kansas; one was a frozen hydrocephalic head specimen submitted from a Kansas herd; and formalin-fixed brains and selected tissue samples from four calves from South Dakota^c.

Specimen Collection and Preparation - Complete necropsies were performed on the six intact calves. Brains were obtained via removal of the dorsal cranium or by parasagittal sectioning of the head by a band-saw. Central nervous system (CNS) tissues were fixed in 10% buffered neutral formalin (BNF) along with other selected and grossly abnormal

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tissues for a minimum of 14 days. Tissues were routinely processed^d, embedded in paraffin, 8 to 10 micra sections of nervous tissue and 6 micra sections of non-nervous tissue were cut^{e,f}, and stained with hematoxylin and eosin in an automatic slide stainer^g or by conventional hand methods^g for light microscopy. Selected sections were stained with azure eosinate (modified Nocht's method), Davenport's method for neuraxons, Holzer's method for glial fibers, luxol fast blue (Klüver-Barrera method) for myelin and nerve cells, Gomori's trichrome method and Mallory's phosphotungstic acid hematoxylin (PTAH)⁸⁻¹⁰. Coronal sections of cerebral hemispheres and midsagittal sections of mid- and hindbrains were utilized when feasible.

Microbiologic Examination - Bacteriologic examination of tissues was performed utilizing standard aerobic techniques. Kidney, lung, spleen, mesenteric lymph node and CNS tissues from suitable carcasses were screened by the direct fluorescent antibody test (FAT)^h for bovine virus diarrhea-mucosal disease (BVD-MD) and infectious bovine rhinotracheitis (IBR) viruses. Virus isolation was utilized in a single case for parainfluenza-3 (PI₃) virus.

^dAutotechnicon Ultra II, Technicon Instruments Corp, Tarrytown, NY

^eSpencer rotary microtome, model 820, American Optical Corp, Buffalo, NY.

^fSpencer sliding microtome, model 860, American Optical Corp, Buffalo, NY.

^gHisto Tek, Technicon Instruments Corp, Tarrytown, NY.

^hDR Howard, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

RESULTS

Herd History and Clinical Findings - These results along with microbiologic findings are tabulated in Table I.

Calves were aborted during late gestation or died shortly after birth. Three were females, two were males, and six unknown. Most came from herds with a previous history of abortions, heavy neonatal death loss, and hydrocephalus. Frequently, the calves had a common sire. Seven of these 11 calves represented four commercial and purebred horned Hereford herds in Kansas and South Dakota. The remaining cases were sporadic in isolated herds.

Microbiologic Findings - Tissues from two of the five carcasses examined for bacteria were negative; enteric bacteria, Micrococcus, Proteus, and Pseudomonas spp were isolated from several tissues from the remaining three. One of the four calves screened for BVD-MD virus by FAT was positive; FAT for IBR virus and isolation for PI₃ virus were negative.

Gross Pathologic Findings - Pathological changes in the CNS, eyes, and skeletal musculature are included in Table II.

Five of the six intact calves were undersized full-term Herefords. Two calves weighed 27 kg each, and a third, 25 kg. Five calves had moderately domed calvaria (Fig 1); the sixth was slightly domed. Narrow refined facial features, swollen protruding tongues, and caudo-dorsal-rostroventral angulation of the palpebral fissures were frequently observed (Fig 2).

Moderate to severe internal hydrocephalus was present in all brains.

Cerebral hemispheres were fluctuant and distended with clear to yellow cerebrospinal fluid (CSF). Caudal displacement of the occipital lobes over the cerebellum and attenuation of sulci and gyri over the dorsal cerebral surface were noted in the most severely affected brains (Fig 3). Remaining cerebral surfaces were corrugated due to multiple small gyri (micropolygyrus) (Fig 3). Cystic dilation of the optic chiasma and subarachnoid hemorrhage at the base of the brain were occasionally observed (Fig 4). Fenestration of the septum pellucidum was present in 10 brains (Fig 5). Lateral and third ventricular dilation, distention of the interventricular foramens, lateral splaying of the dorsal thalamus, and absence of the interthalamic adhesion were present in all brains (Fig 5-9).

Cerebral mantles were thin with proportional reduction in grey and white matter. Circumferential elongation resulted in peripheral shifting of the corpus callosum and deep gyri to the cerebral surfaces (Fig 8,9). Hippocampi were reduced to thin ribbons and choroid plexuses of the lateral ventricles were thin and stretched. Caudodorsal displacement and lateral compression of the mesencephalon at the interpeduncular fossa associated with rostral displacement of the pons and absence of the pontine eminence were present in all calves (Fig 5,7,10,11). Superior and inferior colliculi were indistinct; the tectum was frequently visible in the posterior portion of the longitudinal fissure (Fig 5). The Sylvian aqueduct was represented by a laterally compressed anterior vertical slit and dilated mid-portion (Fig 10,11).

Cerebellums were examined in 10 calves and size reduction of 50% to 60% was present in all (Fig 10).

Eyes were examined in five calves. All had varying degrees of

reduced bony orbits, microphthalmia, and disparity in size of the globes (Fig 12). Optic nerves were reduced in size. The turbid fluid of the vitreous body contained tan to grey flocculent precipitate. and occasional hemorrhage. Retinas were detached and frequently associated with persistent primary vitreous (Fig 13). Lenses were reduced and occasionally ruptured.

Soft, pale spongy skeletal musculature was present in the six intact calves. Pale areas were present in most major muscles of the trunk and limbs. The quadriceps provided the most consistent gross lesions (Fig 14-16).

Microscopic Findings - Alterations in the cerebral mantles were minor (Fig 19). Neurons were normally aligned and occasional degenerated cells and glial satellitosis were observed. Neuraxons were scarce in the subependymal white matter. Ependymal cells were severely attenuated and segmentally denuded. Pedunculated intraventricular ependymal projections (excrecence) were present in modest numbers. Segmental areas of subependymal accumulations of basophilic cells resembled reserve cells. Modified ependymal cells of the choroid plexuses were flattened and vascular spaces within the tela choroidea were dilated.

The mesencephalon was displaced dorsally (dorsal kinking) at the interpeduncular fossa. The dorsal surface of the tectum was rounded. The cleft between the superior colliculi and the brachium colliculi inferior was poorly delineated. A laminar zone corresponding to the superficial and intermediate collicular stria extended from the stalk of the pineal body, over the dorsal surface of the tectum to the anterior medullary velum. Frequently tattered on the surface, it contained few

myelinated and non-myelinated neuraxons and numerous large, tortuous vascular channels surrounded by thick concentric zones of fibrillar gliosis (Fig 17, 18, 20, 21). Similar changes were present in the basal optic tracts coursing caudoventrally on the lateral surface of the mesencephalon and on the ventral surface of the crus pedunculi. The pons, tectospinal and cerebrospinal tracts, and long fasciculi were deficient in myelinated and non-myelinated neuraxons. The anterior third of the Sylvian aqueduct was dorsoventrally elongated and compressed laterally. Pedunculated masses of ependymal covered neurophil, extended from the roof into the aqueduct, producing partial aqueductal obstruction (Fig 22-24). In adjacent areas, numerous ependymal invaginations and isolated ependymal rosettes were present. Occasionally, the aqueduct was subdivided into small ependymal-lined tubules (aqueductal forking). Segmental subependymal accumulations of basophilic cells within a continuous fibrillar glial plate resembled reserve cells. The mid-portion of the aqueduct was dilated. Focal piling of ependyma was usually associated with thickening of the subependymal glial plate.

Cerebellar folia were markedly hypoplastic. Dysplastic changes were present in all portions of the central lobe and to a lesser degree in the lateral ansiform lobe, paraflocculus, and flocculus. The severe dysplasia present in the lingula, nodulus, and uvula was characterized by discontinuance of the external and internal granular layers and pseudorosette formation around blood vessels. Ectopic Purkinje's cells were numerous. Severely affected folia contained a paucity of myelinated and non-myelinated fibers in the white matter, and a relative increase in blood vessels, fibrous astrocytes, and oligodendroglia. Evidence of

tissue destruction was not observed.

Two spinal cords were examined. A paucity of neuraxons in the dorsal and ventral roots resulted in a relative increase in nuclei. Myelinated axons in the dorsal funiculi were scarce. Occasional sections contained bilaterally symmetrical focal malacia in the grey matter.

Optic nerves consisted of scant neurophil and axons surrounded by prominent connective tissue trabeculae extending from the pial sheath (Fig 25). Retinas were detached at the lamina vitrea, and adhered to a central hyaloid artery extending from the optic disc to the posterior lens capsule. Pseudorosettes of retinal tissue surrounded vascular spaces (Fig 26). The bulk of the vitreous was composed of eosinophilic, acellular material, and erythrocytes.

Generally smaller than normal, muscle fasciculi were irregular in size, with uniformly well delineated interfascicular connective tissue and preserved neuromuscular spindles. In some fasciculi, the reduction in the number of myofibers was scarcely perceptible. In others, the myofibers were markedly reduced in number and haphazardly arranged in loose areolar endomyseal connective tissue (Fig 27). Individual myofibers contained areas of swollen, hyalinized regions, adjacent to areas with normal cross striations, or atrophic zones with retained striations (Fig 28). Flocculent and granular degeneration was present in both smaller and atrophic fibers. Severely degenerated fibers were represented by sarcolemmal membranes collapsed around rows of nuclei. Rarely, modest numbers of histiocytes were observed in the most severely affected areas.

DISCUSSION

Hydrocephalic horned Hereford calves consistently had reduced body size and weight, narrow refined facial features, cranial doming, caudodorsal-rostroventral angulation of palpebral fissures, microphthalmia, and protruding edematous tongues. The lethal, familial nature of the condition, and the presenting clinical features agreed with previous reports^{1-4,6,7}. The gross morphologic and histologic findings in the brains, eyes, and skeletal muscles in this investigation confirmed previous studies^{2-4,7}.

Mean body weights of hydrocephalic calves in one study were less than mean body weights of normal controls². Body measurements in these calves generally suggested proportional reduction in body size (dysmaturity) with some predilection for the axial skeleton.

Bacterial isolates in this study are considered to be contaminants. The presence of BVD-MD antigens in one calf is of questionable significance. Since BVD-MD virus is ubiquitous among cattle, cause and effect relationships are difficult to establish. Apparently normal fetuses are as likely to have BVD-MD viral infection as aborted fetuses¹¹.

Micropolygyrus of the cerebral convexities appears to result from the dorsal elevation of gyri located within the longitudinal fissure to the cerebral surface. Shallow sulci form secondarily. Attenuation of convolutions on the dorsal cerebral surface and cystic dilation of the optic chiasma were presumably the effects of pressure of severe internal hydrocephalus. They were not previously observed⁷.

Caudodorsal displacement of the mesencephalon (mesencephalic kinking) at the anterior portion of the Sylvian aqueduct, lateral splaying

of the dorsal thalamus, and absence of the interthalamic adhesion are distinguishing features. Mechanical displacement and resultant tissue reactivity due to pressure has been postulated as the cause of these mesencephalic abnormalities⁷. The sigmoid configuration of the brain conferred by dorsal kinking of the mesencephalon, and the splaying configuration of the thalamus resemble the cephalic flexure and diencephalon of 40-day-old bovine embryos, respectively¹².

Cerebellar hypoplasia and distribution of dysplastic lesions resemble findings of arrested development⁷.

Spinal cord lesions in the two cords examined resemble previous findings⁷, but the small sample size does not allow accurate conclusions to be drawn concerning the consistency of these lesions.

Severe hypoplasia of the collicular and basal optic pathways are postulated to be the cause of the retinal and optic nerve lesions observed in all the eyes studied.

Most major skeletal muscles were affected by degenerative lesions. The quadriceps had the most consistent gross lesions. Similar muscle lesions have been previously reported^{7,13}. Greater than 3-fold elevations in serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), lactic dehydrogenase (LDH), malic dehydrogenase (MHD), and aldolase reported in hydrocephalic calves has been suggested as evidence for a primary myopathy^{7,14}. Although no evaluation of terminal nerve fibers and motor endplates was made, grouped distribution of atrophic fibers, preservation of neuromuscular spindles and cross striations, absence of lipid replacement, little or no inflammatory response, and lack of regeneration are compatible

with neurogenic myopathy¹⁵. Innervation of skeletal muscle takes place during early fetal life, however, it plays no part in muscle morphogenesis. Later in gestation, muscle becomes dependent on its nerve supply¹⁶. Primary maldevelopment and hypoplasia of the mesencephalon is thought to be the cause of apparent neurogenic myopathy. Muscular development and movement in man develops progressively from cephalic to caudal portions, providing a plausible explanation for the severe lesions in the quadriceps.

Two analogous hydrocephalic syndromes in Hereford cattle with genetic implications have been identified¹. Syndrome I was characterized by extreme hydrocephalus without obstruction of CSF pathways, domed forehead, and cerebellar hypoplasia and dysplasia. Microphthalmia, retinal dysplasia, and myopathy were inconsistent findings. Syndrome II was characterized by dorsal kinking and lateral compression of the mesencephalon with Sylvian aqueduct stenosis. Ventricular dilation was less severe than that of Syndrome I. Cranial doming was seldom observed. When it occurred, cerebellar hypoplasia was moderate. Mesencephalic abnormalities in Syndrome II resemble those in the present series; however, associated defects of the cerebellum, eyes, and skeletal muscle were inconsistent features in Syndrome II.

Breeding trials and pathologic studies are needed to determine whether these syndromes represent a spectrum of expression of a recessive gene, or a gene influenced by modifier genes, or the activity of more than one gene.

SUMMARY

Carcasses, brains, and selected tissues from 11 near-term aborted fetuses and neonatal horned Hereford calves with clinical signs suggestive of hydrocephalus were utilized for microbiologic, gross pathologic, and light microscopic study. Previous herd histories of abortions, excessive neonatal deaths, and hydrocephalus in calves of common ancestry accompanied most of the specimens. Reduction in body size, cranial doming, and internal hydrocephalus characterized by maldevelopment of the mesencephalon were considered distinguishing features. Microphthalmia and retinal dysplasia, cerebellar hypoplasia and dysplasia, and skeletal muscle myopathy were additional criteria for diagnosis.

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TABLE I - Herd History and Clinical Findings
Hereditary Internal Hydrocephalus of Horned Hereford Cattle

Case no	State of origin	Age	Sex	Herd history	Microbiology
78-545	KS	Newborn (died)	M	5 calves by this sire, 3 of which died at birth	ND
79-193	KS	Newborn (died)	F	ND	BVD positive (FAT)
79-232	KS	Newborn (died)	ND	ND	ND
79-313	KS	1 day (died)	F	1 of 3 calves with hydrocephalus, common sire	BVD negative (FAT)
79-314	KS	1 day (died)	F	1 of 3 calves with hydrocephalus, common sire	<u>Pseudomonas and Micrococcus</u> from jt fluid BVD negative (FAT)
79-315	KS	Newborn (died)	M	1 of 3 calves with hydrocephalus, common sire	BVD negative (FAT)
79-742	KS	Newborn (died)	ND	ND	ND
79-1291	SD	Abortion	ND	7th abortion 2nd case of hydrocephalus	Negative
79-1293	SD	Newborn (died)	ND	ND	ND
79-1294	SD	Abortion (late term)	ND	2nd abortion in herd of 100 cows	IBR negative (FAT) PI ₃ negative (VI) <u>Proteus</u> from liver and lung
79-1295	SD	Abortion (late term)	ND	3rd abortion in herd	Few enterics from liver and lung

ND - Not determined, for lack of suitable tissues
BVD - Bovine Viral Diarrhea
FAT - Fluorescent Antibody Test
Jt - Joint

KS - Kansas
PI₃ - Parainfluenza - 3
SD - South Dakota
VI - Virus Isolation

TABLE II - Pathological Changes - Hereditary Internal Hydrocephalus of Horned Hereford Cattle

Case No.	Micro- poly- gryus	Lateral ventricu- lar dila- tion	Third ventricu- lar dila- tion	Caudal- dorsal mesen- cephalon displace- ment	Aqueduct stenosis	Cerebellar hypoplasia	Cerebellar dysplasia	Spinal cord de- creased neuraxons (spinal roots)	Myodys- plasia	Micro- phthalmia, retinal dysplasia
78-545	+	+	+	+	+	ND	ND	ND	+	ND
79-193	+	+	+	+	+	+	+	+	+	+
79-232	+	+	+	+	+	+	+	+	+	ND
79-313	+	+	+	+	+	+	+	ND	+	+
79-314	+	+	+	+	+	+	+	ND	+	+
79-315	+	+	+	+	+	+	+	ND	+	+
79-742	+	+	+	+	+	+	+	ND	+	+
79-1291	+	+	+	+	+	+	+	ND	+	ND
79-1293	+	+	+	+	+	+	+	ND	+	ND
79-1294	+	+	+	+	+	+	+	ND	+	ND
79-1295	+	+	+	+	+	+	+	ND	-	ND

ND - Not Determined, for lack of suitable tissues.

+ - Present

- - Absent

Fig 1 - Newborn horned Hereford calf with hereditary internal hydrocephalus. Note moderate calvarial doming.

Fig 2 - Close up view of the head of calf in Fig 1. Note caudodorsal-rostroventral angulation of the palpebral fissure, refined facial features, and protruding tongue.

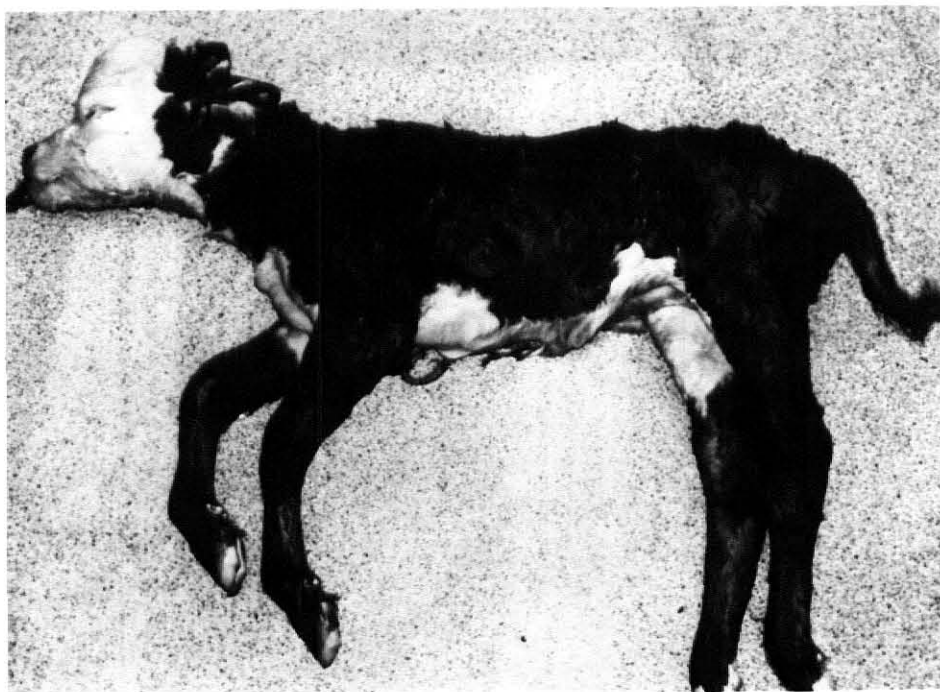


Fig 3 - Dorsal view of hydrocephalic brain. Note attenuation of sulci and gyri over the dorsal surface of the cerebral hemispheres, multiple small gyri on remaining surfaces and caudal displacement of the occipital lobes (a).

Fig 4 - Ventral view of brain in Fig 3. Note cystic dilatation of the optic chiasma (arrow) and subarachnoid hemorrhage at the base of the hindbrain (a).

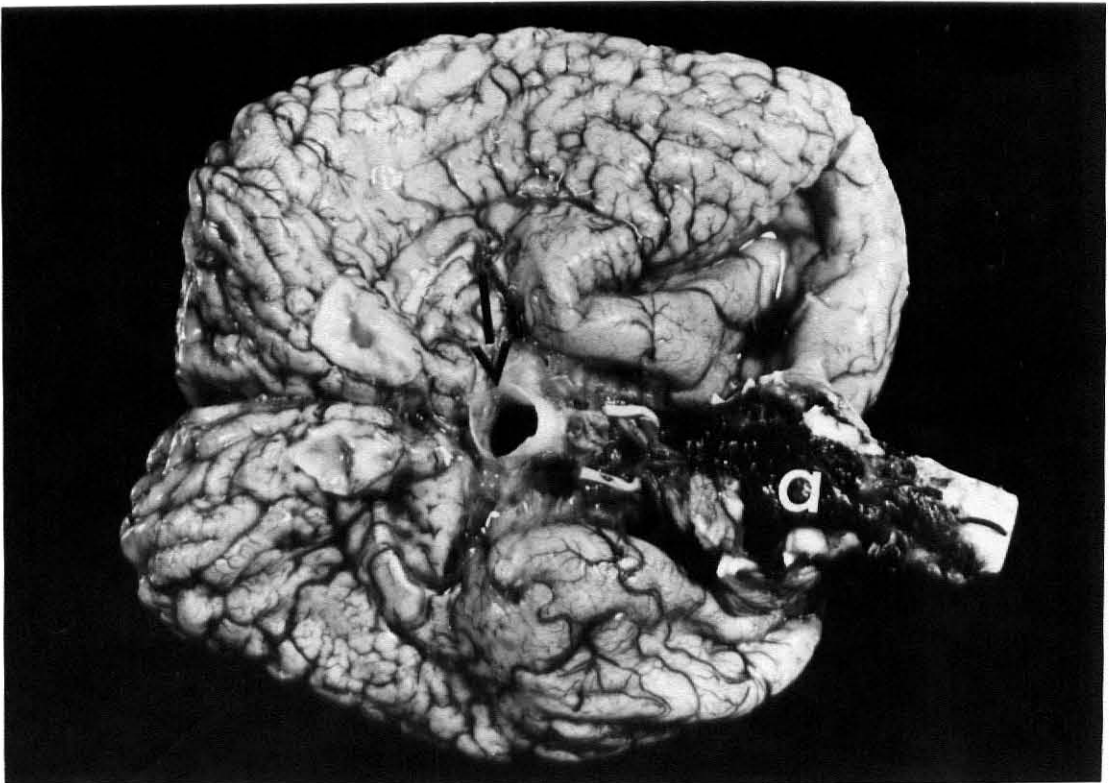
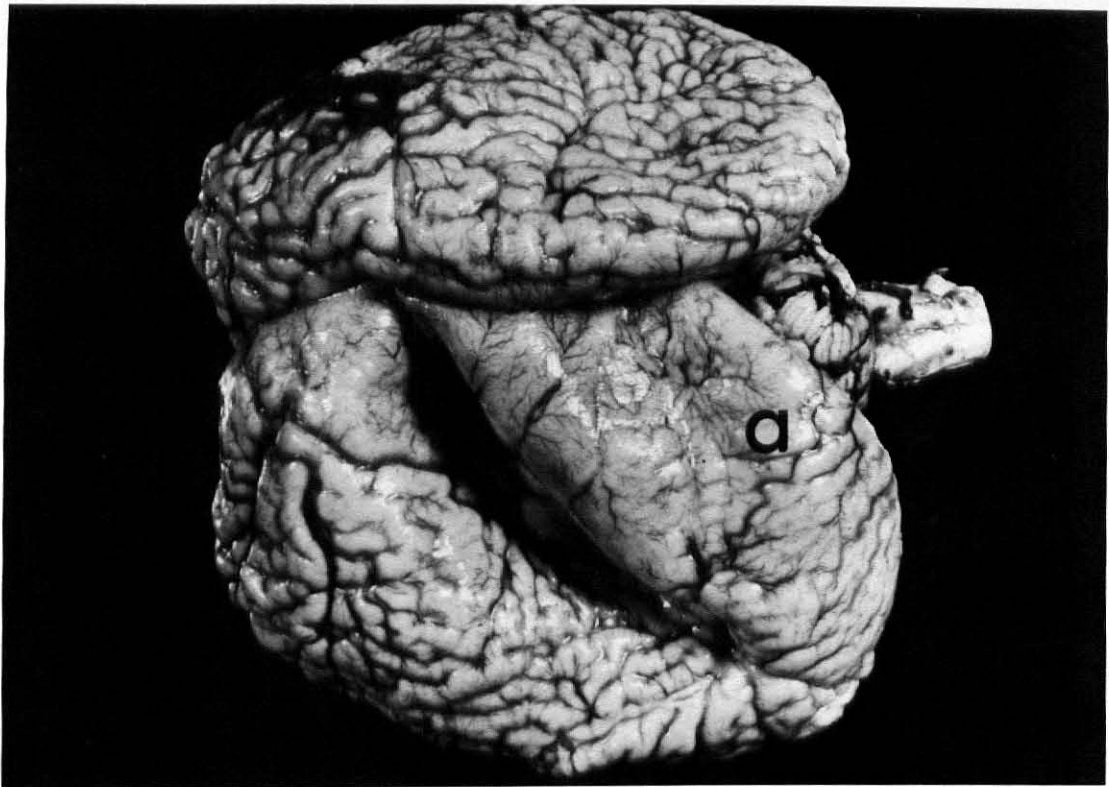


Fig 5 - Lateral view with left cerebral hemisphere removed. Note marked fenestration of the septum pellucidum and lateral and 3rd ventricular dilation. Elevated tectum (arrow) was visible in the posterior longitudinal fissure.

Fig 6 - Dorsolateral view following partial removal of the left cerebral hemisphere. Note lateral and third ventricular dilation and lateral splaying of the 2 sides of the dorsal thalamus (a).

Fig 7 - Dorsal view of the brain stem and cerebellum. Note lateral splaying of the 2 sides of the dorsal thalamus (a), with accentuation of the interlaying 3rd ventricle and absence of the interthalamic adhesion. The mesencephalon (arrows) appears laterally compressed.

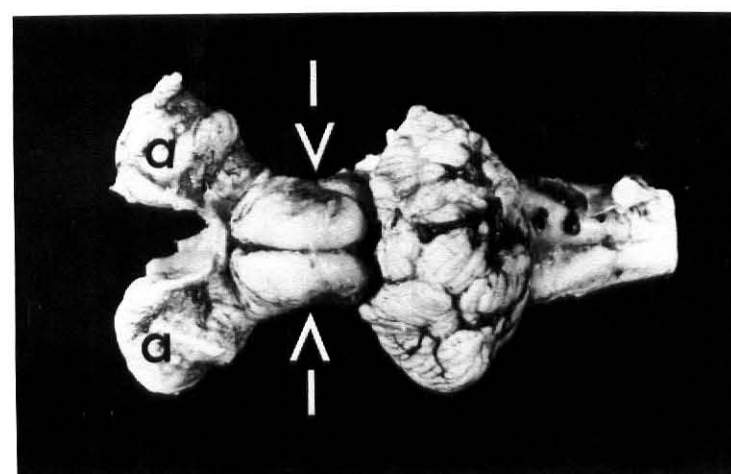
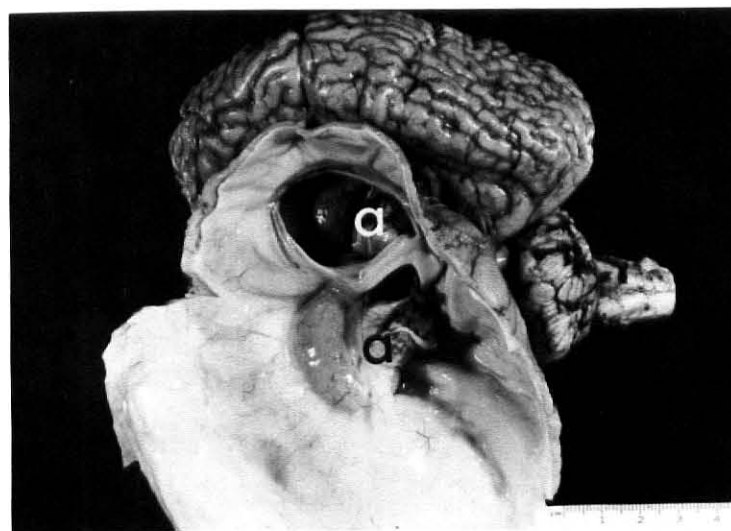
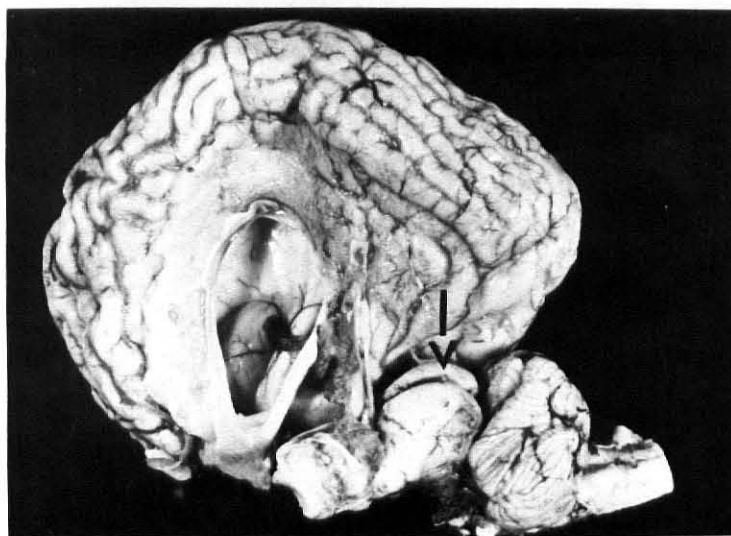


Fig 8 - Coronal section at the level of the mamillary bodies. Note proportional thinning of the cerebral mantle and elevation of deep gyri to the cerebral surface. Basilar portion of the lateral ventricle is dilated (arrow).

Fig 9 - Coronal section slightly posterior to that depicted in Fig 8. Note proportional thinning of the cerebral mantle and dilation of the basilar portion of the lateral ventricle (arrow).

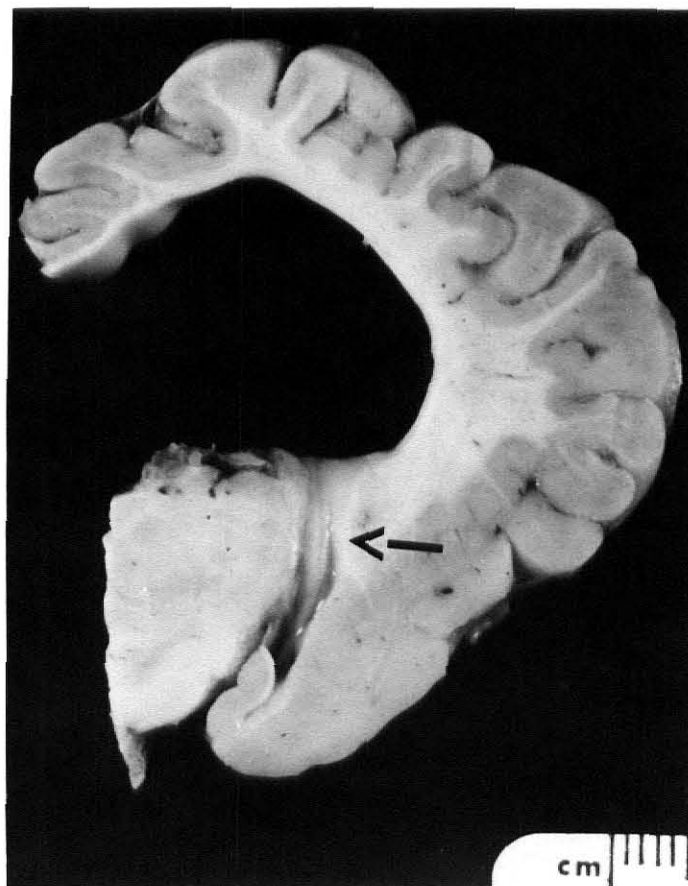
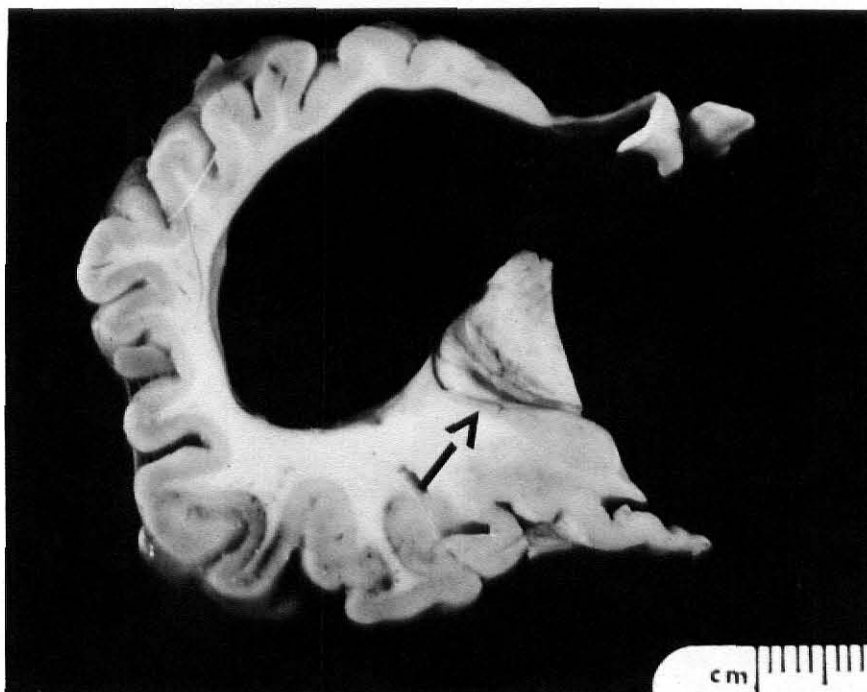


Fig 10 - Lateral view; mid-sagittal sections, brain stem, and cerebellum. Hydrocephalic Hereford calf (Top) normal Hereford calf (Below, n). Note the hypoplastic cerebellum, caudodorsal displacement of the mesencephalon with the apex at the interpeduncular fossa (white arrows), lack of the pontine eminence, anterior stenosis of the aqueduct of Sylvius (black arrow), and dilation of the mid portion of the aqueduct.

Fig 11 - Close up view of Fig 10 (Top). Note the stenotic anterior portion of the aqueduct of Sylvius and dilation of the mid section.

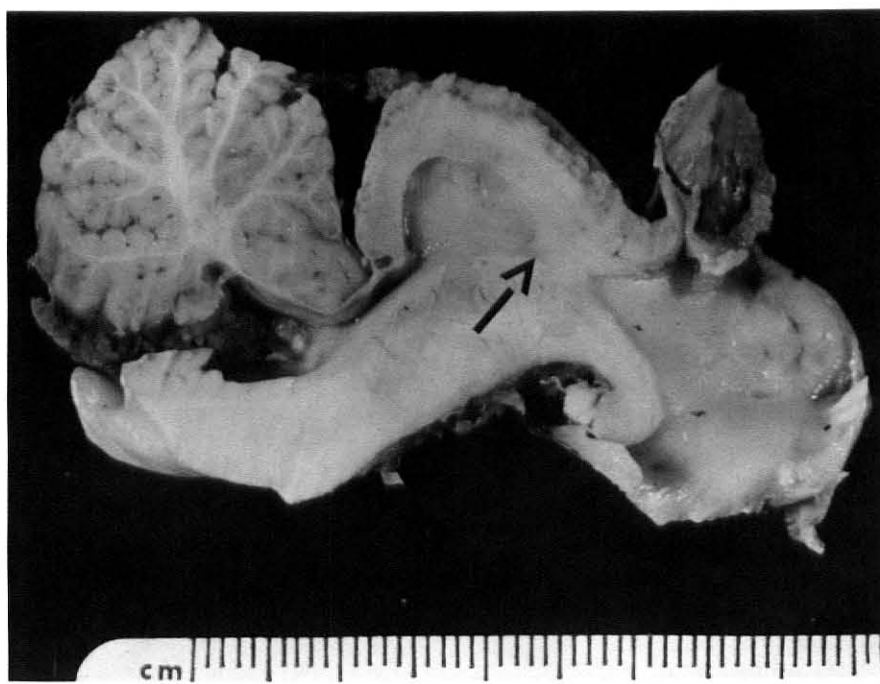
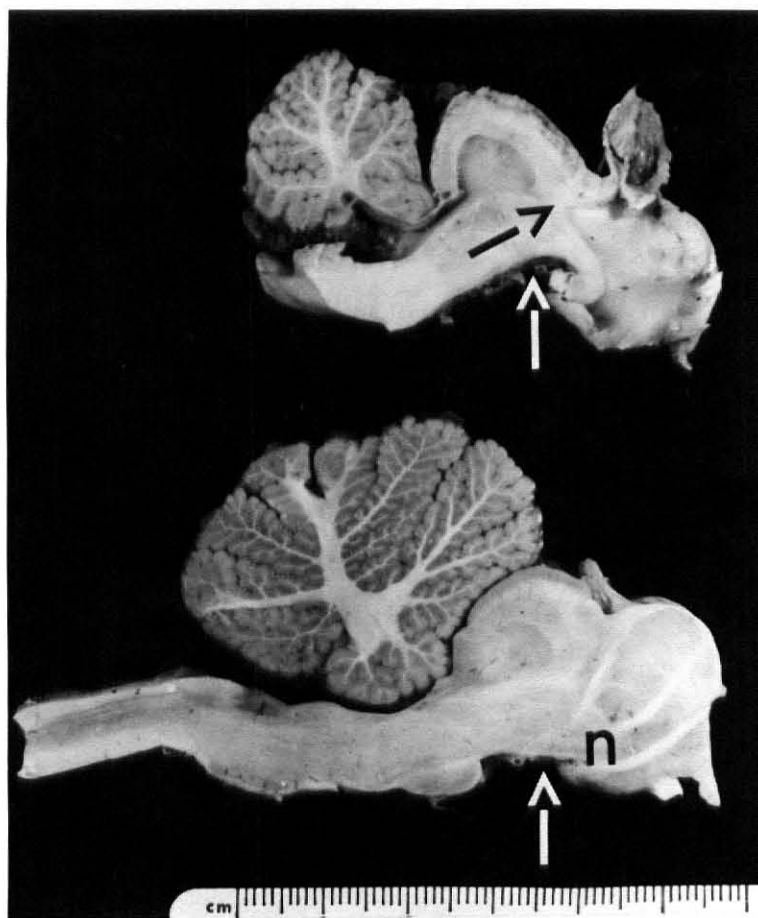


Fig 12 - Eyes from hydrocephalic Hereford calf. Note bilateral microphthalmia and disparity in size.

Fig 13 - Cross sections of the eyes in Fig 12. Note retinal detachment and persistent primary vitreous.

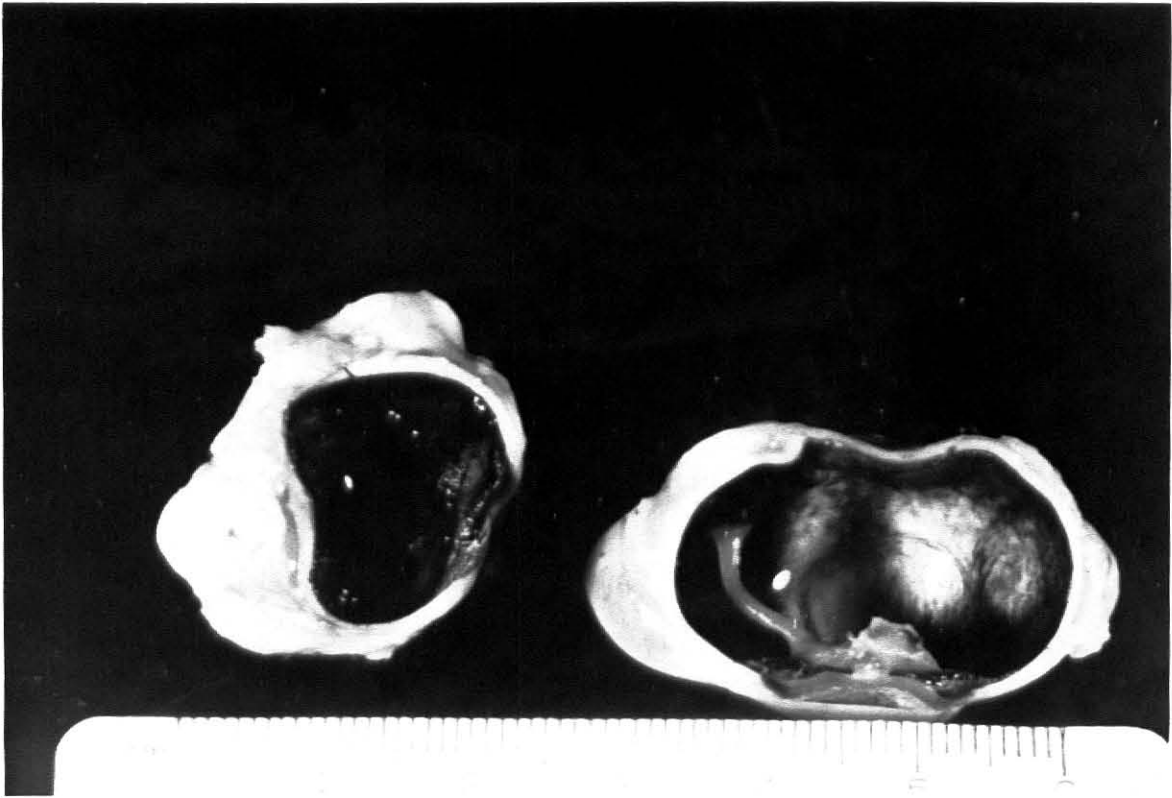


Fig 14 - Quadriceps normal Hereford calf (a) and hydrocephalic calf (b). Note the pale, watery appearance of the musculature from the hydrocephalic calf.

Fig 15 - Close up view of (b) Fig 14.

Fig 16 - Quadriceps muscle removed from hydrocephalic (b) and normal (a) Hereford calves depicted in Fig 14. Note extremely pale watery appearance of the muscle from the hydrocephalic calf.

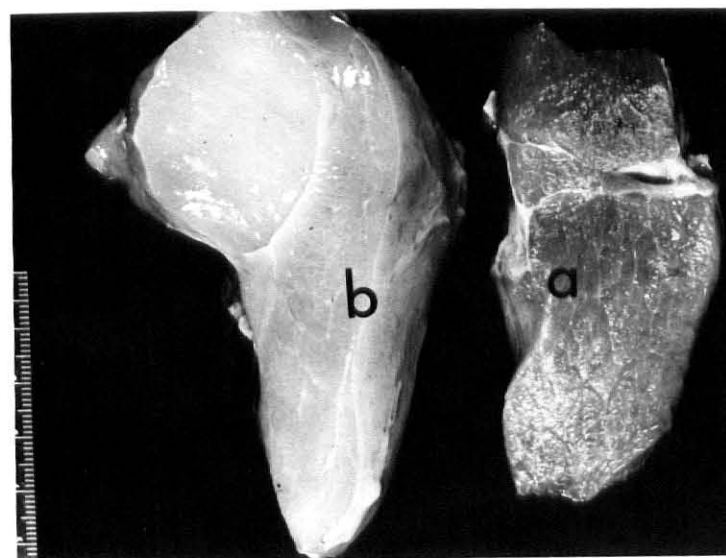
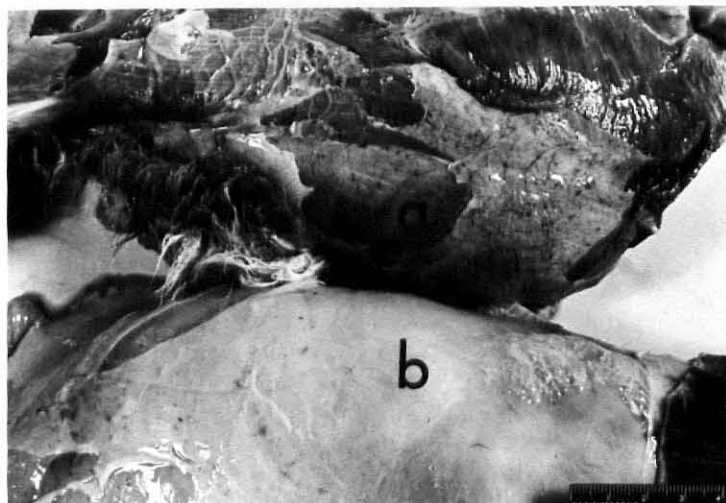


Fig 17 - Parasaggital section of the cerebellum and brain stem from a hydrocephalic horned Hereford calf. The tectum (T) is dorsally displaced and has a tattered dorsal surface. H&E stain; X 1.5.

Fig 18 - Parasaggital section of the cerebellum and brain stem from hydrocephalic horned Hereford calf. The laminar zone on the dorsal surface of the tectum (T) and a portion of the cerebellum (arrow) are devoid of neuraxons. Davenport stain; X 1.5.

Fig 19 - Partial coronal section of the cerebrum from a hydrocephalic horned Hereford calf. Note the thinned cerebral mantle (arrows). H&E stain; X 2.

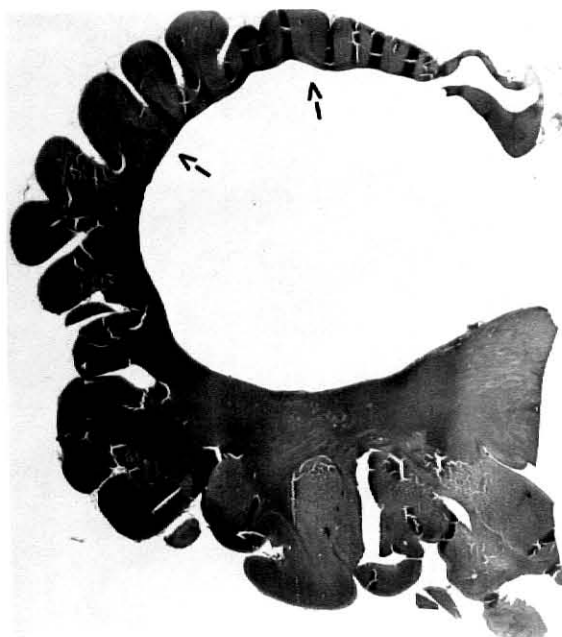
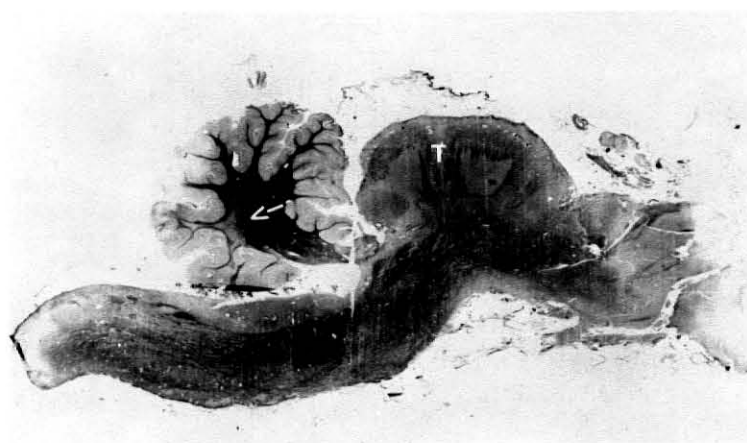
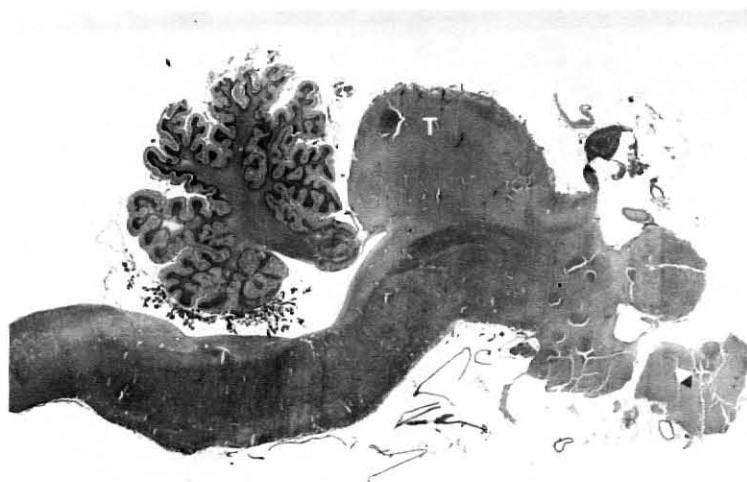


Fig 20 - Parasagittal section of the brain stem and cerebellum from a hydrocephalic horned Hereford calf. The laminar zone on the dorsal surface of the tectum (arrow) contains tortuous vascular spaces. Holzer stain; X 2.

Fig 21 - Higher magnification of the tectal surface depicted in Fig 20. Note the concentric zones of fibrillar gliosis. Holzer stain; X 25.

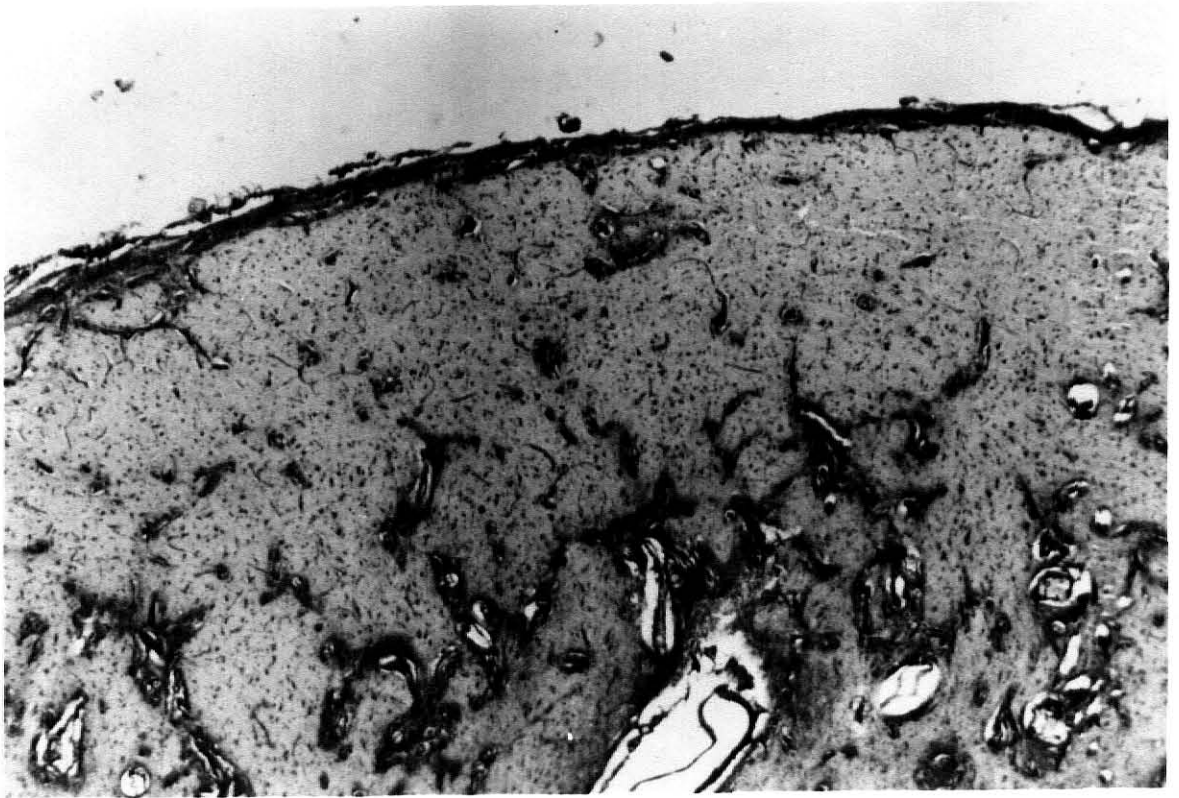
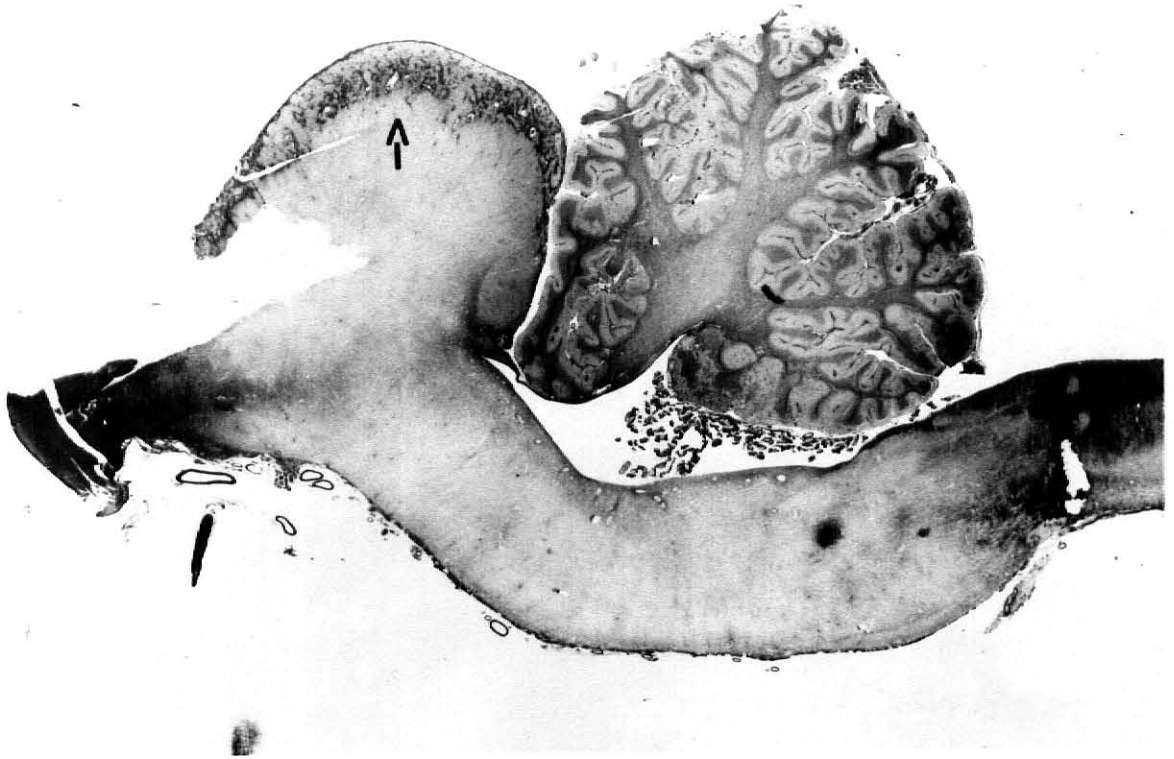


Fig 22 - Midsagittal section of the brain stem and cerebellum from a normal horned Hereford calf for comparison. Pons (P), tectum (A), lingula (L), nodulus (N), and uvula (U) are marked. The normal mesencephalic aqueduct is marked by arrows. H&E stain; X 2.

Fig 23 - Slightly parasagittal section of the brain stem and cerebellum from a hydrocephalic horned Hereford calf. The pontine eminence is missing (P), and the tectum has a tattered appearance. Lingula (L), nodulus (N), and uvula (U) are marked. Note the obstruction in the mesencephalic aqueduct (arrows). H&E stain; X 2.3.

Fig 24 - Midsagittal section of the brain stem and cerebellum depicted in Fig 23. A mass obstructs the anterior portion of the mesencephalic aqueduct (arrows). H&E stain; X 2.3.

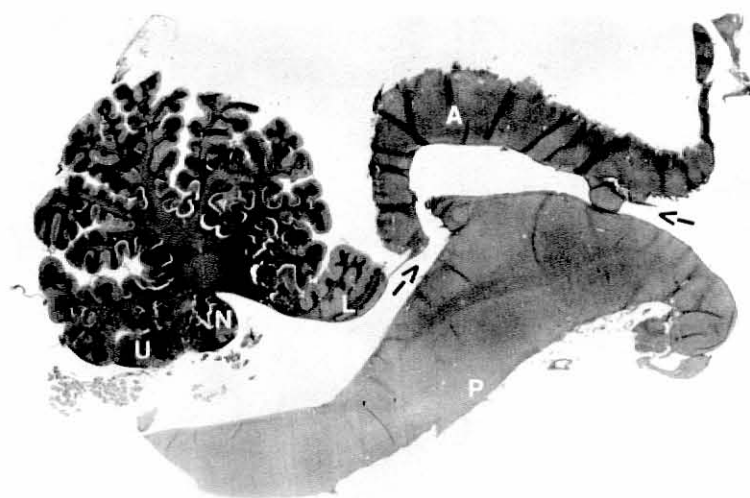
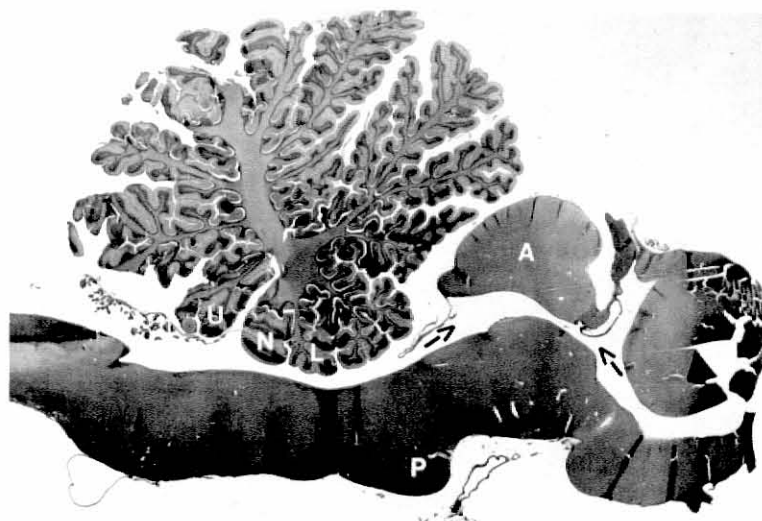


Fig 25 - Longitudinal section of the optic nerve from a hydrocephalic horned Hereford calf (arrows). Nervous tissue is scant, resulting in a relative increase of connective tissue. H&E stain; X 64.

Fig 26 - Photomicrograph of the retina from a hydrocephalic horned Hereford calf. Note the pseudorosettes of retinal tissue. H&E stain; X 160.

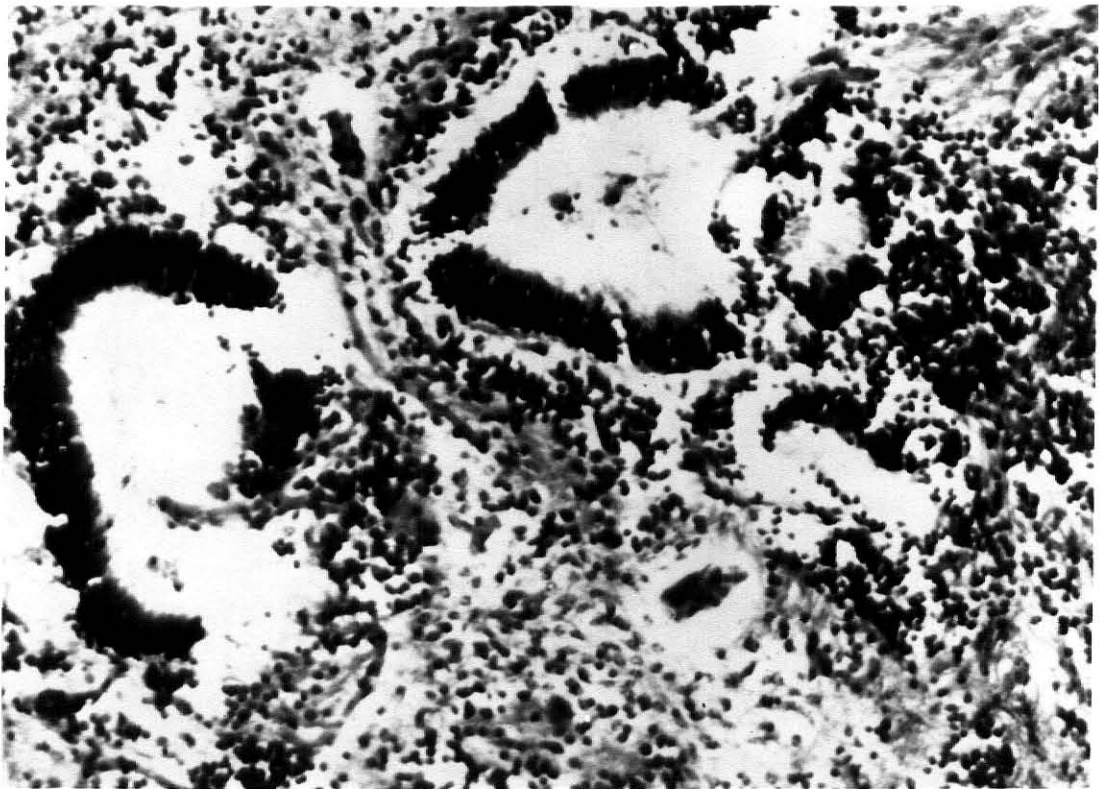
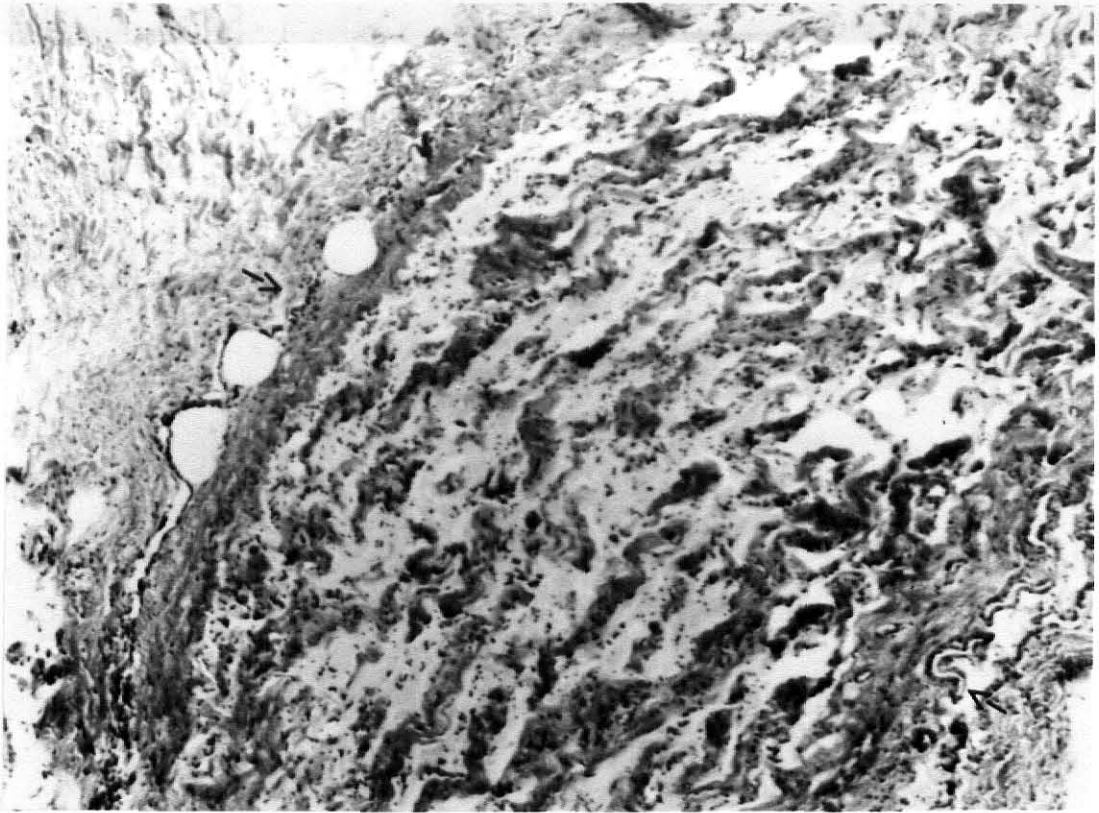
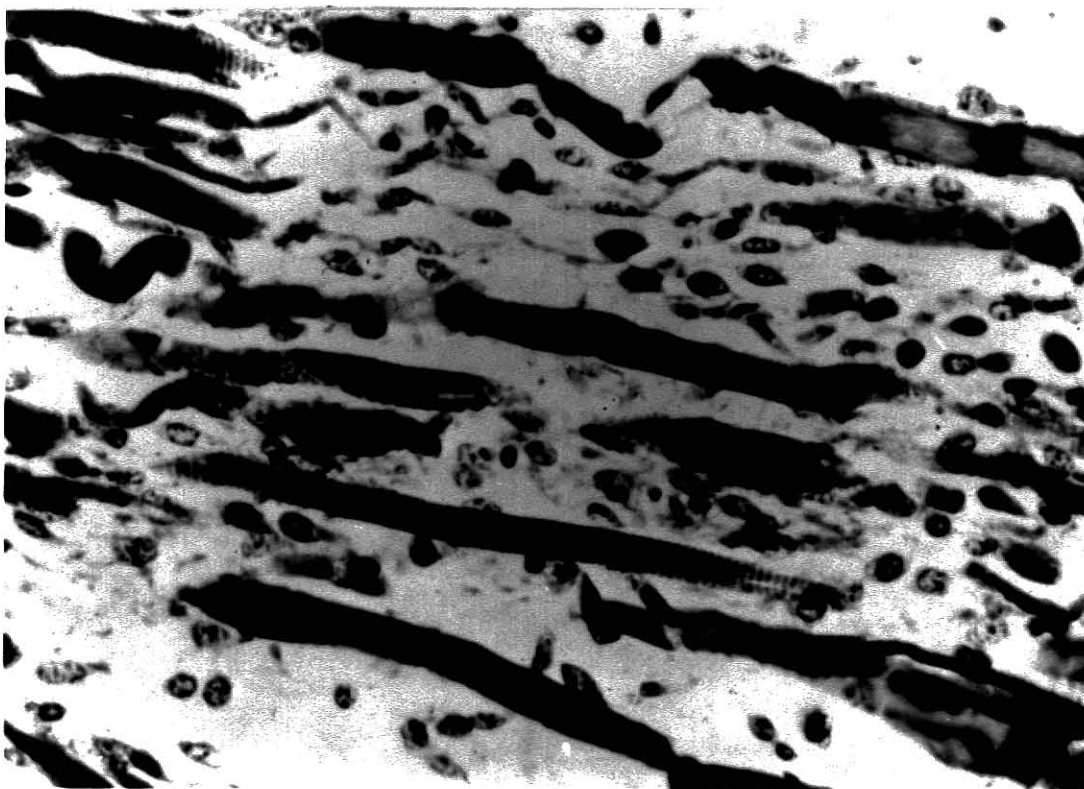
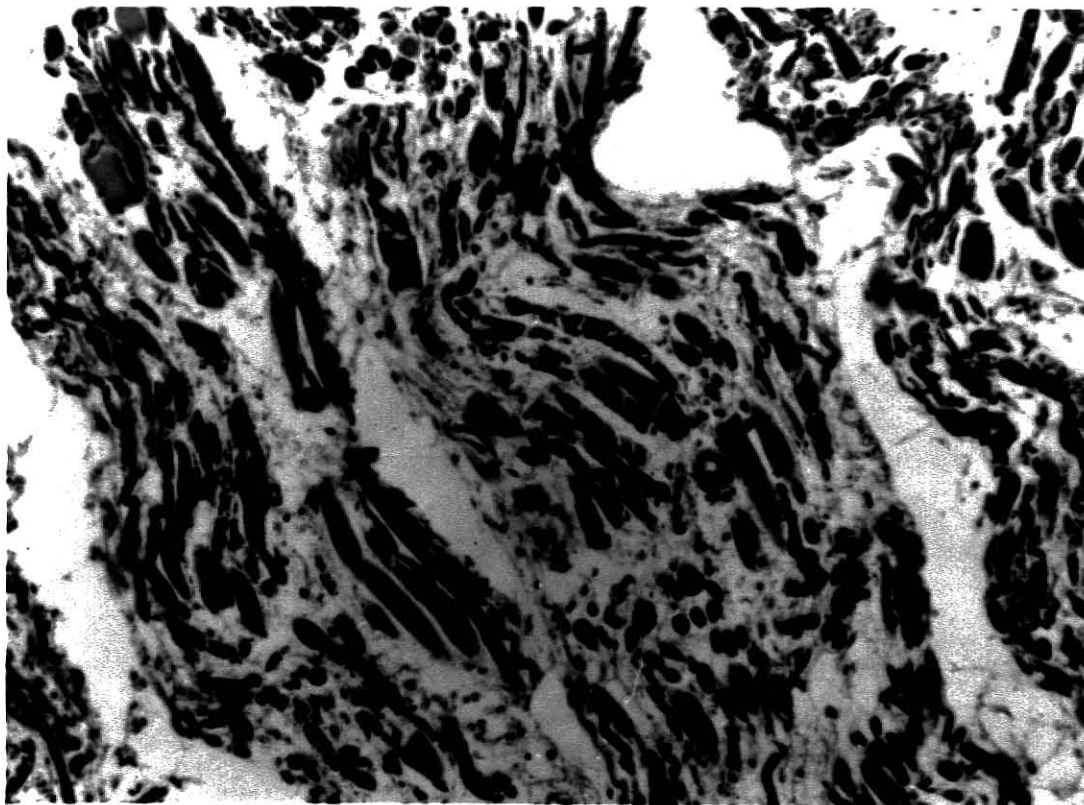


Fig 27 - Photomicrograph of the quadriceps muscle from a hydrocephalic horned Hereford calf. Note the haphazard arrangement of the myofibers. H&E stain; X 160.

Fig 28 - Higher magnification of the quadriceps muscle depicted in Fig 27. Note the transition from swollen, hyalinized zones, to normal, and atrophic zones which retain cross striations. H&E stain; X 320.



III. CONGENITAL HYDRANENCEPHALY IN CATTLE

INTRODUCTION

Hydranencephaly is defined as complete or near complete absence of the cerebral hemispheres in a cranium of normal conformation, with the space filled with cerebrospinal fluid (CSF) surrounded by thin, membranous cerebral tissue^{1,2}. The term includes a group of disorders that vary widely in their presumable time of onset, pathogenesis, regions of involvement of the central nervous system (CNS), and anatomic organization of the brain remnant³.

Several infectious causes of hydranencephalic conditions in cattle have been identified or incriminated, including ephemeral fever, Japanese encephalitis, bluetongue (BT), Akabane, aino, bovine virus diarrhea-mucosal disease (BVD-MD) and border disease (BD) viruses⁴⁻¹³. Recently hydranencephaly was reported from Canada and although no specific cause was determined, environmental factors were implicated¹⁴.

The frequency of hydranencephaly in man is 1 per 500 newborn infants autopsied in university referral centers where neurosurgical practices are active¹⁵. Further, 1% of cases thought clinically to be hydrocephalus have been proved to be hydranencephaly. Few cases have been reported in the United States, and comparable data is not available for cattle.

This paper describes pathologic, microbiologic, and serologic findings in naturally occurring, congenital bovine hydranencephaly.

MATERIALS AND METHODS

Calves - Four calves from the same herd (1-21 days of age) were

submitted to Kansas State University, over a two year period from fall of 1977 to the fall of 1979, with clinical signs referable to the CNS. Information was obtained on a fifth calf from this herd submitted to another laboratory^a. Following clinical examination, calves were euthanatized^b and standardized complete necropsies immediately performed.

Specimen Collection and Preparation - Brains and spinal cords were removed intact via removal of the dorsal calvarium and dorsal spinal arches of the spinal column. CNS tissues were fixed in 10% buffered neutral formalin along with other selected and grossly abnormal tissues for a minimum of 14 days. Tissues were routinely processed^c, embedded in paraffin, 6 to 10 micra sections of nervous tissue and 6 micra sections of non-nervous tissue were cut^{d,e}, and stained with hematoxylin-eosin in an automatic slide stainer^f or by conventional hand methods for light microscopy¹⁶. Selected sections were stained with Davenport's method for neuraxons¹⁷ and luxol fast blue (Kluver-Barrera method) for myelin and nerve cells¹⁶. Coronal sections of cerebral hemispheres and mid-sagittal sections of mid- and hindbrains were utilized where feasible.

^aLE Rice, College of Veterinary Medicine, Oklahoma State University, Stillwater, OK: Personal communication.

^bT-61, National Laboratories, Veterinary Pharmaceuticals, American Hoechst Corp, Somerville, NJ.

^cAutotechnicon Ultra II, Technicon Instruments Corp, Tarrytown, NY

^dSpencer rotary microtome, model 820, American Optical Corp, Buffalo, NY.

^eSpencer sliding microtome, model 860, American Optical Corp, Buffalo, NY.

^fHisto Tek, Technicon Instruments Corp, Tarrytown, NY.

Virologic Examination - Virus isolation techniques utilizing embryonic bovine kidney cells, vero (Maru), and embryonated chicken egg injected intravenously were employed to screen lung, lymph node, spleen, brain, cerebrospinal fluid (CSF), and phosphate buffered saline washed erythrocytes^{g,18,19}.

The viral interference test or direct fluorescent antibody test (FAT)^h was employed for detecting BVD-MD virus in tissue cultures. The FAT was utilized to screen tissues for BVD-MD virus. Additional virus isolation for BT virus was performed by a referral laboratoryⁱ.

Bacteriological Examination - Bacteriologic examination of tissues was performed utilizing standard aerobic techniques.

Serologic Procedures - The virus neutralization test (NT) for infectious bovine rhinotracheitis (IBR), BVD-MD, parainfluenza-3 (PI₃), adeno types 3 and 5 viruses and the complement fixation (CF) test for BT virus were performed on frozen (-160 C) sera obtained from selected calves and dams.

Clinical Pathology - Serum and CSF protein electrophoresis and CSF evaluation were performed utilizing standard techniques^{j,20}.

RESULTS

Herd History and Clinical Findings - Five male hydranencephalic

^gRM Phillips, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

^hDR Howard, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

ⁱJE Pearson, National Veterinary Services Laboratory, Ames, IA.

^jWE Moore, Department of Laboratory Medicine, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

Charolais and Charolais crossbred calves were born in an 80-cow herd over a two year period. No dam produced more than a single abnormal calf, and a change of sire failed to alleviate the condition. Dams with hydranencephalic calves subsequently raised normal calves.

All calves were recumbent at birth and four were unable to stand when assisted. Three calves exhibited fine to-and-fro head tremors, periodic episodes of limb rigidity, and opisthotonos; blindness was evident by lack of pupillary and menace reflexes. The fifth calf was able to stand with assistance and was hand reared until euthanatized at 21 days of age.

Microbiologic Findings - Microbiologic and serologic findings for calves and dams are summarized in Table I.

Evaluation of CSF from one calf revealed four white cells per cubic millimeter, with a 100 cell differential of: 74% large mononuclear cells, 2% lymphocytes, 20% neutrophils, and 4% smudged cells (probably mononuclear cells).

Gross Pathologic Findings - Calvaria were externally normal in all calves. Cranial vaults were reduced in size and cranial bone thickened. All calves were microhydranencephalic. Brains were 2/3 normal size; prominent reduction in the size of cerebral hemispheres made the cerebellums appear abnormally large (Fig 1,2,4). Lateral ventricles were markedly distended with clear CSF, cerebral mantles were thinned to 0.5 cm and superior sulci were abolished. A porencephalic cyst was present in one cerebrum (Fig 7-9); cystic cavitation of the optic chiasma was noted in another.

All cerebellums contained multiple, clear fluid-filled porencephalic

cysts distributed over the surface and in the central portions of all lobes (Fig 1, 3-5).

Focal necrotic mucosal ulceration was present on the superior lip of one calf. Crusty erosions on the muzzle and bilateral hypopyon were observed in another (Fig 6).

Histopathologic Findings - Segmental loss of dorsolateral ventricular ependyma and thinning of the periventricular white matter were consistent findings in the cerebral hemispheres (Fig 12). The laminar zone of white matter in the mantle was compressed. Where ependyma was missing, flattened glial cells lined the ventricular lumina. Focal areas of periventricular white matter had a spongiform appearance, most prominent in the lateral ventricular recesses.

Porencephalic cysts in the cerebrum and cerebellums consisted of central cavities of liquefaction necrosis surrounded by a zone of rarified neuraxonal lattice (Fig 10,11,13-15). Changes in adjacent white matter consisted of severe spongiform alteration characterized by vacuolar disarray of neuraxons with reduced affinity for luxol fast blue and Davenport stains. Large cavities were due to loss of multiple folia. Macrophages were occasionally observed; however, they were not prominent. Cysts were most prominent in the tips of the cerebellar folia. There was an overall paucity of granular cells in all cerebellums. In two calves, dysplastic changes consisted of a disarray of granular cells and ectopic Purkinje's cells. Spongiform alterations of the brain stem white matter was present in two calves.

Three calves had spongiform alteration and liquefaction necrosis of ventral funicular white matter in the spinal cord. Focal malacia of

the ventral horns accompanied degeneration of ventral horn neurons and glial satellitosis.

Additionally, three calves had birefringent renal tubular crystals. Interstitial pneumonia and excessive numbers of plasma cells were observed in the spleen and lymph nodes of two calves. Purulent uveitis, spongiform alteration of the optic nerves (Fig 16,17), and thymic involution were found in one calf.

DISCUSSION

Occurrence of encephalic malformations in crossbreds, absence of "sire effect", and failure of dams to produce more than a single abnormal calf are in keeping with recognized criteria for viral teratogens²¹. Results of the single CSF evaluation were suggestive of viral infection. The relatively low incidence suggests most cows in the herd have immunity to the agent, the agent is poorly transmissible, or husbandry practices are not conducive to transmission. The clinical appearance of affected calves is compatible with previous reports of spontaneous and experimentally-induced congenital encephalic malformations associated with several viruses 5-12,22-27.

The presence of BVD-MD antigens in two calves and absence of serum neutralizing antibody to BVD-MD virus in all calves would not be unusual if infection occurred early in gestation²⁸. The absence of neutralizing antibodies in the single cow tested is difficult to explain. BVD-MD vaccine had been used in non-pregnant cows and replacements in the herd since the spring of 1978. Because of this serologic screening of the

herd was deemed of little value. No dam, however, had received the vaccine prior to birth of the abnormal calves. Bluetongue CF titers of 1:10 are considered suspect and its presence must be considered.

In an extensive study of Akabane virus induced malformations in Australian cattle it was concluded that hydro-micrencephalic (lissencephalic) lesions in the cerebrum and cavitating lesions in the cerebellum resulted from infection in early gestation²⁷. Hydranencephalic calves in this study generally had thickened calvarial bone and reduced cranial vaults. Concurrent serologic confirmation was poorest in this group compared to calves believed infected later in gestation.

Porencephalic cavitations of cerebellar folia resemble experimental BVD-MD induced lesions in calves from two groups of cows inoculated at 100 and 150 days gestation, respectively²⁹. Hydranencephaly, however, was not reported. Hydranencephaly, severe porencephalic cavitation of the cerebrum, and cerebellar dysplasia were reported in one of five calves in England¹²; the calf was seronegative for BVD-MD antigen. BVD-MD antigen was demonstrated in serum from remaining calves and a virus indistinguishable from BVD-MD virus was recovered from their tissues.

While the present evidence does not demonstrate conclusively a cause and effect relationship, BVD-MD virus is believed to be the most likely cause of the encephalic malformations. The cases are thought to represent early fetal infection with the virus. These cases are considered to be unique in that they appear to be the first report of BVD-MD associated microhydranencephalic lesions in the United States.

SUMMARY

Hydranencephaly with porencephalic cavitation of the cerebellum was diagnosed in five calves from an 80-cow herd over a two year period. Affected calves were blind and exhibited fine head tremors and limb rigidity. Bovine virus diarrhea-mucosal disease (BVD-MD) antigens were found in the tissues of two calves and was considered to be the likely cause.

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TABLE I - Microbiologic and Serologic Findings
with Congenital Hydranencephaly

	Bacteri- ology	Virus iso- lation	FAT	Serology					
				IBR ⁴	BVD ⁴	PI ₃ ⁴	Adeno 3 ⁴	Adeno 5 ⁴	BT ⁵
Calf	---	---	BVD ⁺ MD	---	---	---	---	---	---
Calf	---	BVD-MD	---	---	---	---	---	---	---
Calf	Neg	Neg	Neg	1:2	<1:2	<1:2	<1:2	<1:2	Neg
Calf	Neg	Neg	---	<1:2	<1:2	<1:2	<1:2	<1:2	Neg
Calf	---	Neg	---	---	Neg	---	---	---	Neg
Dam ^{1,2}	---	Neg	---	---	Neg	---	---	---	1:10
Dam ²	---	Neg	---	---	---	---	---	---	Neg
Dam ²	---	Neg	---	---	---	---	---	---	Neg
Dam ²	---	Neg	---	---	---	---	---	---	Neg
Dam ³	---	Neg	---	---	---	---	---	---	1:10
Dam ³	---	Neg	---	---	---	---	---	---	Neg
Dam ³	---	Neg	---	---	---	---	---	---	Neg

1. L.E. Rice, College of Veterinary Medicine, Oklahoma State University, Stillwater, OK.
2. Dam with affected calf.
3. Dam with normal calf.
4. Serum Neutralizing Antibody test.
5. Complement Fixation test.

Fig 1 - Dorsal view of a hydranencephalic bovine brain. Cerebral hemispheres are reduced with abolition of superior sulci. Porencephalic cysts are present in the cerebellum.

Fig 2 - Ventral view of the brain depicted in Fig 1.

Fig 3 - Parasagittal section of the hydranencephalic brain in Fig 1,2. Note the ventricular dilation, thinned cerebral mantle, and porencephalic cysts in the cerebellum.

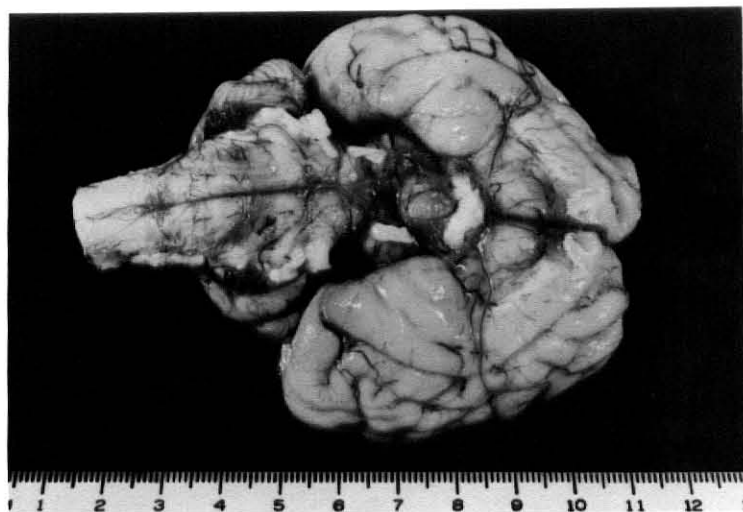
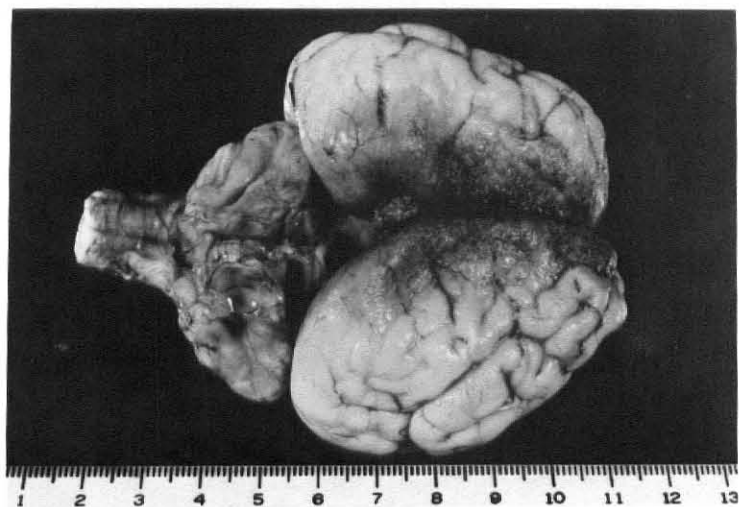


Fig 4 - Dorsal view of a hydranencephalic bovine brain.
The cerebral hemispheres are small, and the
cerebellum contains porencephalic cysts.

Fig 5 - Coronal slice of the cerebellum from the brain
depicted in Fig 4. Porencephalic cysts are
present in all portions of the cerebellum.

Fig 6 - Eyes from a hydranencephalic calf. Purulent
exudate is visible in the lower anterior
chambers.

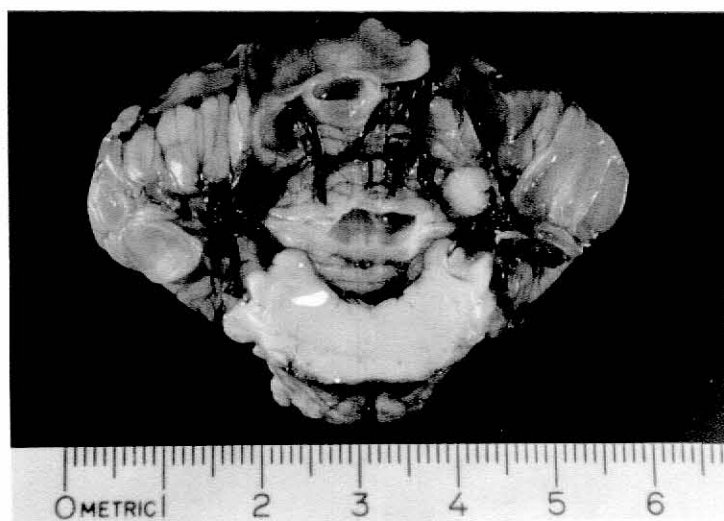


Fig 7-9 - Coronal sections of the cerebrum from a hydran-
encephalic calf. Both lateral ventricles are
dilated. The cerebral mantle is thin, and a
unilateral porencephalic cyst is visible in the
external capsule.

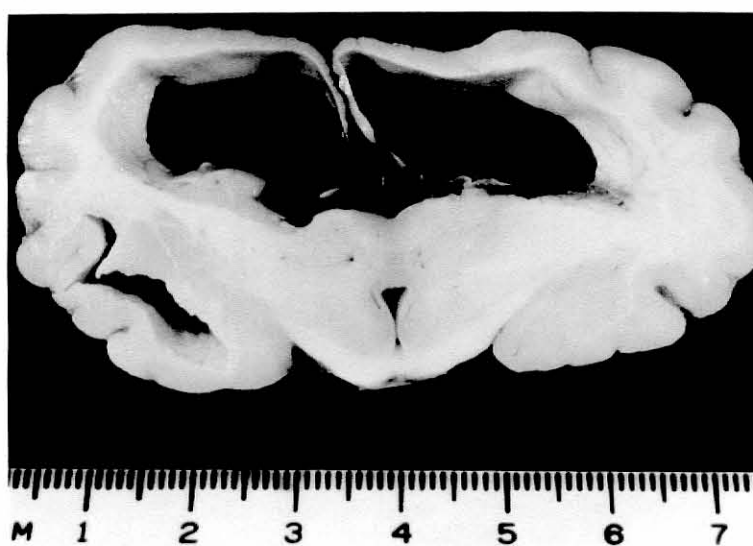


Fig 10 - Sagittal section of cerebellum and brain stem from a hydranencephalic calf. Note the porencephalic cysts (C) and overlying pia mater (arrow). H&E stain; X 2.

Fig 11 - Parasagittal section of cerebellum and brain stem from a hydranencephalic calf. Porencephalic cysts (C) are present. Note the paucity of neuraxons (light areas). Davenport stain; X 2.

Fig 12 - Coronal section of cerebral hemispheres from a hydranencephalic calf. White matter is markedly reduced in the mantle (CM). Davenport stain; X 1.8.

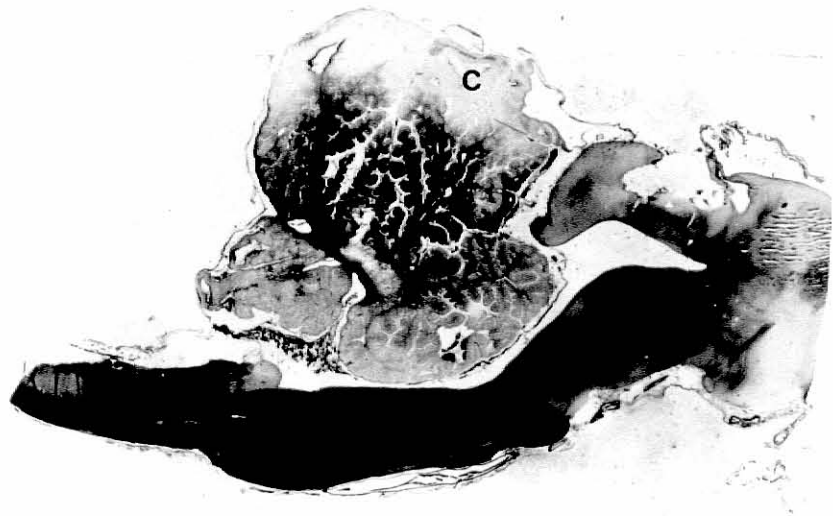
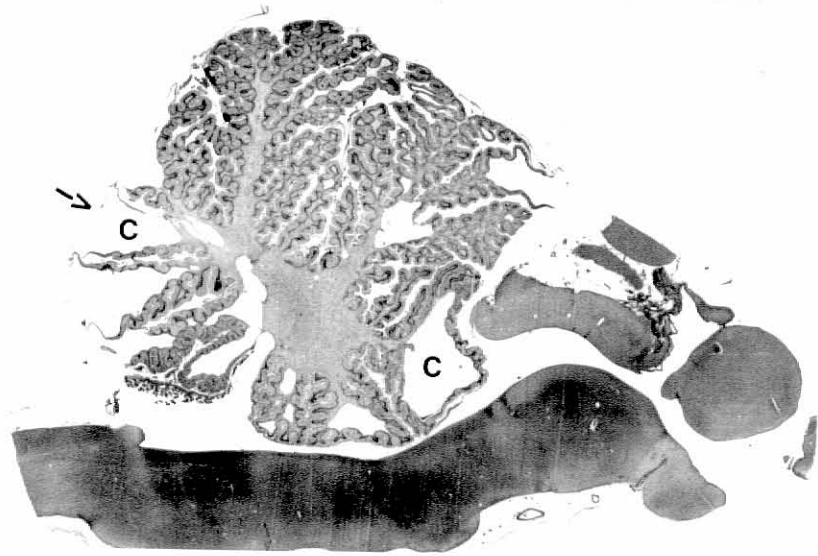


Fig 13 - Cerebellum from a hydranencephalic calf. Note the spongiform appearance of the white matter. H&E stain; X 160.

Fig 14 - Cerebellar folium from a hydranencephalic calf. Liquefaction of the spongiform areas of white matter progress to cyst formation. H&E stain; X 40.

Fig 15 - Cerebellar folium from a hydranencephalic calf. Note the porencephalic cyst. H&E stain; X 64.

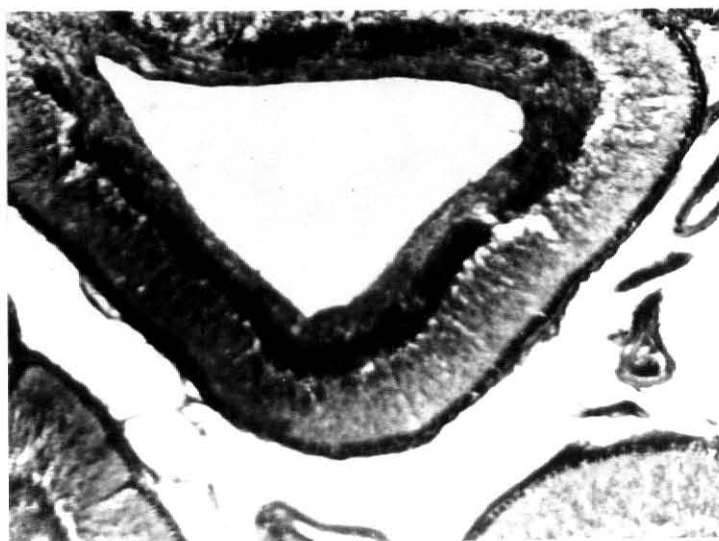
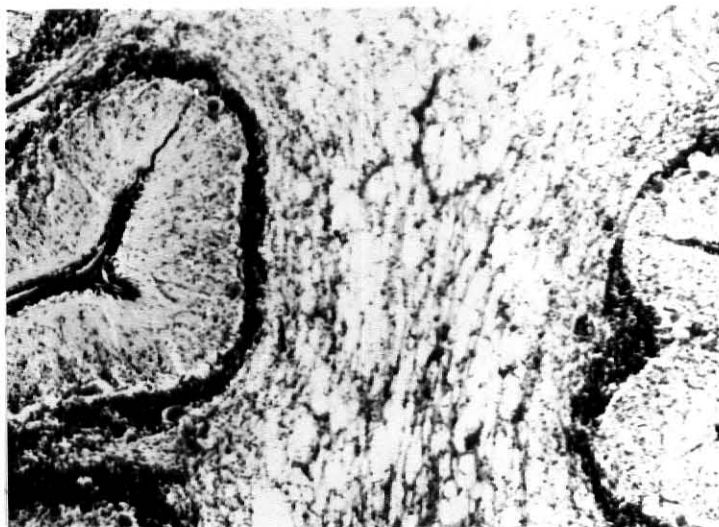
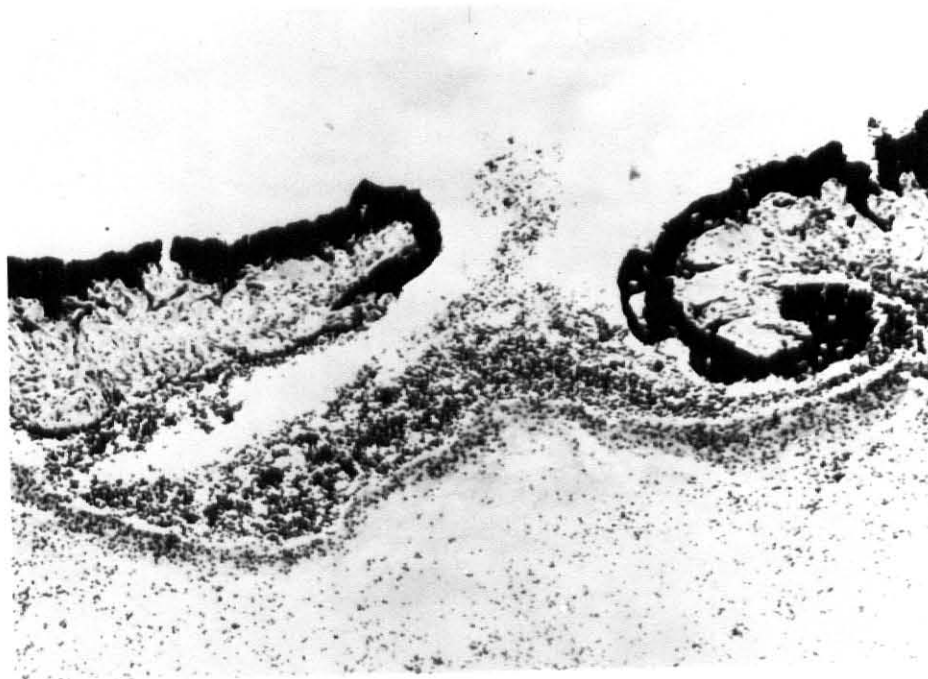
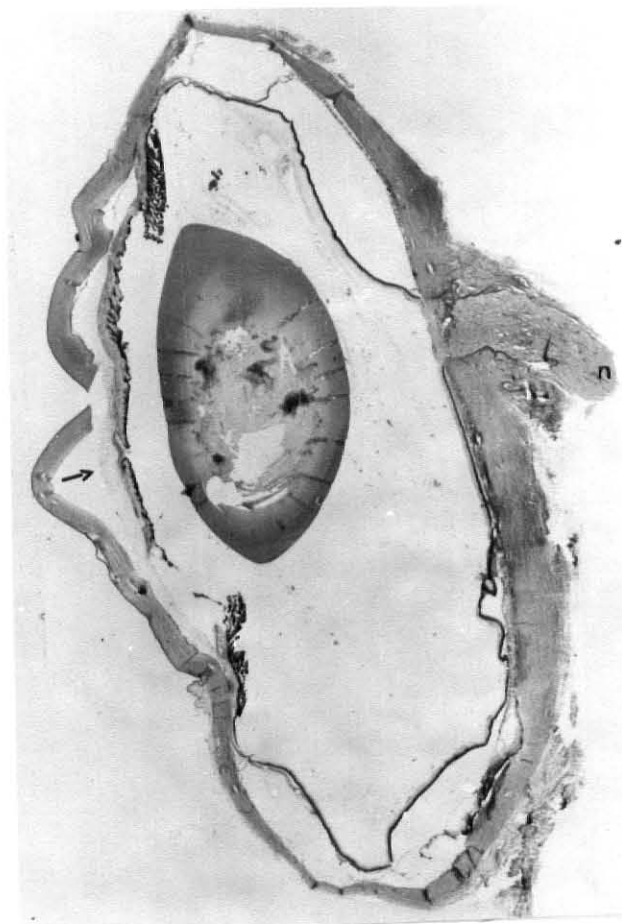


Fig 16 - Longitudinal section of the globe of a hydran-
encephalic calf. The anterior chamber contains
a purulent exudate (arrow), and the optic nerve
(n) has undergone spongiform change. The retinal
detachment is an artifact. H&E stain; X 3.6.

Fig 17 - The iridic aperture from the eye depicted in
Fig 16. Purulent exudate is present in the
anterior chamber. H&E stain; X 64.



IV. CONGENITAL INTERNAL HYDROCEPHALUS IN CALVES ASSOCIATED WITH
BOVINE VIRUS DIARRHEA-MUCOSAL DISEASE VIRUS

INTRODUCTION

Congenital hydrocephalus in cattle may result from genetic or adverse environmental factors. Genetic forms have been extensively reviewed¹. The influence of environmental factors in the pathogenesis of hydrocephalus is difficult to ascertain; few cases have been reported.

The teratogenic effect of bovine virus diarrhea-mucosal disease (BVD-MD) virus has been studied. Experimental infection of susceptible cows has demonstrated that fetal age at the time of infection and the virus strain are apparently the most important factors in determining the subsequent effects on the fetus²⁻⁶. The principal central nervous system (CNS) malformation reported was cerebellar hypoplasia; hydrocephalus was not observed. Pregnant ewes experimentally inoculated with a cytopathic BVD-MD virus on days 22 and 47 post-breeding, produced hydrocephalic lambs⁷. Field cases of hydrocephalus thought to be the result of fetal BVD-MD infection have been reported from Australia⁸ and Hungary⁹, but not the United States.

Reported here are field cases of congenital hydrocephalus in calves associated with BVD-MD virus.

MATERIALS AND METHODS

Calves - Two calves with clinical signs of hydrocephalus were submitted to Kansas State University. Following clinical examination,

the calves were euthanatized^a and complete necropsies performed.

Specimen Collection and Preparation - Brains were removed intact via removal of the dorsal calvarium. Nervous tissue and grossly abnormal non-nervous tissues were fixed in 10% buffered neutral formalin for a minimum of 14 days. Tissues were routinely processed^b, embedded in paraffin, 6 to 10 micra sections of nervous tissue, and 6 micra sections of non-nervous tissue were cut^c, and stained with hematoxylin and eosin in an automatic slide stainer^d. Selected sections were stained with periodic acid Schiff (PAS)¹⁰.

Virology - Previously published virus isolation techniques^e utilizing embryonic bovine kidney cells were employed to screen spleen, lymph node, intestine, and cerebrospinal fluid (CSF)¹¹. The viral interference test was used to detect BVD-MD virus after the third passage.

Direct immunofluorescent test (FAT)^f was used for virus detection in tissues.

^aT-61, National Laboratories, Veterinary Pharmaceuticals,
American Hoechst Corp, Somerville, NJ.

^bAutotechnicon Ultra II, Technicon Instruments Corp, Tarrytown, NY.

^cSpencer rotary microtome, model 820, American Optical Corp,
Buffalo, NY.

^dHisto Tek slide stainer, Technicon Instruments Corp, Tarrytown, NY.

^eRM Phillips, Veterinary Diagnostic Laboratory, College of Veterinary
Medicine, Kansas State University, Manhattan, KS.

^fDR Howard, Veterinary Diagnostic Laboratory, College of Veterinary
Medicine, Kansas State University, Manhattan, KS.

RESULTS

Clinical Findings - The first calf, a day old female Beefmaster, was presented with a severely enlarged calvarium (Fig 1 & 2). Extensive cranial enlargement caused dystocia; the calf was delivered via cesarian section. The calf was able to stand and move about slowly. Severe calvarial enlargement resulted in ventrolateral deviation of the eyes. Blindness was evidenced by lack of pupillary and menace reflexes. Signs of septicemia were observed; the calf died the following day.

The second calf, a 14-day-old male horned Hereford calf, was born with moderate doming of the calvarium. Though depressed, the calf was able to walk and had normal ocular reflexes. He had been hand reared since birth.

Virologic Findings - A non-cytopathic BVD-MD virus was isolated from spleen, intestine, lymph nodes and CSF from the first calf. BVD-MD viral antigens were detected by FAT in spleen, lung and lymph nodes of the second calf.

Gross Pathologic Findings - Severe calvarial enlargement in the Beefmaster calf was accompanied by patency of the fontanelles and thinning of the calvarial bones. Internal hydrocephalus was marked. Ventricles were severely distended with clear CSF and collapsed following partial removal of the calvarium (Fig 3). The cerebral mantle was reduced to a 0.2-0.5 cm membrane of nervous tissue lacking sulci. The septum pellucidum was absent. The hippocampus was atrophic and displaced ventrally between the flattened and abaxially displaced thalamic bodies. The mesencephalic aqueduct was stenotic; the cerebellum was hypoplastic.

Moderate calvarial enlargement of the Hereford calf was accompanied

by slight thinning of calvarial bone. Internal hydrocephalus was marked. Both lateral ventricles were severely distended and the cerebral mantle thinned to a 0.5 cm membrane of tissue that lacked dorsal sulci. The septum pellucidum was fenestrated (Fig 4). A fibrinous exudate was present on the inner surface of the lateral and third ventricles and choroid plexus. The hypothalamic sulcus was dilated and fibrinous exudate was present on the surface of the thalamus (Fig 5). The mesencephalic aqueduct was stenotic (Fig 6). The cerebellum was normal sized.

Histopathologic Findings - The inner surface of the lateral ventricles of the Beefmaster calf consisted of compressed periventricular white matter devoid of ependymal cells. The leptomeninges, perivascular spaces, and the choroid plexus were infiltrated with neutrophils and mononuclear inflammatory cells. The mesencephalic aqueduct was stenotic. Neutrophils and mononuclear inflammatory cells were found in the aqueduct lumen, and perivascular spaces of adjacent nervous tissue (Fig 7). Cerebellar hypoplasia was characterized by reduction in folial size and rarefaction of granular cells. Mild bronchopneumonia, meningomyelitis and retinal atrophy were also present.

The cerebral mantle in the Hereford calf was compressed. Leptomeninges and perivascular spaces were infiltrated with mixed populations of neutrophils and mononuclear inflammatory cells. Large areas of the lateral ventricular lining were covered with inflammatory exudate consisting of neutrophils, fibrin, and erythrocytes. The mesencephalic aqueduct was stenotic and inflammatory exudate was present in its lumen (Fig 8). The cerebellum was normal, except for inflammatory cells in

the leptomeninges and perivascular spaces.

DISCUSSION

Internal hydrocephalus in both calves was associated with aqueductal stenosis and meningoencephalitis. Experimentally viral agents have been found to cause aqueductal stenosis resulting in internal hydrocephalus in laboratory animals¹². Inflammatory lesions have been observed in the brains of fetuses from dams experimentally infected with BVD-MD virus^{4,6}. They differ from the calves in this study; however, as only mononuclear cells were observed and evidence of inflammation was absent 70 days post-infection⁶. Clinical signs of septicemia were present in one calf, and may be responsible for the suppurative inflammatory component. Cerebellar hypoplasia is a consistent finding in experimental congenital BVD-MD infection in calves²⁻⁶. The absence of cerebellar hypoplasia in one calf was surprising. Experimental BVD-MD virus infection in a ewe 22 days post-breeding, however, resulted in the birth of a hydrocephalic lamb without cerebellar lesions⁷. Hydrocephalus in man is thought to result from destructive processes after the fifth month of gestation¹³. Hydrocephalus in the absence of cerebellar lesions may be the result of destructive processes after sufficient cerebellar development has occurred, rendering it less vulnerable to destruction.

Hereditary hydrocephalus in horned Herefords, in our experience, is characterized by a triad of lesions: internal hydrocephalus, cerebellar dysplasia, and dorsal kinking of the mesencephalon at the interpeduncular fossa. These lesions were not present in the Hereford

in the present study.

While no cause and effect relationship was proven, the most likely cause of the two cases of hydrocephalus is congenital BVD-MD infection, though infection could have occurred during, or following birth. The nature of the lesions, however, makes the latter unlikely.

SUMMARY

Congenital internal hydrocephalus was diagnosed in two calves, one and 14 days old, respectively, associated with stenosis of the mesencephalic aqueduct and meningoencephalitis. Cerebellar hypoplasia was present in one calf. Bovine virus diarrhea-mucosal disease virus was detected in the tissues of both calves and was thought to be the causative agent.

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Fig 1 - Lateral view of a hydrocephalic Beefmaster calf.
The severe cranial enlargement has resulted in
ventrolateral deviation of the eye.

Fig 2 - Dorsal view of the same Beefmaster calf in Fig 1.

Fig 3 - Dorsal view of the brain of the Beefmaster calf in
Fig 1 & 2, following removal of part of the calvarium.
The cerebral hemispheres are partially collapsed.

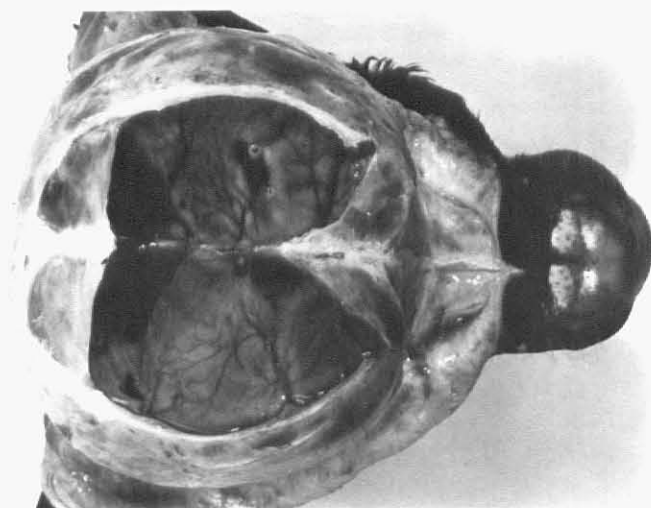
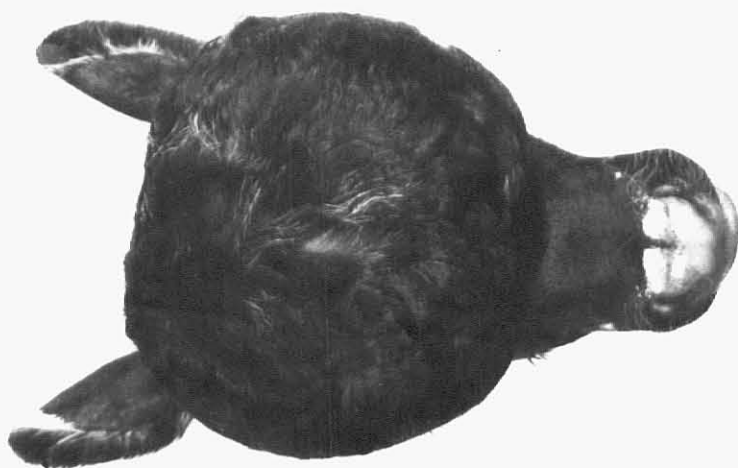


Fig 4 - Lateral view of the brain from a 14-day-old hydrocephalic horned Hereford, following removal of the left cerebral hemisphere. The septum pellucidum is fenestrated (arrow). The interpeduncular fossa has normal conformation (a).

Fig 5 - Dorsal view of the brainstem and cerebellum of the hydrocephalic horned Hereford in Fig 4. The hypothalamic sulcus is dilated. Fibrinopurulent exudate covers the thalamus.

Fig 6 - Serial slices of the mesencephalon from the same hydrocephalic Hereford. The stenotic aqueduct is visible.

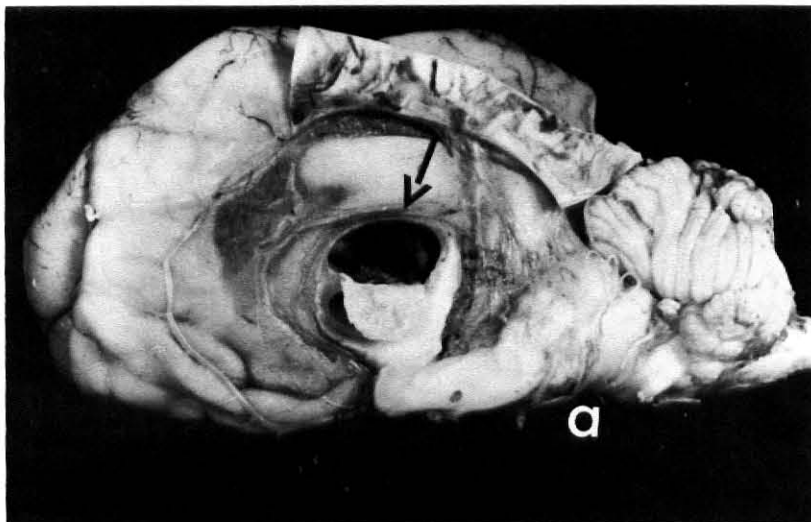
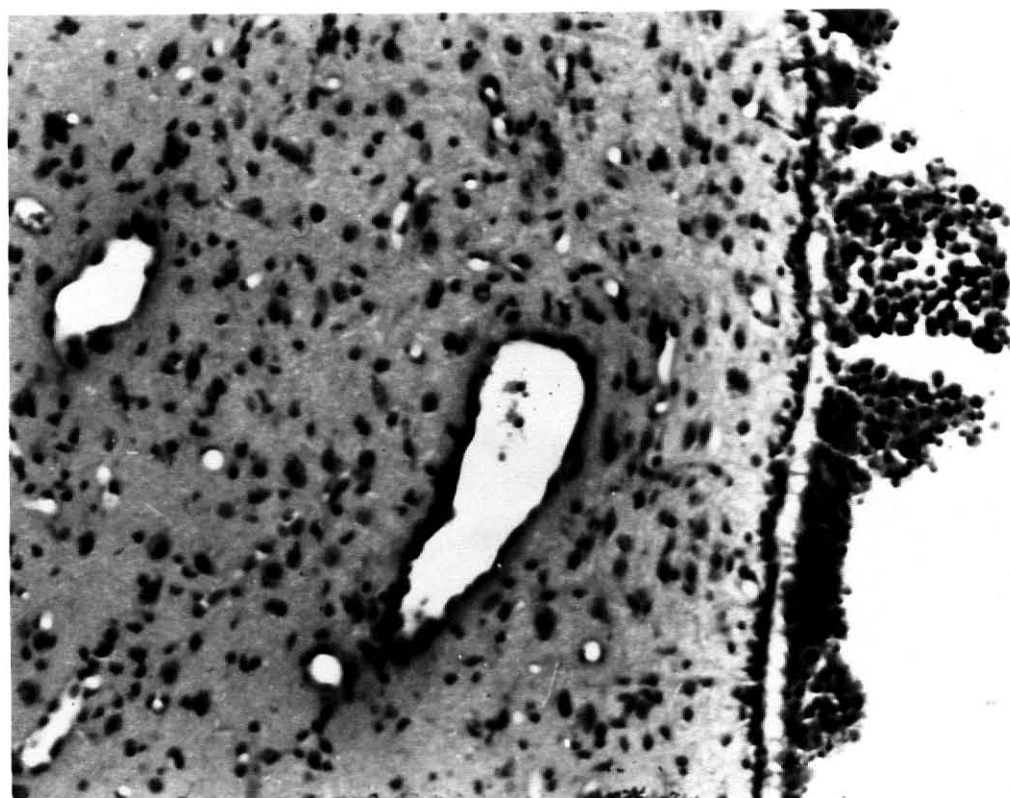
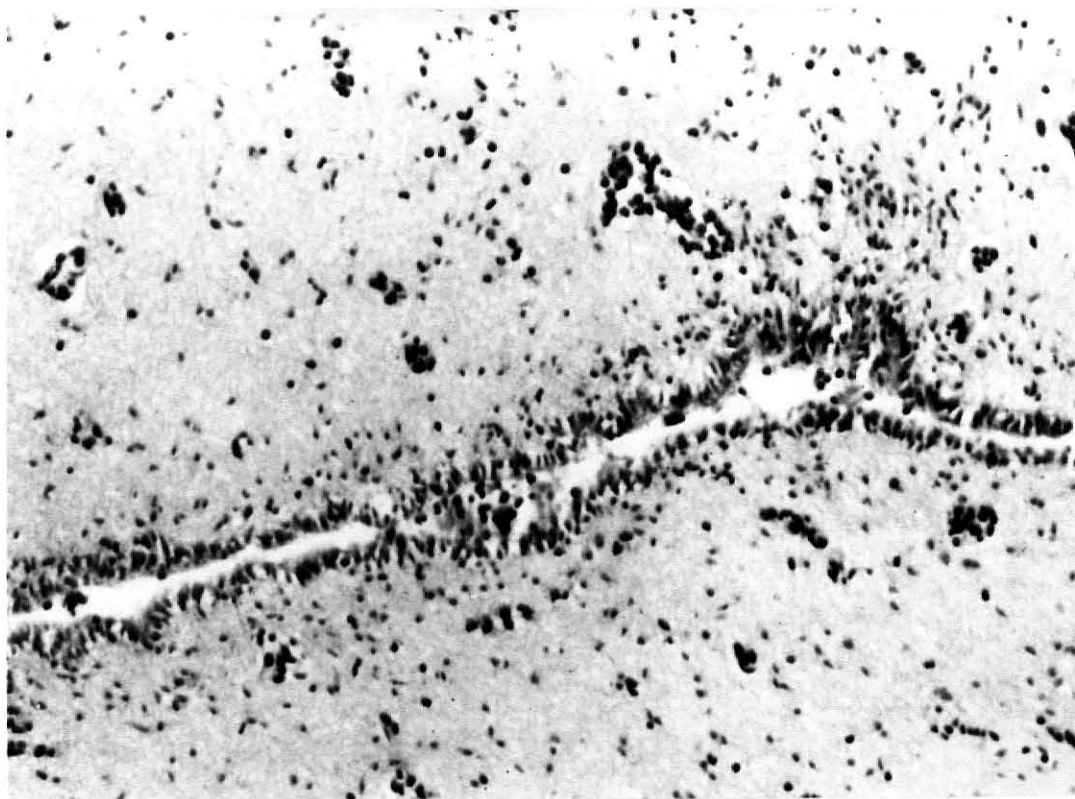


Fig 7 - Mesencephalic aqueduct from the same Beefmaster calf.
Inflammatory cells are visible within the lumen of the
stenotic aqueduct and in the perivascular spaces.
H&E stain; X 160.

Fig 8 - Mesencephalic aqueduct from a hydrocephalic Hereford
calf. An aggregate of inflammatory cells is adhered
to the ependymal cilia. H&E stain; X 320.



V. CONGENITAL INTERNAL HYDROCEPHALUS IN SIMMENTAL CATTLE

INTRODUCTION

Hydrocephalus is the most common central nervous system defect reported in cattle¹. Congenital forms may be inherited or environmental. While virtually all beef and dairy breeds are affected, few cases have been reported in Simmentals²⁻⁶.

This paper reports pathologic findings in congenital hydrocephalus in two calves of Simmental descent.

MATERIALS AND METHODS

Calves - Two calves with clinical signs of hydrocephalus were submitted to Kansas State University; a 14-day-old dead male Simmental and a six-month-old male Simmental-Hereford crossbred. The crossbred was clinically examined and euthanatized^a. Both calves were carefully necropsied.

Specimen Collection and Preparation - Brains were removed intact via removal of the dorsal calvarium. Nervous tissue and grossly abnormal non-nervous tissues were fixed in 10% buffered neutral formalin for a minimum of 14 days. Tissues were routinely processed^b, embedded in paraffin, 8 to 10 micra sections of nervous tissue and 6 micra sections of non-nervous tissue were cut^{c,d}, and stained with hematoxylin and eosin

^aT-61, National Laboratories, Veterinary Pharmaceuticals, American Hoechst Corp, Somerville, NJ.

^bAutotechnicon Ultra II, Technicon Instruments Corp, Tarrytown, NY.

^cSpencer rotary microtome, model 820, American Optical Corp, Buffalo, NY.

^dSpencer sliding microtome, model 860, American Optical Corp, Buffalo, NY.

by an automatic slide stainer^e, or by conventional hand methods⁷.

Virology - Previously published virus isolation techniques utilizing embryonic bovine kidney cells were employed to screen cerebrospinal fluid (CSF), intestine, lymph node, and spleen^{8,f}. The direct fluorescent antibody test (FAT)⁸ was employed to screen tissues and cell cultures for bovine virus diarrhea-mucosal disease (BVD-MD) and parainfluenza-3 (PI₃) viruses. The viral interference test was used for additional screening of cell cultures for BVD-MD virus.

RESULTS

Clinical Findings - Both male calves had exhibited clinical signs of hydrocephalus since birth. The six-month-old Simmental-Hereford cross was emaciated and slightly ataxic. Saliva flowed continuously from the mouth. Moderate calvarial enlargement was apparent (Fig 1,2).

Virologic Findings - Tissues from both calves were negative for BVD-MD virus. The older crossbred was negative for PI₃ virus.

Gross Pathologic Findings - The calvarium of the Simmental calf was severely enlarged and resulted in ventromedial angulation of the eyes. The calvarial bones were thin. Internal hydrocephalus was

^eHisto Tek Slide stainer, Technicon Instruments Corp, Tarrytown, NY.

^fRM Phillips, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

⁸DR Howard, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

characterized by severe distension of the lateral ventricles, and fenestration of the septum pellucidum. The cerebral mantle was thinned to 0.5 cm and the dorsal cerebral convolutions were missing. The leptomeninges in the posterior fossa were thickened and hemorrhagic. Arnold-Chiari malformation (ACM) was evidenced by herniation of the cerebellar vermis through the foramen magnum and caudal displacement and elongation of the medulla oblongata, pons, and fourth ventricle (Fig 4,5). The mesencephalic aqueduct was stenotic, although anatomically patent. Suppurative bronchopneumonia was an additional finding.

Moderate cranial enlargement of the Simmental-Hereford cross was accompanied by thinning of the calvarial bones and ventromedial angulation of the eyes. Internal hydrocephalus was characterized by severe distension of the lateral ventricles and fenestration of the septum pellucidum (Fig 3,6). The cerebral mantle was thinned to 1 cm and dorsal convolutions were absent (Fig 6). The mesencephalon was hypoplastic and the mid-portion was laterally compressed. Superior colliculi were elevated to form two sharply pointed ridges separated by a deep median cleft (tectal beaking). The aqueduct was stenotic, but anatomically patent (Fig 7). Transventricular shunting of CSF was evidenced by cystic distension of the roof of the third ventricle. The cerebellum was normal in size.

Histopathological Findings - The cerebral mantle in the Simmental calf was compressed with focal loss of ependymal cells and attenuation of those present. Subependymal tissues were infiltrated with glial cells and hemosiderin-laden macrophages. The leptomeninges surrounding the caudal cerebellum and brain stem were fibrosed and infiltrated

with neutrophils, erythrocytes, and hemosiderin-laden macrophages (Fig 8,9). The cerebellar vermis was severely compressed. Cortical areas contained numerous vacuoles, focal areas of hemorrhage, and diffuse gliosis (Fig 10,11). Additional findings included meningo-myelitis and retinal dysplasia.

The cerebral mantle of the Simmental-Hereford cross was compressed. Lateral ventricular ependymal tissue was intact and severely attenuated with mild subependymal gliosis. No evidence of inflammation was apparent in the malformed mesencephalon. The cerebellum was normal. Additional findings included spongiform vacuolation of the ventral funiculi in the spinal cord, and rare birefringent crystals in renal tubules.

DISCUSSION

Nineteen reported cases of hydrocephalus in Simmental cattle were found; one occurred in the United States², and eighteen in Germany³⁻⁶. Arnold-Chiari malformation and hydrocephalus was associated with ditetraploid mosaicism in one of the European cases, however, no morphologic description accompanied the report⁴.

Reported cases of ACM in other breeds have usually been associated with spina bifida⁹. A similar combination of malformations was experimentally produced in hamsters with reovirus infection¹⁰. Hydrocephalus resulted from stenosis of the third ventricle and mesencephalic aqueduct, secondary to ependymal damage. The ACM was attributed to compression of the developing cerebellum in the posterior fossa by the expanding lateral ventricles.

The absence of dysplastic changes in the cerebellum in the present case suggests compression took place after it was fully developed. The spinal subarachnoid space is responsible for the bulk of CSF resorption in animals¹¹. Occlusion of the foramen magnum by the cerebellum or pre-existing meningomyelitis could account for reduced CSF resorption and hydrocephalus. Hydrocephalus usually results in compression of the mesencephalon, rather than elongation, as observed in this case, favoring ACM as the cause¹². Chromosome studies were not done and aberrations observed in the previously reported case cannot be eliminated.

Tectal beaking and lateral compression of the mesencephalon, as observed in the Simmental-Hereford cross, resulted from hydrocephalus-induced stenosis of the aqueduct in man¹². The cause of hydrocephalus in both cases was undetermined.

SUMMARY

Congenital internal hydrocephalus was diagnosed in two male calves; a 14-day-old Simmental, and a 6-month-old Simmental-Hereford cross. It was associated with Arnold-Chiari malformation in the Simmental. Mesencephalic malformations characterized by mesencephalic hypoplasia, aqueductal stenosis, and tectal beaking accompanied the internal hydrocephalus in the crossbred. The cause of hydrocephalus in both cases was undetermined.

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Fig 1,2 - Antemortem photographs of a six-month-old male Simmental-Hereford crossbred calf with internal hydrocephalus. The moderate calvarial enlargement resulted in ventromedial angulation of the eyes.

Fig 3 - Dorsal view of the brain from the calf in Fig 1,2. The severely distended lateral ventricles completely cover the cerebellum. The cerebral convolutions have been abolished.

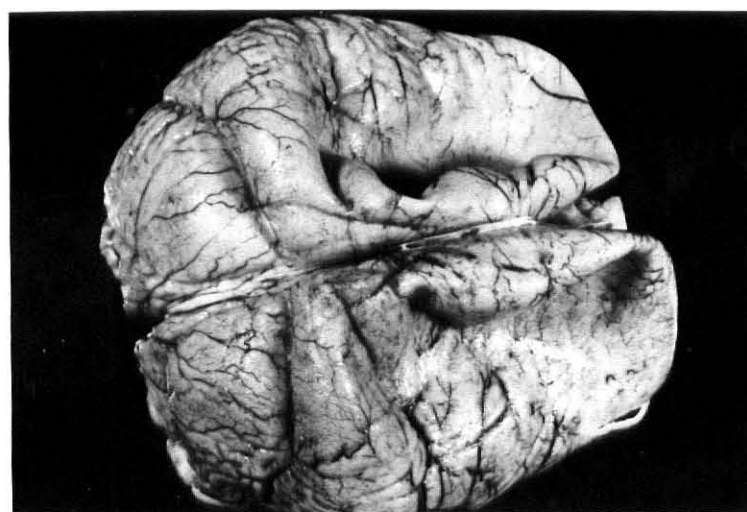


Fig 4 - Midsagittal sections of a brainstem from a normal calf (top section), and from a 14-day-old Simmental calf with Arnold-Chiari malformations (bottom section). Note the abnormally elongated, hemorrhagic cerebellar vermis (arrows), and the flattened brainstem.

Fig 5 - Close-up view of the bovine Arnold-Chiari malformation depicted in the bottom section of Fig 4. Note the elongated fourth ventricle (arrow).

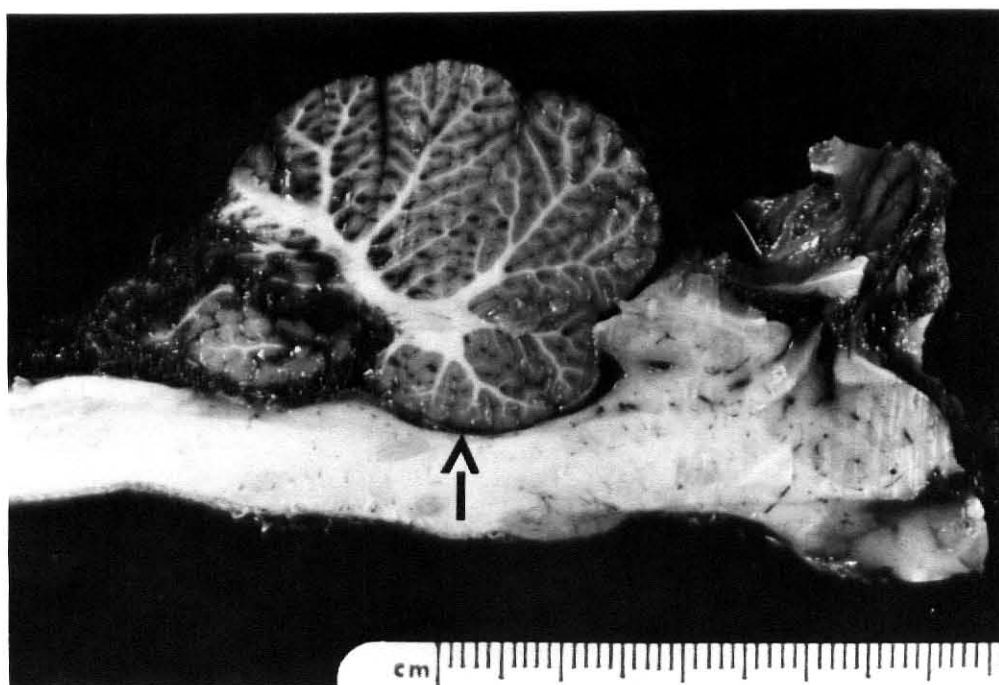
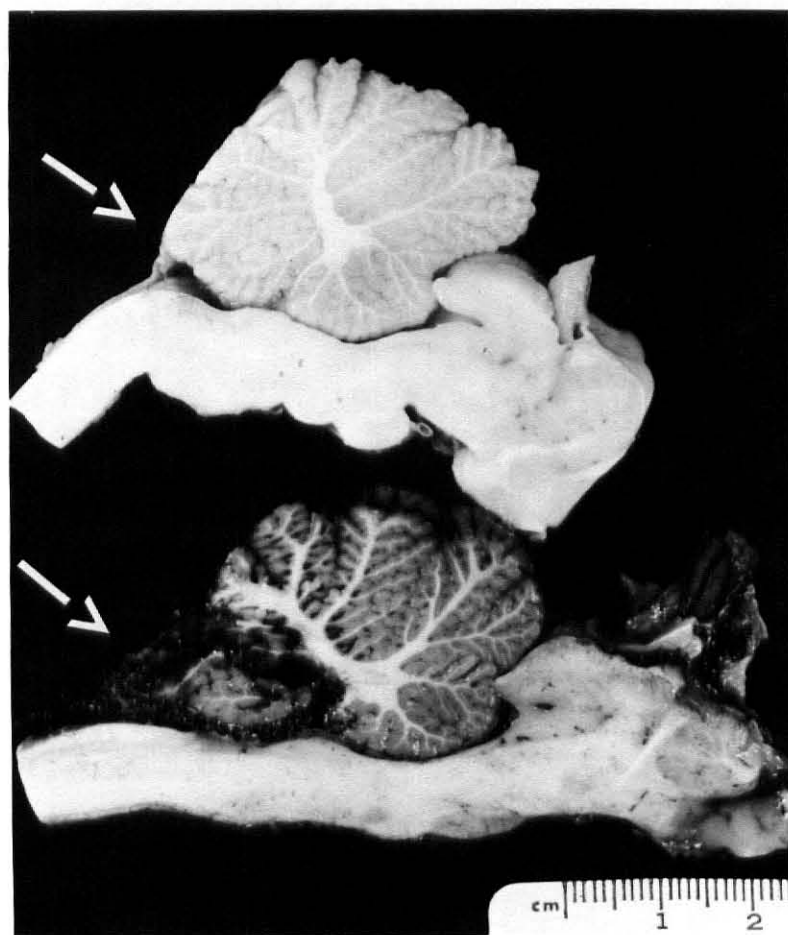


Fig 6 - Lateral view of the brain in Fig 3, from a hydrocephalic Simmental-Hereford calf. The lateral ventricles are severely distended. The cerebral cortex is thinned and septum pellucidum fenestrated.

Fig 7 - Cross sections of mesencephalons from the Simmental-Hereford calf (left), and a normal calf (right). Note the marked tectal beaking (arrows) and hypoplastic appearance. The aqueduct on the left is stenotic, but patent.

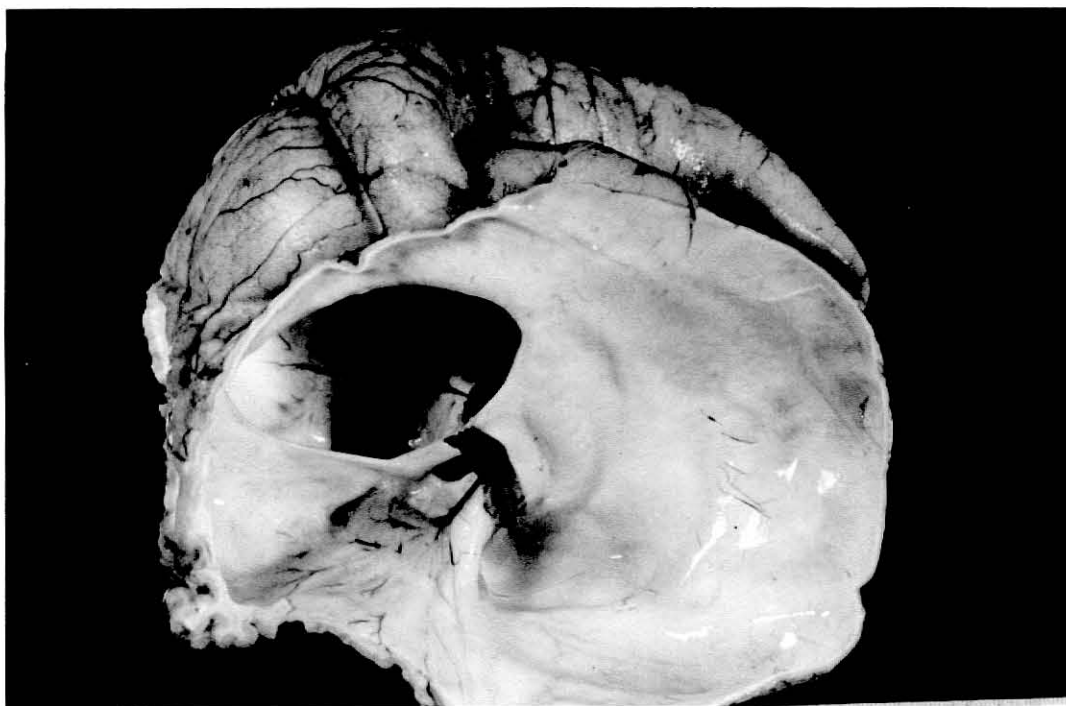


Fig 8,9 - Parasagittal sections of cerebellum and brain stem from a normal calf (top), and from one with Type I Arnold-Chiari malformation. Hemorrhage is present in the "tongue-like" extension of the vermis (arrows), elongated fourth ventricle (4), and elongated mesencephalon. Compare the distances across the interpeduncular fossa from the mammillary bodies (M) to the pons (P). H&E stain; x 2.7.

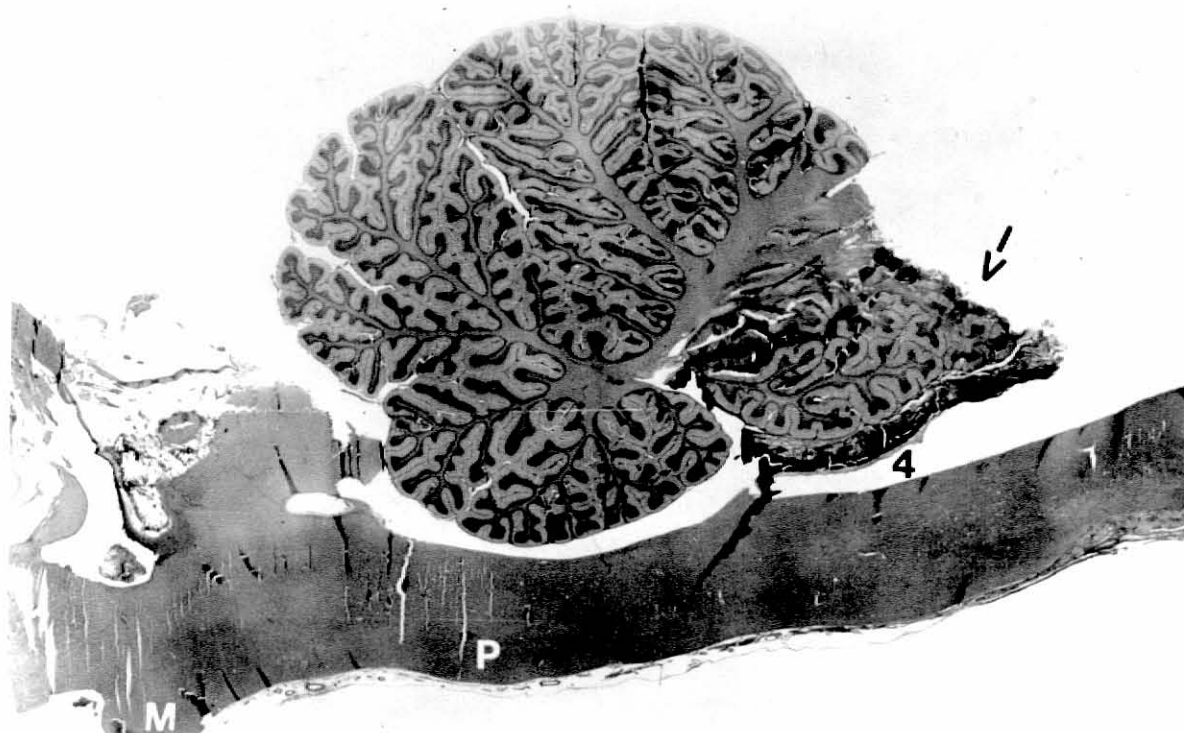
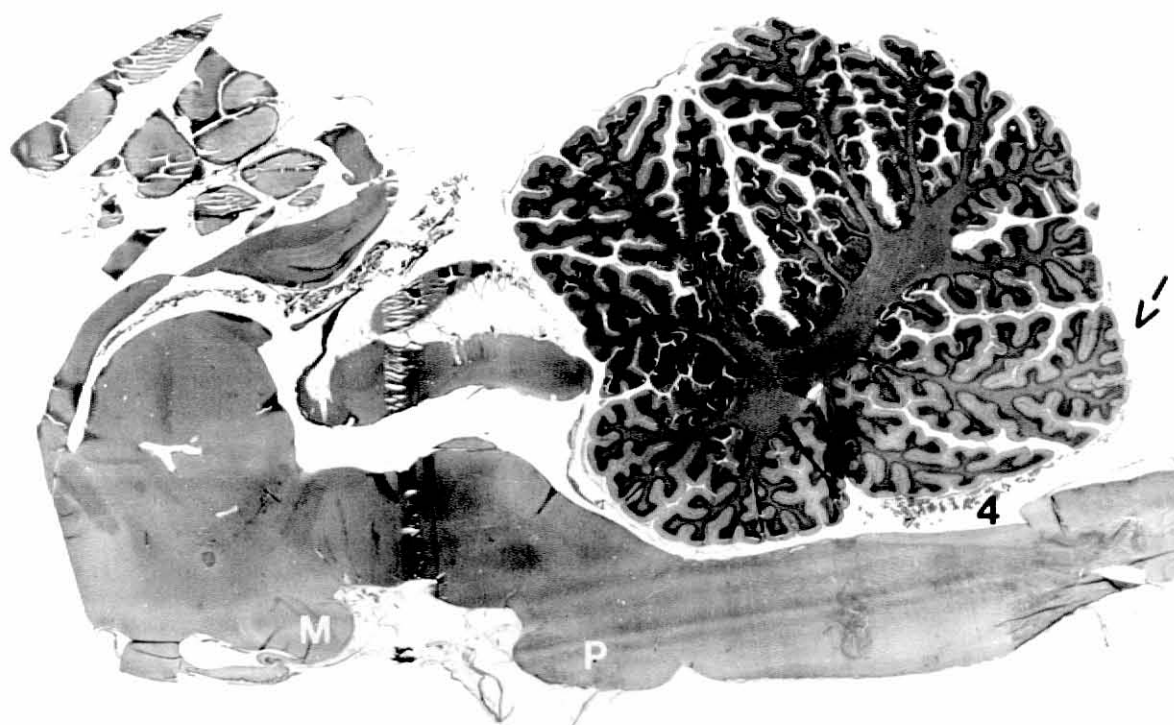


Fig 10 - Cerebellum from a hydrocephalic Simmental calf with Type I Arnold-Chiari malformation. A large area of hemorrhage (arrow) extends from the meninges to the granular cell layer (G). Note the diffuse gliosis. H&E stain; X 64.

Fig 11 - A higher magnification of the cerebellum depicted in Fig 10. The Purkinje's cell layer is vacuolated and contains diffuse gliosis. The granular cell layer (G) is visible. H&E stain; X 160.



VI. CONGENITAL INTERNAL HYDROCEPHALUS IN POLLED HEREFORD
CATTLE

INTRODUCTION

Congenital hydrocephalus in cattle may result from genetic or environmental factors, and occurs in virtually all breeds. Hereditary internal hydrocephalus has resulted in substantial losses in Hereford cattle¹⁻⁴. Morphologic variation in hydrocephalic brains has been described in calves with familial histories supportive of a genetic cause; multiple syndromes may exist^{4,5}.

No distinction was made between Horned and Polled Hereford breeds in previous studies. Both breeds represent different genetic populations that may account for the multiplicity of syndromes. Reporting of field cases of bovine hydrocephalus according to their respective breeds would facilitate recognition of genetic and environmental causes of internal hydrocephalus.

Reported here are the morphologic findings in three hydrocephalic Polled Hereford calves.

MATERIALS AND METHODS

Calves - Three Polled Hereford male calves (1-11 days of age) with domed calvaria suggestive of hydrocephalus were submitted to Kansas State University. Following clinical examination, the calves were euthanatized^a and complete necropsies performed.

^aT-61, National Laboratories, Veterinary Pharmaceuticals, American Hoechst Corp, Somerville, NJ.

Specimen Collection and Preparation - Brains and spinal cords were obtained intact via removal of the dorsal calvarium and dorsal spinal arches of the spinal column. Nervous tissue and other grossly abnormal tissues were fixed in 10% buffered neutral formalin for a minimum of 14 days. Tissues were routinely processed^b embedded in paraffin, 8 to 10 micra sections of nervous tissue and 6 micra sections of non-nervous tissue were cut^{c,d} and stained with hematoxylin and eosin by an automatic slide stainer^e or by conventional hand methods for light microscopy⁶. Selected sections were stained with Davenport's method for neuraxons⁷ and luxol fast blue (Kluver-Barrera method) for myelin and nerve cells⁶. Coronal sections of cerebral hemispheres and sagittal sections of brain stems and cerebellums were utilized where feasible.

Virology - Previously published virus isolation techniques utilizing embryonic bovine kidney cells were employed to screen cerebrospinal fluid (CSF), joint fluid, lung, lymph node, skin, and spleen^{8,f}.

The direct fluorescent antibody test (FAT)^g was used to screen

^bAutotechnicon Ultra II, Technicon Instruments Corp, Tarrytown, NY.

^cSpencer rotary microtome, model 820, American Optical Corp, Buffalo NY.

^dSpencer sliding microtome, model 860, American Optical Corp, Buffalo NY.

^eTechnicon Instruments Corp, Tarryton, NY.

^fRM Phillips, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

^gDR Howard, Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University, Manhattan, KS.

tissues and cell cultures for the presence of bovine virus diarrhea-mucosal disease (BVD-MD) virus.

Serology - Serum neutralizing antibody tests for BVD-MD, infectious bovine rhinotracheitis (IBR), parainfluenza type 3 (PI₃), and adeno types 3 and 5 viruses, and the complement fixation test for bluetongue (BT) virus were performed on serum from two calves^f.

RESULTS

Clinical Findings - All calves had moderate calvarial doming. One calf was delivered via cesarean section and presented at one day of age was unable to stand. The eyes deviated ventrally, and leg paddling in lateral recumbency was noted. A second day-old calf, with tetramelic arthrogryposis, was alert and able to stand with difficulty. The 11-day-old was presented with anterior thoracic scoliosis and torticollis, asymmetry of the upper lip, stenosis of the left naris, multifocal complete and partial alopecia, and bilateral corneal ulceration and opacity. The calf was alert and walked with a swaying, weaving gait.

Microbiologic and Serologic Findings - No attempt was made to isolate viruses from the first calf, and cytopathic effects were not observed in cultures from the other two. Tissues from all calves and cell cultures were negative for BVD-MD virus by the FAT.

A neutralizing antibody titer of 1:64 for PI₃ was obtained from the second day-old calf. The 11-day-old calf had 1:4 and 1:256 titers for PI₃ and BVD-MD, respectively. Serum of the first calf was not tested.

Gross Pathologic Findings - Internal hydrocephalus was the only abnormality found in the first day-old calf. Both lateral ventricles were severely distended; sulci and gyri over the dorsal surface were attenuated. Remaining cerebral surfaces were corrugated due to multiple small gyri (micropolygyrus) (Fig 1). The roof of the third ventricle and tectum were elevated, causing separation of the longitudinal fissure (Fig 1). The leptomeninges were hemorrhagic at the base of the brain (Fig 1,2). The cerebral mantle was thin (2.0 cm) and the septum pellucidum was absent. The brain stem and cerebellum were hypoplastic; dilation of the third ventricle and mesencephalic aqueduct was marked. Tectal elevation was accompanied by dorsal kinking of the mesencephalon at the interpeduncular fossa, and absence of the pontine eminence (Fig 3,4).

Internal hydrocephalus accompanied tetramelic arthrogryposis in the second day-old calf. The leptomeninges of the brain and cord were distended with CSF. Lateral and third ventricles were only moderately dilated; the cerebellum and brain stem were morphologically normal (Fig 5,6). Lateral ventricular dilation was accompanied by fenestration of the septum pellucidum.

Internal hydrocephalus accompanied multiple defects in the 11-day-old calf. Lateral ventricles were distended and cerebral convexities were corrugated, due to many small gyri (micropolygyrus). The tentorium cerebelli transected part of the cerebellum, with no disparity in size of the anterior and posterior chambers (Fig 7-9). Lateral ventricular dilation was accompanied by absence of the septum pellucidum. Dorsal elevation of the tectum and dilation of the central portion of the

mesencephalic aqueduct were the only abnormalities noted in the brain stem (Fig 9).

Scoliosis of the thoracic spine consisted of compression of the right portion of the sixth and seventh thoracic vertebrae and deviation of the spinal column to the left (Fig 10). The spinal canal was stenotic through the affected portion of the column; the spinal cord was small and compressed. The right sixth spinal nerve was reduced to a thin thread (Fig 10).

Histopathologic Findings - Cerebral hemispheres in the first day-old calf consisted of thin, compressed remnants with deep gyri shifted to the exterior (Fig 12). Areas of focal loss of lateral ventricular ependyma were lined by flattened glial cells. The third ventricle was severely dilated; an elongated sac containing the choroid plexus projected dorsally from the roof, anterior to the pineal body (Fig 11). Cerebellar hypoplasia was characterized by ectopic granular cells and Purkinje's cells. Inflammation was not observed in the brain or leptomeninges. Mild suppurative bronchiolitis was noted.

Compression of the periventricular white matter was the only abnormality observed in the cerebrum of the second day-old calf. The ventricular ependyma was intact, but irregular in thickness. The mesencephalic aqueduct was anatomically patent. Projections of piled ependymal cells extended into the lumen. Evidence of inflammation was not observed. Mild hepatic lipidosis, ulcerative keratitis, and rare birefringent renal tubular crystals were additional findings.

Periventricular white matter was compressed and the lateral ventricular ependyma was intact in the 11-day-old calf. The cerebellum

was normal, except for the cleft produced by the aberrant tentorium cerebelli (Fig 13,14). Adjacent folia were mildly distorted. Infiltration of the leptomeninges with macrophages and lymphocytes was focally distributed. The mesencephalic aqueduct was anatomically patent. Perivascular spaces in the subependymal and deeper portions of the brain stem were infiltrated with macrophages and lymphocytes.

The compressed thoracic portion of the spinal cord was distorted (Fig 15). Eccentric shifting of the grey matter was accompanied by absence of the right ventral horn. The central canal was small and distorted or completely absent. Spongiform change was present in the white matter.

DISCUSSION

Internal hydrocephalus and cerebellar hypoplasia in the first day-old calf resembled the hereditary Syndrome I of Hereford cattle⁵. Environmental causes, however, cannot be excluded. The remaining cases have little in common with known or suspected forms of hereditary hydrocephalus in Polled Herefords.

The 11-day-old calf received colostrum; serum neutralizing antibodies to BVD-MD and PI₃ viruses could be either fetal or colostrum in origin. PI₃ virus is known to infect the bovine fetus and cause an immune response⁹. The PI₃ virus titer in the second day-old calf most likely indicated fetal infection. The presence of viral antibody, however, is not proof that the particular virus was responsible for the defects observed. While PI₃ appears to be of some importance in bovine

abortion, its role as a teratogen is largely unknown¹⁰. Intra-amniotic inoculation of PI₂ virus into hamsters pregnant 10-12 days, resulted in hydrocephalus secondary to aqueductal stenosis¹¹. Destruction of the ependyma led to gliovascular outgrowth over the ventricular walls, adhesions, and aqueductal stenosis. As a consequence of repair, the aqueductal lesion resembled a developmental rather than a post-infectious defect.

Fetal infection with BVD-MD virus is known to cause a wide range of congenital defects including ocular and CNS malformations, mandibular brachygnathism, musculoskeletal deformities, and alopecia^{12,13}. Mononuclear inflammatory cell perivascular cuffing in the 11-day-old calf, and ependymal abnormalities in the second day-old calf are compatible with an infectious cause. Fetal viral infection would seem to be the most likely cause of hydrocephalus in these Polled Hereford calves.

SUMMARY

Congenital internal hydrocephalus was diagnosed in three Polled Hereford calves. Internal hydrocephalus and cerebellar hypoplasia in one calf resembled a hereditary syndrome. Fetal viral infection was considered the most likely cause of internal hydrocephalus and musculoskeletal malformations in the other two calves.

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Fig 1 - Dorsal view of a hydrocephalic brain from a day-old Polled Hereford calf. The sulci and gyri are attenuated adjacent to the separation in the longitudinal fissure (arrow). Note the micropolygyrus and small cerebellum.

Fig 2 - Ventral view of the hydrocephalic brain depicted in Fig 1. The leptomeninges are hemorrhagic.

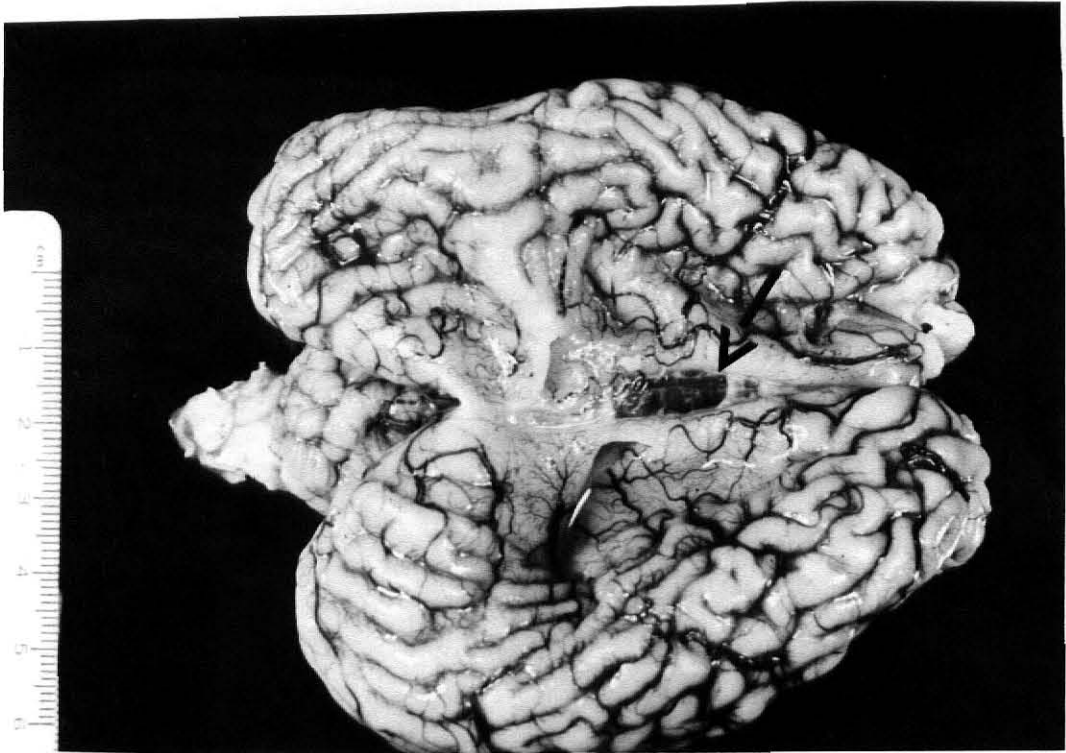


Fig 3 - Mid-sagittal slice of the brain stem and cerebellum from a day-old Polled Hereford calf (top). Normal brain stem and cerebellum (below) is presented for comparison. Note the generalized hypoplastic appearance and dilation of the third ventricle and mesencephalic aqueduct. The pontine eminence (P) is missing along the ventral margin, and the mesencephalon is elevated at the interpeduncular fossa (arrow).

Fig 4 - Close-up view of the brain stem and cerebellum from a day-old Polled Hereford calf depicted at the top of Fig 3. Distention of the mesencephalic aqueduct is marked (arrow).

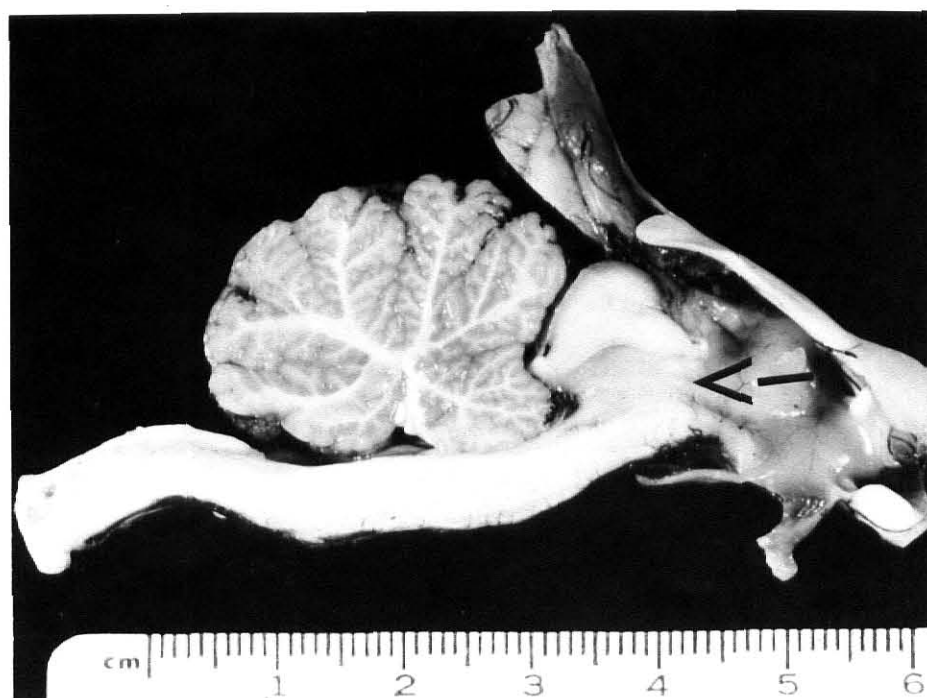
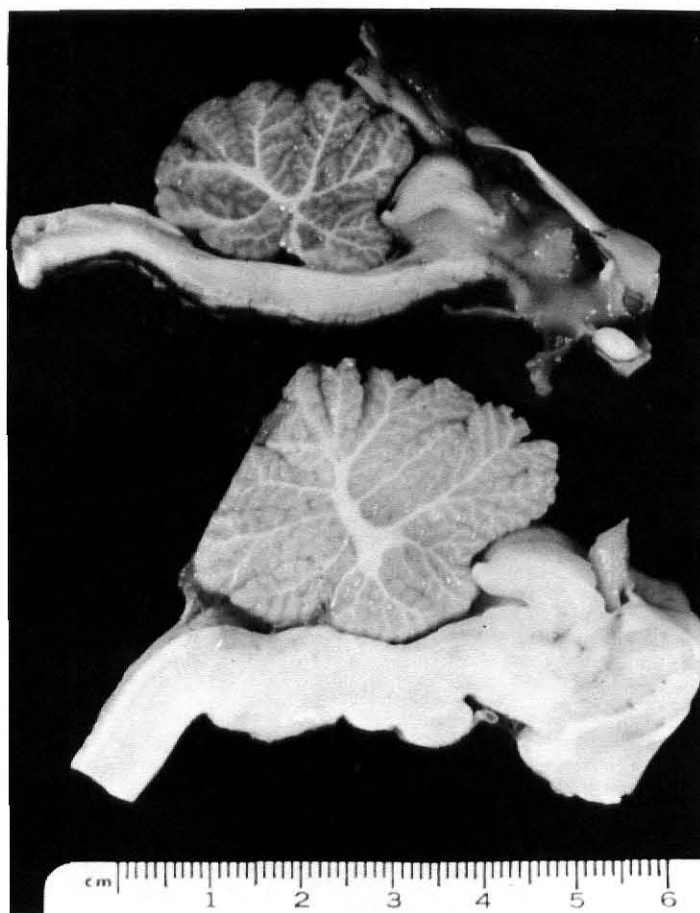


Fig 5 - Coronal slices of the cerebral hemisphere from a hydrocephalic Polled Hereford calf with tetramelic arthrogryposis (left). Normal brain sections are on the right for comparison. Note the lateral ventricular dilation.

Fig 6 - Sagittal slices of the brain stem, cerebellum, and occipital portion of the cerebral hemispheres from the hydrocephalic (top) and normal brains (bottom) depicted in Fig 5. The lateral ventricle is dilated, but the brain stem and cerebellum are normal.

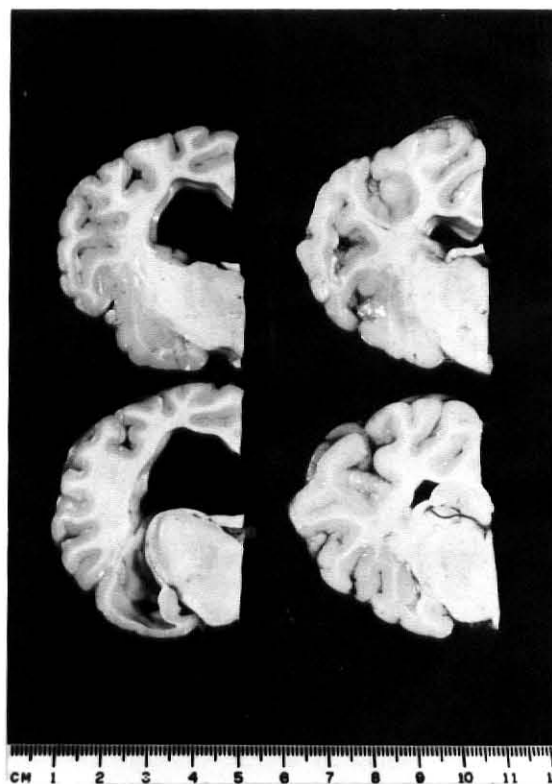


Fig 7 - Dorsal view of a hydrocephalic brain from a 17-day-old Polled Hereford. There is micropolygyrus of both cerebral hemispheres, and a cleft in the cerebellum produced by the aberrant tentorium cerebelli (arrow).

Fig 8 - Lateral view of the brain stem and cerebellum from the brain depicted in Fig 7. The cleft in the cerebellum was produced by the tentorium cerebelli.

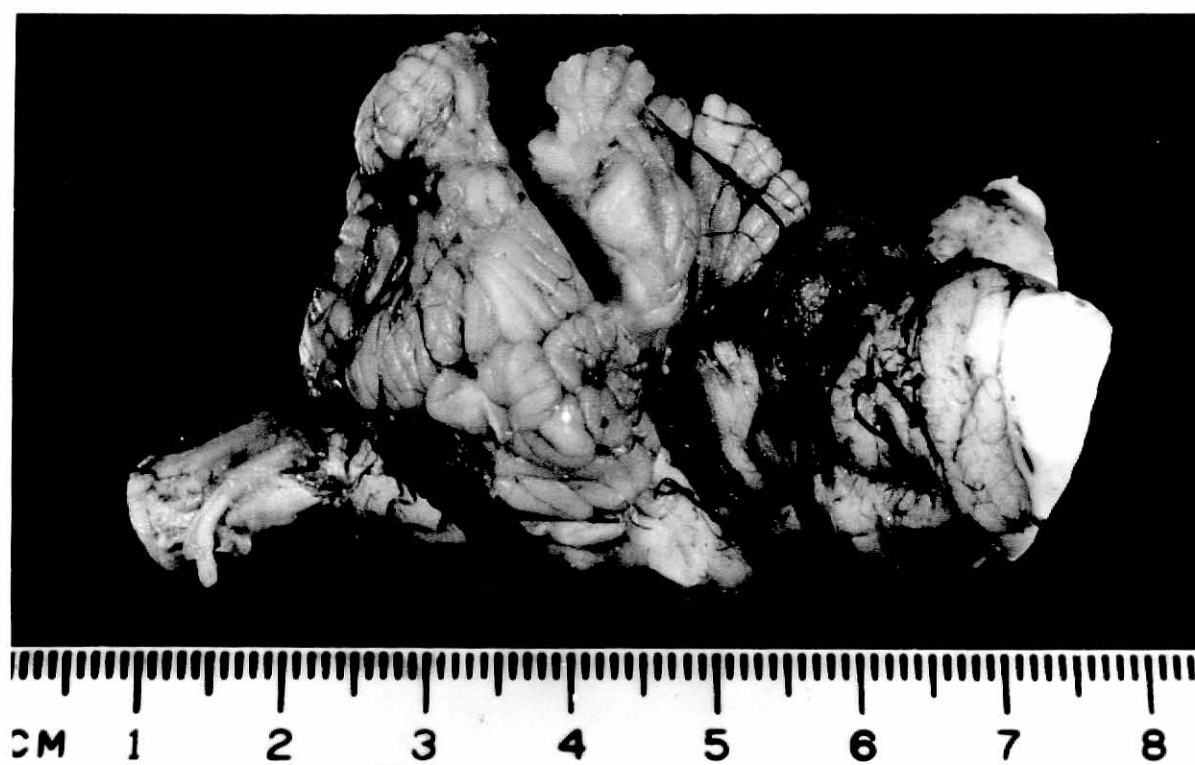
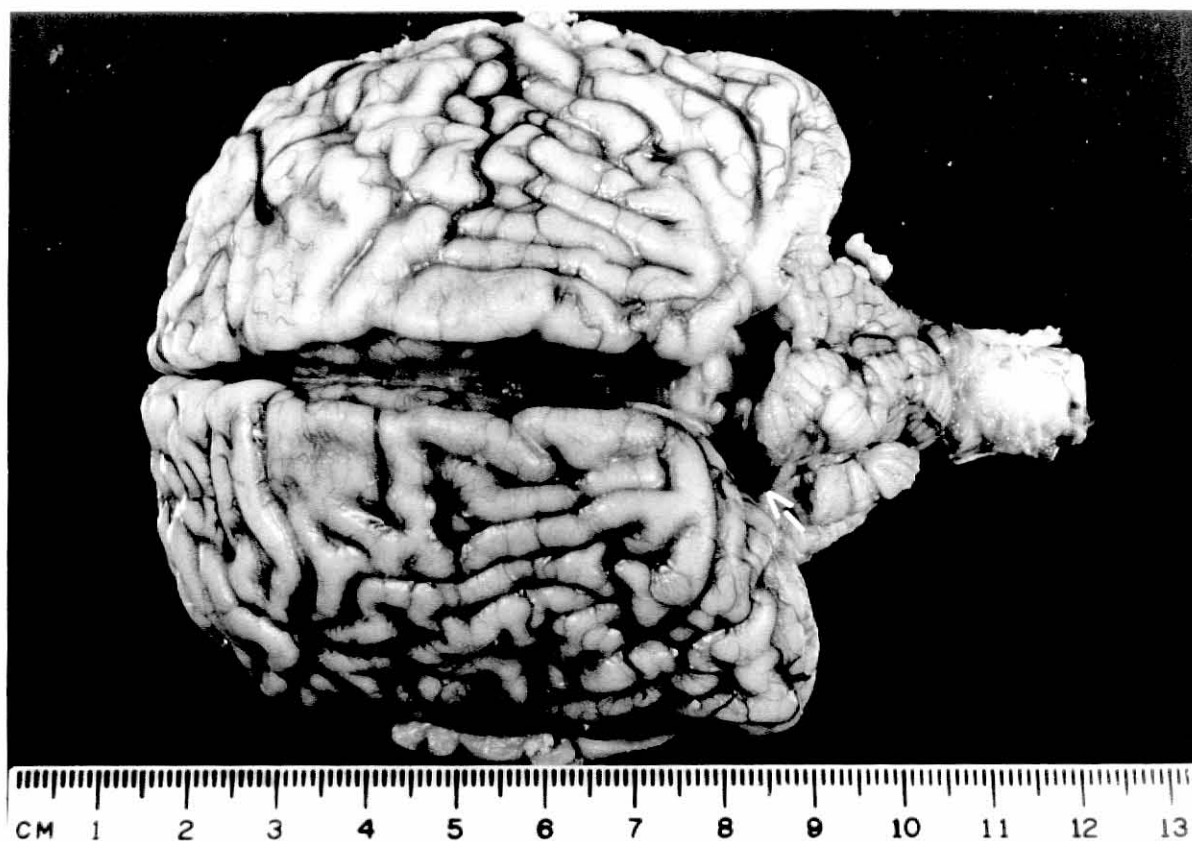


Fig 9 - Sagittal slice of the brain stem and cerebellum (top) and coronal slice of the cerebral hemispheres (bottom) from a 17-day-old hydrocephalic Polled Hereford. The aberrant tentorium cerebelli produced the cleft in the cerebellum. The mesencephalic duct is distended. Note the tectal elevation (T), (above), and marked distension of the lateral ventricles (below).

Fig 10 - Dorsal view of the thoracic spinal column with the dorsal arches removed (above), and spinal cord (below). Scoliosis has resulted in thinning of the spinal cord and marked reduction in the size of the spinal nerve (arrow).

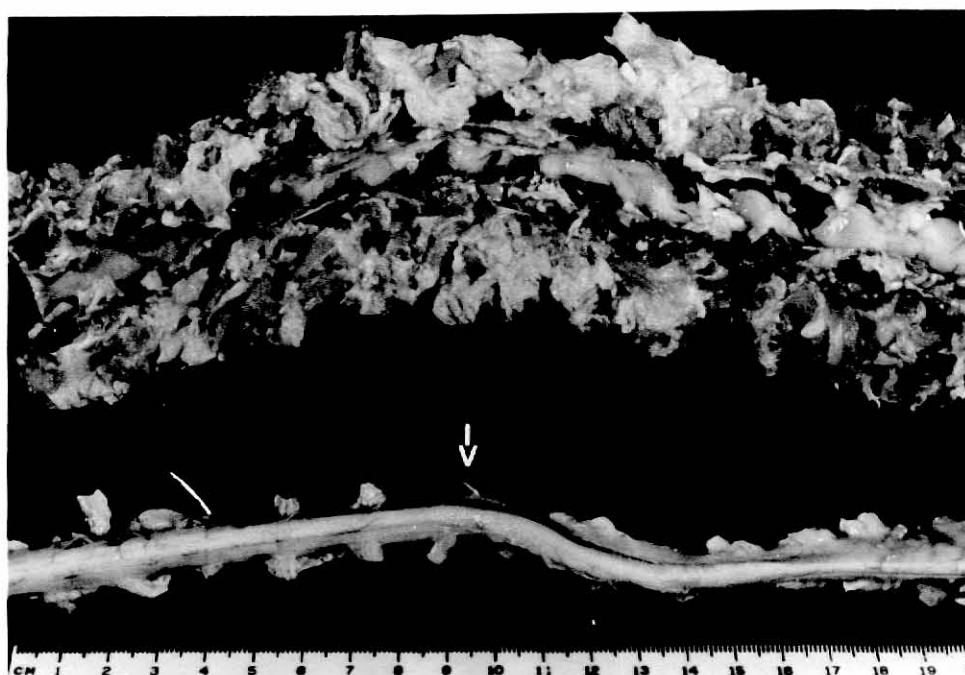


Fig 11 - Sagittal section of the brain stem and cerebellum from a day-old hydrocephalic Polled Hereford. The third ventricle (3) is severely distended. The elongated saccular distension off the roof contains choroid plexus (CP). The pontine eminence (P) and mammillary body (M) are obliterated. The thalamus is indicated for reference (TH). H&E stain; X 2.6.

Fig 12 - Coronal section of the cerebral hemispheres from a day-old hydrocephalic Polled Hereford. Both lateral ventricles are severely distended. The thinned cortical tissue remnant has deep gyri shifted to the surface (arrows). H&E stain; X 2.8.

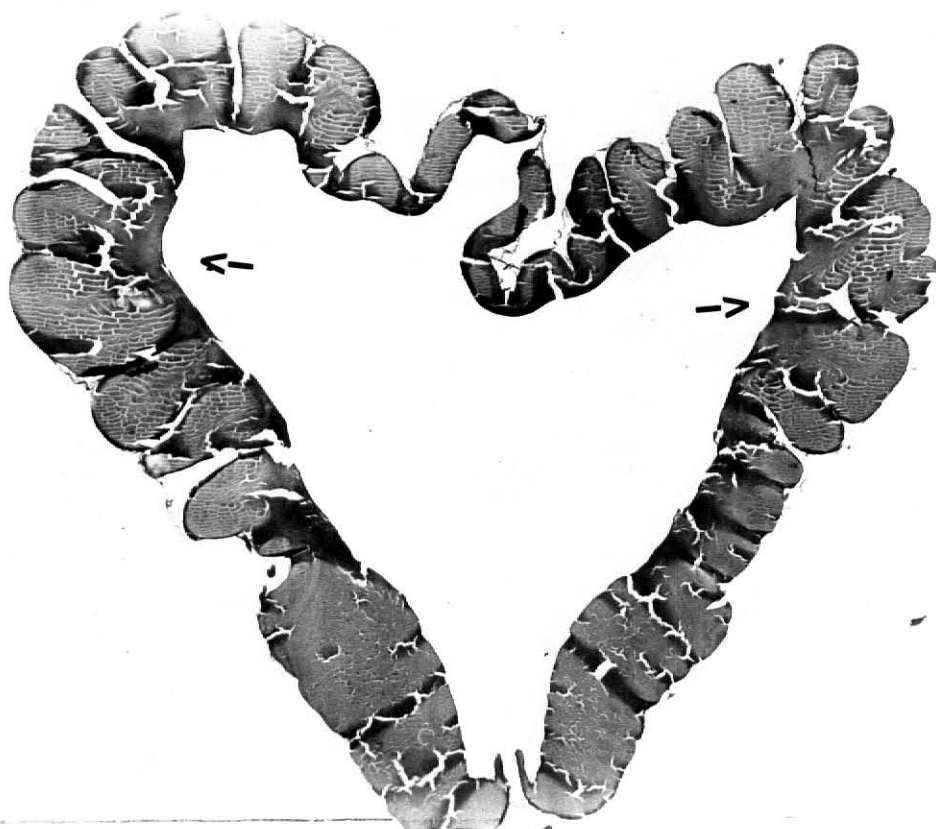
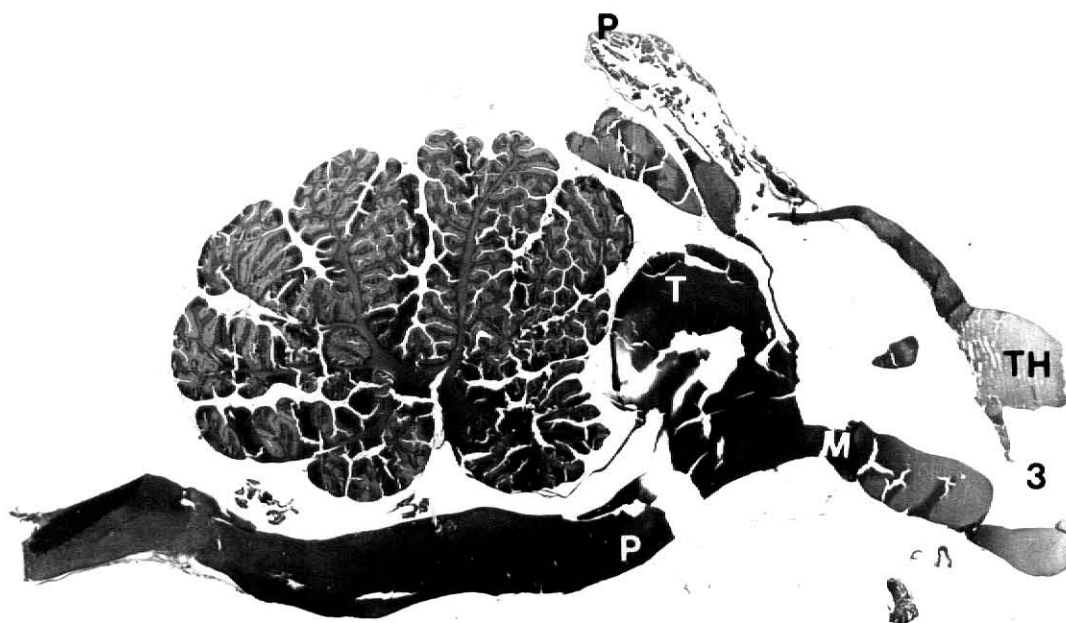


Fig 13,14 - Mid-sagittal section of the cerebellum and brain stem from a 17-day-old hydrocephalic Polled Hereford. The cleft was produced by the aberrant tentorium cerebelli (arrows). The mesencephalic aqueduct is dilated. H&E stain (top), Davenport stain (below); X 2.8.

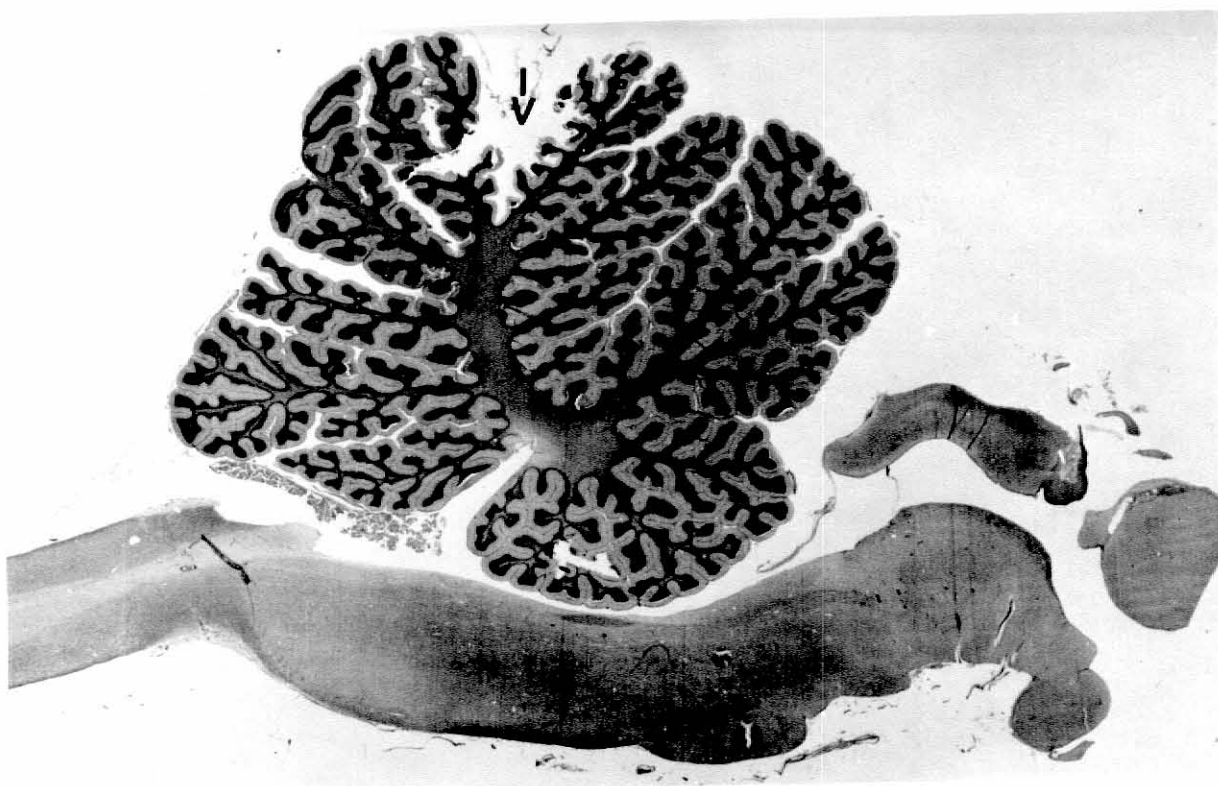
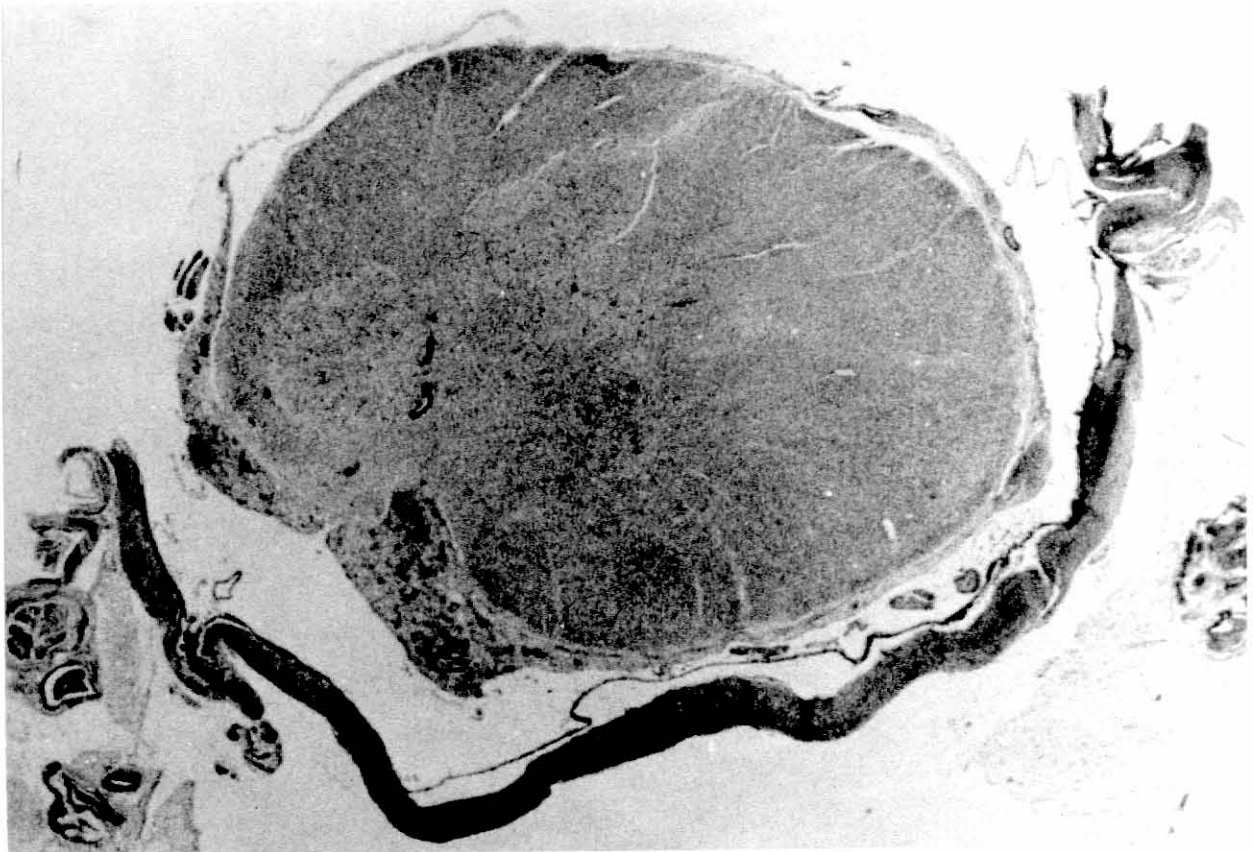


Fig 15 - Cross section of the thoracic spinal cord from an 11-day-old hydrocephalic Polled Hereford with scoliosis. The eccentric grey matter lacks the left ventral horn. The central canal is small and distorted. H&E stain; X 7.5.



CONGENITAL INTERNAL HYDROCEPHALUS
AND HYDRANENCEPHALY
IN CATTLE

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AN ABSTRACT OF A THESIS

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The main objectives of this study were to characterize the gross and histopathologic findings in field cases. Reference tables were developed summarizing reported cases of bovine congenital hydrocephalus into 3 etiologic classifications: hereditary, chromosomal aberrations, and environmental and unknown. Following complete necropsy examination, field cases of congenital internal hydrocephalus and hydranencephaly were placed into 5 categories for histopathologic evaluation. Cases with suspected hereditary or unknown causes were grouped according to breed. Suspected environmentally-induced cases were grouped according to morphologic classification.

Eleven cases of hereditary internal hydrocephalus in Horned Herefords had characteristic mesencephalic malformations considered to be diagnostic. Additional abnormalities in the eyes and musculoskeletal system were present in most cases.

Five cases of congenital microhydranencephaly characterized by cerebellar porencephalic cysts were thought to be caused by fetal bovine virus diarrhea-mucosal disease infection.

Two calves had congenital internal hydrocephalus associated with stenosis of the mesencephalic aqueduct and meningoencephalitis. Fetal BVD-MD virus infection was thought to be the cause.

The cause of internal hydrocephalus in 2 calves of Simmental descent was undetermined. The Arnold-Chiari malformation was present in one calf, and stenosis of the mesencephalic aqueduct in the other.

The cause of congenital internal hydrocephalus in 3 Polled Hereford calves was not determined. Internal hydrocephalus and cerebellar hypoplasia in one calf resembled a suspected hereditary syndrome.

Environmental factors were considered the most likely cause of internal hydrocephalus and musculoskeletal malformations in the others.