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Chapter 19

Bovine Parvoviruses

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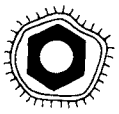
INTRODUCTION

In 1959, Abinanti and Warfield isolated from the intestine of calves a virus that was later identified as a parvovirus (Storz and Warren, 1970; Bachmann, 1971). It is now well established that replication of nondefective parvoviruses depends on cellular functions expressed during the S phase of the eukaryotic cell cycle (Margolis and Kilham, 1965; Tennant et al., 1969; Siegl, 1976). Considering the turnover of intestinal cells and their gradient of differentiation, it is not surprising that parvoviruses were cultured frequently from the intestinal tract of calves when specific attempts for isolation were made (Vincent, 1971; Bates et al., 1972; Hinaidy, 1978; Hinaidy et al., 1979; Wosu et al., 1979). Furthermore, evidence for intrauterine infections of bovine fetuses was found when high titers of HI antibodies of bovine parvovirus (BPoV) were detected in commercial bovine fetal serum (Storz et al., 1972).



VIRUS PROPERTIES

Physical and chemical characteristics

Parvoviruses are extremely resistant to chemical and physical inactivating factors. The most reliable disinfection is achieved with 0.5% chlorox or ethylene oxide in the form of the nonexplosive mixture of 10% ethylene oxide and 90% carbon dioxide.

Antigenic properties

All the parvoviral isolates studied agglutinate guinea pig and human type O erythrocytes. The isolates from cattle of different countries all are antigenically related or identical to prototype BPoV-1 (Abinanti and Warfield, 1961). One BPoV strain isolated in Japan appears to differ and is separated as BPoV-2 (Inaba et al., 1973a). Bovine parvoviruses differ antigenically from parvoviruses isolated from man, pigs, cats, dogs, rats and rabbits. This is further substantiated by comparisons of genomic nucleotide sequences among parvoviruses, which revealed virtually no homology between rodent parvoviruses, Lu III and BPoV (Banerjee et. al., 1983). A defective parvovirus was found associated with BAV types 1, 2 and 3 (Luchsinger et al., 1970; Myrup et al., 1976; Coria and Lehmkuhl, 1978).

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Cultivation

BPoV-1 replicated in all primary bovine fetal cells tested. High levels of hemagglutinin were present in tissue culture fluids following passage in different cell types (Bates and Storz, 1973; Hinaidy et al., 1979; Durham and Johnson, 1985). The virus reached cytopathic and hemadsorption titers of $10^{6.2}$ and $10^{6.8}$ $TCID_{50}$/ml, respectively, on assay after three passages in bovine fetal lung (BFL) cells. Replication occurred to similar titers in bovine fetal testicle (BFT), spleen (BFS), and adrenal (BFA) cells. The least efficient replication of BPoV-1 occurred in bovine fetal kidney (BFK) and bovine fetal intestine (BFI) cells with cytopathic endpoints of $10^{4.2}$ and $10^{3.5}$ $TCID_{50}$/ml, respectively. In all cases, hemadsorption endpoints were approximately 10-fold higher than cytopathic endpoints.

Cell lines from a variety of animal species were tested for their susceptibility to BPoV infection (Bates and Storz, 1973). The line cells examined did not support replication of BPoV-1. Except for decreasing titers observed in the cell strain FB4BN, established from bovine bone marrow, hemagglutinins were not detected in these tissue cultures. Low levels of infectivity and hemagglutinin were detected in BFL cells after three passages of BPoV-1 in MDBK and BHK-21 cells. Plaques resulting from BPoV replication in BFS cells were detected within 5 days after inoculation (Bates and Storz, 1973). The plaque sizes ranged from 1 to 3 mm in diameter at 5 days and increased to 3–5 mm at 7 days p.i. All plaques, irrespective of their size, had fuzzy edges.

The CPE resulting from BPoV replication in actively dividing BFL cells was distinct and reproducible. At 20–24 h after inoculation, infected cells were swollen, refractile, and exhibited a stellate appearance. These cells were scattered over the cell monolayer and ultimately became uniformly round and highly refractile. Soon after rounding, the cells detached from the glass surface. The cytopathic changes continued until all cells were involved, usually by 72 h after inoculation.

Parvovirus-specific fluorescence in infected BFS cells was detected exclusively in the nuclei. Intranuclear inclusions with a unique morphology are formed and can be detected following acridine orange or Giemsa staining (Hinaidy et al., 1979; Leary and Storz, 1980, 1982). Initial changes resulted in a uniformly basophilic nucleoplasm giving the nuclei a glassy appearance. Clumps of dark blue marginated chromatin appeared on the inner nuclear envelope. Along with greater numbers of glassy nuclei, a second nuclear change became apparent, which was characterized by an intensely stained, eosinophilic, finely granular nucleoplasm with a prominent dark blue nucleolus. Thin halos formed around the entire finely granulated nucleoplasm by 18 h after infection. Halo width, intensity of staining, and basophilia of the central inclusion mass increased after 24 h to reach the form of Cowdry type A inclusions (Figs. 82 and 83).

An additional type of inclusion consisting of multiple round, smooth, eosinophilic foci emerged in both glassy and finely granular nuclei at 18–24 h. Halos formed later around individual foci, which remained clearly distinct from nucleoli (Figs. 84 and 85). These foci were often marginally arranged, but they appeared also throughout the nucleoplasm (Hinaidy et al., 1979). All our BPoV strains tested induced multifocal as well as Cowdry type A inclusions (Leary and Storz, 1980, 1982).

Ultrathin sections of many nuclei of infected BFS cells fixed 18–24 h after inoculation contained distinct, fine-grained, electron-dense, circular foci in the nucleoplasm. The foci are local accumulations of viral capsids as revealed by EM (Fig. 86). There appeared to be nuclear compartmentalization of viral replication sites (Bates et al., 1974; Leary and Storz, 1982). Inclusions were not

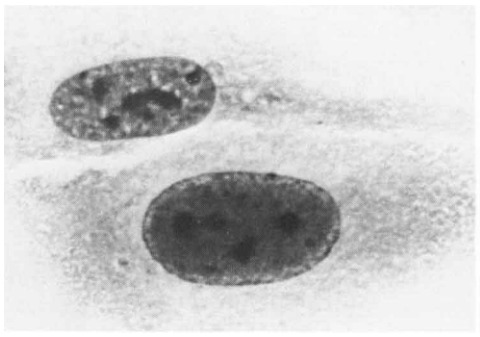

Fig. 82 (left). Early Cowdry type A inclusion within the nucleus of a BFS cell infected with BPoV-1; Giemsa stain (× 1280).

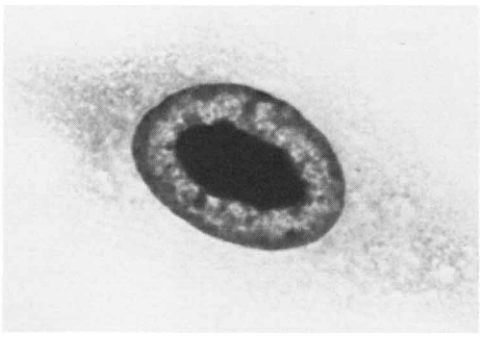

Fig. 83 (right). Mature Cowdry type A inclusion within the nucleus of a BFS cell infected with BPoV-1; Giemsa stain (× 1280).

detectable in infected mitotic cells where the nuclear envelope was dispersed. The presence of characteristic tubular forms in these cells revealed them as infected.

The nucleopathic changes described are characteristic for BPoV and can be used to indicate the infection in cultured cells. Their appearance in infected cells of tissues from animals can be exploited diagnostically.

EPIZOOTIOLOGY

Evidence for parvovirus infection of cattle through detection of antibodies neutralizing infectivity or inhibiting hemagglutination of BPoV was detected in the USA, Algiers, Japan, Brazil, England and Austria (Leary and Storz, 1980). The incidence of cattle with antibodies ranged from 46 to 86% (Table 20). The age of the animals tested was not specified, but the majority of the serum samples involved newborn calves and cattle to 12 months of age. The highest percentage of positive calves was found in February in Austria, where the only attempt was made to analyze seasonal distribution (Hinaidy and Bürki, 1980).

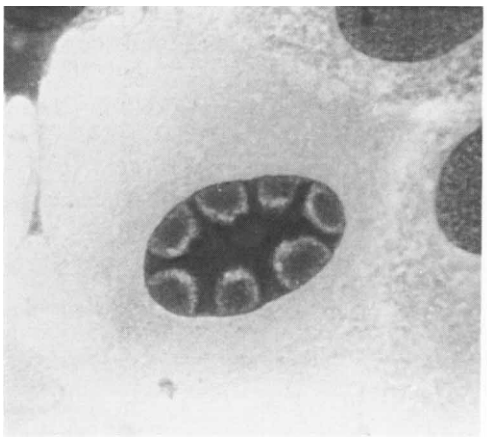

Fig. 84 (left). Multifocal inclusion located peripherally in nucleus of BFS cell infected with BPoV-1; Giemsa stain (× 1280).

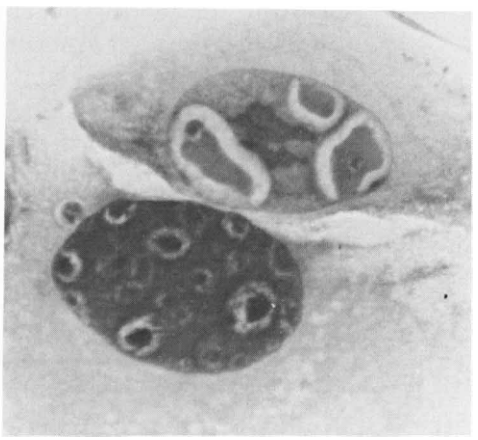

Fig. 85 (right). Large and small multifocal inclusions within the nucleus of BFS cell infected with BPoV-1; Giemsa stain (× 1280).

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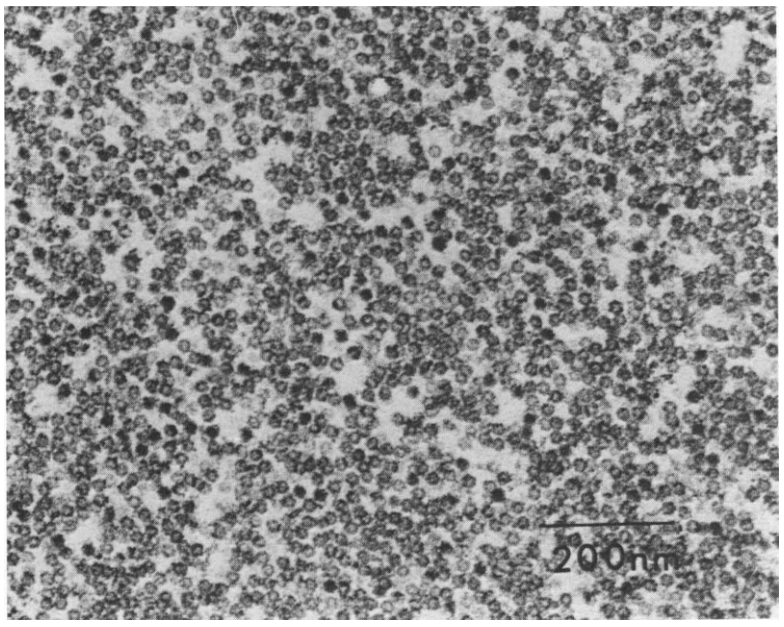

Fig. 86. Ultrastructural detail of section from a nucleus of a BFS cell infected with BPoV-1.

Serum samples from 35 herds of cattle representing 433 animals were tested in the western USA. Antibodies were detected in sera from 243 of 377 animals in 29 herds. Six of the herds did not have cattle with parvovirus antibodies (Storz et al., 1972). Parvoviruses were isolated from cattle of all the countries where serological surveys had been made.

Considering their antigenic properties and minimal homology with parvoviruses of other animal species, one can assume that BPoV antibodies in cattle were not induced through cross-reactions after infection with parvoviruses of other animal species (Bates et al., 1972). In addition, the host cell range of BPoV was found to be virtually restricted to bovine cells. Accordingly, the chain of infection is maintained within the cattle population.

Vertical transmission of BPoV was proven through detection of significant antibody titers in fetal serum and isolation of parvovirus from tissues of a naturally occurring abortion (Storz et al., 1972; Inaba et al., 1973b); it was confirmed through experimental inoculations of pregnant cows or direct fetal inoculations (Storz et al., 1978).

TABLE 20

Parvovirus antibodies in cattle

Country	Positive (%)	Total tested	References
USA, Maryland	86	?	Abinanti and Warfield, 1961
	83	209	Spahn et al., 1966
Colorado	65	377	Storz et al., 1972
Algiers	70	254	Vincent, 1971
Japan	50	48	Inaba et al., 1973b
England	46	114	Huck et al., 1975
Austria	71	148	Hinaidy, 1978
	70	101	Hinaidy and Bürki, 1980

PATHOGENESIS

How do parvoviruses induce enteritis in calves?

The spread of BPoV during infection and its distribution in newborn calves after oral or intravenous inoculations was studied (Storz et al., 1978). Parvoviral antigen was demonstrated by IF test and virus was reisolated.

Calves excreted BPoV 24–48 h after oral as well as intravenous inoculation and continued to do so during the course of the experiment lasting for 11 days. Virus was isolated from mucosal scrapings of the duodenum and lower levels of the intestine for 6 days. The regions most consistently infected were the jejunum, ileum and caecum; the highest titers were measured in the intestinal mucosa of intravenously inoculated calves. Patches of cells with fluorescent nuclei were found in the epithelium of the Lieberkühn crypts, in the transition and intervillous zones of villi, in cells of central lacteals (a site where more fluorescent cells were found after intravenous inoculation) and in cells of the lamina propria. The range and distribution of fluorescent cells was similar to that found in newborn kittens inoculated with feline panleukopenia virus, another parvovirus (Hammon and Enders, 1939; Csiza et al., 1971; Carlson et al., 1977, see volume Virus Infections of Carnivores of this series). It differed from the range of infected cells of adult conventional cats, where the cells of Lieberkühn crypts are the initial sites of intestinal infection.

Viremia associated with leukocytes developed after oral inoculation and reemerged when virus was given intravenously, and more serious diarrhea was then induced. Infections of intestinal cells in crypts, central lacteal and other sites occurred during the systemic phase. Also, infection of cells in the cortex of the adrenal gland (Fig. 87), the thymus, lymph nodes and heart muscle became pronounced during the systemic phase, which is a characteristic feature of the pathogenesis of parvovirus-induced enteric disease.

Fluorescence in intestinal and other lymph nodes was distributed randomly and involved large cells in paracortical areas. The thymus showed fluorescence in large nuclei or reticulum-like cells in the medullar region and cortex. Fluorescent cells were present in the nodular areas of the spleen. The adrenal

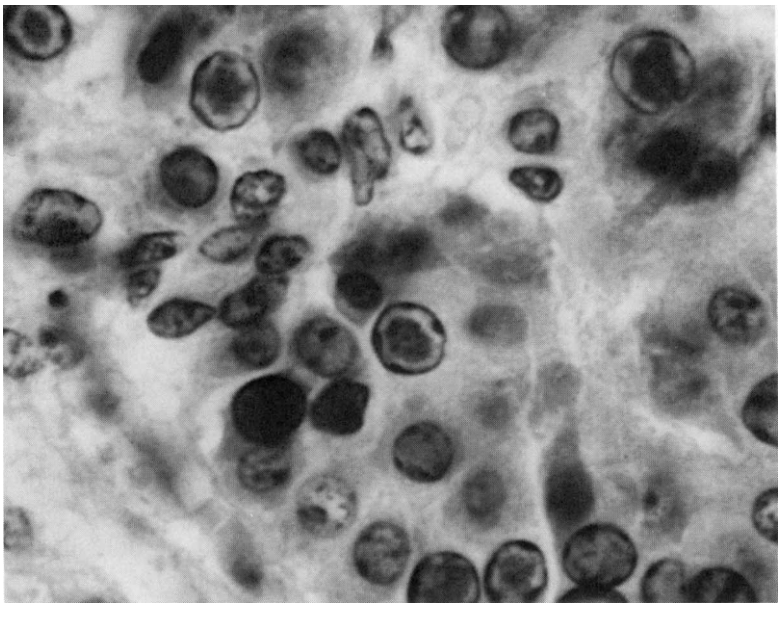

Fig. 87. Section of adrenal gland of a calf infected with BPoV-1; several nuclei have inclusions.

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glands examined had abundant fluorescence in the zona glomerulosa and fasciculata. Net-like pronounced fluorescence was present in heart muscle cells. Fluorescent cells were not found with parvovirus-specific conjugates in the corresponding tissues of one normal control calf or calves inoculated with bovine enteroviruses.

Conventional calves inoculated orally or intravenously with parvovirus propagated in BFS or BFK cells for 8–10 passages developed diarrhea (Storz et al., 1978). Also 2–8-month-old calves became diarrheic 4–7 days after oral or intranasal inoculation with BPoV-1 of an unspecified passage level (Spahn et al., 1966). Calves inoculated intravenously had more severe diarrhea, which was initially watery and then mucoid, than orally inoculated calves. Since parvoviruses were also isolated from conjunctival and tonsillar specimens, it appears that the oropharyngeal and respiratory routes of infections are more common under natural conditions than direct oral intestinal infections. The oropharyngeal and respiratory or parenteral routes of infection are most effective in experimental induction of feline panleukopenia (Csiza et al., 1971).

The most reliable inocula for inducing enteric disease with clinical signs comparable to those observed under natural conditions were suspensions of wild-type virus derived from diarrheic fluid and intestinal mucosal samples in experimental coronaviral and rotaviral enteritis (Storz et al., 1978; Storz and Leary, 1979). Similarly, a reliable inoculum for inducing panleukopenia in cats was a wild-type parvovirus maintained by intestinal infections in pathogen-free cats (Carlson et al., 1977). Cell culture propagated BPoV did not reproducibly cause diarrhea. Evidently, enteropathogenic viruses rapidly become attenuated during passage in cell culture due to mutation and selection of host range mutants with reduced virulence. Although enteritis was induced in our experiments involving parvovirus passed serially in cultured cells at least eight times, we may not have reproduced the naturally occurring infection.

Parvoviruses were detected in mixed intestinal viral infections of calves involving enteroviruses, adenoviruses, pestiviruses and coronaviruses. Because multiple viral infections in enteric diseases are quite common but seldom mentioned and hardly studied, the significance of a parvovirus component should be investigated. The parvoviral infection involves the host cell niche left unoccupied by intestinal coronaviruses or rotaviruses.

Pathogenesis of fetal infections

The pathogenic potential of BPoV to establish infection of the placenta and fetus was investigated by intravenously inoculating pregnant cows or by direct fetal inoculation during laparotomy (Storz et al., 1978). Following intravenous inoculation of pregnant cows, virus was isolated from their blood leukocytes 3 and 6 days later, and placental as well as fetal infection occurred. Fetuses of the first trimester of gestation were highly susceptible. Nuclei of cells of the cotyledonary villi fluoresced in a honeycomb pattern when stained with parvovirus-specific antibodies. The uterine mucosal glands contained some fluorescent cells which were also present in the adrenal glands, lungs, spleen, heart muscle, kidneys and thymus of the fetuses. Virus was isolated from uterine fluid and the fetal organs.

Also fetuses from the second trimester of gestation were susceptible to BPoV infection. When gravid uteri were removed 5–13 days after exposure of the fetuses, parvovirus could be isolated from placental fluids and most organs, including the intestinal tract. The infectivity levels of placental fluids varied from 10^4 to 10^6 PFU per ml. The liver of one fetus contained 7×10^5 PFU/g, and titers of similar levels were detected in adrenal glands, lymph nodes and intestinal tissues. Immunofluorescence findings corresponded with viral isola-

tion results. If fetuses survived and were tested 2 weeks after inoculation or later, virus isolation was irregular because the fetuses had produced antibodies.

Fetuses of the third trimester of gestation became infected, developed antibodies and recovered. These calves were born alive at term, and virus was isolated from them irregularly.

Repeat breeders and embryonic death

A serological survey in 12 commercial dairy herds indicated that BPoV may be involved in other reproductive problems (Barnes et al., 1982). The BPoV seroreactor cows commonly experienced higher rates of embryonic mortality and required more services per conception than did nonreactor cattle. The cows in these herds were adequately protected against the major reproductive diseases. Regular disease prevention programs and vaccination against brucellosis, leptospirosis, BVD, IBR and parainfluenza were applied in these herds. Bluetongue virus infection also was not associated with reproductive problems in these herds.

DISEASE SIGNS

Calves with naturally occurring parvoviral infections proven by isolation had various clinical signs and varied in age from 1 week to 12 months (Abinanti and Warfield, 1961; Vincent, 1971; Bates et al., 1972; Huck et al., 1975; Hinaidy et al., 1979). Diarrhea affected most calves from which we recovered parvoviruses. Calves surviving the diarrheic episode developed circulating antibodies, but parvoviruses could be isolated intermittently from their feces. Most isolates were made from fecal specimens of calves suffering from enteritis, combined occasionally with febrile respiratory illness and conjunctivitis (Table 21). In some instances parvoviruses were isolated from feces of clinically normal young cattle. Holstein calves that had recovered from episodes of parvovirus diarrhea appeared retarded in growth.

Newborn calves deprived of colostrum or given colostrum free of parvoviral (HI) antibodies developed enteritis 24–48 h after oral or intravenous inoculation with cell culture propagated strain 71-1-20W of the eighth–tenth passage in BFS cells (Storz et al., 1978). The diarrhea was mild to moderately severe in orally inoculated calves. Calves given the inoculum intravenously developed a more severe, watery diarrhea and became prostrate. The body temperatures reached 41°C 2 days after exposure. The calves were listless, but they usually drank the offered milk. Others observed diarrhea in 2–8-month-old calves 4–7 days after oral or intranasal inoculation with BPoV-1 of an unspecified passage level in cell cultures (Spahn et al., 1966).

Pregnant cows did not develop clinical signs immediately following inoculation. Their temperature and behavior remained normal. Abortions occurred in the first and early second trimester. The aborted fetuses were edematous, and the placentas were edematous and had necrotic cotyledons (Storz et al., 1978).

PATHOLOGY

Most calves infected with BPoV had a catarrhal enteritis. The levels of the gastrointestinal tract consistently infected were the jejunum, ileum and cecum. Single small patches of fluorescent cells were found in the epithelium of the crypts, in the transition and intervillous zones of villi, the central

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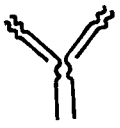
TABLE 21

Clinical signs, age, and specimens of calves yielding parvovirus isolates

Country	Specimens yielding isolates	Clinical signs and age	Types and number of isolates	References
USA, Maryland	Feces	Normal, 3 weeks–4 months	BPoV-1 (6)	Abinanti and Warfield, 1961
Colorado	Feces	Diarrhea and normal, 1 week–12 months	BPoV-1 (10)	Bates et al., 1972
Colorado	Lymph Node	Diarrhea, 6 months	BPoV-1(1)	Storz et al., 1976
South Dakota	Feces	Diarrhea (coccidiosis), 6 months	BPoV-1 (1)	Bates et al., 1972
Oregon	Feces Conjunctiva Tonsils	Diarrhea, conjunctivitis Normal, 1–3 months	BPoV-1 (4)	Storz et al., 1978
Algiers	Feces	Normal	BPoV-1 (4)	Vincent, 1971
Japan	Feces	Diarrhea, respiratory signs, 4–12 months	BPoV-1 (4) BPoV-2 (1)	Inaba et al., 1973b
	Fetus	Abortion	BPoV-1 (1)	Inaba et al., 1973a
England	Feces	Diarrhea, 3 months	BPoV-1 (1)	Huck et al., 1975
Austria	Feces	Normal, 6–11 weeks	BPoV-1 (10)	Hinaidy et al., 1979
Australia	Feces	Normal, 6 months	BPoV-1	Wosu et al., 1979

lacteals, and in cells of the lamina propia mucosae. Clusters of fluorescent epithelial cells were also found in the crypts of Lieberkühn. Fluorescence in lymph nodes was distributed randomly and involved single large cells, probably lymphoblasts, in paracortical areas; they were also seen in the germinal centers. Fluorescence in large nuclei of reticulum-like cells in the medullar regions of the thymus and infrequently in cells of the cortex was observed. Similarly, fluorescent cells were found in the nodular areas of the spleen. The adrenal glands examined showed large numbers of fluorescent cells in the zona glomerulosa and fasciolata. The nuclei of numerous heart muscle cells had net-like fluorescence. Histological samples were taken from the experimental calves that were studied virologically. Evaluations of these tissues were not fruitful because of fixation problems. Recognizable nuclear changes (see Fig. 87) were detected in the adrenal glands, which had high titers of infectious virus (Storz and Bates, 1973).

Fetuses aborted during the first and early second trimester of gestation were edematous and had increased amounts of pleural and peritoneal fluid. Intranuclear inclusions were formed in cells of the small intestine, liver, lymph nodes, and the cerebellum. Microscopic lesions consisted of excessive cellular necrosis in the external granule cell layer of the germinative sites of the cerebellum. Lymphoid hyperplasia was also observed in fetuses examined at 10 days p.i. There was no evidence of lymphoid depletion or necrosis in lymph nodes, spleen, or thymus (Storz et al., 1978; Barros, 1980).



IMMUNE REACTION

Newborn calves and pregnant cows inoculated intravenously had a brisk HI antibody response within 5–7 days. These antibodies also neutralized virus infectivity as tested in the plaque assay. A high percentage of cattle in different herds had antibodies, but there were closed herds found free of this infection (Spahn et al., 1966; Vincent, 1971; Storz et al., 1972; Hinaidy and Bürki, 1980).

The humoral immune response of bovine fetuses to BPoV infection during the second and third trimesters was studied by the single radial immunodiffusion, HI, indirect IF test, micro-neutralization (MN), plaque-neutralization (PN), and double ID tests (Storz et al., 1978; Hayder et al., 1983). Serum samples collected from 23 virus-inoculated and several control fetuses were tested. The IgM concentration reached 355 mg/100 ml at 10 days after fetal inoculation and then decreased. The IgG concentration increased 10 days after inoculation and was maximal 142 days later. A correlation between Ig concentrations and antibodies reacting in the HI, MN, PN, IF, and ID tests existed in all samples. Neutralizing and HI antibodies were detected 10 days after fetal inoculation. The highest MN titer of 4096 was detected in a fetus 10 days after inoculation done during the third trimester. Six sera were positive in the IF test. These samples were collected 10–60 days after the fetuses had been inoculated; they had IgG concentrations of 615 mg/100 ml or higher and titers of 16–64.

Between 5 and 10 days p.i. fetal blood lymphocyte counts tripled, due primarily to an increase in E-rosetting lymphocytes. Peripheral blood lymphocytes of all fetuses reponded well to nonspecific mitogens of phytohemagglutinin, concanavalin A, and pokeweed (Liggitt et al., 1982).

LABORATORY DIAGNOSIS

The BPoV isolates established by investigators in different countries were cultured in BFK or calf testicle cells. Considering the high incidence of cattle

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with antibody titers it is apparent that isolation of parvovirus from natural infections was relatively sporadic and inefficient with the various methods used. Optimal replication and pronounced cytopathic changes were observed in BFL and BFS cells (Bates and Storz, 1973). These were used as actively growing cultures in a state of parasynchrony. The cellular requirements of BPoV must be considered before attempting in vitro studies, in viral isolation trials, and in the interpretation of pathogenetic mechanisms. Cultures of BFS cells synthesize DNA in a parasynchronous manner between 18 and 48 hours after passage (Leary and Storz, 1982). Optimum interaction of BPoV with DNA-synthesizing, S-phase cells was insured by infecting cells 18 h after passage. Intracellular infectivity rose 18–24 h p.i., at which time both cytopathic changes and intranuclear inclusions were detected.

Three methods of BPoV isolation from IF pretested samples of experimentally inoculated calves were compared (Storz et al., 1978): (1) parasynchronous BFS cells with freezing and thawing between subpassages to disrupt cells; (2) direct culture of cells from selected organs; and (3) parasynchronous BFS cells and cell-associated virus techniques to maintain cell viability on subpassages.

Cell-free virus techniques with parasynchronous BFS cells detected parvovirus in only 25.5% of the samples that were IF positive. Direct culture of cells from kidneys or testicles produced parvovirus where this technique failed. The cell-associated virus technique employing parasynchronous BFS cells was most reliable and recovered parvovirus from 82.5% of IF-positive tissue specimens. Reports of investigations of parvoviral infections in other animal species, mainly the cat, also infer that it is difficult to isolate virus from infected organs. Method 3 is recommended and should be employed to isolate field strains. Serum free of antibodies against BPoV and of HI inhibitors must be used for successful isolation and virus propagation (Storz et al., 1972).

Direct EM examination of diarrhea fluid is not reliable because of the possible presence of many other small particles, including enteroviruses, caliciviruses, astroviruses, togavirus cores and even small bacteriophages. Recourse to the use of immune EM would be more specific, and enzyme immune assays should be developed.

A unique variety of nucleopathic changes was detected in cultured BFS cells infected with BPoV (Leary and Storz, 1980). They consisted of Cowdry type A as well as multifocal inclusions (see Figs. 82–85). Formation of distinct halos occurred in both instances. The appearance of these nucleopathic changes in infected host tissues has to be analyzed further to establish its diagnostic value.

A most efficient method to detect antibodies against BPoV is the HI test employing guinea pig or human type O red blood cells (Abinanti and Warfield, 1961; Storz et al., 1972). In some serum samples, nonspecific inhibitors of BPoV hemagglutination may be present and must be removed before testing for BPoV antibodies. The HI antibody titers corresponded well with results obtained through infectivity neutralization tests and other methods for the detection of antibodies (Hayder et al., 1983).

Recently, a competitive ELISA was introduced for detection and titration of antibodies to BPoV. The antibodies, if present in the cattle sera, are competing in this assay with two monoclonal antibodies to the parvoviral hemagglutinin. The antibody titers determined in ELISA correlated with the titers in VN tests (N. Juntti, personal communication, 1987).

PROPHYLAXIS AND CONTROL

A high percentage of cattle in the USA and other parts of the world has antibodies resulting from natural infections (Storz and Leary, 1979). However,

there are herds of seronegative cattle and thus without experience with this infection. Attempts to vaccinate cattle have not been described. As we learn more about the infection and the pathogenic potential of BPoV, efforts to develop vaccines may be warranted, particularly for the prevention of reproductive disease problems. This approach would be of benefit in reducing parvovirus-induced disease during the neonatal period of calves.

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