PASSIVE IMMUNITY AGAINST ENTERIC VIRAL INFECTIONS OF PIGLETS

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ABSTRACT

An immunologic system has evolved whereby newborn animals derive an appreciable degree of protection from enteric infections by means of passive immunity. This report explores some of the facets of this system, using infections of swine with transmissible gastroenteritis virus, rotavirus, or enterovirus as examples. In swine, and probably in most monogastric animals, passive immunity against enteric infections is dependent on the ingestion - at normal intervals for the particular species - of colostrum or milk which contain appropriate levels of specific antibodies, with those of the IgA class being most protective. In swine, and probably in most monogastric animals, antibodies of the IgA class appear to occur in mammary secretions only, or primarily, as a result of an appropriate antigenic stimulation of the intestinal tract. This type of information, and the variables involved, is of special value when attempting to design an immunisation programme which will provide passive immunity against enteric infections.

Many enteric infections occur as enzootics, wherein young animals become infected during the suckling period or shortly after weaning. Pigs are usually protected from rotaviral or enteroviral infections during the first 2 to 5 weeks of age because of passive immunity, after which time an intestinal infection usually occurs. The occurrence and possible significance of boosting lactogenic immunity by natural re-infection or by vaccination are discussed and some results given.

F. J. Bourne (ed.), *The Mucosal Immune System*

INTRODUCTION

From the time of birth, most animals are reared in an environment of limited sanitary conditions and, consequently, are generally exposed to potential pathogens. This is well illustrated when an attempt is made to rear orphan newborn animals. Invariably, under conventional husbandry conditions, they become sick and often die. However, a protective immunologic system has evolved which tends to safeguard the newborn against those pathogens normally found in its environment. With most animals, this system depends on the ingestion of colostrum and milk, which provides a temporary degree of passive immunity. Fortunately, during the period of passive immunity, the young become partially susceptible to infection with ubiquitous pathogens; allowing for only mild, if any, clinical signs, and for development of semi-permanent active immunity which replaces the temporary passive immunity.

Although animal husbandrymen and scientists have long been aware of this protective system, only recently have some of its mechanisms and intricacies been better understood. This is especially true as it relates to the protection of mucosal surfaces against infectious agents.

This report will discuss some characteristics of the passive immune system as it applies to enteric viral infections of pigs, with emphasis on rotavirus and transmissible gastroenteritis virus (TGEV). Some of this information should be relevant to other animal species, especially monogastric animals.

INFLUENCE OF PASSIVE IMMUNITY ON ENZOOTIC ENTERIC INFECTIONS

As a preface to discussing passive immunity, a few comments on the immunoglobulin system in swine are indicated. Pigs are essentially born agammaglobulinaemic. Immunoglobulins are absorbed from colostrum for only the first 12 to 36 hours after birth (Payne and Marsch, 1962). IgG accounts for about

80% of the total immunoglobulin in colostrum but rapidly declines so that a 30-fold decrease occurs during the first week of lactation, and remains a minor component of milk during the remainder of lactation (Curtis and Bourne, 1971). Although the level of IgA in colostrum is only 16% of that of IgG, it declines only 3-fold and soon becomes the predominant immunoglobulin in milk (Curtis and Bourne, 1971; Porter and Allen, 1972). IgM is at low level in both colostrum and milk. In colostrum, nearly all of the IgG and 40% of IgA are derived from serum; but in milk more than 90% of IgA and IgM, and 70% of IgG are produced in the mammary gland (Bourne and Curtis, 1973). Thus, colostrum can be considered a concentrated serum transudate, while milk is a secretion. The transition from colostrum to milk occurs during the first 3 to 7 days of lactation, with the predominant change occurring during the first 24 hours. As used in this report, milk refers to mammary secretions occurring only after 72 hours post-partum.

Many enteric viral infections of swine occur at a young age when pigs have a variable degree of passive immunity acquired from nursing immune mothers. A similar situation occurs with most species of animals and to a lesser extent with man, depending on sanitary conditions. Most of these enzootic viral infections will be either subclinical or will result in clinical signs which are less severe than would usually occur in immunologically susceptible animals. Since many infections cannot be prevented, the objective is to provide satisfactory immunity, sanitation, nutrition, and environmental conditions so as to prevent or minimise disease. Thus, there is interest in how an optimal level of passive immunity can be routinely and consistently provided to young animals so as to minimise disease from enzootic enteric infections.

Two types of studies are indicated: (1) How can existing immunity in females best be boosted so as to provide passive immunity? This will be discussed later. (2) What might be the overall benefits derived from improved passive immunity to the young? In regard to the latter, little may be accomplished if

immunity provided to suckling animals is of such high degree that infection would occur only after weaning, at a time when animals may be more susceptible to a severe infection. Weanling diarrhoea is often a serious problem in pigs, other animals, and children, especially when sanitation, nutrition, and environmental conditions are poor. An absence or decline in lactogenic immunity - due to antibodies in milk - or humoral immunity probably contributes to the occurrence or severity of weanling diarrhoea.

Enzootic infections of pigs occur with enteroviruses (Wenner et al., 1960), TGEV (Bohl, 1975; Morin et al., 1978), and rotaviruses (Bohl et al., 1978; de Leeuw et al., 1979). Faecal excretion of these viruses generally occurs in 3- to 9-week-old pigs during the latter part of the suckling period or shortly after weaning. Whether faecal excretion of virus at this time results from (1) an initial infection, or (2) a massive viral replication from a previous low-grade or latent gut infection is not known. Regardless, it is probably related to a decline or interruption in lactogenic or humoral immunity, with the former, generally, being more important.

Enteroviruses

About 11 serotypes of porcine enteroviruses have been described (Knowles et al., 1979). Primary replication of enteroviruses are thought to occur in the alimentary tract, especially the ileum. However, clinical signs result from a secondary localisation in other organs; such as, central nervous system, lungs, or foetuses. Most young pigs become infected with some serotypes, usually while they have some degree of lactogenic or humoral passive immunity; and disease is seldom observed (Wenner et al., 1960; Singh and Bohl, 1972).

TGE virus

This virus is a member of the coronavirus genus (Tajima, 1970). It causes a devastating disease in susceptible newborn pigs, characterised by vomiting, diarrhoea, dehydration and,

generally, a 100% death loss; although swine of all ages can be infected and show diarrhoea. Viral replication occurs in the villous enterocytes, which accounts for the clinical signs. There is no safe and effective vaccine, nor practical method of treatment. Herd infections can be either enzootic or epizootic, with losses much more severe in the latter (Bohl, 1975). In enzootic infections, diarrhoea does not usually occur in pigs less than 8 days old, due to lactogenic immunity derived from the sow.

Porcine rotavirus

This virus was first reported as a cause of diarrhoea in piglets in 1976 (Woode et al., 1976). Rotaviruses have been associated with diarrhoea in several animal species including man (Flewett and Woode, 1978). The pig serves as a good model for the study of rotaviral infections. Rotavirus is most commonly associated with 'white scours' in 2- to 4-week-old pigs (Bohl et al., 1978; de Leeuw et al., 1979). Viral replication occurs primarily in villous enterocytes. There is probably more than 1 serotype of porcine rotavirus, but precise information is lacking.

All serum samples from adult, conventionally reared swine which we have tested contained neutralising antibodies against porcine rotavirus. Serum and milk samples have been sequentially collected from 5 sows during lactation and tested for neutralising antibody against porcine rotavirus (OSU strain). Results have been similar and those from one sow are summarised in Table 1. Antibody titres in milk are usually similar or often higher than those in serum, as occurred with this sow. This information suggests that the milk antibodies are primarily of the IgA class. Of special interest was the marked increase in antibody titres in milk which occurred between post-partum day 20 and 48. We think this was due to severe viral exposure of the sow resulting from contact with her infected pigs. Pigs in this litter began shedding rotavirus when 23 days old (Table 1). This phenomenon has been

observed in several other sows, with antibody titres increasing more in milk than in serum. This may be due either to (1) an increased migration of rotaviral sensitised IgA immunocytes from the re-infected gut of the sow to the mammary gland, or (2) a lacteal entrance of the virus from infected suckling pigs.

TABLE 1

ANTIBODY TITRES OF SOW (NO. 36-1) DURING LACTATION. FAECAL SHEDDING OF ROTAVIRUS WAS FIRST DETECTED IN PIGS WHEN 23 DAYS OLD

Day post-partum	Rotaviral antibody titre*	
	Serum	Milk
1	98	280
13	110	125
20	150	95
34	420	460
48	480	1 400

* Reciprocal of dilution giving an 80% plaque reduction with porcine rotavirus.

When milk whey is fractionated by gel filtration, rotaviral antibody is primarily associated with the IgA fractions, as previously reported (Saif and Bohl, 1979). Thus, the IgA class of antibody is similar to that which occurs when swine are naturally or experimentally infected with virulent TGEV (Bohl et al., 1972).

We have followed the course of infection in about 6 litters of pigs from the same herd by obtaining rectal swabs at various time intervals and testing for rotavirus by a cell-culture-immunofluorescent test (Bohl, 1979). Findings were similar in all litters, in that rotaviruses were detected when pigs were 3 to 7 weeks of age. The findings in one litter are summarised in Table 2. In this litter, rotaviruses were detected in at least one rectal swab sample from all 9 pigs between 31 to 34 days of age. In some pigs, only a very mild diarrhoea was associated with the infection. However, pig number 9 had severe diarrhoea and was euthanatised (Table 1).

Smears from the small intestinal mucosa revealed that a high percentage of the epithelial cells contained rotaviral antigen as determined by immunofluorescent staining.

From several pigs (numbers 3, 5, 6; Table 2) of this litter, rotavirus was again detected after several days of negative findings, suggesting either a sporadic shedding of virus or infection with a different porcine rotavirus serotype. We think the latter more probable. De Leeuw et al., 1979 have also reported similar findings.

TABLE 2

DETECTION OF ROTAVIRUS FROM RECTAL SWABS OF PIGS IN 1 LITTER (41-2), USING A CELL CULTURE-IF TEST. PIGS WERE WEANED WHEN 42 DAYS OLD.

Pig no.	Days of age													
	11	13	24	31	32	33	34	35	38	42	45	49	53	56
1		-	-			+	+	+		+	-	-	-	-
2	-			+	+	+			-					
3	-	-				+	-	-	-	+	-	-	-	-
4							+		-	-	-	-	-	-
5							+		-	-	+	-	-	-
6	-	-	-	-	+	+	+	+	-	-	+	-	-	-
7						-	+	-	-	-	+	-	-	-
8						-	+	+	-	-	-	-	-	-
9	-		-			+*								

* Pig no. 9 had severe diarrhoea when 33 days old, and was euthanatised. Enterocytes were IF positive for rotavirus.

VIRAL CELLULAR TROPISM AS RELATED TO IMMUNITY

With any infectious disease, the mechanism of immunity is largely determined by its pathogenesis. Thus, a few comments on cellular tropism of enteric viruses. The ability of a virus to cause diarrhoea appears to result from a massive infection of either villous enterocytes or crypt enterocytes. Because of their importance, a few relevant characteristics of enterocytes are described. Enterocytes of the small intestines proliferate in the crypts and migrate to the tips of the villi where they are sloughed. During migration, which takes from 2 to 10 days in the pig depending on many factors, the enterocytes become

more differentiated and enzymatically mature (Moon, 1971; Lipkin, 1973). The enzymatic maturity and proliferative rate of enterocytes appear to determine their suitability for replicating sites by different viruses (Moon, 1978).

TGEV and rotavirus infect villous enterocytes and it is their malfunction or destruction that results in diarrhoea. Thus, the objective of passive immunity is to protect these enterocytes against viral infection. This is normally accomplished by having a constant supply of IgA antibodies in the lumen of the gut, as occurs when pigs nurse - every 1 to 2 hours - immune sows. Haelterman (1965) has referred to this immunologic mechanism as lactogenic immunity. Ingested IgA antibodies apparently protect enterocytes either by neutralising the ingested virus before cellular adsorption or by 'coating' the luminal surface of enterocytes. Credence of the latter is provided by the report that milk IgA binds specifically to the luminal surfaces of villous epithelium in the proximal small intestine of the rat (Nagura et al., 1980). In contrast, serum antibodies have not been shown to protect villous enterocytes against TGE viral infection.

Some parvoviruses infect crypt enterocytes, resulting in villous atrophy and diarrhoea. Examples are the feline panleucopaenia virus (Carlson and Scott, 1977) and canine parvovirus (Appel et al., 1978). A porcine parvovirus has been reported to infect lymphoid cells of the gut but not crypt enterocytes, and there was an absence of diarrhoea (Brown et al., 1980). We know of no reports of viruses infecting crypt enterocytes of swine or man, but this situation could change as it recently did in the dog. Epizootics of canine parvoviral diarrhoea have been reported from several countries since 1978. It appears to be a new disease, as no canine serum samples have been found positive before June 1978 in USA (Carmichael et al., 1980).

Immunity against viral infections of crypt enterocytes seems to be associated with the presence of serum antibodies.

At least, these are the conclusions which can be drawn from studies on feline panleucopaenia (Davis et al., 1970). This is in marked contrast to the local or lactogenic immunity which is necessary with viral infections of villous enterocytes.

A major difference in pathogenesis between viral infections of villous enterocytes and crypt enterocytes may be the pathway by which viruses arrive at these cells. This may well be the basic characteristic which determines the effective immune mechanism. There is every indication that rotavirus and TGEV infect villous enterocytes from the luminal surface after having been ingested. In contrast, it is thought that feline panleucopaenia virus infects crypt enterocytes by a haematogenous route (Carlson and Scott, 1977). If such is the case, then it is easy to understand the role of serum antibodies in protecting crypt enterocytes.

The intestinal cell tropism of some enteric viruses have not been determined; such as, enteroviruses, reoviruses, and adenoviruses. It is reasonable to believe that some enteric viruses principally infect gut lymphoid tissue, without causing diarrhoea. If this situation exists, what is the immune mechanism for protecting such cells?

VACCINATION PROCEDURES FOR PROVIDING PASSIVE IMMUNITY AGAINST ENTERIC VIRAL INFECTIONS

Since TGE is such a highly fatal disease in newborn pigs, there has been much interest in development of a vaccine for use in pregnant swine, which would provide passive immunity to suckling pigs. The problem posed in developing such a vaccine has been rather unique, in that the objective is to protect villous enterocytes. TGE was apparently the first disease for which any attempt had been made to develop this type of vaccine. Interest in this area now extends to rotaviruses and other enteric coronaviruses as they also infect villous enterocytes of a number of different species. However, at this point it should be reiterated that immunity against viral infections of

crypt enterocytes is probably due to circulating antibodies; thus, vaccination procedures which provide systemic immunity should suffice against parvoviral diarrhoea.

In this section, we will comment on some of the characteristics and variables associated with lactogenic immunity in newborn pigs, with emphasis on TGEV and rotavirus.

Immunoglobulin classes of antibodies in milk as related to immunity

TGE antibodies in mammary secretions occur primarily in two immunoglobulin classes, IgG and IgA (Bohl et al., 1972). In milk of sows which have been naturally or experimentally infected with virulent TGEV, antibodies are principally associated with IgA (Saif et al., 1972). When milk whey of these sows is fractionated by gel filtration on Sephadex G-200, antibody activity is mainly associated with IgA fractions (Figure 1). TGE antibody titres are usually higher in milk than in serum throughout lactation. These sows provide good immunity to their suckling pigs against TGEV.

Intramuscular or intramammary inoculations of serologically negative pregnant swine with live virulent or attenuated TGE viral preparations have resulted in milk antibodies which have been almost entirely of the IgG class (Bohl et al., 1972; Saif et al., 1972; Bohl and Saif, 1975). Antibody titres were highest in colostrum, less in serum, and declined rapidly in milk to low levels in 5 to 10 days post-partum. Figure 2 illustrates the gel filtration (Sephadex G-200) results conducted on a milk whey sample from a sow which had been injected intramammarily with virulent virus, 42 and 17 days pre-partum. TGE neutralising antibodies were associated primarily, if not solely, with IgG. Antibody titres were higher in serum and milk from sows inoculated intramammarily than intramuscularly, which also correlated with the ability of the intramammarily inoculated sows to provide better protection to suckling pigs. Generally, limited to poor

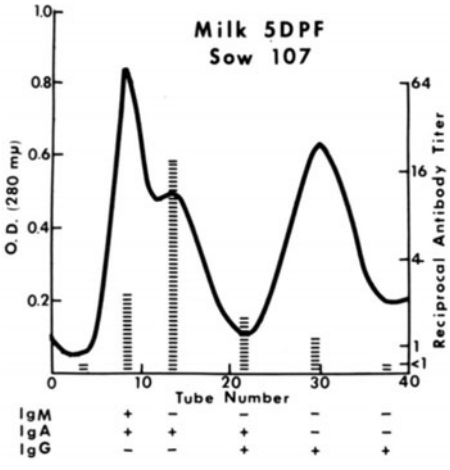

Fig. 1. Gel filtration on Sephadex G-200 of a 5-day post-partum milk sample from a sow which had been infected orally with virulent TGE virus 32 days pre-partum. Reproduced from Bohl et al., 1974, with kind permission of Plenum Press, New York.

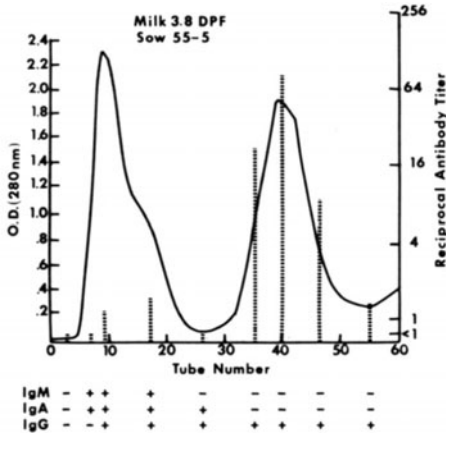

Fig. 2. Gel filtration on Sephadex G-200 of a 3.8-day post-partum milk sample from a sow which had been injected intramammarily with virulent TGE virus 17 and 42 days pre-partum. Reproduced from Bohl et al., 1974, with kind permission of Plenum Press, New York.

protection has been provided to pigs nursing sows which had been intramuscularly inoculated with live attenuated TGE vaccines (Bohl et al., 1972; Tamoglia, 1972; Bohl et al., 1975). However, when a vaccine of very high titre was inoculated intramuscularly and, later, intranasally, very high levels of colostral antibodies occurred, and there was a 100% survival of challenged pigs, although only a few litters were studied (Kaji and Shimizu, 1978). Adsorption studies indicated that about equal amounts of low levels of IgA and IgG antibodies occurred in milk.

Live attenuated virus vaccines have also been administered by the oral and/or intranasal routes, which would seem to be the procedure of choice. However, the resulting TGE antibodies in milk were of low titres; and in only about 50% of the sows could IgA antibodies be detected, and then in low levels (Bohl and Saif, 1975). Protection of suckling pigs was limited or poor, but better than when vaccine was given intramuscularly. Pensaert (1979) also reported poor results when pregnant swine were vaccinated, first orally and then intramuscularly, as mortality of challenged pigs was 65%. We interpret these results as due to the inability of attenuated virus adequately to infect the gut of orally vaccinated swine. In contrast, Hess et al., 1978 have reported that oral administration of their B1 attenuated strain resulted in high levels of IgA antibodies in milk and a 90% survival of challenged pigs. These results look very promising but more work should be done to determine the stability of the avirulent state of the viral vaccine.

Leucocyte cell-cultured TGEV vaccine

This is an unique and interesting type of experimental vaccine. A small plaque variant strain of TGEV was derived from a persistently infected swine leucocyte cell line originally infected with virulent virus (Woods, 1978). The virus vaccine was avirulent for 3-day-old pigs. When administered, by a variety of routes, to pregnant swine,

relatively high levels of antibodies were detected in 3-day post-partum milk. Challenge of 3-day old suckling pigs resulted in fairly good protection as only 14 and 29% died in 2 studies, respectively (Woods, 1978; Woods and Pedersen, 1979). As a result of passage in leucocyte cell cultures, the cell tropism of the variant virus had changed so that unidentified cells within the lamina propria of young pigs were infected rather than villous enterocytes, as judged by immunofluorescence (Woods et al., 1980).

Boosting of antibody in mammary secretions

Since many enteric infections are enzootic in nature, adult females will usually have been previously infected, but possibly only when they were young. Thus, immunisation may more often involve a boosting effect rather than a priming, or initiating, effect. This is especially true with rotaviral and enteroviral infections. Only limited information is available on the variables which are involved in boosting the titre and immunoglobulin classes of antibodies in milk of immunologically primed animals or humans. Parenteral immunisation with *Vibrio cholerae* lipopolysaccharides boosted the level of IgA antibodies in milk of primed women (Svennerholm et al., 1977). Our studies show that colostrum and milk antibody titres can be markedly boosted by parenteral vaccination of sero-positive pregnant or lactating swine with a rotavirus or TGEV vaccine. For example, Table 3 summarises the antibody responses in serum and milk of a sow which was intramuscularly vaccinated 7 days pre-partum with a TGEV and a porcine rotavirus vaccine. Antibody titres for both viruses increased markedly in serum, and were higher in colostrum and in milk for the first few days post-partum than normally occurs in non-vaccinated animals. Faecal shedding of rotavirus was first detected in pigs of this litter when 31 days old, which is about the normal age for faecal shedding in non-vaccinated litters (See Table 2). We interpret the rotaviral infection as being due either to ineffective immunisation or to a different rotavirus serotype than the vaccine strain. Following

infection of the pigs, there was a 4-fold increase in antibody titre in milk but only a slight increase in serum of the sow. Similar results for a non-vaccinated animal were previously discussed and shown in Table 1.

TABLE 3

ANTIBODY TITRES OF SOW (NO. 48-1) VACCINATED WITH PORCINE ROTAVIRUS (OSU STRAIN) AND TGEV. LIVE CELL-CULTURED VIRUSES WERE INTRAMUSCULARLY INJECTED 7 DAYS PRE-PARTUM. FAECAL SHEDDING OF ROTAVIRUS WAS FIRST DETECTED IN PIGS WHEN 31 DAYS OLD.

Day pre- or post-partum	Antibody titres*			
	TGEV		Rotavirus	
	Serum	Milk	Serum	Milk
-7	40		150	
0.5	400	2 000	370	4 200
7	1 800	500	1 600	340
14	740	350	1 020	270
28	520	310	450	120
42	450	210	540	520

* Reciprocal of dilution giving an 80% plaque reduction of porcine rotavirus or TGEV.

About 50% of the swine herds in Ohio, USA, contain TGE serologically positive animals. Thus, some animals will need to be immunologically primed and others boosted. Some vaccination procedures may be better for priming, and others for boosting, immunity. Parenterally administered TGE vaccines can appreciably boost antibody titres in serum, colostrum and milk of previously infected swine and, presumably, provide increased protection to suckling pigs. This effect may be the principal justification for using parenterally injected TGE vaccines (Stepanek et al., 1979). We usually recommend this procedure for helping control enzootic TGE infections but have no precise information on its value.

It is important to know the immunoglobulin classes of TGE viral and rotaviral antibodies in milk which result from vaccinating previously infected animals, using a variety of

vaccination procedures. Such studies are underway in our laboratory.

Neonatal colibacillosis

The immunologic findings with TGE prompted our research group to try similar vaccination procedures using enterotoxigenic *Escherichia coli* (EETC). Pregnant swine were vaccinated with live EETC either by oral exposure with high dosages or by intramuscular injections. When newborn pigs from these vaccinated or non-vaccinated sows were orally challenged with EETC, protection was much more effective in pigs suckling the orally vaccinated sows (Kohler et al., 1975). Kohler (1978) then took this procedure to the field and very favourable results have been obtained; to the extent that it is a commonly used immunising procedure in midwestern USA for protecting newborn pigs against *E. coli* diarrhoea. By this procedure, the previously isolated strain or strains of EETC from the involved herd are grown in commercial pasteurised milk, usually in quart or gallon containers. The 'cultured' milk is then fed to pregnant swine about 4 weeks before parturition. A recent report has shown that oral immunisation of lactating sows with EETC (O8 : K88) stimulated an IgA antibody response in mammary secretions (Evans, et al., 1980).

PROCEDURES FOR INITIATING THE PRODUCTION OF IgA ANTIBODIES IN MAMMARY SECRETIONS

We initially reported evidence for an immunologic gut-mammary link in 1972, stating that TGE viral antibodies of the IgA class occurred in milk of swine only as a result of a previous infection of the gut (Bohl et al., 1972; Saif et al., 1972). We also postulated that the most appropriate explanation for this immunologic finding was 'a relocation of TGE viral sensitised immunocytes from the lamina propria to the mammary gland, possibly via lymphatic and blood vessels' (Bohl et al., 1972). These conclusions were drawn from investigations involving the administration of virulent or attenuated TGEV using a variety of routes - oral, intramuscular, or intramammary.

These immunologic concepts have since been either confirmed or elaborated upon, using a variety of antigens, in swine (Bohl and Saif, 1975; Saif and Bohl, 1977; Hess et al., 1978; Evans et al., 1980), rabbits (Montgomery et al., 1974), man (Goldblum et al., 1975), rats (Michalek et al., 1976), and mice (Roux et al., 1977). A gut-mammary link which provides high levels of IgA antibodies in colostrum and milk is highly advantageous for protecting the newborn against those enteric infections which are enzootic or endemic in the parent population.

We were interested in knowing if there is an immunologic respiratory-mamary link, similar to the gut-mammary link. Consequently, pregnant swine were intranasally exposed to pseudorabies virus, which causes an infection, mainly, of the upper respiratory tract. The ensuing antibodies in milk were primarily, if not solely, of the IgG class; and although high titres occurred in colostrum, they declined rapidly to very low levels in milk after 6 to 12 days' lactation (Saif and Bohl, 1977). This suggests that such a link does not occur. Nor do we know of any direct evidence that IgA antibodies in milk protect the young against respiratory infections. This information discouraged us from attempting to use a respiratory infection as a means of stimulating the production of IgA antibodies in the mammary gland; as might occur if a modified enteric virus were to replicate in the respiratory tract.

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DISCUSSION

H. Miller *(UK)*

Does pseudorabies infect epithelial cells in the upper or lower respiratory tract?

E. Bohl *(USA)*

It is my understanding that it is the upper respiratory tract.

H. Miller

Do you get an IgA response?

E. Bohl

We get an IgG response in the mammary gland. We have not tested the respiratory secretions. I assume there would be an IgA response there.

K. Petzoldt *(FRG)*

You mentioned antibody response in defence against enteric diseases. Is there any evidence that cellular immune mechanisms also play a role. There has been work in humans for example which shows that following breast feeding tubercle negative babies become tubercle positive, for a short period of time.

E. Bohl

There are both lymphocytes and macrophages in milk and there is much interest in what role they play. I know of no evidence to suggest that they are involved in passive immunity, however, they probably do contribute and the reason I say this is that if you have a sow which is immune to TGE, and you take pigs off that sow for about eight hours, then they become susceptible to TGE. If you want to have good lactogenic immunity, it is imperative that the pigs keep nursing about every hour and a half, this is the normal nursing period of pigs. This may go against the idea of establishment of live cells in the gut which

would give a semi-permanent type of immunity from cells rather than from immunoglobulins, but I can envisage that it would play a considerable role in passive immunity.

J. Soothill *(UK)*

First a comment: there is evidence from Pitt that the macrophages are of value as a passive protective factor. Now a question - you said that you thought that villus tip infections were transmitted by faeces and protected for by secreted antibody and that crypt infections were transmitted by blood and perhaps protected by serum antibody. What evidence underlies this association which is an intriguing one?

E. Bohl

There is a good deal of evidence that serum antibodies play a very small role in protecting villus enterocytes against virus infection with TGE virus or rotavirus, either passively or actively acquired serum antibodies. There does seem to be protection passively by so-called lactogenic immunity, or local active immunity. Now, the evidence in regard to the crypt enterocyte is probably a little more indirect. We immunise cats against panleucopaenia by parenteral injection. Some people think that feline panleucopaenia virus gets to the crypt enterocytes by way of the blood and not by way of the lumen. Obviously, serum antibodies would be protective if the route to the crypt was by the haematogenous route. This is very important in regard to knowing what type of immunising agent is effective.

P. Brandzaeg *(Norway)*

I just wondered, with regard to the lack of a respiratory mammary link in pigs, do the pigs have tonsils?

E. Bohl

Yes.

P. Brandzaeg

Are they as well developed as in the human species?

E. Bohl

I would think they are.

A. Ferguson *(UK)*

Is there solid evidence that IgA antibody completely prevents rotavirus infection, or does it just alter the course?

E. Bohl

I should have emphasised this more. Most passive immune states do not give complete protection. In fact, it is not to the advantage of the animal to be completely protected. There may be complete protection for the first two weeks of life and then partial protection at 3, 4 or 5 weeks.

A. Ferguson

I completely follow your argument that amelioration of the clinical features is the ultimate objective. But is there evidence that immunity rather than other factors such as motility, acidity and mucous, is involved? Is there proof that active IgA antibody prevents infection by rotavirus? Could it be that antibody has nothing to do with protection against rotavirus?

E. Bohl

Infection occurs in pigs at one, two or three days of age. Maybe there is a very latent infection in the gut which is held in check by antibodies or certain physiological conditions. Then, at 3 or 4 weeks of age, physiological conditions change or the milk antibody level declines, and latent infection develops with excretion - this doesn't answer your question. I don't know if we can say for absolutely sure that it is the IgA that is preventing these infections. I just think it is the most likely explanation at the present time.

T.J. Newby *(UK)*

Thank you very much Professor Bohl. There will be an opportunity to continue this discussion later.