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Abstract

It is well established that there normally is no transmission of maternal immunoglobulins across the placenta of the pig and calf. The passive transfer of colostral immunoglobulins from mother to neonate is for pig and calf the most important way of giving immediate immunological protection.
The proteolytic activity in the digestive tract is low, and is further minimized by the presence of trypsin inhibitor in colostrum. The small intestine is lined with highly vacuolated, immature mucosal epithelial cells which are capable of absorbing macromolecules. Immunoglobulins in the lumen of the intestine are first internalized by enterocytes via pinocytosis in the uptake phase, and internalized macromolecules are thereafter transported to the blood. In pig and calf, the uptake and transport of macromolecules is qualitatively nonselective, including a variety of homologous and heterologous proteins. The absorption of immunoglobulins has dropped to a relatively low level after 24-36 hours. What regulates closure is not fully known, but appears to be controlled by endocrine influences and coordinated with the development of the enzymes that characterize the mature microvillus surface.
Many factors influence the absorption of colostral immunoglobulins in the newborn e.g. starting age of colostrum feeding, feeding before colostrum feeding, amount of colostrum fed, concentration of immunoglobulins in colostrum, exposure to stress, permeability changes in the intestine.

Antibody transfer from mother to offspring has been the subject of numerous studies since the 1890's and certain differences between species have been disclosed. The transmission of passive immunity from mother to young may occur prenatally via the placenta, postnatally by way of colostrum or by both routes. It is well established that there normally is no transmission of maternal immunoglobulins across the placenta of the pig and calf (Brambell, 1970). As a result the pig and calf are born devoid of immunoglobulins and rely on colostrum as a source of circulating antibody during the early part of their life, (Bourne *et al.*, 1978; Kruse, 1980; Watson, 1980; Klobasa *et al.*, 1981).

If immunoglobulins are found in fetal or newborn pig and calf sera they must be of fetal origin following antigen stimulation or have been passively transferred from the dam across a damaged placenta. It has been readily demonstrated that the fetal pig, like many other mammalian fetuses, is immunocompetent to a variety of antigens when exposed either naturally or by artificial means (Redman, 1979). However, under normal circumstances antigen exposure does not occur until soon after birth. In consequence, the newborn emerges from its protective shelter equipped with a rudimentary immune system, which has not hitherto been primed to function. Pigs and calves are therefore born with poor resistance against the intensive microbial challenge of the outside world.

The passive transfer of colostral immunoglobulins from mother to neonate is for pig and calf the most important way of giving immediate immunological protection. Colostrum is well adapted to the

immunological roles, because the immunoglobulins are derived almost entirely from the serum of the dam (Bourne, 1977; Watson, 1980). The intestinal tract of the newborn pig and calf is capable of absorbing colostral immunoglobulins without change in amounts sufficiently large to alter the composition of blood plasma. The mechanism by which this transfer of colostral immunoglobulins occurs mainly in pigs and the effect of certain factors on the amount of immunoglobulins reaching the blood are reviewed in this paper.

Colostral immunoglobulins

The importance of colostral immunoglobulins in the resistance to infectious diseases in newborn is universally recognized (McCallum *et al.*, 1977; Bourne *et al.*, 1978; Chidlow and Porter, 1979). It has been reported that 90 % of piglets deprived of colostrum died before weaning (McCallum *et al.*, 1977). In our studies where cow colostrum and cow milk were fed to newborn pigs the mortality was almost 100 % during the first 3 weeks of life. However, the results indicate that cow colostrum gives the piglets certain protection, as the piglets fed cow milk all died before they were two days old. Sow colostrum was found very important and irreplaceable. However, when the sows immune response is carefully regulated to meet particular requirements, a great amount of colostrum is not needed for the passive immunisation of the neonatal pig. Studies showed that 175 ml colostrum with a total amount of 15.8 g immunoglobulins were able to protect newborn pigs under normal environmental, conditions.

Isolation and characterization of colostral immunoglobulins have been undertaken in many studies in the last decade (Bourne, 1969a,b; Svendsen *et al.*, 1971; Porter and Allen, 1972; Bourne and Curtis, 1973; Jensen and Pedersen, 1979; Kruse, 1979, 1980).

There is approximately 15 g of whey proteins in 100 ml colostrum whey from sows and 60-70 per cent of these proteins are immunoglobulins (Kruse, 1980). The immunoglobulins known to be related to immunity in pigs are IgG, IgM and IgA (Porter and Allen, 1972). As it can be seen from table 1 the main immunoglobulin of colostrum is IgG. With the onset of lactation there is a rapid decline in the IgG concentration over the first week of lactation and immunoglobulin A, which is a minor component of colostrum, predominates in milk (table 1).

As is the case with immunoglobulins from other mammalian species, also porcine colostral immunoglobulins are sensitive to different proteolytic enzymes, including trypsin (Stone *et al.*, 1979). Therefore trypsin inhibitor present in colostrum (table 1) may have a positive influence on the acquisition of passive immunity by newborn piglets.

Studies with pigs have shown that milk IgA takes longer to pass along the gut than the normal interval between suckings and this milk IgA forms a continuous defence protecting the sucking piglet from disease caused by enteric pathogens (Chidlow and Porter, 1978, 1979). Secretary IgA from sow's milk is relatively more resistant than IgG or IgM against proteolytic digestion (Stone *et al.*, 1979).

The immune system of the bovine would appear to be deficient in IgA when compared to other mammalian species (Watson, 1980). The major immunoglobulin of bovine colostrum and milk is IgG1 and bovine milk contains very little IgA. Bovine IgG1 is thought to possess similar importance in local immunity to secretory IgA in pigs (Bourne *et al.*, 1978).

Absorption of immunoglobulins

Colostral proteins fed to the newborn pig and calf are not degraded and used as a food source but reach the small intestine intact. Because the proteolytic activity in the digestive tract is low, and is further minimized by the presence of trypsin inhibitor in colostrum. IgG-rich colostral whey passes quickly through the stomach and into the small intestine. For the first 24-36 hours after birth the small intestine is lined with highly vacuolated, immature mucosal epithelial cells which are capable of absorbing macromolecules. The colostral immunoglobulin is thus transported from the lumen of the intestine, via the absorptive epithetial cells and intestinal lymphatic system, to the blood (Murata and Namioka, 1977; Moog, 1979).

Table 1. — Immunoglobulins and specific sow colostrum trypsin inhibitor (SCTI) in colostral and milk whey from 9 sows (Jensen and Pedersen, 1979).

Day	IgG (g/l ± s)	IgM (g/l ± s)	IgA (g/l ± s)	SCTI (mg/l ± s)
0	57.8 ± 19.0	10.7 ± 6.9	24.0 ± 9.3	1 305 ± 232
1	14.2 ± 5.5	3.2 ± 2.3	7.5 ± 3.0	445 ± 277
2	4.5 ± 2.8	1.8 ± 0.7	4.0 ± 1.9	89 ± 74
3	2.0 ± 1.1	1.6 ± 0.7	3.6 ± 1.6	36 ± 39
7	0.7 ± 0.3	1.2 ± 0.3	3.2 ± 0.9	3 ± 5
15	0.3 ± 0.1	1.2 ± 0.8	2.8 ± 0.7	0.2 ± 0.3

The phenomenon of intestinal absorption of maternal immunoglobulins has been extensively examined by nutritionists and immunologists. Macromolecules in the lumen of the intestine are first internalized by enterocytes via pinocytosis in the uptake phase, and internalized macromolecules are thereafter transported to the blood (Harvey and Lecce, 1976, 1979; Bush and Staley, 1980).

Studies have shown that the absorption of macromolecules is specific also between the different immunoglobulin classes (Perry and Watson, 1967). However, many studies since then have shown, that the uptake and transport of macromolecules is qualitatively nonselective in pig and calf, including a variety of heterologous and homologous proteins, dextrans and polyvinylpyrolidone (Hansen, 1968; Harvey and Lecce, 1976, 1979). Proportions of the different classes of immunoglobulins in serum after ingestion of colostrum reflect therefore the proportions in colostrum when absorption is completed.

The intestinal epithelium of the newborn pig and calf retains the ability to pinocytose macromolecules for only a short time before the highly vacuolated epithelium is replaced by mature epithelial cells (Moog, 1979). The length of the absorptive period is a matter of debate among authorities, but as a general rule absorption of immunoglobulins has dropped to a relatively low level after approximately 24-36 hours (Porter, 1969; Bourne and Curtis, 1973; Murata and Namioka, 1977). In general, permeability is highest immediately after birth and declines rapidly thereafter.

The cessation of pinocytosis, a phenomenon called «closure», apparently signals a shift in the membrane producing capacity of the epithelial cells, the endocytotic type of membrane is no longer being synthesized (Moog, 1979). The intestinal cells that absorb immunoglobulins are replaced by a more mature cell population with enzymes that characterize the mature microvillus surface and the cells are no longer engaged in pinocytosis. What regulates closure is not fully known, but appears to be controlled by endocrine influences and coordinated with the development of the enzymes that characterize the mature microvillus surface.

The relationship between adrenocortical hormones and intestinal maturation have been abundantly supported, in a large number of investigations carried out with other mammals than pigs and calves. (for review see Moog, 1979). Experiments on intact sucklings or those derived of hypophysis, adrenal or thyroid glands show that epithelial maturation depends on adequate titers of corticosteroids and thyroxine, with either hormone eliciting nearly normal redifferentiation in the absence of the other (Yeh and Moog, 1979). Cessation of the uptake of colostral immunoglobulins occur from the proximal to the distal part of the small intestine. There is evidence from work that pinocytosis in the epithelium disappeared 2 hours after birth in the duodenum but not before 72 hours in the ileum (Murata and Namioka, 1977). The period of absorption, however, is not limited to a certain critical time period after birth but is dependent upon the type of food ingested.

Factors effecting the amount of immunoglobulin absorbed

There is a wide variation among newborn pigs (table 2) and calves in concentration of immunoglobulins in serum after cessation of absorption of colostral immunoglobulins (Curtis and Bourne, 1971; Jensen and Pedersen, 1979; Kruse, 1980). Peak serum levels of immunoglobulins are observed at 24 hours of age and thereafter there is a steady decrease until the active immunity takes place (table 1).

There may be many factors during the prenatal period including nutrition (Kruse, 1980) genetics (Spooner *et al.*, 1975) environment (Chidlow and Porter, 1979), etc., which may influence the immune competence of the neonate. In our own studies with a total of 90 sows there was found a considerable sow to sow variation in the concentration of total immunoglobulins in colostrum

Table 2. — Immunoglobulins in serum from 23 piglets — offspring of 4 sows — in relation to age (Jensen and Pedersen, 1979).

Age (days)	IgG (g/l ± s)	IgM (g/l ± s)	IgA (g/l ± s)
1	24.4 ± 8.8	3.5 ± 1.8	17.0 ± 5.1
3	21.5 ± 8.5	1.5 ± 0.7	8.7 ± 3.1
6	18.5 ± 7.4	0.7 ± 0.3	2.7 ± 1.4
15	11.7 ± 4.8	0.4 ± 0.2	0.4 ± 0.1
22	7.7 ± 2.7	0.7 ± 1.1	0.4 ± 0.2
30	11.1 ± 7.3	0.9 ± 0.7	0.8 ± 0.4

whey from 5.2 to 12.9 g/100 ml whey. The composition of colostrum was also altered by dietary horse beans in the sows feed. An increase in dietary horse beans significantly reduced the protein content in colostrum ($P < 0.001$). As to the various protein fractions, albumin and immunoglobulins showed the greatest decline (Kruse, 1980). The efficiency of protein absorption by the piglet is increased if concentration of ingested protein is increased (Pierce and Smith, 1967). With the advent of sucking a very marked fall occurs in colostral immunoglobulin concentration, and 50 per cent of this fall occurs within four to six hours of the birth of the first piglet (Bourne, 1969a, b). In normal farrowing, particularly with large litters, piglet born late in parturition will meet with greater competition and will only be able to obtain colostrum of a lower protein concentration than those born earlier. This situation will be aggravated by prolonged parturition.

The starting age of colostrum feeding, feeding before colostrum feeding and the amount of colostrum fed will also influence the rate of absorption of colostral immunoglobulins. The time of closure is a function of feeding regime in that the intake of whole colostrum or some fractions initiates closure. Starved piglets will keep their ability for pinocytotic activity for some days. However, generally absorption efficiency is decreased when ingestion of first colostrum is delayed, indicating the importance of colostrum intake soon after birth (Bush and Staley, 1980). Even more important is that transmigration of pathogenic bacteria can be prevented by colostrum in the intestinal lumen.

Stress is also a factor which is influencing the absorption of colostral immunoglobulins. Cold exposure early in the life of pigs (Blecha and Kelly, 1981) and calves (Olson *et al.*, 1980) lowered the rate of absorption of colostral immunoglobulins. However, the reason why cold exposed pigs and calves have lower concentrations of colostral immunoglobulins in the systemic circulation is unknown.

When considering colostrum quality, it is not only a question of the total amount of immunoglobulins, but also a question of the antibody activity in all immunoglobulin classes in colostrum. Newborn piglets are therefore most susceptible to infections when they are born into environments other than those in which their dams had been reared, because of a lack of specific antibodies to infections present in the new environment (Kruse, 1980).

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Question

From Dr. Bourne to Dr. Kruse

An observation made in our laboratory in the early 1970's suggested that initial level of colostrum was very important in establishing higher levels of serum antibody. Could this be positively influenced by withholding piglets from the sow right after farrowing has finished and by so doing reduce the wide variations in piglet serum levels that is commonly observed?

Answer

The efficiency of protein absorption by the newborn pig and calf is increased if concentration of ingested protein is increased. With the advent of sucking, a very marked fall occurs in colostral immunoglobulin concentration. Prolonged parturition will therefore influence the rate of the passive immunization of newborn pigs, and this can be positively influenced by restricting suckling until the parturition process is complete.

Question

From Dr. Michell to Dr. Kruse

Could you comment on the local protective value of colostrum if ever it is not absorbed?

Answer

Colostral immunoglobulins, which are left in the intestinal lumen are also of great importance to the local immunity in the gastro-intestinal tract. For the defense of mucosal surfaces IgA is especially important in colostrum and milk with appropriate antibody specificity. The functions of secretory IgA are to prevent the adherence of bacteria and viruses to mucosal surfaces and also to agglutinate particles and neutralize viruses and toxins. The last two functions are also typical functions of IgG and IgM in colostrum and milk.