Colostrum and Immunologic Competence

M. L. Kaeberle, D.V.M.

The ability of a subject to respond to antigenic stimulation with the production of antibodies or increased sensitivity to the antigen (hypersensitivity) has been called "immunologic competence." However, the term may be used in a broader sense to describe the relative ability of an animal to establish resistance to a disease process. This concept of immunologic competence not only relates to the responsiveness of the animal to antigenic stimulation but also to other mechanisms of resistance to infectious disease. While the significance of antibody-mediated immunity cannot be questioned, mechanisms such as those associated with natural immunity, cellular or tissue immunity, and immunity to viral diseases are of equal or greater importance. Immunologic competence will be used in its broader connotation in this presentation since several aspects of resistance are under consideration.

Immunity to infectious agents may be either natural or acquired. Genetically controlled native immunity is mediated by several humoral factors including natural antibodies, properdin, complement, lysozyme, and β-lysins and by cellular factors such as phagocytosis. Acquired immunity includes that mediated by antibodies and the less well understood cellular or tissue immunity. These factors acting alone or in concert possess the capability of inactivating or destroying infectious agents and are the basis of an animal's resistance to disease.

The young pig is an excellent experimental animal for immunologic studies since the newborn pig lacks immunologic competence. This observation is supported by the acknowledged marked susceptibility of young pigs to infectious disease. Pigs deprived of colostrum are even less competent since they lack the protection provided by maternal antibodies and the ability to respond to immunization as well as normal pigs. The incompetence of colostrum-deprived pigs to form antibodies was first reported by Hoerlein[2] and has been confirmed in other experimentation.[5,6] Only Kim *et al.*[3] question this thesis for they have reported 3-day-old Minnesota miniature pigs taken by Caesarean section and deprived of colostrum to respond normally to antigenic stimulation.

The immunologic behavior of young pigs changes with age and may be influenced by such a factor as colostrum. The experimentation to be reported demonstrated the influence of age and colostrum upon several factors associated with immunologic competence.

EXPERIMENTAL ANIMALS

The animals used in these studies were young pigs, either colostrum-deprived or colostrum-fed. Colostrum-deprived (CD) pigs were taken by Caesarean section,[1] raised in isolation, and fed modified cow's milk or SPF-lac[2]. Colostrum-fed (CF) pigs were naturally farrowed, reared on the sow and weaned at approximately 3 weeks of age. Both groups of pigs were fed a commercial pre-weaner, starter and grower.[3]

From the Department of Veterinary Microbiology and Preventive Medicine, Iowa State University, Ames, Iowa.

1. Colostrum-deprived pigs used as serum donors for the bactericidal experiment were naturally farrowed and removed from the dam prior to nursing.
2. The Borden Co., New York 17, N.Y.
3. Kindly supplied in part by the Walnut Grove Products Co., Atlantic, Iowa.

ANTIBODY PRODUCTION

The response of young pigs to several soluble and precipitated antigens has been studied. Not only have these experiments demonstrated a marked difference in the responsiveness of CF and CD pigs but also the influence of the antigen. Early experiments utilized alum-precipitated tetanus toxoid in 3 groups of newborn and 3-week-old pigs. In each age class a group of CD pigs was injected intraperitoneally with toxoid alone, a second group of CD pigs with antigen mixed with a small quantity of tetanus antiserum and a group of CF pigs with toxoid alone. Serum was collected at weekly intervals and tested for tetanus antibodies. The results are shown graphically in Figures 1 and 2. CD and CF pigs in both age groups responded to the toxoid with production of antibodies. Two observations are particularly interesting, (1) the enhancing effect on antibody production of a small quantity of specific antibody and (2) the superior response of 3-week-old CF pigs but inhibition of the response in newborn CF pigs.

The circulating antibody responses of 3-week-old CD and CF pigs to several different antigens are summarized in Table 1. CF pigs consistently responded with a higher titer than CD pigs. The experiments also indicated the superior antigenicity of tetanus toxoid and equine

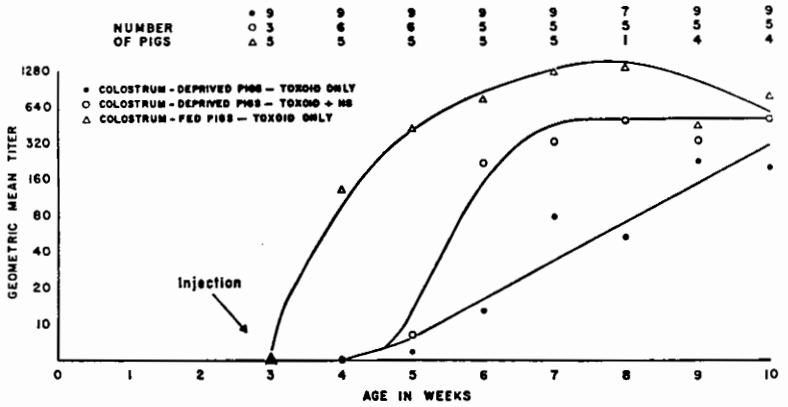

Figure 1. Antibody responses of 3-week-old CD and CF pigs.

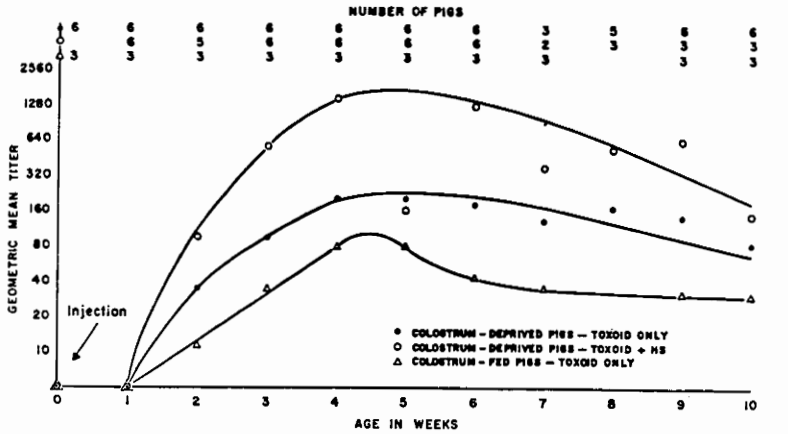

Figure 2. Antibody responses of newborn CD and CF pigs.

ferritin for young pigs. Experimentation utilizing dosages of the same antigens ranging from 6.25 to 25 mg has not resulted in significantly different responses indicating that dosage was not a major consideration.

TABLE 1—CIRCULATING ANTIBODY RESPONSES OF 3-WEEK-OLD CD AND CF PIGS TO SEVERAL ANTIGENS. THE ANTIGENS WERE ADMINISTERED INTRAPERITONEALLY IN A DOSAGE OF ONE ML OF COMBINED DIPHTHERIA-TETANUS TOXOID CONTAINING 50 LF UNITS DIPHTHERIA TOXOID AND 15 LF UNITS TETANUS TOXOID OR ONE ML OF HEMOCYANIN, SHEEP GLOBULIN OR FERRITIN CONTAINING 12.5 MG OF THE RESPECTIVE PROTEIN.

Antigen	Type of Pigs	Titer by Week[a] 4	5	6	7	8
Tetanus Toxoid (Alum Precipitated)	CF	120	460	640	950	970
	CD	0	5	15	70	50
Diphtheria Toxoid (Alum Precipitated)	CF	20	20	110	230	80
	CD	0	0	0	0	5
Keyhole Limpet Hemocyanin (Soluble)	CF	15	35	60	80	55
	CD	0	0	10	5	10
7S Sheep Globulin (Soluble)	CF	0	35	40	40	45
	CD	0	0	0	0	0
Equine Ferritin (Soluble)	CF	290	610	410	590	200
	CD	120	150	190	220	180

[a]—Mean passive hemagglutination antibody titer of serum.

SERUM COMPLEMENT

Complement activity has been assayed in serum obtained from CD and CF pigs at weekly intervals from birth (cord serum) to 8 weeks of age. Titration of serum for complement activity was performed in a hemolytic system utilizing sheep erythrocytes and rabbit hemolysin. Average serum complement titers for pigs of different ages are shown in Table 2.

TABLE 2—SERUM COMFLEMENT TITERS IN CD AND CF PIGS OF DIFFERENT AGES.

Type of Pig	Complement Titer by Week[a] O[b]	1	2	3	4	5	6	7	8
CD	10.0	15.24	25.62	49.22	46.97	49.27	56.96	79.68	78.73
CF		44.18	63.58	74.14	70.55	62.71	62.88	56.63	78.55

[a]—Average CH_{50} units per ml
[b]—Cord serum

Serum complement titers increased with age and CF pigs reached a stable level somewhat earlier than CD pigs.

SERUM LYSOZYME

Lysozyme activity has been measured in serum from CD and CF pigs of different ages. A standard lysozyme assay was utilized with the test system measuring the lytic activity of 0.25 ml of serum on a suspension of *Micrococcus lysodeikticus* cells. The results of these titrations are shown in Table 3 and indicated that serum lysozyme activity increases with age and more rapidly in CF pigs.

TABLE 3—SERUM LYSOZYME ACTIVITY IN CD AND CF PIGS OF DIFFERENT AGES.

Type of Pigs	Lysozyme Titer by Week[a] 1	2	3	4	5	6	7	8
CD	0.60	0.78	1.10	1.79	1.57	2.27	2.05	2.08
CF	0.85	1.29	1.53	1.37	4.30	3.58	2.20	2.29

[a]—Average lysozyme activity in μg

BACTERICIDAL ACTIVITY OF SERUM

The bactericidal activity of serum for *Escherichia coli* and *Salmonella choleraesuis* was determined by plate count assays and release of P-32 from radiolabeled bacteria. Serum from young CD pigs did show some bactericidal activity (Table 4) but serum from young or old CF pigs possessed far greater activity. Serum from older pigs was much more bacteriolytic than serum from young pigs but this was not reflected in the plate count assays. Antibacterial activity of serum increased with the age (Table 5) of the donors with the increased effectiveness particularly evident in serum from CD pigs.

TABLE 4—BACTERICIDAL ACTIVITY FOR *Escherichia coli* AND *Salmonella choleraesuis* OF THREE SWINE SERUMS. THE SERUMS WERE POOLED SAMPLES FROM 3-DAY-OLD, COLOSTRUM-DEPRIVED PIGS (CD), 3-DAY-OLD COLOSTRUM-FED PIGS (CF), AND 16-WEEK-OLD, COLOSTRUM-FED PIGS (FD). ACTIVITY WAS DETERMINED BY QUANTITATION OF BACTERIA SURVIVING INCUBATION WITH 0.4 ML OF SERUM AND BY P-32 RELEASED BY INCUBATION OF RADIOLABELED BACTERIA WITH 0.4 ML OF SERUM.

Serum	*Escherichia coli* % Killed	*Escherichia coli* % P-32 Released	*Salmonella choleraesuis* % Killed	*Salmonella choleraesuis* % P-32 Released
CD	6	3.76	40	14.28
CF	79	9.56	74	30.39
FD	47	19.04	68	38.64

TABLE 5—BACTERICIDAL AND BACTERIOLYTIC ACTIVITY OF SERUM FROM COLOSTRUM-DEPRIVED (D) AND COLOSTRUM-FED (F) PIGS OF DIFFERENT AGES. CORD SERUM AND POOLED SERUM SAMPLES OBTAINED AT WEEKLY INTERVALS WERE TESTED IN 0.4 ML QUANTITIES FOR ABILITY TO KILL OR RELEASE P-32 FROM *Escherichia coli*.

Age of Pigs in weeks	% Bacteria Killed D serum	% Bacteria Killed F serum	% P-32 Released D serum	% P-32 Released F serum
0	51[a]		0.47[a]	
1	86	78	7.50	19.55
2	63	93	7.12	19.39
3	93	94	15.23	18.01
4	93	91	21.21	19.25

[a]—cord serum

DISCUSSION

A number of factors that contribute to immunologic competence of young pigs

have been studied in experiments utilizing CF and CD pigs. The influence of age and physiologic state of these animals on their immunologic competence is quite apparent. While the neonatal pig is quite deficient immunologically, colostrum and increasing age contribute to the development of competence.

Colostrum is an extremely important contributing factor not only for the passive immunity conferred by its antibody content but also through its contribution to physiologic processes. Maternal immunity resulting from the transfer of antibodies across the intestinal wall to the circulation provides protection against infectious agents during that early period of life when the pig's capacity to produce antibodies is limited. However, these same maternal antibodies may interfere with the development of active immunity. Presence of appreciable quantities of antibody in the circulation apparently ties up the antigen and blocks the induction of antibody formation. This has been observed commonly in hog cholera immunization and is demonstrated experimentally in Figures 1 and 2. While 3-week-old, CF pigs respond very well to tetanus toxoid as compared to their CD counterparts, newborn CF pigs were somewhat less responsive. The presence of interfering quantities of antitetanus antibodies in newborn pigs is probably responsible for this happening. In contrast, a small quantity of antibody acts to enhance active antibody formation. This adjuvant effect of antibody has been observed in experiments utilizing tetanus toxoid, diphtheria toxoid or equine ferritin as antigens in CD pigs. The possibility exists that colostrum may contribute to immunologic competence by contributing a small quantity of specific antibodies.

The role of complement in the immunologic maturation of the young pig is demonstrated by the capacity of CF pigs to form antibody and the earlier achievement of normal complement and lysozyme levels in their serum. Cochrane, *et al.*[1] also titrated pig serum for hemolytic complement and reported similar results. Colostrum apparently contributes factors that aid in the physiologic development of the young pig. The increased production of serum complement and lysozyme is associated with this physiologic maturation.

Antibodies, complement and lysozyme are important reactants in bactericidal activity of serum, particularly against Gram negative organisms. The *in vitro* bactericidal assay is, therefore, a determinant of these materials acting in concert. Bacteriolytic activity is thought to require the participation of antibody. The observation that newborn CD pig serum has some activity is, therefore, quite interesting. Schwab and Reeves[4] reported essentially similar findings and concluded that serum from the newborn pig must contain some antibody. Such a conclusion is in contrast with the generally accepted thesis that newborn pigs are completely devoid of gamma globulin. Contrary to previous beliefs that the newborn pig derives maternal antibody only from the ingestion of colostrum, the possibility exists that minute quantities of gamma globulin are transferred across the placenta to the circulation of the fetus *in utero.*

The correlation between serum complement and lysozyme titers and bactericidal activity is indirect evidence for the participation of these materials. These factors undoubtedly are active under *in vivo* circumstances and provide protection against infectious agents. The marked susceptibility of newborn and CD pigs to infectious disease must relate to a deficiency of these and other materials that contribute to immunologic competence.

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