Post-weaning diarrhea is a complex disease resulting in significant losses in the period immediately following weaning. Although closely associated with the presence of enteropathogenic E. coli, this pathogen is not the sole cause of post-weaning diarrhea. Enteropathogenic E. coli strains isolated from diarrheic animals show a high degree of genetic diversity, and the pathogenic potential of these strains varies widely. The persistence of these strains in the environment and their ability to re-infect newly weaned piglets contribute to the recurrence of diarrhea.

Several explanations have been advanced in an attempt to explain this increase in susceptibility. These include:

1. Disruption of the protective effects of milk.
2. Reduction of the bactericidal activity of neutrophils.
3. Some unknown stress associated with the introduction of solid food.

We have performed a number of experiments to test these possible explanations. In a preliminary study, piglets were infected with milk while still suckling the sow at 7 days of age with a marked enteropathogenic E. coli strain isolated from a case of post-weaning diarrhea. After two or three days this bacteria was no longer detectable in fecal samples obtained from the animals or from the environment. Seven days after weaning however, the bacteria reappeared in the feces and persisted for several days without producing clinical signs of disease. This persistence of infection suggests that the appearance of enteropathogenic E. coli in post-weaning diarrhea is due to an increase in numbers of a bacterial population already established in the intestine rather than through infection via ingestion.

The removal of antibody in sow's milk may well be a significant factor in the reappearance of pathogenic E. coli in the intestinal tract in large numbers after weaning but further experiments suggest that this is not in itself sufficient to provoke diarrhea. Pigs were weaned at three weeks of age and fed for a further 14 days on cows milk. During this period no diarrhea was seen but five days after a high protein weaner ration was introduced all the animals had diarrhea. This experiment appeared to exclude the possibility of milk antibody as a prime cause of post-weaning diarrhea and pointed to the importance of the diet and the method of its introduction in the etiology of this condition. These experiments and the field observations that post-weaning diarrhea is often associated with the abrupt introduction of weaner diets, often in excessive amounts, support an alternative explanation. This explanation is that the antigenicity of the food is in the young animal, leading to a transient period of immunological hyperreactivity: the intestine that has not been pre-imprinted with specific antibodies, may then be at risk for post-weaning diarrhea and also predispose the gut to infection with enteropathogenic E. coli.

This hypothesis grew out of studies performed in mice which indicated that mice naturally fed under appropriate conditions could result in a lifelong state of small intestine injury as indicated by malabsorption and by histological changes. The conditions necessary for producing such an immunologically-mediated injury involved a short initial exposure to the antigen followed after a latent period by a longer period of exposure. Prolonging the first exposure on the other hand induced a state of immunological tolerance which abolished the damaging response.

This hypothesis has been tested by weaning pigs in experimental conditions designed to investigate two predictions of this hypothesis.

These predictions are firstly, that the severity of the diarrhea can be altered by changing the amount of weaning diet fed to the baby pigs before weaning. In particular, piglets fed large amounts of the weaning diet before they reach weaned should become immunologically tolerant and so be relatively unaffected by weaning. On the other hand, piglets fed small amounts of the weaning diet before weaning should be immunologically primed and should suffer severe diarrheal disease following weaning. Piglets not exposed to the solid food prior to weaning should occupy an intermediate position and should suffer little injury at weaning.

Piglets from four litters were assigned at random to one of four groups. One group was maintained throughout the experiment on the sow without access to the weaning diet. A second group was fed small amounts of the weaning diet for 3 days only at each week of age. A third group was fed no solid food before weaning while the fourth group was encouraged to eat a large amount of the weaning diet from 1 week of age.

The latter three groups were weaned at two weeks and monitored for signs of diarrhea. Clinical diarrhea was seen in some groups 7 days after weaning and as can be seen in Table 1 the results are in agreement with the concept of an immunological mechanism underlying the disease, since exposure to the weaning diet for only 2 days at 1 week of age significantly increased the severity of the diarrhea seen at 7 days post weaning.

Table 1

<table>
<thead>
<tr>
<th>Post-weaning Diarrhea</th>
<th>Fed for 3 days only</th>
<th>Fed for 7 days only</th>
<th>No pre-weaning feeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No diarrheal</td>
<td>0</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Diarrheal</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>96.05</td>
<td>94.02</td>
<td></td>
</tr>
</tbody>
</table>

Another prediction of the immunological hypothesis is that weaning diets with reduced antigenicity would be substantially less harmful to pigs post-weaning than conventional diets. To study this possibility pigs were weaned onto diets in which the protein source, which was casein, was included as the native protein or in a hydrolysed form that was non-antigenic. All other dietary components were non-antigenic. Casein was taken to ensure that the two diets were nutritionally identical. It was found that all animals that were weaned onto diets containing native casein displayed changes in fecal water content which frequently resulted in clinical diarrheas. It was striking however that animals weaned onto the hydrolysed casein diet showed virtually no changes in water content and no signs of diarrheal disease.

These experiments appear to support the suggestion that immune mediated diarrheas may be a significant factor in the etiology of this condition and these results are supported by observations in the field that intractable outbreaks of post-weaning diarrhea can be controlled by altering the way in which piglets are introduced to weaning rations, in such a way as to minimize the immune response to dietary antigens.