

## THE SIGNIFICANCE OF DIETARY ANTIGENS IN THE AETIOLOGY OF POST-WEANING DIARRHOEA.

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Post-weaning diarrhoea is a complex disease resulting in significant losses in the period immediately following weaning. Although closely associated with the process of weaning the precise aetiology of the condition remains obscure. Enteropathogenic strains of *E. coli* are frequently isolated from affected animals and in severe cases are undoubtedly responsible for the profuse diarrhoea, but experimental infection of pigs with *E. coli* strains isolated from cases of post-weaning diarrhoea usually does not result in clinical disease. It is clear that some factor or factors associated with weaning increase the susceptibility of the animal to diarrhoea induced by pathogenic *E. coli*.

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

- 1) Withdrawal of the protection afforded by milk antibody.
- 2) Reduction of the bactericidal effect of low stomach pH brought about by the introduction of solid food.
- 3) Some undefined stress associated with the introduction of solid high protein diets.

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

The removal of antibody in sows 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 diarrhoea. Pigs were weaned at three weeks of age and fed for a further 14 days on cows milk. During this period no diarrhoea was seen but five days after a high protein weaner ration was introduced all the animals had diarrhoea. This experiment appeared to exclude the withdrawal of milk antibody as a prime cause of post-weaning diarrhoea and pointed to the importance of the diet and the method of its introduction in the aetiology of this condition. These experiments and the field observation that post-weaning diarrhoea is often associated with the abrupt introduction of weaner diets, often in excessive amounts, suggested an alternative explanation. This explanation is that the antigenicity of the food may, in the young animal, lead to a transient period of immunological hypersensitivity in the intestine that can bring about gut damage, and this may in itself produce diarrhoea and also predispose the gut to infection with enteropathogenic *E. coli*.

This hypothesis grew out of studies performed in mice which indicated that new antigens fed under appropriate conditions could result in a short-lived state of small intestine injury as indicated by malabsorption and by histological changes. The conditions necessary for producing this immunologically mediated injury involved an initial short 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 diarrhoea 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 are 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 more severe diarrhoea 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 sows without access to the weaning diet. A second group was fed small amounts of the weaning diet for 3 days only at 1 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 three weeks and monitored for signs of diarrhoea. Clinical diarrhoea 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 diarrhoea seen at 7 days post weaning.

Table 1 Effect of solid food before weaning on post-weaning diarrhoea

	Fed from 7 days	Fed for 3 days only	No pre-weaning feeding
Diarrhoea	0	7	2
No diarrhoea	7	0	4
	P < .001		P < .02

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 constituents were non-antigenic. Care 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 faecal water content which frequently resulted in clinical diarrhoea. It was striking however that animals weaned onto the hydrolysed casein diet showed virtually no changes in faecal water content and at no time suffered diarrhoea.

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