ROLE OF NUTRITION IN THE PATHOGENESIS OF PORCINE *ESCHERICHIA COLI* ENTEROTOXAEMIA

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Abstract

The role of nutrition in the pathogenesis of *E. coli* enterotoxaemia was studied in weaned pigs inoculated with a field strain of *E. coli* O139:K82:B:H 4. Feeds extremely low in nutrients (5 % crude protein, 4.6 MJ/kg digestible energy, 17 % crude fibre) completely prevented the disease by inhibiting proliferation of the pathogenic bacteria in the intestine. This protective effect of the diet could not be used for disease control, because the pigs did not develop immunity. A diet moderately low in nutrients (8 % crude protein, 9 MJ/kg digestible energy, 11 % crude fibre) allowed proliferation of the inoculated bacteria to the point, where most of the pigs developed solid immunity and losses were significantly reduced. This diet combined with inoculation of the pigs with herd specific organisms allowed control of the disease in the field.

Characterization of the disease

*E. coli* enterotoxaemia continues to cause significant losses in pig production in Switzerland. It occurs predominantly in weaned pigs but exceptionally it is also seen in suckling pigs over two weeks of age and even in adult sows. Since the 1950s it is known, that the disease is associated with massive growth of a few serotypes of haemolytic *E. coli* in the small intestine. Correspondingly to *E. coli* diarrhoea the massive bacterial proliferation is accomplished by adhesion of the organisms to the intestinal mucosa (Bertschinger and Pohlenz, 1983). These adhesive bacteria are producers of the so-called oedema disease producing principle (EDPP) which more recently was named neurotoxin or, due to its effect on blood vessels, vaso-toxin. The latter term is derived from the lesions observed in diseased pigs in the walls of arterioles of a variety of organs, most often of the intestine and the CNS. The resulting disturbances of the circulation are the cause of the various clinical symptoms of the disease. Some strains also produce enterotoxins, which lead to diarrhea preceding the appearance of oedema disease.

Effect of diet

Even before the association of the disease with bacterial toxins was known, the prophylactic effect of reduced rations was empirically noticed. Smith and Halls (1968) reported prevention of the disease by a feed extremely low in nutrients. They found significantly lower numbers of pathogenic *E. coli* in the intestines of pigs on such an experimental diet. In view of the lack of an efficacious control of oedema disease, we extended the studies of Smith and Halls (1968) and investigated the role of nutrition in the pathogenesis of *E. coli* enterotoxaemia with regard to a possible application to disease prevention. The investigations were conducted on an experimental farm, where *E. coli*...
enterotoxaemia had caused losses every year. The predominant serogroups of *E. coli* were 0139:K82(B) and 0141:K85a,c(B). In addition rotavirus was detected in suckling and weaned pigs.

The general design of the experiments was the following: Pigs were weaned at four to seven weeks, when they weighed 7 to 11 kg. Immediately after weaning they were allotted to groups identical in respect of weight and parentage. It is well-known that individual litters differ in their susceptibility to *E. coli* enterotoxaemia. The experimental diets were given *ad libitum* for variable periods after weaning. Thereafter they were replaced by a commercial complete feed for suckling and weaned pigs. Between days 1 and 4 after weaning, the pigs were orally inoculated either individually or via feed with a field isolate of *E. coli* 0139:K82(B).

The experiments were started with a comparison of a commercial-type diet A with a diet B consisting mainly of an oat mill by-product and apple pomace. Diet B was extremely low in crude protein and in digestible energy but high in crude fibre (table 1).

As long as pigs were fed on diet B, they remained healthy and shed reduced numbers of pathogenic *E. coli* in their faces as compared to pigs on diet A. The latter suffered a loss of 26% during the experimental period (table 2). These results suggest a competition for essential nutrients between the absorptive enterocytes of the host and the pathogenic bacteria closely adhering to them. Own results (Bertschinger et al., 1979a) corroborate the

**Table 1.** — Composition and nutrient content of diets A and B.
(Modified from Bertschinger et al., 1979 a).

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Diet A</th>
<th>Diet B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barley</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Maize</td>
<td>36</td>
<td>6</td>
</tr>
<tr>
<td>Oat</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Barley and oat flakes</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Dried apple pomace</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Oat mill by-product</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Soybean meal</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>Fishmeal (anchovy)</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>Animal fat</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Monocalciumphosphate</td>
<td>1.5</td>
<td>2</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Trace elements and vitamins</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Content (air dry basis)*

| Crude protein (N, 6.25) (%)       | 19     | 7      |
| Crude fibre (%)                   | 4      | 16     |
| Digestible energy (MJ/kg)         | 13.5   | 6.9    |
| Calcium (%)                       | 1.1    | 1.0    |
| Phosphorus (%)                    | 0.8    | 0.6    |
| Lysine (%)                        | 1.1    | 0.2    |
| Methionine and cystine (%)        | 0.6    | 0.1    |

**Table 2.** — Comparison of the diets A and B in weaned pigs inoculated with *E. coli* O139:K82 (B).
(Modified from Bertschinger et al., 1979 a).

<table>
<thead>
<tr>
<th>Diet</th>
<th>Number of pigs</th>
<th>Mean daily gain/g</th>
<th>Loss of pigs due to <em>E. coli</em> enterotoxaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>68</td>
<td>167</td>
<td>18 (26 %)</td>
</tr>
<tr>
<td>B</td>
<td>70</td>
<td>15</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>: 7 pigs lost after termination of experiment.
findings of Smith and Halls (1968), who found that the essential substance is contained in fish meal. We assume this to be protein and the products of protein degradation. The greater intake of crude fibre seems to play no decisive role, because a mere reduction of the ration had a similar effect as a diet low in nutrients and high in fibre (Smith and Halls, 1968). These conclusions may not be universally valid, since they were derived from situations, where protein appeared to be the factor limiting not only the proliferation of the bacteria in the small intestine, but also the growth of the pigs.

Use of diet for disease control

However, experimental diet B turned out to be of no use for disease control, because after change to normal diet, 7 (10%) of the pigs died of E. coli enterotoxaemia in most experiments. The pigs received a second inoculation one to two days after termination of the experimental diet. In the light of the present knowledge this second inoculation would not have been necessary. The pathogenic E. coli were still present in the faecal flora, when the experimental diets were replaced by normal feed. From this moment on, the number of faecal E. coli developed in the opposite direction than during the experimental diets (fig. 1).

Pigs previously fed on diet A showed only a moderate increase, whereas pigs previously fed on diet B shed numbers of pathogenic E. coli nearly as high as those in pigs on diet A. This effect can be explained by insufficient active immunization of pigs on diet B, due to the very limited proliferation of the inoculated bacteria in the small intestine. Recent work published by Newby et al. (1981) indicates that multiplying live bacteria induces a more vigorous local immune response than even large numbers of dead organisms.

By mixing diets A and B in different proportions, seven additional experimental diets with nutrient contents between diets A and B were created and tested in a similar way as diets A and B. Thus a diet was found, which allowed bacterial proliferation to the point, where losses were significantly reduced, and where most pigs developed protective immunity. However, when such a diet was used under field-like conditions, i.e. without inoculation, active immunization did not regularly take place. It was concluded, that the diet suppressed the spontaneous spread of the infection through the pigs and should be used only in conjunction with inoculation of the pigs with pathogenic E. coli.

An experiment was set up to determine the time necessary for optimal protection by a diet low in nutrients. A diet was chosen consisting mainly of oats, barley and apple pomace and with a content of 8% crude protein, 9 MJ/kg digestible energy and 11% crude fibre. This diet was given for variable periods after weaning (table 3), replacing the normal feed. One and 2 days after weaning all pigs were inoculated with 2 x 10⁹ CFU of a broth culture of an E. coli strain 0139: K82 via feed. In the full-fed control pigs the loss amounted to more than 30%. Feeding the experimental diet reduced mortality. When the period of diet was extended

<table>
<thead>
<tr>
<th>Period of diet (days)</th>
<th>Number of pigs</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (control)</td>
<td>97</td>
<td>30.9</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>15.1</td>
</tr>
<tr>
<td>8</td>
<td>95</td>
<td>6.3</td>
</tr>
<tr>
<td>10</td>
<td>149</td>
<td>6.0</td>
</tr>
<tr>
<td>12</td>
<td>78</td>
<td>2.6</td>
</tr>
<tr>
<td>14</td>
<td>122</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Table 3. Mortality due to E. coli enterotoxaemia in pigs fed a diet low in nutrients for variable periods and inoculated with a culture of E. coli 1 and 2 days after weaning. (Bertschinger et al., 1981).
from 6 days after weaning to 12 days, this effect was more marked. A longer period of diet did not allow a further reduction of the loss, which was about one tenth of the loss in the control pigs. Of the residual losses in the 200 pigs fed the special diet for 12 and 14 days respectively, two were due to insufficient protection by the diet and three to a lack of immunity. This distribution of the losses demonstrates, that the feed formula chosen represented a nearly optimal compromise between the diets A and B, and that a further amelioration was not possible.

The growth of weaners receiving this diet for 14 days was reduced to about 100 to 150 g/day as compared to 200 to 300 g in the controls. After changing to normal feed the growth of pigs from different treatments was similar and depended on the body weight at the start.

A similar diet low in nutrients combined with inoculation of the pigs with cultures of virulent E. coli originating from the herd concerned has been used in the last five years with more than 110 000 pigs. Written reports were obtained from 19 farms, where 6 233 pigs had been treated with the method described. The mortality due to E. coli enterotoxaemia (often confirmed by laboratory examination of dead pigs) amounted to 0.2% during the period of diet and to 0.6% after the change to normal feed.

However, the pig producers are not enthusiastic about this method of disease prevention. First of all they object to the reduced growth of the pigs during the period of diet. Secondly they dislike the continuous application of the virulent organisms, which is part of the procedure. The second disadvantage might be overcome by the use of an attenuated live vaccine.

Outlook

In the therapy or prevention of E. coli infections in the weaned pig feeding of diets with a low content of nutrients in combination with oral vaccination is a promising alternative to antimicrobials. With regard to the threatening increase of bacterial resistance to antimicrobials, their use has to be drastically reduced. Multiple antimicrobial resistance is very common in strains of E. coli from pigs with edema disease. The mean number of resistance determinants per strain rose from about 2 ten years ago to about 4 in 1982 with a maximum of 9. More research is needed to improve dietetic and immunological methods for prevention of the disease.

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References


Question

From Dr V. Danielsen to Dr H.V. Bertschinger

In a comparison, diets A and B, a reduction in gastro-intestinal disorders was found for diet B. Could a similar effect be expected if the daily ration of diet A was reduced to the same?

Answer

We did not investigate this question. Smith and Halls (1968) found reduction of the ration as effective as nutrient dilution.