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Hazards involved in the use of furazolidone for the prevention of salmonellosis in broiler chickens

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SUMMARY

The purpose of this work was to study the effects of interrupted, continuous and post-salmonella inoculation treatment with furazolidone in the feed on the colonization of *Salmonella infantis* in the intestines of chickens, as well as the influence of furazolidone *in vitro* on the effect of a mixed culture used for the prevention of salmonellosis in chickens.

It was shown that chickens given interrupted treatment with 0·01 % furazolidone had significantly more salmonellas in the caeca than either chickens fed continuously with this drug or chickens without any treatment. The use of 0·01 % furazolidone after inoculation with *Salmonella infantis* had no effect on *Salmonella infantis* in the caeca of chickens.

The mixed bacterial culture from the normal intestinal flora lost its preventive effect on salmonellosis when cultured with 0·01 % furazolidone.

INTRODUCTION

Broiler chickens reared in the modern way have previously been shown to be highly susceptible to colonization by *Salmonella infantis* (Nurmi & Rantala, 1973). Furazolidone has been used in the feed of broiler chickens as a preventive drug. There is, however, considerable evidence of various hazards connected with the use of antibiotics and chemotherapeutics, one of which is their possible unfavourable effect on the normal intestinal flora. This effect may involve an enhanced susceptibility to certain infections.

Treatment with furazolidone is a fairly easy remedy in cases of manifested infections caused by certain salmonella strains other than *Salmonella infantis*, as has been shown by Wilson (1955) and Perry, Herbert & Braemer (1972). Salmonellas in the intestines of symptom-free carriers are more difficult to eliminate, according to Knivett & Tucker (1972). *Salmonella infantis*, which caused a widespread outbreak of salmonellosis in broilers in Finland in 1971, usually colonizes the intestines of birds without any signs of illness.

The purpose of this work was to study the effect of interrupted treatment with the most commonly used dose of furazolidone (0·01 %) in the feed on the susceptibility of broiler chickens to *Salmonella infantis*, and to test the effect exerted on chickens experimentally inoculated with *Salmonella infantis* by this drug when continuously used, on one hand both before and after inoculation and on the other hand after inoculation only. The purpose of the last part of the work was to study the effect of furazolidone on the growth of the cultured intestinal flora which inhibits the colonization of *Salmonella infantis* in the intestines of chickens. The preventive effect of the intestinal flora cultured from adult cocks has been described earlier (Rantala & Nurmi, 1973).

MATERIAL AND METHODS

The chickens used in the work were the offspring of Cornish cocks and Pilch de Kalb hens. The basal feeds contained no antibiotics or coccidiostats. *Salmonella infantis* was isolated from a field case.

Media used for the detection of salmonellas were bromo-thymol blue–lactose–saccharose–agar, triple-sugar–iron–agar and urea–agar. Selenite broth was used for enrichment. All these were products of the Orion Pharmaceutical Co., Helsinki, Finland. The sera used for typing were produced by Behring-Werke AG, Marburg-Lahn, Germany. The furazolidone came from Pharmacia, Uppsala, Sweden. The feeding of the chickens was started at the age of 2 days in all experiments.

Expt 1. Ten chickens were fed with 0·01 % furazolidone in the feed during 1 week from the age of 2 days onward (group A). Another 10 chickens were kept as controls and fed with the same feed, without furazolidone (group B). The treatment with furazolidone was discontinued at the age of 9 days, and all chickens were inoculated with 10^6 *Salmonella infantis* 1 day later. The chickens were killed 1 week after the inoculation.

Expt 2. Twenty chickens were fed with 0·01 % furazolidone in the feed during the first week after hatching, from the age of 2 days onward. Ten chickens were fed without furazolidone. The furazolidone treatment was interrupted at the age of 1 week in the case of 10 chickens. One day later all chickens were inoculated with 10^3 *Salmonella infantis*. The other 10 chickens from the group fed with furazolidone initially received the same treatment all the time. All chickens were killed at an age *ca.* 2 weeks and studied for salmonellas. There were thus three groups:

Group A: Chickens fed all the time without furazolidone (control group).

Group B: Chickens fed with 0·01 % furazolidone in the feed before inoculation with salmonellas, but not subsequently.

Group C: Chickens fed all the time with 0·01 % furazolidone.

Expt 3. Twenty chickens were inoculated with 10^3 *Salmonella infantis* at the age of 2 days. Feeding was started after the inoculation. Ten of the chickens were then treated during 1 week with 0·01 % furazolidone (Group A), while the other ten received no treatment (group B). All chickens were killed at the age of 9 days and examined for salmonellas.

Expt 4. Six chickens in group A were pretreated at the age of 1 day with a flora cultured from the intestinal contents of adult cocks. The cultivation was performed

Table 1. *Number of salmonellas in the caeca of experimentally infected chickens fed with furazolidone before inoculation, compared with chickens fed without furazolidone. The chickens were inoculated with* 10^6 Salmonella infantis *at the age of* 10 *days and killed* 1 *week later.*

	Number of chickens with different salmonella counts	
	Group A	Group B
No. of salmonellas in 1 g caecal contents	Treated with furazolidone	No treatment
10^8–10^9	1	0
10^7–10^8	9	4
10^6–10^7	0	0
10^5–10^6	0	0
By enrichment only	0	2
Not detected	0	3
Total no. of chickens	10	9

The difference between groups A and B is significant according to the t-test ($t = 2{\cdot}9$, $P < 0{\cdot}01$).

in the VL-medium described by Barnes & Impey (1971), transferring twice to a new medium. The chickens in group B received an identical treatment except that the VL-medium contained 0·01 % furazolidone. Group C served as a control, without pretreatment. All chickens were inoculated with 10^3 *Salmonella infantis* at the age of 2 days and were killed at the age of 1 week.

The caeca of all chickens in each group were studied for salmonellas quantitatively and by enrichment.

The statistical method used was Student's t-test with logarithmic transformation of the values.

RESULTS

In Expt 1 it was shown that chickens fed with furazolidone before inoculation with *Salmonella infantis* had significantly more salmonellas in the caeca 1 week after the inoculation than the controls, which were fed all the time without furazolidone. During the experiment 1 chicken in the control group died. The figures are presented in Table 1.

The chickens in Expt 2 showed the same results as in Expt 1, but with a smaller salmonella inoculum. The chickens fed all the time with furazolidone had eliminated salmonellas as effectively as the controls. The figures from this experiment are given in Table 2.

The third experiment was performed in order to determine the effect of 0·01 % furazolidone used only after inoculation with *Salmonella infantis* on the number of salmonellas in the intestines of chickens. There was no difference between the treated group and the control group. One chicken in the unmedicated group died during the experiment. The counts are given in Table 3.

Expt 4 showed that a culture grown with 0·01 % furazolidone in the medium had no preventive effect on the colonization of salmonellas, whereas the culture

Table 2. *Effect of interrupted feeding of furazolidone on* Salmonella infantis *in the caeca of chickens, compared with continuous treatment with furazolidone, and no treatment. The chickens were inoculated at the age of* 1 *week with* 10^3 Salmonella infantis *and killed* 1 *week later*

	Number of chickens with different salmonella counts		
	Group A	Group B	Group C
No. of salmonellas in 1 g of caecal contents	No treatment	Interrupted treatment with furazolidone	Continuous treatment with furazolidone
10^8–10^9	0	1	0
10^7–10^8	0	3	0
10^6–10^7	1	1	0
10^5–10^6	0	2	0
10^4–10^5	0	2	0
By enrichment only	0	1	0
Not detected	9	0	10
Total no. of chickens	10	10	10

The differences were highly significant according to the *t*-test between groups A and B ($t = 7{\cdot}1$, $P < 0{\cdot}001$) and between groups B and C ($t = 11{\cdot}0$, $P < 0{\cdot}001$).

Table 3. *Effectiveness of* 1 *week's use of* 0·01 % *furazolidone in the feed on the* Salmonella infantis *after inoculation with* 10^3 *organisms to chickens at the age of* 2 *days*

	Number of chickens with different salmonella counts	
	Group A	Group B
No. of salmonellas in 1 g of caecal contents	0·01 % furazolidone in the feed	No treatment
10^9–10^{10}	0	1
10^8–10^9	10	8
Not detected	0	0
Total no. of chickens	10	9

There is no significant difference between the two groups.

grown without antimicrobial additives was highly effective in this respect. All the chickens pretreated with the culture grown with furazolidone had more than 10^7 salmonellas in 1 g. of caecal contents, as did also the chickens in the control group; no salmonellas were detectable in the caeca of chickens pretreated with the culture grown in the same way as the preceding culture, but without furazolidone.

DISCUSSION

The first two experiments show that if the feeding of a normal furazolidone dose is interrupted, increased susceptibility to salmonellosis may result. The chickens fed without this drug have all the time a resistance against salmonella colonization which is significantly higher than that in the group receiving the interrupted

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Table 4. *The effect of pretreatment with flora cultured from intestines of an adult cock both with and without furazolidone on the number of* Salmonella infantis *detected in the caeca of experimentally infected chickens at the age of* 1 *week*

	Number of chickens with different salmonella counts		
No. of salmonellas in 1 g of caecal contents	Group A Pretreatment with flora cultured without antibiotics	Group B Pretreatment with flora cultured with 0·01 % furazolidone	Group C No pretreatment
10^9–10^{10}	0	2	0
10^8–10^9	0	3	6
10^7–10^8	0	1	0
10^6–10^7	0	0	0
Not detected	6	0	0
Total no. of chickens	6	6	6

The difference between groups A and B was highly significant according to the t-test ($t = 27$, $P < 0{\cdot}001$). There was no significant difference between groups B and C.

treatment. The chickens fed with furazolidone all the time were as resistant as the control groups against the salmonella dose used. The susceptibility of some animals to various infections following therapy with antibiotics is well known. The preventive influence of the normal intestinal flora on the colonization of *Salmonella infantis* in chickens has previously been shown (Nurmi & Rantala, 1973). The results obtained in the experiments described here may thus be due to a disturbance in the development of the normal intestinal flora. This has not been shown to occur with the usual feed additives, such as zinc bacitracin or nitrovin. The results of the experiments with furazolidone show that the use of furazolidone in broiler feeds may result in an increased risk of salmonellosis after the treatment. The treatment should in any case be discontinued before slaughter in view of the possible residues in the meat. The period varies, depending on the legislation in different countries. It follows that a hazard of infection may be present just before slaughter.

The third experiment reported here shows that the usual dose of furazolidone is not effective against *Salmonella infantis* when used after inoculation. Hence, the potential colonization of *Salmonella infantis* induced by the interrupted use of furazolidone cannot be eliminated by a subsequent use of this drug. The opportunity of the *Salmonella* organisms to effect colonization before the treatment may be the reason for the ineffectiveness of the drug.

When furazolidone was used in the medium in which the mixed culture from the intestines of adult cocks was grown, the culture had no preventive effect on the colonization of *Salmonella infantis* in the caeca of chickens. The chickens pretreated with a culture grown in the same way, but without furazolidone, had no salmonellas in the caeca. It thus seems that furazolidone has an unfavourable effect on that part of the intestinal flora which protects the animal against salmonellosis.

Chickens with colonization of their intestines by *Salmonella infantis* show no signs of infection, although the salmonella count in the intestines may be higher than 10^8 organisms in 1 g. of caecal contents. *Salmonella infantis* is able to cause a severe disease in man, and infected chickens thus constitute a serious problem in food hygiene. In view of the results reported here, some drawbacks appear to be associated with the use of furazolidone, which may require practical measures.

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