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The effect of cobalt compounds on uninfected and *Ascaridia galli*-infected chickens: a kinetic model for *Ascaridia galli* populations and chicken growth

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Abstract

The effect of dietary cobalt from three different sources on uninfected and *Ascaridia galli*-infected Hisex chickens, has been studied. The chicken diet was supplemented with 0.06 Co^{2+} kg^{-1} food either in the form of two glycine–cobalt compounds or mixed zinc–cobalt basic salt. An excess of dietary cobalt in small doses increases the gain of body weight and decreases host mortality. A greater bioefficiency of cobalt was established in infected chickens. A mathematical model has been used to provide a quantitative interpretation of the observed results. The model solutions of the kinetics of worm numbers and body weight are in a good agreement with experimental data. The model is valid for different degrees of *A. galli* infections and for treatment with different trace elements. The value of the kinetic parameter, regarded as a phenomenological constant of the host immune response, depends on the degree of infection.

Introduction

Ascaridiasis is widespread in birds and influences their growth, reproductive function and mineral balance. Therefore there is a need to treat *Ascaridia*-infected chickens with compounds of essential microelements to improve the survival and body weight gain of chickens, to correct mineral imbalances and to prevent secondary pathological symptoms. The effects of essential trace elements such as copper, zinc, copper–zinc mixture and manganese on *A. galli*-infected chickens have previously been reported by Gabrashanska *et al.* (1986, 1993, 1999a,b), Galvez-Morros *et al.* (1995) and Teodorova & Gabrashanska (2002). In the present work the effect of cobalt on uninfected and *A. galli*-infected chickens was investigated.

Cobalt is an essential trace element and its biological activity is mainly confined to the action of vitamin B_{12} coenzymes (Hughes, 1981) which play a significant role in the production of erythrocytes and the prevention of anaemia (Vellema *et al.*, 1996). The biological importance of cobalt for animals infected with parasites is not fully understood, despite the work of Southern & Baker (1981, 1982), Brown & Southern (1985) and Gabrashanska *et al.* (1986). Cobalt deficiency in birds infected with *A. galli* leads to anaemia, disturbance in protein metabolism, calcium and phosphorus absorption (Vassilev *et al.*, 1973). The supplementation of cobalt salts in poultry diets stimulates chicken growth and performance (Berenschtein, 1968) and cobalt has been added to most commercial diets either as $CoCl_2.H_2O$ or $CoSO_4.4H_2O$. Flachowsky (1997) suggests that chelated or complexed trace elements may improve the bio-availability of minerals for animals. Our previous work has shown that basic salts of zinc and copper (pure or mixed) and glycine–manganese complexes are appropriate sources for these trace elements, producing few side effects (Gabrashanska *et al.*, 1993, 1999b; Galvez-Morros *et al.*, 1995).

In the present paper the effect of dietary cobalt from three different sources, i.e. $2Gly.CoCl_2.2H_2O$, $Gly.CoSO_4.5H_2O$ and $(Zn_xCo_{1-x})_4.(OH)_6.SO_4.2H_2O$ on

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worm burden, mortality and body weight gain of chickens infected with *A. galli* is studied. A mathematical model is presented of the establishment of *A. galli* populations in untreated chickens or those treated with cobalt compounds and also of the body weight gain in control and infected hosts. Some kinetic parameters which characterize the phenomenological structure of the parasite–host system have been determined. The model has been developed for *A. galli* populations and the body weight gain of birds infected and treated with mixed salts (neutral and basic) of copper and zinc (Gabrashanska *et al.*, 1999a). Thus, the objective is to compare theoretical results, i.e. the time course of infection and mean chicken weight and kinetic parameters, including the reduction rate constant of the parasite population and the relative rate of gain in body weight, for chickens treated with cobalt compounds and those treated with zinc–copper salts to establish the possibility of a more widespread application of these models.

Materials and methods

Three different sources of cobalt (2Gly.$CoCl_2$.$2H_2O$, Gly.$CoSO_4$.$5H_2O$ and $(Zn_xCo_{1-x})_4$.$(OH)_6$.SO_4.$2H_2O$) were used in the chicken's diet. The salts 2Gly.$CoCl_2$.$2H_2O$ and Gly.$CoSO_4$.$5H_2O$ are soluble in water and synthesized from their respective aqueous solutions (Balarew *et al.*, 1970). The salt $(Zn_xCo_{1-x})_4$.$(OH)_6$.SO_4.$2H_2O$ contains Zn^{2+}69% and Co^{2+}31% and the mixed crystals of this salt are synthesized by continuous coprecipitation using diluted zinc and cobalt sulphate solution (Balarew *et al.*, 1994). The composition of the crystals was determined by chemical, X-ray and thermal analyses.

One-day-old male chickens belonging to the Hisex breed (interlinear crossbreeding of Dutch Leghorn), were divided into eight groups as follows: group 0, control (uninfected and untreated); group 1, infected with *A. galli* and untreated; group 2, uninfected and treated with 2Gly.$CoCl_2$.$2H_2O$; group 3, infected and treated with 2Gly.$CoCl_2$.$2H_2O$; group 4, uninfected and treated with Gly.$CoSO_4$.$5H_2O$; group 5, infected and treated with Gly.$CoSO_4$.$5H_2O$; group 6, uninfected and treated with $(Zn_xCo_{1-x})_4$.$(OH)_6$.SO_4.$2H_2O$; group 7, infected and treated with $(Zn_xCo_{1-x})_4$.$(OH)_6$.SO_4.$2H_2O$.

Control and experimental chickens were reared in a vivarium, placed on pine shavings in 1.2×3.6 m pens and maintained on a 24 h constant light schedule in heated (35°C), thermostatically controlled, stainless steel starter batteries with raised wire floors. Feeders and water containers were also of stainless steel construction to minimize environmental cobalt contamination. All chickens were fed on a conventional corn-soybean meal diet, formulated to meet the nutrient requirements of growing chickens (US National Research Council, 1994). The diet was Co^{2+} free and chickens were allowed access to food and water *ad libitum*.

Each chicken from groups 1, 3, 5 and 7 was orally infected by pipette with 1450 embryonated *A. galli* eggs as described by Permin *et al.* (1997) on the first day post-hatching. Cobalt compounds were given orally and individually to each chicken, commencing 5 days post infection (p.i.). Treatment was carried out for 5 days, followed by a 7-day interval. The therapy quantities for each chicken were as follows: for groups 2 and 3, 0.06 g Co^{2+} kg^{-1} food and 0.15 g Gly kg^{-1} food in the form of 2Gly.$CoCl_2$.$2H_2O$; for groups 4 and 5, 0.06 g Co^{2+} kg^{-1} food and 0.12 g Gly kg^{-1} food in the form of Gly.$CoSO_4$.5-H_2O; for groups 6 and 7, 0.06 g Co^{2+} kg^{-1} food and 0.08 g Zn^{2+} kg^{-1} food in the form of $(Zn_xCo_{1-x})_4$.$(OH)_6$.SO_4.2-H_2O.

Chickens were killed by CO_2 inhalation after 60 days and their alimentary tract opened longitudinally from the gizzard to the cloaca. The contents were washed into a 100 μm sieve, transferred to a Petri dish, examined for the presence of a immature and mature *A. galli* under a microscope and the number of worms counted. Body weight gain and mortality were determined on days 1, 10, 20, 30, 40, 50 and 60 p.i. Data were tested using analysis of variance (Steel & Torrie, 1980). Duncan's new multiple range test was used to separate significant differences between the means (Duncan, 1955).

Mathematical model

In order to study the development of *A. galli* populations, the host's infected organ (the intestine) is viewed as a unique 'cultivator' and it is assumed that the therapeutic agent (the cobalt compound) is supplied evenly and constantly into it. The compounds are exerted from the 'cultivator' at a rate proportional to their concentration. The rate of flow is accepted as being equal to the average rate of the passage in the chicken's alimentary tract. It is assumed that the nematodes and the therapeutic agent are distributed evenly and form an homogenous mixture as this allows differential equations to be used.

Following infection the number of larval and adult nematodes decreases as a result of an immune response by the host. This process may be described in infected untreated chickens (group 1) with the differential equation:

$$\frac{dN}{dt} = -\nu N$$

where N is the worm number in the host intestine, dN/dt is the rate of reduction of the worm population and $\nu([\nu] = [\text{day}^{-1}])$ is the relative reduction rate constant.

As host immunity results in a reduction in worm burden, ν is considered an integral characteristic of the host immune status and ν is defined as a phenemenological constant of the host immune response, i.e. the immunological constant.

The weight of healthy chickens increases almost linearly as indicated by the experimental data. This is in good agreement with data provided by the Dutch Company Euribrigh regarding the development of hybrid Leghorn birds (Hisex white hybrid, Euribrigh-Holland) during the first 20 weeks after hatching. We suggest that a nutritional substrate is not a limiting factor. Thus, the following differential equation is proposed for describing the growth of healthy uninfected chickens:

$$\frac{dP}{dt} = \mu$$

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where P is the weight of the chicken and $\mu([\mu] = [\mathrm{g\,day^{-1}}])$ is the relative rate of gain in body weight.

During the development of *A. galli*, worms are likely to disturb the nutrient digestibility of the host, which in turn reduces its growth rate. To a certain degree, worms reduce the nutritional reserves of the host and at the same time the toxins of *A. galli* adversely influence enzyme systems in the intestinal mucosa and interfere with normal absorptive processes (Ackert, 1942; Vassilev *et al.*, 1973). The decrease in gain in body weight in chickens infected with *A. galli* is assumed to be proportional to the number of worms:

$$\frac{\mathrm{d}P}{\mathrm{d}t} = \mu - kN$$

The kinetics of worm establishment in the intestine of chickens and of the gain in body weight with or without cobalt compound treatment can be presented by the following ordinary non-linear differential equations:

$$\frac{\mathrm{d}S_j}{\mathrm{d}t} = \frac{\psi S_{j0}^2 - \beta_j S_j^2}{2S_{j0}} \quad j = 3,5,7 \tag{1}$$

$$\frac{dN_1}{\mathrm{d}t} = -\nu N_1 \tag{2a}$$

$$\frac{\mathrm{d}N_j}{\mathrm{d}t} = -\nu N_j - aS_jN_j \quad j = 3,5,7 \tag{2b}$$

$$\frac{\mathrm{d}P}{\mathrm{d}t} = \mu \tag{3a}$$

$$\frac{\mathrm{d}P_i}{\mathrm{d}t} = \mu + \mu_s - k_iN_i \quad i = 1,3,5,7 \tag{3b}$$

under initial conditions:

$$t_0 = 0, \;\; S_j(t_0) = 0, \;\; N_i(t_0) = N_0, \;\; P_i(t_0) = P_0 \tag{4}$$

where t_0 is the time moment corresponding to 24 h p.i. We postulate: $t_0 = 0$. S_j ($j = 3,5,7$) are the quantities of cobalt compounds in the worm biomass, respectively for groups 3, 5 and 7, at a given time t, S_{j0} are the quantities entering the host's alimentary tract (the average daily dose of Co^{2+} + Gly for groups 3 and 5 and $Co^{2+} + Zn^{2+}$ for group 7, given orally to each chicken), $\psi([\psi] = [\mathrm{day^{-1}}])$ is the flow or dilution rate constant, determined as an average flow of passage through the alimentary tract divided by the average daily dose of compounds), $\beta_j = \psi + \alpha_j$, where α_j is the rate constant of the resorption of compounds in the host's intestine (the resorption constant). α_3 and α_5 correspond to $2Gly.CoCl_2.2H_2O$ and $Gly.CoSO_4.5H_2O$ respectively; α_7 corresponds to the mixed basic Zn–Co salt. $a([a] = [\mathrm{day^{-1}}])$ is a rate constant of decreasing worm populations due to the influence of cobalt compounds. The parameter $k([k] = [\mathrm{g\,day^{-1}}])$ is the relative rate constant of a decrease in body weight gain caused by *A. galli* infections, i.e. the retardation constant. The parameter μ_s is introduced as a relative rate of body weight gain resulting from cell stimulating processes.

Equation 2a describes the establishment of the worm population in experimental group 1; equation 2b describes the establishment of worm populations in experimental groups 3, 5 and 7 respectively. Equation 3a presents the gain in host body weight for control (group 0) and equation 3b for other groups.

For equations 1, 2 and 3 under the conditions (4) we obtain analytical solutions in the form:

$$S_j = S_{j0}\frac{\sqrt{\psi}(1 - e^{-\sqrt{\psi\beta j}\,t})}{\sqrt{\beta_j}(1 + e^{-\sqrt{\psi\beta j}\,t})} \quad j = 3,5,7 \tag{5}$$

$$N_1 = N_0e^{-\nu t} \tag{6a}$$

$$N_j = N_0 2^{2\theta}\frac{e^{-(\nu+\theta\sqrt{\psi\beta j})t}}{(1 + e^{-\sqrt{\psi\beta j}\,t})^{2\theta}} \quad j = 3,5,7 \tag{6b}$$

$$P = P_0 + \mu t \tag{7a}$$

$$P_1 = P_0 + (\mu + \mu_s)t - \frac{kN_0}{\nu}(1 - e^{-\nu t}) \tag{7b}$$

$$P_i = P_0 + (\mu + \mu_s)t - \frac{2^{2\theta}kN_0}{\nu + \theta}(1 - e^{-(\nu+\theta\sqrt{\psi\beta j})t}) \quad i = 1,3,5,7 \tag{7c}$$

where $\theta_j = \frac{aS_{j0}}{\beta_j} \quad j = 3,5,7$

The solutions are: 7a for group 0; 6a and 7b for group 1; 5, 6b and 7c for groups 3, 5 and 7. The immunological constant ν may be determined from the solution (6a) after taking in a logarithm:

$$\ln N_1 = \ln N_0 - \nu t \tag{8}$$

This is an equation of a straight line with an angular coefficient ν. Using the values of N_1 determined by the experiment, a plot of ln N_1 as a function of time can be constructed.

Results and Discussion

The cobalt–glycine compounds did not change mortality in healthy chickens (groups 2 and 4) but the Zn–Co salt slightly improved chicken survival (group 6) (fig. 1). The mortality on day 60 of control and healthy chickens treated with $Gly.CoSO_4.5H_2O$ was 6.67% compared with 10% in healthy chickens treated with $2Gly.CoCl_2.2H_2O$ and 3.33% in healthy chickens treated with $(Zn_xCo_{1-x})_4.(OH)_6.SO_4.2H_2O$. Survival was lowest in infected, untreated chickens from group 1 where a 40% mortality was recorded. As in the case of *A. galli* infected chickens treated with mixed salts of copper and zinc (Gabrashanska *et al.*, 1999a), the majority of chickens did not survive beyond day 30 p.i. Supplementations of glycine–cobalt compounds reduced mortality in infected chickens (fig. 1), probably due to increased erythropoiesis. The chickens treated with a Zn–Co basic salt (group 7) showed a lower mortality (16.7%) compared with chickens treated with $2Gly.CoCl_2.2H_2O$ and $Gly.CoSO_4.5H_2O$, where 30% and 26.7% values were respectively recorded. This may be due to the positive effect of the mixed Zn–Co crystals of the basic salt,

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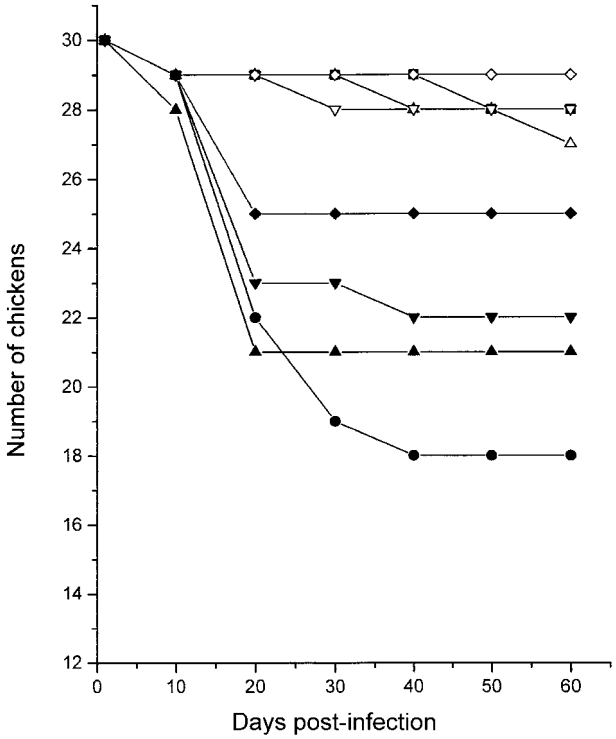

Fig. 1. The survival of chickens experimentally infected with *Ascaridia galli* up to day 60 post-infection. ■, group 0; ●, group 1; △, group 2; ▲, group 3; ▽, group 4; ▼, group 5; ◇, group 6; ◆, group 7.

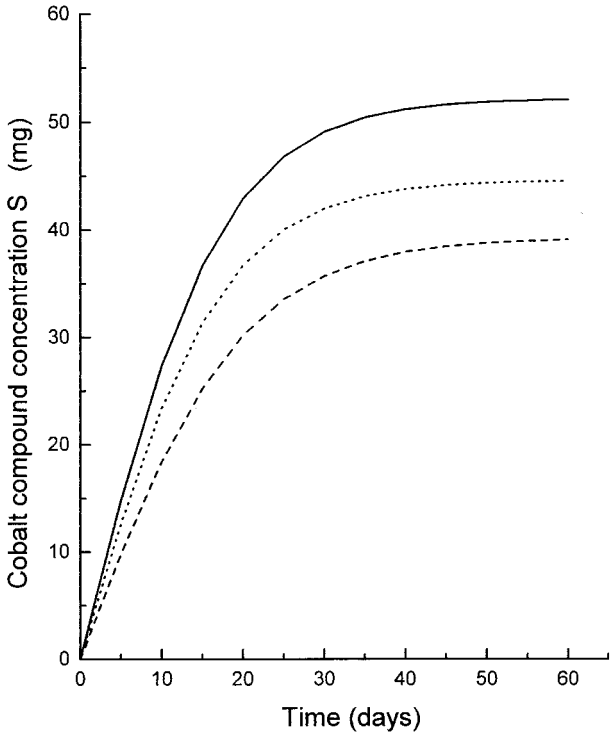

Fig. 2. The relationship between the biomass of *Ascaridia galli* in the alimentary tract of chickens and the quantity of cobalt compounds used during the experimental period (model solutions). –, S_3 – 2Gly.$CoCl_2$.$2H_2O$; …, S_5 – Gly.$CoSO_4$.$5H_2O$; —, S_7 – $(Zn_xCo_{1-x})_4$.$(OH)_6$.SO_4.$2H_2O$.

whereby zinc stimulates immunity (Babenko & Reshetkina, 1971; Goyer, 1996). In addition, the action of basic salts on the host is prolonged and with a lower toxicity compared with neutral salts (Gabrashanska & Timanova, 1995). Statistically significant difference ($P < 0.05$) was established between chicken groups 1 and 7 with regard to host mortality using a Student t-test.

In the model solutions for the therapeutic agents (cobalt compounds) we take into account the lower utilization of basic salts with the value of the parameter α_7: α_7 is smaller than α_3 and α_5, i.e. resorption of the basic salt in the alimentary tract is smaller, resulting in a higher concentration of basic salts in the intestine of the chicken (fig. 2). The dilution rate constant ψ was determined on the basis that the time required for the passage of salts along the intestinal tract is 4 h and the length of the tract is 1.00–1.50 m (Bell & Freeman, 1971).

It should be noted that in equation 1, dS/dt is the total change of the quantity S with time, where dS/dt increases with the salt flow $\psi S_0/2$ entering the alimentary tract of the host and decreases with the flow $[(\psi + \alpha)/2](S^2/S_0)$ from the tract. The exiting salt flow is proportional to the square of the salt concentration in the alimentary tract at a given moment t, divided by S_0. Such a form of dependence, i.e. the square of the concentration is justified by the good agreement of the solutions (5) of equation 1 with experimental data relating to the establishment of *A. galli* in the alimentary tract and also avoids complex calculations connected with special functions, which should be apparent by the solving of equation 3b.

Figure 3 demonstrates the change with time of *A. galli* populations in the host. The mean ± SD for each group was calculated and the data were compared using a Student t-test. Especially, on day 60, means ± SD are as follows: group 1: 95.17 ± 18.45, group 3: 52.7 ± 21.95, group 5: 61.93 ± 23.27, group 7: 70.05 ± 21.15. Our statistical analysis shows: $P_{13} < 0.001$, $P_{15} < 0.001$, $P_{17} < 0.001$, $P_{35} > 0.1$, $P_{37} < 0.01$, $P_{57} > 0.1$. In all cases worm numbers decrease and this is likely to be due to the effect of immune and allergic reactions of the host leading to the elimination of some helminth parasites (Bykoryukov & Tachistov, 1965). The number of *A. galli* is highest in group 1 chickens without treatment whereas differences between worm burdens in groups 3 and 5 and groups 5 and 7 are not statistically significant. The lower number of *A. galli* in group 3 compared with group 7 may be due to the higher average daily dose of 2Gly.$CoCl_2$.2-H_2O, i.e. 0.076 g kg^{-1} food compared with 0.05 g kg^{-1} food in group 7. The higher number of *A. galli* in group 7 after day 45 could be due to the stimulating action of Zn^{2+} from the mixed basic Zn–Co salt. As an essential part in protein metabolism, Zn^{2+} stimulates the sexual development and vitality of *A. galli* (Ikeme, 1977), which leads to lower reduction in worm burden. These results are in a good agreement with the theoretical solutions (6a) and (6b) and support our concept that the *A. galli* population

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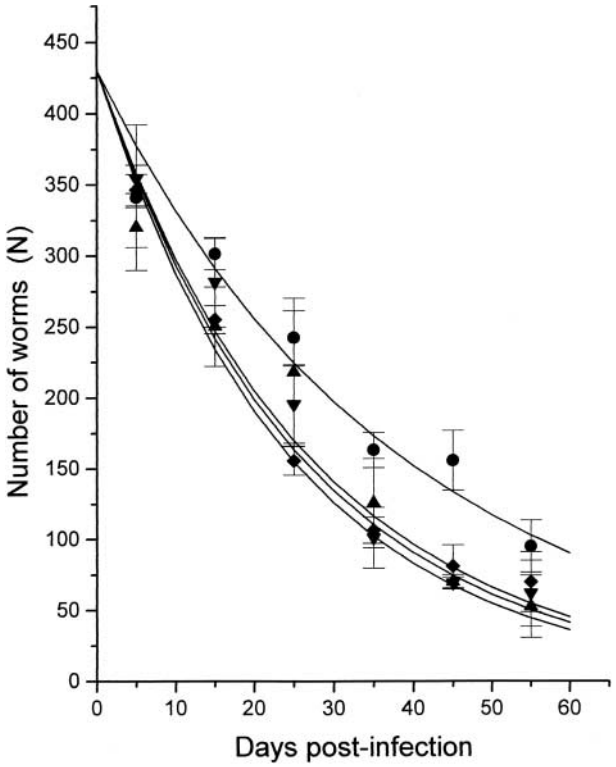

Fig. 3. The establishment of *Ascaridia galli* in the alimentary tract of four groups of Hisex chickens (theoretical curves and experimental points). ●, group 1; ▲, group 3; ▼, group 5; ◆, group 7.

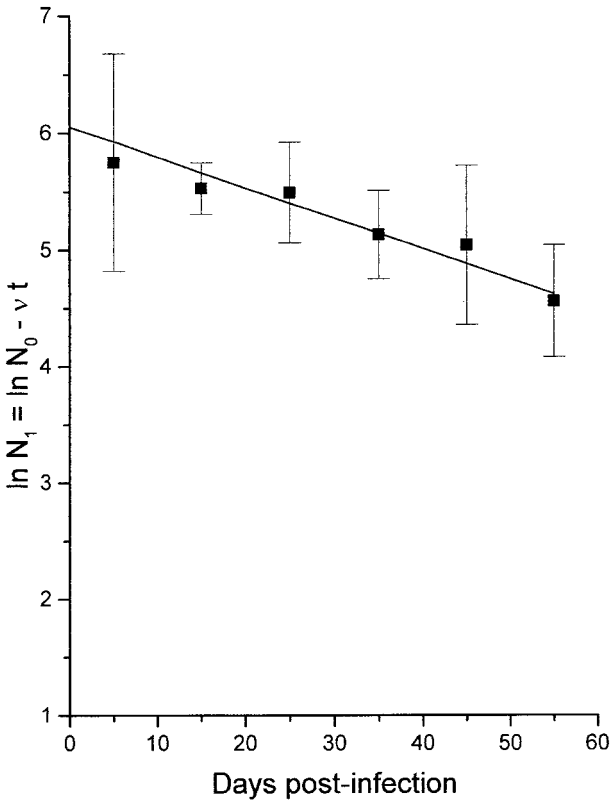

Fig. 4. Determination of the phenomenological constant of the host immune response ν on the basis of equation (8) using experimental measures of *Ascaridia galli* numbers in chicken Group 1 (infected untreated chickens).

in the host intestine decreases exponentially. The phenomenological constant of immune response ν was calculated on the basis of experimental data. According to equation 8, ν is the angular coefficient of the straight line (fig. 4). We obtained:

$$\nu = 0.026\,\text{day}^{-1} \tag{9}$$

We calculated $\nu = 0.0167\,\text{day}^{-1}$ for chickens infected with *A. galli* in our previous experiment (Gabrashanska *et al.*, 1999a). The difference between the values of the immunological constant ν in both cases is likely to be due to the different degrees of infection. Gabrashanska *et al.* (1999a) infected chickens with 450 embryonated *A. galli* eggs compared to 1450 eggs in the present experiment and thus a higher infection stimulates a stronger immune response. In addition, a heavy infection causes more unfavourable conditions for parasite development and a higher rate of elimination.

We chose for the resorption constants α_3, α_5 and α_7 the values determined by the program 'Minuit' in our previous mathematical model describing *A. galli* populations in chickens treated with mixed salts of copper and zinc: $\alpha_3 = \alpha_5 = 0.09\,\text{day}^{-1}$ and $\alpha_7 = 0.05\,\text{day}^{-1}$.

In our previous study (Gabrashanska *et al.*, 1999a) we defined a as an antinematode constant because of the antiparasitic action of used mixed salts containing copper. There are no data for the antiparasitic action of cobalt. In the present study cobalt compounds were used in pharmacological doses and were not toxic to the host, although it is possible that these compounds are slightly toxic to *A. galli*. Cobalt inhibits oxidative enzymes and thus disturbs oxyreduction processes (Ershov & Pleteneva, 1989). In this context we define the constant a as an influence constant. By the program 'Minuit' we obtained $a = 3.10^{-4}\,\text{day}^{-1}$. Here a is smaller compared with antinematode constant from the previous experiment ($a = 9.79.\ 10^{-4}\,\text{day}^{-1}$).

A good correlation was observed between host survival and changes in body weight gain (figs 5 and 6). The growth of infected and untreated chickens (group 1) is considerably reduced in comparison with that of healthy control chickens ($P_{01} < 0.001$ on day 60 p.i.) and this is clearly evident up to day 30 p.i.

The addition of cobalt salts in small doses to the diet increased the body weight in healthy chickens (groups 2, 4 and 6) and the differences are more evident on day 60 p.i. (fig. 5). Using a Student t-test, we obtained respective P values of $P_{02} < 0.001$, $P_{04} < 0.001$, $P_{06} < 0.001$. The most significant gain in body weight was observed in group 6 ($P_{24} > 0.05$, $P_{26} < 0.001$, $P_{46} < 0.001$). With regard to host mortality, the basic Zn–Co salt shows a stronger effect compared with GlyCo compounds.

A loss of body weight caused by *A. galli* infections was compensated for by the addition of GlyCo salts ($P_{13} < 0.001$, $P_{15} < 0.001$). But differences between the

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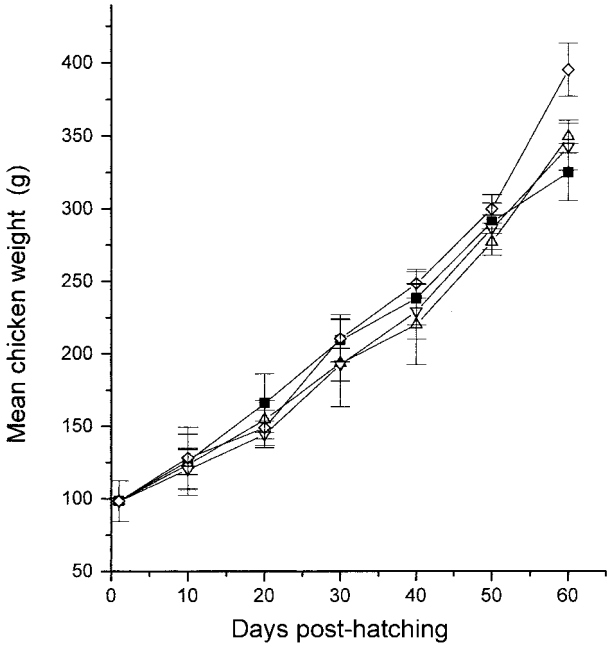

Fig. 5. Time course of the mean body weight in control (group 0) and healthy chickens treated with: $2Gly.CoCl_2.2H_2O$ (group 2), $Gly.CoSO_4.5H_2O$ (group 4) and $Zn_xCo_{1-x})_4.(OH)_6.SO_4.2H_2O$ (group 6) up to 60 days post-hatching. ■, group 0; △, group 2; ▽, group 4; ◇, group 6.

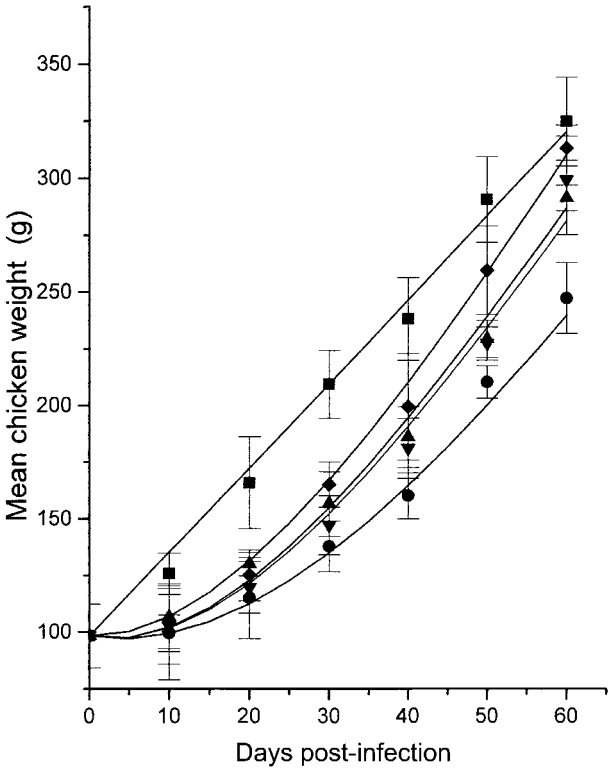

Fig. 6. Time course of the mean body weight in control chickens (group 0) and chickens infected with *Ascaridia galli* treated with $2Gly.CoCl_2.2H_2O$ (group 3), $Gly.CoSO_4.5H_2O$ (group 5) and $(Zn_xCo_{1-x})_4.(OH)_6.SO_4.2H_2O$ (group 7) up to 60 days p.i. (model solutions and experimental points). ■, group 0; ●, group 1; ▲, group 3; ▼, group 5; ◆, group 7.

weight gain of chickens from groups 3 and 5 were not established ($P_{35} > 0.1$). Growth retardation was lowest in infected chickens (group 7) treated with basic Zn–Co salt ($P_{17} < 0.001$, $P_{37} < 0.001$, $P_{57} < 0.001$).

The model appropriately explains experimentally observed time courses of body weight gain in chickens in groups 0, 1, 3, 5 and 7 (fig. 6). We calculated the value of the relative rate of the weight gain of control chickens μ according to solution 7a, on the basis of experimental data:

$$\mu = 3.7\,\mathrm{g\,day^{-1}} \qquad (10)$$

Using parameter μ_s, a stimulating effect is taken into account. It is well known that there is a wide range of stimulatory processes, which develop after some unfavourable influences on living organisms. The organism then enters a characteristic state with a higher metabolism and physiological activity (Popoff, 1931). In general, these effects are related to an increase in enzyme activity and protein synthesis. Our analyses relate to phenomenological aspects and we cannot comment further on mechanisms at the cellular or molecular levels. But we introduce as a phenomenological parameter a stimulation weight gain rate μ_s and assume a linear dependence. Our theoretical results, solutions 7b and 7c, are in a good agreement with experimental data (fig. 6).

The retardation constant k and stimulation constant μ_s were calculated also using the program 'Minuit': $k = 0.014\,\mathrm{g\,day^{-1}}$; $\mu_s = 1.7\,\mathrm{g\,day^{-1}}$.

The theoretical curves in the figs 2, 3 and 6 have been calculated using the following initial conditions: $S_{03} =$ 76 mg, $S_{05} = 65$ mg, $S_{07} = 50$ mg, $N_0 = 430$, $P_0 = 98.36$ g, the parameter value $\psi = 0.08\,\mathrm{day^{-1}}$ and using (9), (10) and the above presented values of parameters α_3, α_5, α_7, a, k and μ_s.

In conclusion, it is clear that an improvement in the survival and body weight gain is observed in uninfected and *A. galli*-infected chickens treated with cobalt compounds in pharmacological doses. The results show that cobalt supplementation in form of complex compounds *per os* have a greater positive effect on infected chickens with cobalt deficiency than on those with a normal cobalt content. Gly–Co and Zn–Co compounds may be utilized better when there is a cobalt depletion in the organism. Our investigation is in a good agreement with other authors (Southern & Baker, 1981; Kratzer & Vohra, 1986). The present results, suggesting an effective action by cobalt from the complex compounds, are similar to data of Smith *et al.* (1995) and Gabrashanska *et al.* (1999b) concerning manganese and also to data of Aoyagi & Baker (1993) concerning zinc and copper. These studies indicate that Mn^{2+}, Cu^{2+}, Zn^{2+} from complex compounds or chelates improve the bioavailability of these elements in healthy chickens and in chickens with trace element deficiencies. The improved utilization of cobalt from complex compounds allows lower levels of cobalt in feed, which reduces the risk of environmental contamination.

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The mathematical model allows us to formulate quantitatively some regulation of the establishment of *A. galli* populations under the conditions of host immune responses and also to explain changes in the body weight gain of hosts treated or untreated with cobalt compounds. The kinetic parameter ν ('immunological constant') could be accepted as a characteristic phenomenological parameter in host–parasite systems and its value might be determined more precisely. It would be interesting to attempt to express ν as a function of some innate physiological parameters of the host and also of some characteristics of the helminth parasites (for example, intensity of infection and helminth toxicity).

The good correlation between theoretical and experimental data, both in our previous (Gabrashanska *et al.*, 1999a) and present studies suggests that the model for ascaridiasis in chickens could have wider applications in other host–parasite systems. The model is likely to be valid in low and heavy doses of infection and also provides a basis for determining regimes for anthelminthic treatment with optimum effect.

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