into mice caused marked changes in their susceptibility to experimental *Escherichia coli* infection. During the first hour after zymosan injection, the mice became highly susceptible to infection with an *E. coli* strain that was avirulent for normal mice. Moreover, during the period between 2 and 5 days after injection of zymosan, the mice were highly resistant to a different *E. coli* strain that was fully virulent for normal mice. In addition, Rowley found that rats which are naturally resistant to *E. coli* infection were killed by this organism if zymosan had been injected with 1 hr preceding challenge.

These experiments suggest that the initial fall and secondary rise in blood properdin that we have found to follow zymosan administration may influence the increase and decrease in natural resistance of the animals in Rowley's experiments. Experiments to be published in detail elsewhere (*5*) also show that the injection of zymosan into mice or rats can markedly increase or decrease their susceptibility to the effects of lethal doses of total-body irradiation depending on the dose and the time of injection.

References and Notes

1. L. Pillemer *et al.*, *Science* **120**, 279 (1954).
2. L. Pillemer and E. E. Ecker, *J. Biol. Chem.* **137**, 139 (1941).

3. This investigation was supported in part by a grant from Lederle Laboratories Division, American Cyanamid Co., Pearl River, N.Y. We wish to acknowledge the technical assistance of Leona Wurz.
4. Kindly furnished by Lederle Laboratories Division and by Fleischmann Laboratories, Standard Brands, Inc., Stamford, Conn.

5. O. A. Ross *et al.*, *Federation Proc.* **14**, 496 (1955).

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Observations on Growth Responses to Antibiotics and Arsonic Acids in Poultry Feeds

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During the past few years the relative growth responses that we have obtained when low levels of antibiotics and arsonic acids were added to poultry feeds have been progressively decreasing. Recent tests have sometimes shown a total lack of response.

Several different antibiotics, arsonic acids, basal rations, and breeds of chickens have been used in our experiments (*1*). However, equipment, management, and sanitation practices were reasonably uniform from year to year. The facilities for growing chickens have been in use almost continuously for many years, so that the environment may be considered "old" rather than "new."

Birds were started at 1 day of age and were carried for 3 to 6 wk on wire floors in batteries or up to 10 wk on corncob litter in a brooder house with heated floors. Feeds and water were offered *ad libitum,* and lights were used for 24 hr a day in the battery room and 14 hr a day in the brooder house.

Table 1 gives the yearly percentage growth response of birds fed rations containing antibiotics or arsonic acids over those fed control rations without these additives. Although the data for arsonic acids are not as extensive as those for antibiotics, both substances showed a similar trend—a progressive percentage decrease in response. Inasmuch as these chemicals exert their influence on nutrition in the same manner (*2*), their data are combined in column 3. This table contains data on 3900 chicks in 146 comparisons between groups of birds that were simultaneously fed the control rations or these same rations containing dietary levels of antibiotics or arsenicals.

It is seen that during the first year these substances considerably improved the early growth of chicks. This occurred on all basal diets. The response to antibiotics and arsonic acids, however, has since been progressively decreasing. Waibel (*3*) recently noted this in the case of dietary penicillin and Aureomycin during a 3-yr period.

At first sight this decreasing response appeared to be in accord with the idea that antibiotics may lose their effectiveness with continued usage, because of the gradual establishment of a microflora resistant to the antibiotics (*4*). If this were the case, the value of such additives would decrease in the course of time with prolonged use in the same place.

However, before this inference is drawn from the data presented, the growth rate of birds that were not fed antibiotics or arsonic acids should be noted. As is

Table 1. Growth responses from dietary antibiotics and arsonic acids and the mortality by years. The figures in parentheses indicate number of comparisons with control birds.

Periods	Increase in weight with respect to birds fed the control ration (%)			Increase in weight of control birds with respect to 1950–51 control birds (%)	Mortality to 6 wk of age (%)
	Birds fed antibiotics	Birds fed arsonic acids	Average		
1950–51	19.0 (75)	16.0 (2)	18.9	0	8.5
1951–52	12.8 (32)	(0)	12.8	7.4	8.2
1952–53	10.0 (4)	3.8 (5)	6.5	15.3	4.6
1953–54	3.3 (19)	3.2 (9)	3.2	19.1	2.8

evident in column 4, the weights of the control birds have been gradually increasing. For example, in 1950–51 certain groups of White Leghorn cockerels weighed 330 g at 5 wk of age, whereas in 1953–54 the same breed and strain of birds, on the same ration and in the same batteries, weighed more than 400 g. During the same period, the 4-wk weights of New Hampshire chicks that had antibiotics in their ration increased from 385 g to 406 g. Thus, both control and antibiotic-fed birds increased in weight during the last 4 yr, but the former gained at a much greater rate than the latter. The apparent decreased effectiveness of the growth promotants, therefore, is caused by a relatively greater increase in the rate of growth of birds fed the control ration.

These data, thus, do not furnish support for the theory that the continued use of antimicrobial agents in feeds results in the proliferation of resistant strains of organisms that eventually cause these agents to become ineffective. Rather, the data can be interpreted from an entirely different viewpoint—that is, that their continuous use over a long period produces an environment with a lowered germ load or disease potential. After long-time usage, these growth promotants are still capable of suppressing the germ load, but less of a challenge is presented. Thus, birds that are grown on the premises where birds have or have had antibiotics or arsonic acids in their feeds benefit to some extent from the improvement in environment.

The reduction in the mortality of chicks that we have observed during the last 4 yr adds support to the postulation that a reduced germ load develops. As can be seen in column 5, prior to the inclusion of antibiotics and arsenicals in chick rations, the mortality of battery-raised chicks up to 6 wk of age was about 8.5 percent, whereas the mortality of birds in these same batteries in recent years has declined to less than 3 percent. In addition, fewer cull chicks and less variability in growth rate within pens are now being noted.

From the practical point of view, this study indicates that antibiotics and arsonic acids would be of greatest value in promoting growth (i) when first used in a poultry-feeding enterprise and (ii) under the environmental conditions usually surrounding farm feeding. If once used and then discontinued, feeding performance may still be somewhat improved, because the contamination level has been lowered. Continued use of these substances at low levels, however, would help to insure maximum results, because an "infected" area can be reestablished through disuse (*5*). Indications are that such use of antibiotics and arsonic acids in feeds will not build up a resistant microflora that future poultry populations will have difficulty to live with.

From the point of view of the laboratory that attempts to evaluate antibiotics and arsonic acids for growth promotion, it would be desirable to be able to create at will a controlled level of contamination so that these substances can be tested under conditions more comparable to those in the field. Investigations along these lines are under way.

References and Notes

1. This paper is Journal article 1714, Michigan Agricultural Experiment Station.
2. T. L. Jukes, *Feedstuffs* (11 Sept. 1954) ; D. V. Frost and H. C. Spruth, Symposium on nontherapeutic uses for antibiotics, 124th meeting Am. Chem. Soc., Chicago, Ill. (1953).
3. P. E. Waibel *et al., Poultry Sci.* **33**, 1141 (1954).
4. P. Gyorgy, *Ann. N.Y. Acad. Sci.* **57**, 925 (1954).
5. M. E. Coates, *Chemistry & Industry* 1333 (1953).

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Straight-Line Function of Growth of Microorganisms at Toxic Levels of Carbon Dioxide

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Although CO_2 is essential for the growth of many heterotropic organisms (*1*), at high concentrations it becomes toxic (*2–4*). Such toxic action may, in part, be upon the CO_2-fixation mechanism itself (*5*).

Studies have been conducted to determine the influence of various concentrations of CO_2 upon the growth of several fungi (*2–4*). It has been found that these data will fit a straight-line dosage-response curve when they are plotted on a log-log scale, examples of which are shown in Fig. 1. Bateman's (*6*) method was employed by plotting the logarithm of the CO_2 concentration versus the logarithm of the

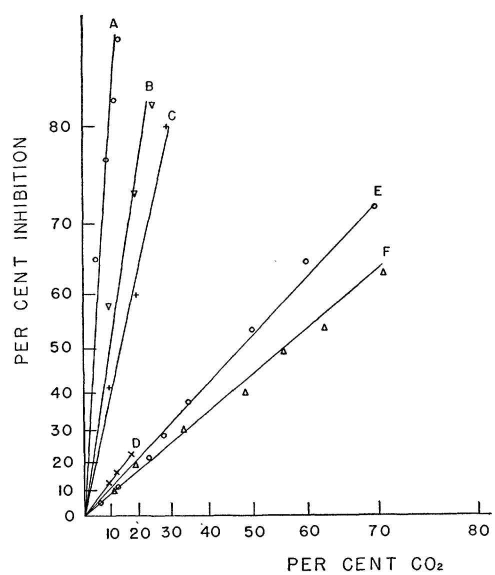

Fig. 1. Inhibition of growth at various levels of CO_2 for (*A*) *Penicillium nigricans,* (*B*) *Alternaria grossulariae,* (*C*) *Cladosporium herbarum,* (*D*) *Ophiobolus graminis,* (*E*) *Fusarium oxysporum, and* (*F*) *Fusarium solani* f. *eumartii.*