LETTERS TO THE EDITORS

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Mode of Action of Antibiotics in Stimulating Growth of Chicks

The stimulating effect on chick growth of antibiotics given by mouth has been reported by Stokstad and Jukes[1] and many other workers. Their finding has been confirmed at Reading[2] on several occasions with a variety of diets including practical rations, but not at Greenford, where only practical rations were tested.

The first set of results reported here was obtained independently in the two laboratories. The diet was a practical chick-rearing meal to which procaine penicillin was added to supply 25 mgm. of the antibiotic/kgm. Day-old Rhode Island Red × Light Sussex chicks were used in both laboratories, but were obtained from different sources. Their mean body-weights in grams after three weeks on the diets were :

Laboratory	No. of chicks/group	Without penicillin	With penicillin
Greenford	10 (mixed sexes)	181	183
Reading	20 ♂	143	191

The second experiment was designed to eliminate sources of variation between the two laboratories. One large batch of National Baby Chick Mash was obtained and divided between them. Similarly, equal groups of cockerel chicks (Rhode Island Red × Light Sussex) from the same supplier were distributed to each on the day of hatching, and their housing conditions were made as nearly as possible the same. The chicks were given the experimental diets for three weeks and their mean body-weights in grams at the end of this period were :

Laboratory	No. of chicks/group	Without penicillin	With penicillin
Greenford	20 ♂	188	191
Reading	20 ♂	167	192

The reasons for this marked discrepancy between results in the two laboratories is being investigated further ; but the findings so far support the suggestion that the growth-stimulating effect of antibiotics results from their suppression of micro-organisms detrimental to the host. It is possible that at Reading, and in other laboratories, where chicks have been kept regularly for a number of years, such organisms may have become established, with a slightly retarded rate of growth as their only manifestation. Chicks are not normally kept in the Greenford laboratories, and it is therefore unlikely that such organisms would be present there. If this explanation proves correct, it could certainly account for some of the dramatic results obtained by many workers with antibiotics in practical poultry management.

Quite possibly, with chicks deprived of the animal protein factor or other vitamins, antibiotics may stimulate growth also by creating in the gut conditions more favourable to the synthesis and uptake of missing factors.

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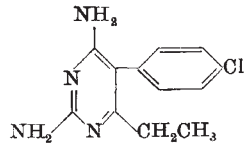
[1] Stokstad, E. L. R., and Jukes, T. H., *Proc. Soc. Exp. Biol., N.Y.* **73**, 523 (1950).
[2] Coates, M. E., Harrison, G. F., Kon, S. K., Mann, M. E., and Rose, C. D., *Biochem. J.*, **48**, xii (1951).

A 2 : 4-Diamino Pyrimidine in the Treatment of Proguanil-resistant Laboratory Malarial Strains

A series of 2 : 4-diamino pyrimidines substituted in the 5- and/or 6-position has recently been described[1] as having activity against malaria infections of laboratory animals. In particular, 2 : 4-diamino-5-*p*-chlorophenyl-6-ethyl pyrimidine (I), termed 50-63 here, showed a high degree of activity.



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This compound has been tested against strains of malaria parasites showing experimentally induced resistance to proguanil. Its activity against these resistant strains falls little short of that which it exercises against normal strains.

Three resistant strains were used in these experiments. The proguanil-resistant *P. gallinaceum* was obtained from the Liverpool School of Tropical Medicine and is strain 6 as described by Williamson and Lourie[2]. This strain was tested for proguanil-resistance before proceeding further and was found to be at least 55 times more resistant to the action of proguanil than the normal sensitive strain. (Minimum effective dose for proguanil is 0·9 mgm./kgm. for the normal strain and more than 50 mgm./kgm. for the resistant strain, the minimum effective dose being defined as the dose which effected a 50 per cent reduction in parasitæmia compared with untreated controls, this being estimated graphically from dose-response curves.)

Two drug-resistant strains of *P. berghei* were used : the first a strain which had been subjected to sub-curative doses of proguanil, and the second to sub-curative doses of sulphadiazine. The method of inoculation and dosing is similar to that described by Goodwin[3]. After their respective courses of treatment, both strains were tested for proguanil- and sulphadiazine-resistance along with the untreated parent strain.

It had previously been shown[4] that treatment of *P. gallinaceum* infections in chicks by sub-curative doses of sulphadiazine had very quickly induced a high degree of proguanil-resistance in that strain, even before sulphadiazine-resistance became mani-