Brit. J. Nutr. (1960), **14**, 499

Further studies on antibiotic, copper and zinc supplements for growing pigs

By R. S. BARBER, R. BRAUDE and K. G. MITCHELL
National Institute for Research in Dairying, Shinfield, Reading

(*Received* 31 *March* 1960)

The growth-promoting effect of the addition of 0·1 % of copper sulphate (supplying 250 p.p.m. of copper) to a diet for growing pigs has been demonstrated in a number of reports after the communication of Barber, Braude, Mitchell & Cassidy (1955). In a number of these reports it was shown that the improvement in performance arising from supplementation with copper was very similar to that obtained from the inclusion of an antibiotic in the diet. Evidence on the effect of adding both copper and an antibiotic to the diet is inconclusive. Barber, Braude & Mitchell (1955) gave rations containing a high-copper mineral mixture together with chlortetracycline to growing pigs and found no additional improvement in performance above that recorded for each of the supplements separately, whereas results reported by Lucas & Calder (1957) suggested a further improvement, at least during the first half of the growing period, when chlortetracycline was added to a diet already supplemented with 250 p.p.m. of copper.

Allen, Barber, Braude & Mitchell (1958) confirmed the growth-promoting effect of a supplement of 250 p.p.m. of copper. No effect was noted on supplementing the diet with 250 p.p.m. of zinc, nor did a combination of copper and zinc produce any better response than copper alone. The amount of copper stored in the liver of the pigs that received the high-copper diet was, however, reduced when zinc was added to the ration.

In the present paper, the results of a further three experiments are reported in which the diet of growing pigs was supplemented with copper, chlortetracycline or oxytetracycline, and zinc in various combinations.

EXPERIMENTAL

In the three experiments weaners from the virus-pneumonia-free Large White herd of this Institute were used and were all individually fed. Each experiment was designed as a randomized block; blocks corresponding to litters, and treatments were allocated at random to the pens in a Danish-type piggery, there being no direct communication between the pigs on the different treatments. The number of pigs on each treatment was 10, 8 and 7 on Expts 1, 2 and 3 respectively. All pigs were given twice daily as much meal as they would consume within 30 min, up to a maximum of 6½ lb/day, water at the rate of 3 lb to every 1 lb meal being added immediately before feeding. The pigs were weighed once weekly throughout the experiment and were sent

to slaughter individually when their live weight at the weekly weighing exceeded 203 lb. At the factory all carcasses were commercially graded on the basis of carcass length and shoulder and loin back-fat thickness. The liver was taken from four of the litter-mate replicates on Expt 3 and stored at $-20°$. The copper content of a sample of liver tissue adjacent to the bile duct was subsequently determined by the method of Andrus (1955); it had been previously established that the copper content of such a sample approximates closely to the mean copper content of the whole liver (Allen, Barber, Braude & Mitchell, unpublished).

Table 1. *Percentage composition of the basal diet used in all experiments*

Barley meal	52
Fine miller's offal	38
White-fish meal	10
Rovimix (Roche Products Ltd) (containing 50 000 i.u. vitamin A and 12 500 i.u. vitamin D_3/g)	4·5 g/100 lb

Table 2. *Details of supplements of copper, zinc, oxytetracycline and chlortetracycline used in the experiments*

Supplement	Form in which added	Amount added to diet
Copper	$CuSO_4.5H_2O$	0·1 %, supplying 250 p.p.m. Cu
Zinc	$ZnCO_3.2ZnO.3H_2O$	0·045 %, supplying 250 p.p.m. Zn
Oxytetracycline	T.M. 5*	2·24 lb/ton of diet
Chlortetracycline	Aurofac 2A†	2·80 lb/ton of diet

* Pfizer Ltd, containing 5 g oxytetracycline/lb.
† Cyanamid of Great Britain Ltd, containing 3·6 g chlortetracycline/lb.

Table 3. *Details of the treatments in the three individual experiments*

Expt 1		Expt 2		Expt 3	
Treatment no.	Dietary supplement	Treatment no.	Dietary supplement	Treatment no.	Dietary supplement
1	None	1	None	1	Copper
2	Copper	2	Copper	2	Copper + oxytetracycline
3	Oxytetracycline	3	Copper + chlortetracycline	3	Copper + zinc
4	Copper + oxytetracycline			4	Copper + oxytetracycline + zinc

The composition of the basal diet used in all three experiments is given in Table 1. Details of the supplements used in the various experiments and of the treatments in the three individual experiments are shown in Tables 2 and 3 respectively.

RESULTS

The mean results for daily gain, food conversion, rate of food consumption, carcass dressing percentage and carcass length, together with the approximate standard errors, for Expts 1, 2, and 3, are given in Tables 4, 5 and 6 respectively. Values for copper

content of livers of pigs on Expt 3 are also included in Table 6. The standard errors were calculated from randomized block analyses of variance, no adjustments being made for variation in either initial live weight or cold dead weight (Barber, Braude & Mitchell, 1957). The results of commercial grading of the carcasses from the three experiments are presented in Table 7. In Table 8, results for pigs receiving the basal control diet alone or with the supplement of copper in Expts 1 and 2 have been

Table 4. *Expt* 1. *Effect of diets supplemented with copper or oxytetracycline or both on mean daily gain, food conversion, rate of food consumption, dressing percentage and carcass length*

	Treatment no.					
	1	2	3	4		
Dietary supplement ...	None	Copper	Oxytetracycline	Copper + oxytetracycline	Standard error of means*	Significance of treatment mean square
No. of pigs	10†	10†	10	10	—	—
Initial weight (lb)	51·0	52·8	51·2	51·5	—	—
Final weight (lb)	207·6	206·3	209·2	207·2	—	—
Daily gain (lb)	1·40	1·55	1·52	1·65	0·029	***
Food conversion (lb meal/lb live-weight gain)	3·52	3·36	3·43	3·18	0·054	**
Rate of food consumption (lb/day)	4·90	5·21	5·20	5·24	0·057	**
Dressing percentage	73·3	74·0	74·1	74·4	0·37	N.S.
Carcass length (mm)	789	774	777	786	5·3	N.S.

N.S., $P > 0.05$. ** $0.01 > P > 0.001$. *** $P < 0.001$.
* Based on 25 degrees of freedom.
† One pig taken off experiment after a few weeks for reasons unconnected with the experiment, and missing values calculated by missing-plot technique (Yates, 1933).

Table 5. *Expt* 2. *Effect of diets supplemented with copper or with copper and chlortetracycline on mean daily gain, food conversion, rate of food consumption, dressing percentage and carcass length*

	Treatment no.				
	1	2	3		
Dietary supplement	None	Copper	Copper + chlortetracycline	Standard error of means†	Significance of treatment mean square
No. of pigs	8	8	8	—	—
Initial weight (lb)	46·5	46·9	48·1	—	—
Final weight (lb)	208·5	208·1	209·0	—	—
Daily gain (lb)	1·48	1·64	1·70	0·037	**
Food conversion (lb meal/lb live-weight gain)	3·18	3·02	3·02	0·060	N.S.
Rate of food consumption (lb/day)	4·70	4·95	5·15	0·099	*
Dressing percentage	71·5	73·3	72·4	0·40	*
Carcass length (mm)	809	791	800	5·4	N.S.

N.S., $P > 0.05$. * $0.05 > P > 0.01$. ** $0.01 > P > 0.001$.
† Based on 14 degrees of freedom.

combined. Similarly in Table 9, results for pigs receiving the diet with a supplement of either copper or both copper and oxytetracycline or chlortetracycline in Expts 1–3 have been combined. As the standard errors were very similar for each variable studied in all three experiments, in the combined results given in Tables 8 and 9 the errors over Expts 1 and 2, or 1, 2 and 3, respectively, were pooled.

Table 6. *Expt* 3. *Effect of diets supplemented with copper, copper and oxytetracycline, copper and zinc, or copper and oxytetracycline and zinc, on mean daily gain, food conversion, rate of food consumption, dressing percentage, carcass length and liver storage of copper*

	Treatment no.				
	1	2	3	4	
Dietary supplement	Copper	Copper + oxytetracycline	Copper + zinc	Copper + oxytetracycline + zinc	Standard error of means*
No. of pigs	7†	7	7	7	—
Initial weight (lb)	50·0	51·1	50·6	49·0	—
Final weight (lb)	206·7	207·0	209·1	207·1	—
Daily gain (lb)	1·61	1·68	1·53	1·67	0·038
Food conversion (lb meal/lb live-weight gain)	3·25	3·11	3·34	3·19	0·069
Rate of food consumption (lb/day)	5·23	5·22	5·11	5·31	0·072
Dressing percentage	73·7	73·4	74·4	74·3	0·35
Carcass length (mm)	779	790	791	797	7·0
Copper in liver‡ (mg/kg dry tissue):					
Value	836	458	332	410	131·6
Range	(226§–1219)	(307–600)	(128–554)	(158–660)	

* Based on 17 degrees of freedom. (Liver copper values based on 9 degrees of freedom.) None of the treatment mean squares was significant ($P > 0{\cdot}05$).

† One pig taken off experiment after a few weeks for reasons unconnected with the experiment, and missing values calculated by missing-plot technique (Yates, 1933).

‡ Means for four pigs on each treatment.

§ Next lowest value was 919.

Daily gain, food conversion, rate of food consumption, dressing percentage and carcass length

Expt 1 (*Table* 4). Supplementation of the basal diet with either copper, oxytetracycline, or both together, resulted in a significant increase in both rate of gain and rate of food consumption. Efficiency of food conversion was also significantly improved by the supplement of copper or of copper with oxytetracycline. Treatment differences in dressing percentage and carcass length were not significant at the 5 % level.

Both rate of gain and efficiency of food utilization were significantly better in pigs that received copper with oxytetracycline than in those that received only one of these two supplements. Differences in rate of food consumption between the three supplemented groups were very small and were not statistically significant.

Expt 2 (*Table* 5). Supplementation of the basal diet with either copper or with copper and chlortetracycline resulted in a significant increase in rate of gain; the rate of food consumption was significantly increased only in pigs receiving both

Table 7. *Results of commercial grading of carcasses of pigs on Expts 1–3*

Expt no.	Dietary supplement	No. of carcasses: Total	AA+	AA	A	Total A and above	B+	B	C	F	Grade A on: Loin	Grade A on: Shoulder
1	None	9	2	1	0	3	4	0	2	0	7	5
	Copper	9	0	2	3	5	2	0	2	0	8	6
	Oxytetracycline	10	1	1	1	3	3	4	0	0	5	5
	Copper + oxytetracycline	10	1	3	0	4	3	1	2	0	7	7
2	None	8	6	2	0	8	0	0	0	0	8	8
	Copper	8	1	4	0	5	3	0	0	0	6	6
	Copper + chlortetracycline	8	4	2	0	6	2	0	0	0	6	7
3	Copper	6	0	2	1	3	2	1	0	0	4	5
	Copper + oxytetracycline	7	1	2	0	3	2	1	1	0	5	4
	Copper + zinc	7	0	2	1	3	2	0	1	1	4	3
	Copper + oxytetracycline + zinc	7	3	1	0	4	0	0	3	0	6	4
1+2	None	17	8	3	0	11	4	0	2	0	15	13
	Copper	17	1	6	3	10	5	0	2	0	14	12
1+2+3	Copper	23	1	8	4	13	7	1	2	0	18	17
	Copper + oxytetracycline or chlortetracycline	25	6	7	0	13	7	2	3	0	18	18

supplements, and the dressing percentage only in pigs receiving the copper supplement alone. Treatment differences in efficiency of food conversion and in carcass length were not significant at the 5 % level.

Differences between the two supplemented groups for any of the variables measured were all small and not significant.

Table 8. *Combined results of Expts* 1 *and* 2 *showing effect of supplementation of diet with copper*

	Dietary supplement		Response to copper as percentage of (*a*)	Standard error of difference between means†	Significance of difference between means
	None (*a*)	Copper (*b*)			
No. of pigs	18	18	—	—	—
Daily gain (lb)	1·44	1·59	10·4	0·032	***
Food conversion (lb meal/lb live-weight gain)	3·36	3·21	−4·5	0·057	*
Rate of food consumption (lb/day)	4·81	5·09	5·8	0·074	***
Dressing percentage	72·5	73·7	1·7	0·38	**
Carcass length (mm)	798	782	−2·0	5·4	**

* $0{\cdot}05 > P > 0{\cdot}01$. ** $0{\cdot}01 > P > 0{\cdot}001$. *** $P < 0{\cdot}001$.
† Based on 39 degrees of freedom.

Table 9. *Combined results of Expts* 1–3 *showing effect of supplementation of a high-copper diet with oxytetracycline or chlortetracycline*

	Dietary supplement		Response to antibiotic as percentage of (*a*)	Standard error of difference between means†	Significance of difference between means
	Copper (*a*)	Copper + oxytetracycline or chlortetracycline (*b*)			
No. of pigs	25	25	—	—	—
Daily gain (lb)	1·60	1·68	5·0	0·028	**
Food conversion (lb meal/lb live-weight gain)	3·22	3·11	−3·4	0·049	*
Rate of food consumption (lb/day)	5·13	5·21	1·6	0·060	N.S.
Dressing percentage	73·7	73·5	−0·3	0·31	N.S.
Carcass length (mm)	781	792	1·4	4·8	*

N.S., $P > 0{\cdot}05$. * $0{\cdot}05 > P > 0{\cdot}01$. ** $0{\cdot}01 > P > 0{\cdot}001$.
† Based on 56 degrees of freedom.

Expt 3 (*Table* 6). None of the treatment differences for any of the variables measured was significant at the 5 % level. For the daily gain the treatment mean square only just failed to reach the 5 % level of significance and a *t* test indicated that the pigs that received the supplement of copper with zinc grew significantly more slowly than those given copper and oxytetracycline with or without the zinc supplement. There was also an indication that the slower growth of the pigs given the copper and zinc supplement was accompanied by a poorer conversion of the food consumed.

The mean values in Table 6 for liver copper show a marked reduction in liver copper when oxytetracycline, zinc or both were added to a diet containing the copper supplement. Although the treatment mean square did not quite reach the 5 % level of significance, a *t* test indicated that the addition of zinc, with or without the antibiotic, to the high-copper diet significantly reduced the liver-copper stores of the pigs.

Commercial grading results

Expts 1–3 (*Table* 7). No marked and consistent differences between any of the treatments arising from changes in thickness of back fat were apparent. There was, however, a trend towards more A and AA carcasses and fewer AA+ carcasses from pigs receiving the diet supplemented with copper alone than from those given the unsupplemented diet or one supplemented with copper and an antibiotic. This change in the proportions of the three categories of grade A carcasses is a function of carcass length and is consistent with the somewhat shorter mean length of the carcasses from pigs given the diet supplemented with copper alone, as compared with the other two treatments, shown in Tables 4–6, 8 and 9.

DISCUSSION

The marked growth-promoting effect of a supplement of 250 p.p.m. copper in the diet of growing pigs and its similarity to the effect of antibiotic supplementation were again confirmed. The mean improvement in growth rate of 10·4 %, and in food conversion of 4·5 %, resulting from supplementation of the diet with copper, as shown in the combined results given in Table 8, agree closely with previously reported findings. The magnitude of the mean response to copper is very similar to the mean responses to antibiotic supplementation obtained under British conditions (Lucas, 1957).

It seems clear from the results reported now and previously that when pigs are fed in a way that allows some expression of appetite, as in the present experiments, the improvement in rate of growth resulting from supplementing the diet with copper is the direct consequence partly of an improvement in the efficiency with which the food consumed is utilized and partly of an increase in the daily amount of food consumed. This finding also appears to apply in general to supplementation of pig diets with antibiotics (Lucas, 1957). However, in experiments in which pigs have been fed according to a scale based on live weight, so that no expression of appetite should be possible (Allen, Barber, Braude & Mitchell, unpublished; Lucas & Calder, 1957), growth responses to copper supplementation were also obtained.

The mode of action by which copper, or an antibiotic, initiates these effects remains obscure. It is of interest to note the close similarity in so many respects between the total effects of supplementing a diet for growing pigs with copper sulphate or with an antibiotic, suggesting the possibility that the mode of action of the two substances may at least be similar. On the other hand, the evidence in Table 9 showing some additional response when both copper and an antibiotic are added to the diet suggests that their modes of action are, at least to some extent, different.

The further mean improvement in growth rate of 5·0% and in food conversion of 3·4%, arising from the addition of either oxytetracycline or chlortetracycline to a diet already supplemented with 250 p.p.m. copper, as shown in Table 9, is in general agreement with results reported by Lucas & Calder (1957) in this country, and by Hawbaker, Speer, Jones, Hays & Catron (1959) in America, although in an earlier trial Barber, Braude & Mitchell (1955) obtained no further response when chlortetracycline was added to a diet supplemented with a high-copper mineral mixture.

The significant increase observed in dressing percentage resulting from copper supplementation of the diet had also been noted by Lucas & Calder (1957) in one of their trials. Some increase in mean dressing percentage was also apparent when the basal diet was supplemented with oxytetracycline in Expt 1. This effect of antibiotic has been observed by a large number of workers in this field (see Lucas, 1957). A tendency for some antibiotics to reduce liver and gut weight in pigs has been reported by several workers and a suggestion that copper supplementation has similar effects was made by Barber, Braude, Mitchell, Rook & Rowell (1957), but there is insufficient evidence as yet to draw any conclusions on the extent to which such changes in organ weights may be correlated with the observed effects on dressing percentage. Moreover, the influence on dressing percentage of such factors as the interval between final feed, final weighing of the live pig and time of slaughter, add to the difficulties in making comparisons between different experiments. Nevertheless, real increases in dressing percentage, although only small, are of economic importance when the producer is paid on a dead-weight basis.

The observed reduction in length of carcass shown in Tables 8 and 9 from pigs fed on a diet supplemented with copper, compared with those fed on either an unsupplemented diet or one to which both copper and an antibiotic are added has not previously been reported, and further work will be required to determine whether this observation represents a real treatment effect or is due to chance selection of the animals in our experiments. Treatment differences in commercial grading were mainly associated with these carcass-length differences, as indicated by the changes in the proportions of the three grade A classifications shown in Table 7.

From the practical economic aspect, results obtained so far do not permit a definite answer to be given to the question whether both copper and an antibiotic should be added to a growing-pig diet, or only one or the other. The large variation in response to antibiotics from one farm to another is well established, although the reasons for it are still not understood. Against this background of variation, it would appear most likely that the use of both copper and an antibiotic will prove to be economic under some conditions, whereas under others the incorporation of only one of the two materials will be found worth while. A large-scale co-ordinated trial conducted by the Agricultural Research Council involving twenty-two centres, now in progress, should provide further information on this question.

The finding reported by Allen *et al.* (1958) that the addition of 250 p.p.m. zinc to a diet supplemented with 250 p.p.m. copper did not produce a better response than that given by copper alone was confirmed (see Table 6). In addition, it was

shown that the addition of the zinc supplement to a diet supplemented with both copper and oxytetracycline caused no additional response.

The effect of zinc in reducing the amount of copper stored in the liver of pigs given the high-copper supplement was again demonstrated. There was also a suggestion that the addition of oxytetracycline to the diet containing 250 p.p.m. copper tended to reduce liver-copper stores. The reasons for this latter observation are obscure and further investigation is required to determine whether it represents a true treatment effect. It would seem most probable that the observation of Wallace (1956) that the addition of zinc to the diet enhanced the growth-promoting effect of copper supplementation, was associated with conditions conducive to development of parakeratosis in the pigs used by this worker, and absent in the pigs used in the experiments reported here. The marked effect of zinc in preventing the development of parakeratosis is now well established.

SUMMARY

1. Ninety-two individually fed, virus-pneumonia-free Large White weaners were used in three experiments to compare the effects of dietary supplements of copper sulphate, oxytetracycline or chlortetracycline, and zinc carbonate in various combinations on the performance of growing pigs from weaning to bacon weight.

2. Copper sulphate or oxytetracycline significantly and similarly increased growth rate, efficiency of food conversion, and rate of food consumption.

3. The addition of zinc carbonate to a diet supplemented with either copper sulphate alone or with copper sulphate and oxytetracycline had no significant effect on the performance of the animals.

4. Combined results from the three experiments showed that copper sulphate alone significantly increased growth rate by 10·4%, efficiency of food conversion by 4·5%, rate of food consumption by 5·8%, and dressing percentage by 1·7%, and significantly reduced carcass length by 2·0%. Oxytetracycline or chlortetracycline, added to a diet already supplemented with copper sulphate, significantly increased growth rate by 5·0%, efficiency of food conversion by 3·4% and carcass length by 1·4%, but had no significant effect on rate of food consumption or dressing percentage.

5. There were no marked or consistent treatment differences in results of commercial grading apart from a tendency for pigs given copper alone to yield fewer AA+ carcasses and more AA and A carcasses, a function of the reduction in carcass length of the animals on this treatment.

6. The addition of zinc to a diet supplemented either with copper alone or with copper and oxytetracycline resulted in a reduction in the mean copper stores in the liver of the pigs. There was also an indication that the addition of oxytetracycline to a high-copper diet reduced liver-copper stores.

We wish to thank Mr M. M. Allen and Professor J. P. Bowland for carrying out the liver-copper analyses, and Miss Z. D. Hosking for advice in connexion with the statistical analysis of the results. Our thanks are also due to Cyanamid of Great Britain Ltd, and Pfizer Ltd, for the gift of Aurofac 2A and of T.M. 5 respectively.

REFERENCES

Allen, M. M., Barber, R. S., Braude, R. & Mitchell, K. G. (1958). *Proc. Nutr. Soc.* **17**, xii.
Andrus, S. (1955). *Analyst*, **80**, 514.
Barber, R. S., Braude, R. & Mitchell, K. G. (1955). *Brit. J. Nutr.* **9**, 378.
Barber, R. S., Braude, R. & Mitchell, K. G. (1957). *J. agric. Sci.* **48**, 347.
Barber, R. S., Braude, R., Mitchell, K. G. & Cassidy, J. (1955). *Chem. & Ind.* p. 601.
Barber, R. S., Braude, R., Mitchell, K. G., Rook, J. A. F. & Rowell, J. G. (1957). *Brit. J. Nutr.* **11**, 70.
Hawbaker, J. A., Speer, V. C., Jones, J. D., Hays, V. W. & Catron, D. V. (1959). *J. Anim. Sci.* **18**, 1505.
Lucas, I. A. M. (1957). *Vet. Rec.* **69**, 233.
Lucas, I. A. M. & Calder, A. F. C. (1957). *J. agric. Sci.* **49**, 184.
Wallace, H. D. (1956). Private communication.
Yates, F. (1933). *Emp. J. exp. Agric.* **1**, 129.

Printed in Great Britain