whom the arterial pressure is at or below normal levels.

The fact that dibenamine, a sympatholytic agent, prevented the formation of pulmonary edema(3) is not necessarily an indication that it is blockade of the pulmonary sympathetics which alters the outcome. Cameron and De (5,6) produced rapid, lethal pulmonary edema in the rabbit with the intracisternal injection of thrombin and fibrinogen, and Cruchaud and Vermeil(7) demonstrated that this type of pulmonary edema is also prevented by dibenamine. However, in recent studies on the dog it became clear that the striking elevation of pulmonary capillary pressure that occurs soon after the intracisternal injection of thrombin and fibrinogen is due not to activity of pulmonary sympathetics but rather to impulses traveling over sympathetics to the peripheral vascular bed(8-10). The increased peripheral vascular resistance, as well as the shift of blood from periphery to lung, was shown to be mainly responsible for the elevations of pulmonary capillary pressure that occurred.

Summary. (1) Ammonium chloride was administered intraperitoneally to 12 cats under sodium pentobarbital anesthesia with measurement of left auricular, femoral arterial, and vena caval pressures. (2) Left auricular and vena caval pressures rose significantly in all experiments. Arterial pressures were generally, but not always, lower during the period of the sustained elevation of left auricular pressure than during the control period. (3) Two of the 12 cats developed generalized pulmonary edema. These 2 had sustained left auricle pressures of 24 and 40 cm of water. (4) Although the above experiments do not preclude the possibility that other mechanisms may also be operating, they do suggest that left ventricular failure plays a role in the development of ammonium pulmonary edema in the cat.

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Function and Metabolic Significance of Penicillin and Bacitracin in the Chick.* (19235)

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Elam, Gee, and Couch(1) reported that the fecal microflora of the growing chick was influenced by the feeding of penicillin. These workers reported further that this antibiotic stimulated growth and egg production. Aureomycin has also been shown to increase egg production and hatchability(2). The growth promoting effect of penicillin and terramycin has been explained as an inhibition of *Clostridium perfringens* in the intestinal tract of turkeys by Sieburth *et al.*(3). Halick and

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TABLE I. Supplementation to Basal Diet.

Group	Penicillin					Bacitracin		Vit. B_{12}, μg
	Oral, mg	Inj., mg	Autoclaved, inj., mg	Autoclaved, oral, mg	In sesame oil, units	Oral, mg	Inj., mg	
1	0							
2								1‖
3	33*							
4		1.2†						
5			1.2‡					
6				33				
7					15000§			
8	33							1
9		1.2						1
10			1.2					1
11				33				1
12					15000			1
13						33		
14							1.2	
15						33		1
16							1.2	1

* Per kg of diet. † Inj. per bird per wk. ‡ Autoclaved 15 min at 15 lb. § Inj. per bird every other day. ‖ Inj. per bird per wk.

Couch(4) fed aureomycin and penicillin to hens receiving a purified diet containing soybean protein and sucrose and found that these antibiotics apparently assisted in the depletion of the birds of vit. B_{12} and possibly of an unidentified factor necessary for normal hatchability and embryonic development. Shortly after the isolation of vit. B_{12}(5), the pure vitamin was reported to promote a growth response in chicks equivalent to that obtained with crude sources of the animal protein factor(6,7). It has been demonstrated that unidentified factors over and above vit. B_{12} are necessary for maximum chick growth(8-13). Further, Stokstad and Jukes(14) and Whitehill *et al.*(15) reported that aureomycin, streptomycin, penicillin, and sulfasuxidine promoted the growth of chicks adequately supplied with vit. B_{12}.

This experiment was designed to determine the effect of oral and parenteral administration of penicillin, bacitracin, and autoclaved penicillin on growth and aerobic fecal microflora.

Experimental. The New Hampshire chicks used in these studies were obtained from hens which had been fed a diet composed of 20% ground yellow corn, 45.6% ground milo, 20.5% soybean oil meal, 4% fish meal, 2% oyster shell, 3% alfalfa leaf meal, 2% dried whey, 0.25% Lederle APF-B_{12} concentrate, 0.5% NaCl, and 0.175% fortified fish oil (2250A-300D). In addition 2 mg riboflavin, 5 mg calcium pantothenate, 500 AOAC chick units of vit. D_3, and 100 mg $MnSO_4$ were fed per pound of feed. Four hundred and eighty chicks were randomized into 16 groups of 30 chicks each and were kept in batteries with raised screen floors. Feed and water were supplied *ad libitum*. The birds were weighed at weekly intervals during an experimental period of 10 weeks. The basal diet (G-1) used in this study was the same as that reported earlier by Couch and Olcese(16). The basal diet was fed alone and supplemented as shown in Table I. The autoclaved penicillin used in this experiment was prepared according to information from Dr. David Hendlin(17). Sixty mg of procaine penicillin G was added to 20 ml of water and autoclaved for 15 minutes at 15 lb of pressure at 120° to 125°C. In one assay (disc plate technic) no growth inhibition was observed even when the autoclaved material was tested at undiluted strength.† In the other instance (cup plate procedure) the solution of autoclaved procaine penicillin G showed a potency of less than 0.2 unit per ml (less than 0.07 unit per mg)‡. The procaine penicillin G sample (from original aliquot and used as a standard) assayed 1130 units per mg by microbiological

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‡ Dr. David Hendlin, Merck and Co., Rahway, N. J.

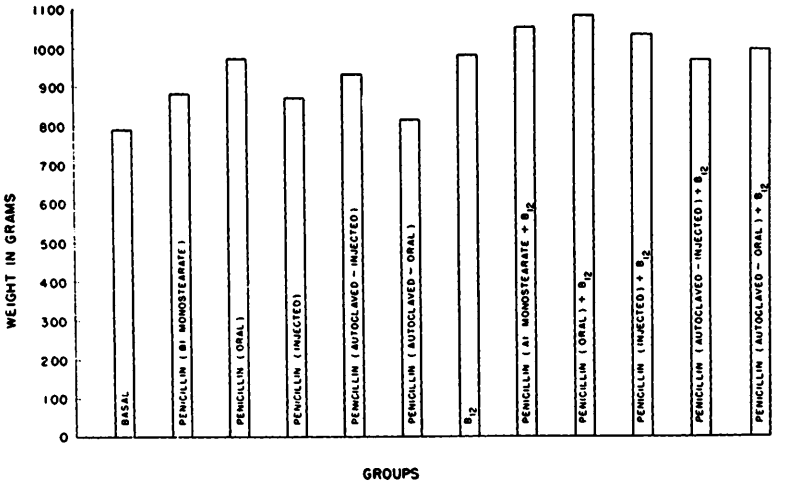

FIG. 1. Effect of oral and parenteral administration of penicillin, autoclaved penicillin, and injecting vit. B_{12} on growth of New Hampshire chicks.

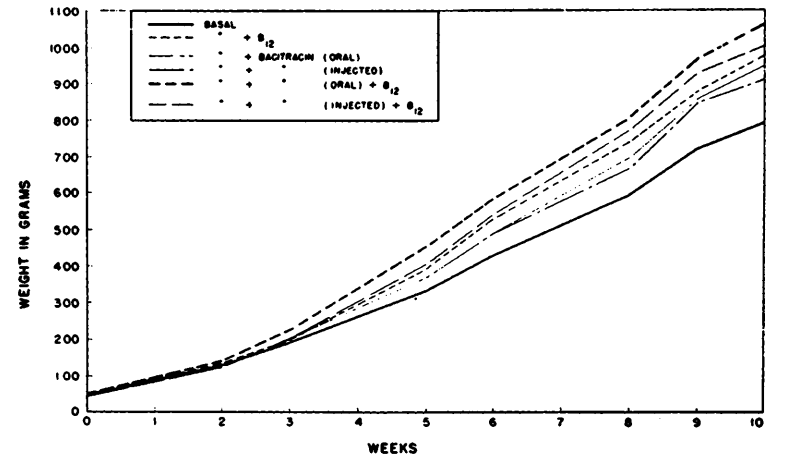

FIG. 2. Effect of oral and parenteral administration of bacitracin and injecting vit. B_{12} on growth of New Hampshire chicks.

assay and 1017 units per mg by chemical assay which are in good agreement with the theoretical value of 1009 units per mg.

Results and discussion. The administration of oral or injected penicillin increased the rate of chick growth (Fig. 1). A somewhat greater growth increase was also apparent when penicillin in sesame oil (containing aluminum monostearate) and autoclaved penicillin were each injected. This is possibly traceable to the fact that penicillin in sesame oil remained in the tissues for a longer period of time and was made available more slowly. The fact that the injection of autoclaved penicillin increased growth is of particular significance since the feeding of autoclaved penicillin had no effect on the growth of the birds. The injection of vit. B_{12} resulted in an increase in growth. When the birds received both vit. B_{12} and penicillin the weight of the birds was increased above that of those which were given B_{12} without penicillin.

Bacitracin administered orally or parenterally produced an increase in growth over that of the birds fed the basal diet unsupplemented (Fig. 2). This increase in growth was about the same as that observed when vit. B_{12} alone was added to the basal diet. Birds which received bacitracin orally or parenterally with vit. B_{12} weighed more at the end of the 10

TABLE II. Summary of Statistical Analysis of Enumerative Data from Fecal Droppings of Chickens from 2-10 Weeks of Age.

		Penicillin						
	Basal	Oral	Inj.	Auto. inj.	Auto. oral	Al mono-stearate	F-value†	LSD§
Penicillin‖	4.91*	6.66	5.75	6.09	6.26	6.67	3.88‡	1.22
Aureomycin¶	2.33	4.06	2.62	3.21	2.72	3.03	3.65‡	.85
Potato-dextrose (yeast)	2.08	3.24	2.24	2.31	2.04	2.36	5.57‡	.59
		Penicillin plus B_{12}						
Penicillin‖	6.03	7.60	5.64	6.18	5.75	7.61	3.88‡	1.22
Aureomycin¶	2.43	3.84	3.31	3.21	3.03	3.25	3.65‡	.85
Potato-dextrose (yeast)	2.27	3.42	2.32	2.32	2.44	2.98	5.57‡	.59

* Avg No. of microorganisms in logarithms. † F-value calculated for all 12 groups. ‡ Significant at the 1% level. § Least significant difference—calculated for all 12 groups. ‖ Penicillin resistant. ¶ Aureomycin resistant.

week test period than did those of any other group.

Effect on flora. The oral administration of penicillin produced an increase in the penicillin resistant organisms, aureomycin resistant organisms, and in the yeast counts (Table II). There was no significant increase in the total dilution count, enterococci, lactics, or coliforms when penicillin was administered orally to the birds over those receiving the basal diet. In an earlier study from this laboratory the oral administration of penicillin increased the total number of bacteria and the enterococci (1). This was not observed in the present study. It should be pointed out that vit. B_{12} depleted chicks were used in the first study (1), whereas chicks from hens on an adequate diet were used in this investigation.

The parenteral administration of penicillin in water did not have any effect on the aerobic fecal microflora. When penicillin was administered in sesame oil, containing aluminum monostearate, there was an increase in the penicillin resistant organisms and in the yeast counts. These data might be explained by the fact that the penicillin in sesame oil was injected every other day and was released slowly. Such a procedure might have led to the excretion of the antibiotic into the intes tinal tract and thus an effect on the microflora was produced. The administration of autoclaved penicillin had little effect upon the fecal microflora.

Since the parenteral administration of penicillin and of autoclaved penicillin failed to have any appreciable effect upon the microflora, and yet stimulated the rate of growth, it might be surmised that a fragment of the penicillin molecule may have acted as a metabolite within the body of the bird.

Bacitracin when administered orally or parenterally, with or without vit. B_{12}, failed to have any effect upon the thioglycollate count, enterococci, lactics, yeasts, coliforms, penicillin resistant, or bacitracin resistant organisms. This observation appears to be rather significant in that bacitracin produced a significant increase in growth. Such an observation lends support to the theory that the antibiotic molecule or fragment of same might possibly have stimulated growth by acting as a metabolite within the body of the bird.

Summary. (1) The feeding of penicillin, but not of autoclaved penicillin, stimulated the growth of birds fed an all-vegetable protein diet. The injection of either penicillin or autoclaved penicillin similarly increased growth. (2) Bacitracin when administered orally or parenterally increased the rate of growth. (3) Under the conditions of the experiment reported herein the feeding of penicillin increased the penicillin and aureomycin resistant organisms and increased the yeast count. The parenteral administration of penicillin had no effect on the fecal microflora. Autoclaved penicillin had little effect upon the fecal microflora. Bacitracin when administered orally or parenterally failed to have any effect on the fecal microflora. (4) Since the parenteral administration of antibiotics and autoclaved penicillin increased the rate of growth and yet had little effect on the fecal

aerobic microflora count it seems possible that the antibiotics may have stimulated growth by some other mechanism. Thus, it might be surmised that the antibiotic molecule or a fragment of same might act as a metabolite within the body of the bird.

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Beneficial Effects of Liver on Cortisone Acetate Toxicity in the Rat.* (19236)

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Considerable data are available indicating that, in addition to the known nutrients, substances are present in our diet which may be required in increased amounts during conditions of stress. Such factors are apparently dispensable under normal conditions, or their requirements are so small they may readily be met by amounts present in the diet or through the synthetic activity of the intestinal flora or the animals' own tissues. Certain drugs or other "stress factors" may, however, increase requirements for these substances to such an extent that deficiencies occur, manifested by retarded growth or tissue pathology, and preventable by the administration in appropriate amounts of the missing nutrient (1,2). Whole liver is a potent source of such unknown nutrients. Thus whole liver or fractions thereof has been shown to counteract the deleterious effects of massive doses of strychnine(3), sulfanilamide(4), promin(5,6), atabrine(7,8) and dinitrophenol(9). Similar results have been observed following the administration of toxic doses of diethyl-stilbestrol(4), alpha-estradiol(10), desiccated thyroid(11-14), and thyroxin, thyroglobulin and iodinated casein(15). In the present communication data are presented on the comparative effects of whole liver and the known B vitamins on cortisone acetate toxicity in the immature rat.

Procedure. Exp. 1. The basal ration employed in the present experiment consisted of sucrose, 61%, casein,† 24%; salt mixture,‡

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