TABLE II.
Electrolytes in mEq. per 1000 g of Dry Tissue.

	R.A.	L.A.	R.V.	L.V.
Calcium	12.6	12.7	9.0	9.1
Chloride	83.4	86.8	91.5	93.0
Iron	7.2	7.4	12.6	13.8
Magnesium	41.1	43.6	74.8	79.7
Phosphorus	169.0	185.0	248.0	257.0
Potassium	111.0	121.5	268.6	270.0
Sodium	152.2	165.8	306.0	326.0
Total Nitrogen %	2.38	2.53	2.91	2.97
Water %	74.3	75.2	76.9	77.5

TABLE III.
70% Alcohol (10 Animals).
Electrolytes in mEq. per 1000 g of Dry Tissue.

	R.A.	L.A.	R.V.	L.V.
Calcium	16.2	15.9	11.3	11.5
Chloride	80.0	83.4	86.5	87.6
Potassium	141.5	156.6	277.8	277.7
Sodium	102.5	118.6	249.0	260.5
Water %	75.2	75.4	76.7	76.6

loss of potassium and calcium (Table IV). Ventricular muscle showed an absolute increase in sodium in the absence of any other significant changes. The loss of potassium from auricular muscle may be explained on the basis of the vagal component of the action of digitalis, since vagal stimulation causes an outflow of potassium from auricular muscle.[2,3] The mechanism of an absolute increase in sodium in heart muscle is not understood, but may be related to the poisonous actions of digitalis since an increase in sodium above the physiological ratio of this ion to potassium and calcium produces toxic effects upon the heart.[4,6]

TABLE IV.
Total Change in Electrolytes.*
(Milli-equivalents per 100 g of dry tissue.)

	R.A.	L.A.	R.V.	L.V.
Control Potassium	137.0	154.0	277.0	279.0
Experimental Potassium	111.0	121.5	268.6	270.0
Loss of Potassium	26.0	33.5	8.4	9.0
Control Sodium	96.6	121.0	253.0	255.5
Experimental Sodium	152.2	156.8	306.0	326.0
Gain in Sodium	55.6	35.8	53.0	70.5
Control Calcium	16.6	16.3	11.5	11.2
Experimental Calcium	12.6	12.7	9.0	9.1
Loss of Calcium	4.0	3.6	2.5	2.1

* From a statistical analysis of the data, only potassium, sodium, and calcium showed P-values not greater than 0.02.

Summary. 1. Maximal digitalization caused a decrease in the potassium and calcium content of auricular muscle and a gain in sodium which does not appear to compensate for the loss of potassium and calcium. Ventricular muscle showed a gain in sodium which does not appear to compensate for the loss of potassium and calcium. Ventricular muscle showed a gain in sodium in the absence of any other significant changes. 2. The changes in sodium, potassium and calcium following digitalization occurred in the absence of significant changes in the water content of the digitalized heart.

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Effects of Pyribenzamine and Benadryl on Chick Embryo and on Vascular Phenomenon Induced by Normal Serum.

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During the last few years extensive studies have been carried out on the toxic, antihistaminic and antianaphylactic properties of pyribenzamine, benadryl and related compounds. Data on the effects of antihistaminic drugs on the chick embryo and upon the inverted anaphylactic shock induced by Forssman antibodies are presented in this communication.

Material and Methods. Fertilized chicken

eggs were incubated at 42°C for 3 days. The eggs were removed from the shell, placed in a glass beaker (150 ml), and kept at 37°C. The vascular phenomenon was induced by the addition of normal rabbit serum, as described by Witebsky and associates.[1,2]

Pyribenzamine hydrochloride (N'pyridil-N'benzyl-N-dimethylethylenediamine HCl) was supplied by Ciba Pharmaceutical Products, Inc. through the courtesy of Dr. F. L. Mohr; benadryl hydrochloride (β-dimethylaminoethyl benzohydryl ether HCl) by Mr. F. H. Nelden of Parke, Davis and Co.; hetramine (N,N-dimethyl-N'benzyl-N' [α-pyrimidyl] ethylene-diamine) by Dr. John V. Scudi of the Pyridium Corp. The drugs were dissolved in buffer solution (pH 7.4) prepared with Na_2HPO_4 and KH_2PO_4.

Experimental. A representative experiment illustrating the toxic effects of pyribenzamine and benadryl upon the embryonated chick ensues. Decreasing amounts of the drugs (volume 1 ml) were slowly dropped on the chick embryo; 4 eggs were used for each concentration. Both pyribenzamine and benadryl in amounts of 2.5 mg caused almost immediate bradycardia, followed within 2 minutes by stoppage of the heart beat and death of the embryo. In some instances, hemorrhages appeared in the embryo or in the vascular network. In smaller amounts (1.25 mg and 1 mg) both compounds caused bradycardia and apparent stoppage of the heart beat. Often, complete recovery took place after a lapse of several hours. Hemorrhages were noted only occasionally. Addition of the drugs in amounts of 0.5 mg and 1 mg resulted in bradycardia and only rarely in transitory stoppage of the heart beat. In yet smaller amounts (0.1 mg to 0.0001 mg) the compounds did not cause any visible changes. Hetramine,[3] another antihistaminic compound, too, caused transitory bradycardia or stoppage of the heart beat, depending upon the amounts used.

The vascular phenomenon, which was studied in detail by Witebsky and co-workers,[1,2] is due to the reaction between the Forssman antigen of the chick embryo and the corresponding antibodies. It resembles closely the inverted anaphylactic shock. In view of the relationship between true anaphylaxis and histamine poisoning, it seemed of interest to determine whether or not antihistaminic compounds affect the inverted anaphylactic shock of the embryonated chick. However, since histamine even in large amounts (up to 50 mg of histamine diphosphate) has no effect upon the 3-day-old chick embryo, it can be postulated that the antihistaminic compounds do not prevent the vascular phenomenon. That this is actually the case has been shown in numerous experiments, in which nontoxic doses of pyribenzamine and benadryl, administered prior to or concomitant with Forssman antibodies (normal rabbit serum), failed to prevent the vascular phenomenon.

Discussion and Summary. The experiments reported here revealed that the antihistaminic compounds pyribenzamine, benadryl and hetramine in the 3-day-old chick embryo cause bradycardia, stoppage of the heart beat and occasionally hemorrhages. It appears likely that the chick embryo can be used to advantage in studies on the relative toxicity of various antihistaminic compounds. The drugs do not prevent the inverted anaphylactic shock, which is due to factors other than histamine.

[1] Baumann, A., and Witebsky, E., *Ann. Inst. Pasteur*, 1934, **53**, 282.

[2] Witebsky, E., and Neter, E., *J. Exp. Med.*, 1935, **61**, 489.

[3] Feinstone, W. H., Williams, R. D., and Rubin, B., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 158.