TABLE IV (Series 3).
Effect of Lyophilized Yeast and Liver Concentrate upon Growth of Chicks.

Supplement level	%	Avg daily gain (%) — Without aureomycin: Exp. 10	Exp. 11	Exp. 12	Avg	Plus aureomycin: Exp. 10	Exp. 11	Exp. 12	Avg
0		6.28	6.12	6.03	6.14	6.45	6.34	6.17	6.32
Lyophilized yeast	2	6.32	6.40	5.94	6.22	6.44	6.40	6.39	6.41
Liver concentrated	.5	6.48	6.37	6.22	6.36	6.59	6.49	6.35	6.48
Lyophilized yeast + liver concentrate	2 .5	6.24	6.50	6.28	6.34	6.36	6.35	6.21	6.31

Least difference for significance at 5% level, .21 and at 1% level, .30.

TABLE V (Series 4). Effect of Antibiotic and Yeast Supplements upon Growth of Poults.

Supplement	Level	Avg of ♂ and ♀ gains (g) Exp. 13	Exp. 14
0		434	659
Streptomycin	50 mg/kg	464	
Procaine penicillin	50 "	538	669
Yeast E-16	1%	433	640
Streptomycin + yeast E-16	50 mg/kg 1%	502	
No./group		17	13
Duration, days		28	31

duced gains equal to aureomycin and terramycin. The level of streptomycin used here should have been adequate to give its maximum growth response.

The few strains of yeast isolated for these trials represent only a minute segment of the total microbial population; hence the present study does not provide conclusive evidence that alterations in the yeast or other microbial flora are not responsible for the antibiotic growth increase.

Summary. A 5- to 10-fold increase was noted in the yeast population of the intestinal contents of turkey poults when they were fed a ration containing streptomycin. When the yeasts were isolated and fed to other poults and chicks there was no consistent increase in growth, although very slight increases were noted in some trials. The growth increase observed with the feeding of antibiotics apparently cannot be simulated by feeding the particular strains of yeast isolated.

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Induction of Precocious Opening of Immature Rat Vagina with Neostigmine.* (19862)

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It has been possible to affect the genital cycle of adult polyestrous animals and to re-establish function in senile females by various drugs which act on the autonomic nervous system, but it has been generally held that the ovaries of immature rats or mice cannot

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be influenced in this manner(1-4). This report deals with the induction of precocious ovarian activity with consequent opening of the vaginal introitus of immature rats following the administration of the parasympathetic stimulant neostigmine.

Methods. A total of 106 immature rats of the Sprague-Dawley strain were employed. A group of 23 normal untreated animals in the colony were observed for the day of spontaneous vaginal opening. Twenty-eight rats 21 days of age at the beginning of the experiment received 0.5 cc (.025 g) of a solution of neostigmine (Prostigmine-Hoffmann-La Roche) subcutaneously 3 times daily, except on intervening Sundays, and were sacrificed in small groups at various times from age 26 to 56 days; a control group of 30 were similarly treated using plain water for injection. Five rats age 21 days, with 5 controls, were given injections of the same dose of neostigmine twice daily for 20 days. Six rats were castrated at age 21 days and injected 3 times daily for 15 days with neostigmine. The hypophysectomized animals were of the same strain but were obtained from a commercial laboratory. They were operated upon on day 21, and injections were begun at 30 days of age. An attempt was made to give the same high dosage of neostigmine but this was impossible owing to toxic effects and they actually only received a total equivalent to 2 injections of .025 g daily. Of these hypophysectomized rats only 3 experimental and 6 control survived treatment for 16 days. In all experiments body, uterine and ovarian weights were recorded at autopsy. The ovaries, uteri, and vaginas were fixed in Bouin's solution for section and microscopic examination.

Results. The 23 untreated animals of our colony showed that vaginal opening normally occurs at from 37 to 45 days inclusive, with 41 days as the mean.

The effect on vaginal opening of the injection of neostigmine 3 times daily as described above, is shown in the accompanying illustration (Fig. 1). Except for 4 rats autopsied at 26 days, the vaginas of all the experimental animals opened at times varying from 29 to 35 days. The vaginas of 18 control rats autopsied before age 36 days were closed, and

Age	Expt'l	Controls
41		oo
40		
39		oo
38		oo
37		oooooo
36		
35	o	xxxxxx
34	oooo	xxx
33	oooo	xxx
32		
31		x
30	oooooooo	
29	ooooooo	
28		
27		
26	xxxx	xxxxx
25		

o=Day vaginal opening
x=Closed at autopsy

FIG. 1. Each symbol (○ or ×) represents one animal. Vaginal opening occurred at 29 to 35 days of age in all the experimental animals except those autopsied at 26 days. In the control group vaginal opening was noted at from 37 to 41 days of age.

opening did not occur until 37 to 41 days in the 12 observed for longer periods of time.

The toxic effect of neostigmine was apparent in lesser body weight, and ovarian weights were also less except in the rats observed long enough for cyclic ovarian function to have become established. The histologic examination of the ovaries of the experimental rats did not show any abnormal picture, but in the group under 35 days of age with opened vaginas a more advanced stage of ovarian development over the controls was discernible. This was seen in the presence of larger and more mature follicles, luteinization, and a marked development and hypertrophy of interstitial tissue both of thecal and germinal epithelial origin.

The importance of the dosage of neostigmine required for this effect is seen in the fact that the vaginas of the rats injected only twice daily opened one day later (39 days) than those of their controls. Also of interest, if not significant, is the observation that 2 Sundays with no injections intervened in the group with vaginal opening at 33 days, and with those at 34 and 35 days there was a long holiday weekend, again with a diminution in the number of injections. On the other

hand, only one Sunday intervened in the groups with vaginal opening at 29 and 30 days.

The necessary involvement of ovarian function to produce vaginal opening is indicated not only by the histological findings given above but by the fact that it was not achieved after 15 days of treatment 3 times daily in 6 immature castrates.

Since it was not possible to give adequate amounts of neostigmine to the hypophysectomized rats used in this study, the question of anterior pituitary involvement in this regard remains unsettled. Other workers(5), however, have been able to stimulate ovarian function in normal adults by direct application of this drug to the hypophysis.

Summary. The daily subcutaneous administration of adequate doses of neostigmine to immature rats has resulted in a premature development of ovarian function with a precocious opening of the vagina.

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Plasma "Thrombocytopenic Factor" as Measured by Direct and Indirect Platelet Methods.* (19863)

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A prompt decrease in the blood platelets as measured by the indirect method occurred in 8 of 10 human subjects following the intravenous administration of normal human plasma. However, no decrease was observed when the platelets were evaluated by the direct citrate method.

Harrington *et al.*(1) demonstrated a "thrombocytopenic factor" in the blood and plasma of patients with idiopathic thrombocytopenic purpura (ITP) but observed no such effect of normal whole blood. Stefanini and Chatterjea(2) reported a temporary but significant decrease in platelets in 32 of 36 subjects when compatible blood plasma or serum from non-thrombocytopenic donors was transfused. These investigators measured the platelets by the indirect method of Dameshek(3). We previously confirmed the observations of Harrington *et al.* as to the thrombocytopenic effect of plasma from subjects with ITP as measured by the indirect method but observed no decrease in platelets as measured by the direct citrate method(4). The effect of normal plasma was not studied.

Materials and methods. Fresh pooled normal plasma was obtained from the blood of normal donors. The blood was collected in acid citrate dextrose solution. Irradiated pooled human plasma was obtained commercially in the lyophilized state. Dextrose solution, 5% in H_2O, was used as a control to be certain that the platelet decrease was not due to a speed-shock reaction. See Table I for recipient data. No transfusion reactions occurred. All intravenous fluids were administered within 30 minutes. Platelets were counted at intervals (Fig. 1, 2) by the direct citrate method of Rees and Ecker(5) and the indirect method of Dameshek(3). The following platelet levels were considered normal: Rees and Ecker method, 225000 to 350000 per cu mm; Dameshek method, 500000 to 900000 per cu mm.

Results. a) *Effect of intravenous 5% dextrose in H_2O.* The two subjects were observed. There was no effect on the platelet levels as measured by either the direct or indirect methods.

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