TABLE I.
Relation Between Resistance to Penicillin and Production of an Inhibitor.
A. Strains Developing Resistance to Penicillin in the Human Body.

Strain	Parent strains (Control)		Resistant variant-strains	
	Oxford units penicillin per cc inhibiting growth	Presence or absence of penicillin inhibitor	Oxford units penicillin per cc inhibiting growth	Presence or absence of penicillin inhibitor
22J	0.05	Absent	1.0	Present
23B	0.05	"	2.0	"
Long	0.05	"	1.0	"
Eden	0.1	"	0.8	"
B. Strains Developing Resistance to Penicillin *in vitro*.				
Rutgers	0.2	Absent	40.	Absent
Ked	0.2	"	200.	"
Nelson	0.2	"	10.	"
Eden II	0.2	"	20.	"

of commercial penicillin in culture medium containing a standardized inoculum of penicillin-sensitive staphylococci. After incubation at 37°C for 48 hours, the presence or absence of viable bacteria was determined by culturing the contents of each tube on blood agar plates.

Results. In Table I is presented a summary of findings concerning the presence or absence of penicillin inhibitor in the extracted organisms of the 16 strains of staphylococcus studied. The significant feature is that an inhibitor of penicillin was obtained only from those 4 strains which had developed resistance to penicillin in the human body. No penicillin inhibitor was demonstrated in the dried, extracted bacteria of the remaining 12 strains even in a concentration of 1 mg of the dried bacteria per cc of penicillin solution. The extracted bacteria of strains which yielded inhibitor produced varying degrees of penicillin inactivation. The penicillin-resistant strain 23B produced the most potent inhibitor. A concentration of 0.1 mg of dried bacteria inhibited the action of 400 units of sodium penicillin per cc.

Summary. Strains of staphylococci which have developed resistance to penicillin in the human body yield an inhibitor for penicillin. Penicillin inhibitor was not present in 4 strains which had been made highly resistant by exposure *in vitro*. Resistance developed *in vivo* was found, among the strains tested, to be a more permanent characteristic of staphylococci than that acquired *in vitro*.

15028 P

Effect of Pituitary Implants and of Estradiol on Newly Metamorphosed Frogs, *Rana pipiens*.

S. SCHREIBER AND R. RUGH.

From the Washington Square College of Arts and Science, New York University, N. Y. City.

Primary and secondary sex organs respond markedly to treatment with hormones. It has been shown that the treatment of some immature salamanders with pituitary extracts results in marked testicular hypertrophy and increased spermatogenesis.[1] Also, other experiments have demonstrated that some estro-

[1] Burns, R. K., and Buyse, A., *J. Exp. Zool.*, 1934, 67.

genic substances cause increased growth of Mullerian ducts in the male and oviducts in female amphibians.[2]

In the preliminary experiments reported in this paper, newly metamorphosed and laboratory raised *Rana pipiens* were divided into 3 groups, one implanted with pituitaries, the second injected with estradiol, and the third constituting the controls. Both sexes were used. Whole pituitaries taken from adult preovulating female frogs were implanted subcutaneously 3 times weekly in the experimental animals. Each of the estradiol group of young frogs received .03 mg of estradiol, dissolved in sesame oil, per week, and the injections were intraperitoneal. The controls consisted of untreated, newly metamorphosed frogs, and some injected with sesame oil equivalent in amount to the experimental animals. Experimentals and controls were killed and the tissues fixed weekly up until 4 weeks after the initial treatment.

The gonads of the pituitary-treated animals showed marked growth, the testes becoming 5 to 10 times, and the ovaries 2 to 4 times the size of the corresponding controls. Histological observations demonstrated an increase of spermatogenesis in the treated males with the production of primary and secondary spermatocytes and some spermatids and the formation of well developed and enlarged seminiferous tubules. The tubules in the animals 1-2 weeks, after the initial treatment, were in most cases filled with the products of spermatogenesis, but those in the older animals were even more enlarged and practically empty, showing that the contents of the tubules had been forced out of the testes. No gross or microscopic effect was observed on the male Mullerian ducts.

The male controls showed slight seminiferous tubule formation, but these tubules were very small and in all cases were full of spermatogonia and some primary spermatocytes, but contained very few if any secondary spermatocytes and no spermatids. No mature spermatozoa were found in any of the experimentals or controls during the month following metamorphosis.

The ovaries of the pituitary-treated females were enlarged to 2 or 3 large lobes, while no more than one or 2 very small lobes were found in any of the controls. The oöcytes of these enlarged ovaries were slightly larger than those in the control ovaries. Both the experimental and control females had open oviducts, but these were minute, and the experimentals were only very slightly larger than controls.

Neither testes nor ovaries of the estradiol-treated animals showed any differences from the controls, but the estradiol-treated frogs showed a decided hypertrophy of the oviducts of the female and the Mullerian ducts of the male 8-10 days following initial injection. In all observed cases, both the Mullerian ducts and the oviducts were larger at the posterior ends. Sections of these ducts, 4 weeks after initial injection, showed large open tubules lined with columnar, granulated epithelium.

The controls, fixed at the same ages as the experimentals, showed very little growth, if any, of either the Mullerian ducts or oviducts. The Mullerian ducts of the 4-week-old control male and the oviducts of corresponding females were very thin and hardly visible strands. When sectioned, the Mullerian ducts appeared to very minute, closed circles of undifferentiated cells. Open oviducts were present in the female controls, but these were also extremely small and consisted of undifferentiated cells.

Summary. The ovaries and testes of recently metamorphosed frogs (*Rana pipiens*) responded by rapid growth and the testes also by cellular differentiation when the animals were treated with whole pituitary glands from mature females of the same species. Estradiol had no effect on the gonads but, in contrast with the pituitary hormone, estradiol brought about hypertrophy of both the oviducts and Mullerian ducts, causing the latter to simulate functional oviducts.

[2] Foote, C. L., *Anat. Rec.*, 1939, **72**, suppl.; Puckett, W. O., *Anat. Rec.*, 1940, **75**, 127, suppl.; Eversole, W. J., and D'Angelo, S. A., *J. Exp. Zool.*, 1943, **92**, 215; Saunders, G. S., and Rugh, R., *J. Exp. Zool.*, 1944, **95**, 5; Glass, F. M., and Rugh, R., *J. Morph.*, 1944, **74**, 3; Adams, E. A., *Anat. Rec.*, 1945, **91**, 4, suppl.