TABLE I. Sensitivity of *Staphylococcus aureus* to Penicillin in Casein Hydrolysate Media Containing Various Carbohydrates.*

	Acetic acid	Lactic acid	Pyruvic acid	Glucose	Nutrient broth	Casein hydrolysate, no carbohydrate (control)
Autoclaved medium	.15†	.2	.025	.1	.025	>.2
Seitz filtered medium	.15	.2	.05	.1	.025	>.2

* Results were read after 96 hr of incubation at 37°C.
† Maximal concentration of penicillin (u/cc) in which growth appeared.

penicillin may be affected by the carbon source of the medium. Similar findings were reported for *E. coli*(14) which was found to be more sensitive to penicillin in the presence of xylose or ribose than with glucose.

Summary. The effect of the composition of the medium on the sensitivity of *Staphylococcus aureus* to penicillin was tested. Pyruvic acid or glucose, when added to a casein hydrolysate medium, increase the antibacterial effect of the antibiotic. Lactic or acetic acids, on the other hand, have no such effect. The possible mechanisms of the enhanced penicillin activity in presence of pyruvic acid are discussed.

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Metabolic Studies of Desaminothyroxine. (22682)

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Desaminothyroxine (3,5 diiodo-4 (3', 5', diiodo-4 hydroxy phenoxy) phenyl-propionic acid) was synthesized by Clayton, *et al.*(1) at the Glaxo Laboratories, Middlesex, England, and by Kharasch *et al.** at the University of Southern California.

Bruice, Winzler and Kharasch(2) reported that in tadpoles (*Rana catesbiana*) at about 24°C, desaminothyroxine possesses 130 times the metamorphosing activity of L-thyroxine. Roth(3) has recently reported that it has 1000 times the activity of L-thyroxine in this test at 16°C. In comparison, Roche(4) has shown desaminothyroxine to have about 75% the antigoitrogenic activity of D-L-thyroxine in rats. Selenkow and Asper(5) reported it to have only 20 to 25% the antigoitrogenic activity of L-thyroxine. No reports on its calorigenic activity in mammals have been found.

* Personal communication.

Method. Measurements of the oxygen consumption of rats were conducted in a 5-unit basal metabolic rate machine at 30°C(6). Individual studies usually lasted 4½ hours, using the first half-hour as a calibration pe-

TABLE I. Comparison of O_2 Consumption of Desaminothyroxine on Na L-Thyroxine.

Drug	Body wt, g	Initial body wt, baseline	O_2 consumption (g O_2/100 g rat/hr) 3 days	7 days	10 days	Avg increase O_2 consumption at 10 days (g O_2 /100 g/rat/hr)
		A. Dosage—.025 mg/day				
Desaminothyroxine	210 ± 50	.141	.155	.172	.186	.045
Na L-thyroxine	200 ± 30	.143	.201	.214	.218	.075
Controls	195 ± 25	.136	.127	.138	.144	
		B. Dosage—.075 mg/day				
Desaminothyroxine	215 ± 55	.141	.161	.158	.194	.053
Na L-thyroxine	200 ± 30	.143	.230	.262	.275	.132
Controls	190 ± 10	.135	.135	.135	.143	

riod on rats fasted 24 hours. Four control runs were performed on each of 10 Long-Evans rats, weighing 160 to 230 g. The average oxygen consumption was .142 g O_2/100 g rat, per hour. The studies were carried out under conditions similar to those obtained by other investigators(8). Each animal acted as its own control and another control animal was evaluated with each group to check the variations of the machine. Four rats were injected intraperitoneally with coded Na-L-thyroxine, 0.025 mg/day; and four rats were given intraperitoneal injections of desaminothyroxine, 0.025 mg per day, in a double blind procedure. Individual studies were made at 3- to 4-day intervals for 2 weeks, reaching maximum oxygen consumption at 10 days. At this dosage the desaminothyroxine was found to be 60% as active as L-thyroxine, measured by the increase of oxygen consumption computed as grams of oxygen per 100 g of rat/hour. The 2 groups were then injected intraperitoneally with 0.075 mg daily, per rat, of desaminothyroxine, or L-thyroxine, for 2 weeks under the double-blind procedure. After 10 days on the tripled dosage, desaminothyroxine had only 40% the oxygen consumption of L-thyroxine. It was also noted that this drug produced only a 40% increase of oxygen above the control level, as compared to a 100% increase produced by L-thyroxine. (Table I).

Results. In trial studies at dosages of 0.15 and 0.30 mg daily/rat, desaminothyroxine was shown to have about 30% the calorigenic activity.

All animals returned to the pretreatment oxygen consumption levels after cessation of the drugs. No toxic signs or symptoms were noted during the one month course of drug administration, or in the one month following cessation of the medications. One rat died because of machine failure. The observation of Freinkel, *et al.*(9) of the marked absorption of thyroxine by glassware was confirmed. All drug containers were siliconized.

Discussion. The results, though variable with respect to the dosage, show that the metabolic effect of desaminothyroxine is of the same magnitude as that found in studies of its antigoitrogenic activity. In this respect the drug is less potent than L-thyroxine, but in comparison with the process of metamorphosis in amphibians, there is a wide variance (130 times more potency than Na L-thyroxine at 24°C(3) to 1000 times at 16°C)(4). These effects suggest the multiple activities of these drugs; perhaps separate or multiple metabolic pathways are involved.

Summary. Desaminothyroxine was shown to have 60% of the calorigenic activity of L-thyroxine at dosages of 0.025 mg/rat/day; 40% at the dosage of 0.075 mg/rat/day; and about 30% at dosages of 0.150 and 0.300 mg/rat day.

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Inhibitory Effect of Chlorpromazine on Arterial Lipid Deposition in Cholesterol Fed Rabbits.* (22683)

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Reduced arterial lipid deposition in cholesterol fed rabbits has been achieved in a number of ways(1). Most of these inhibitory procedures cause weight loss, debilitation or other injurious effects. Chlorpromazine can be administered to animals for long periods of time without causing apparent impairment of health. Nevertheless, it is said to depress cellular activity, lower body temperature and arterial blood pressure, and, possibly, lower oxygen consumption of tissues(2). It is therefore reasonable to assume that this drug might alter cholesterol metabolism and influence the usual responses of rabbits to cholesterol feeding. The present experiment was designed to study the effect of chlorpromazine in this connection.

Method. Twenty-four albino rabbits weighing from 1810 to 2320 g initially were used. Nine received daily, 10 mg/kg intramuscular injections of chlorpromazine (Thorazine hydrochloride; Smith, Kline and French Laboratories)† and were fed rabbit food pellets containing 1% cholesterol(3). Nine rabbits were given equivalent injections of chlorpromazine but were fed the stock diet without added cholesterol. Six rabbits received only the cholesterol diet. The animals were given a daily ration of 100 g and food consumption was recorded daily. Body weights were determined every other week. Blood (9-10 cc) was drawn by ear vein initially and at the end of the 1st, 3rd, 6th, and 9th weeks. Free and esterified cholesterol, phospholipid, total lipid, proteins and sugar were determined on the serum as described previously(3). Determinations of serum bilirubin (Evelyn and Malloy) were also attempted but the levels were always too low to obtain quantitative readings. All animals survived and were sacrificed at the end of the tenth week. Complete gross and microscopic studies of the viscera were performed. The aortas were stained grossly with Sudan IV and the distribution of lipid plaques charted as previously described(3).

Results. Blood chemistry: Cholesterol levels rose progressively in all cholesterol fed animals but by the end of the third week it was apparent that the chlorpromazine group had significantly lower values (Table I). At the ninth week the total cholesterol of this group was only about one-half as high (Mean 985, Max. 1368, Min. 760 mg/%) as that of those fed the 1% cholesterol diet only (Mean 1834, Max. 2166, Min. 1535 mg/%). The ratio of free to esterified cholesterol did not change significantly in either group. Total cholesterol rose slightly and transiently in 8 of 9 chlorpromazine rabbits on stock diet reaching its peak during the third week. In these 8 rabbits the mean cholesterol was 322 mg/% (Max. 457, Min. 234). No explanation can be given for the failure of the 9th rabbit to show this change. It fell in all 8 to a mean level of 157 mg/% by the sixth week and was within normal limits at the ninth week. The free and ester fraction ratios were not altered during this temporary rise.

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