tempt to induce "tolerance." Skin grafting experiments demonstrated that both males and females so treated did acquire a slight degree of tolerance. When the partially tolerant female mice were used as donors or hosts in homologous bone marrow transplantation experiments (with the opposite strain), the date of appearance of the secondary disease was delayed, an effect attributable to acquired tolerance. However, when partially tolerant males were used, survival did not increase, but actually decreased. The animals died in a very short time, as if hypersensitized. It has been proposed that the "tolerant" animals are chimeras; if so, the male animals may contain female cells already hypersensitized against "male," and these "hypersensitized" cells may be responsible for the short survival.

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A Goitrogenic Rat Diet Producing Normal Body Weight Gain.* (27037)

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The first demonstration of low iodine goiter in the rat was reported by Levine, Remington and Von Kolnitz(1), and the diet they designed is, with minor modifications, still in general use today and has come to be known as the Remington diet. Attempts to improve the slow rate of body weight gain produced by this diet by adding animal proteins(2) have shown that such additions reduced the goitrogenic effect of the diet, making it less suitable for use in experimental goiter studies. Thus Parker *et al.*(3) observed good growth in rats fed a diet similar to the Remington diet with addition of DL-methionine, dried beef and "animal protein factor," but only the second generation of animals showed substantial thyroid enlargement, whereas growing rats consuming the standard Remington diet consistently develop goiter in 5 weeks.

The present paper describes a new low iodine goitrogenic rat diet, formulated without animal proteins, that supports a normal rate of body weight gain.

Materials and Methods. Brewers type dry

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yeast (iodine 0.06 μg/g) at 40% by weight of the diet, supplemented with DL-methionine at 0.5% by weight of the diet, was employed as the principal protein source in the diet coded YST in Table 1. To provide comparisons with a low iodine semipurified diet containing an animal protein, the diet coded CAS in Table 1 was designed to contain casein at a level of 20% by weight. The remaining ingredients of these diets are listed in the table footnotes.

The Remington diet (code REM) was also included in the experiment. The formula employed was the standard one(2), modified only to include a complete vitamin mixture, in order to match diets YST and CAS in this regard. Finally, a commercial rat chow (coded PUR) was fed to provide data from "normal" animals. Thus 3 low iodine diets of known composition, one containing an animal protein, were fed in parallel with a widely used rat chow whose quantitative composition is not revealed but which contains a variety of animal proteins and an ample amount of iodine.

Male albino rats, descendants of the Sprague-Dawley strain, were weaned at 3 weeks of age, when their body weights ranged from 45 to 55 g, and averaged close to 50 g. The rats were held in separate cages with wire mesh bottoms, were provided *ad libitum* with demineralized water from an ion exchange column, and were fed one of the 4 experimental diets *ad libitum* for 7 weeks, while records of individual food intake and body weights were kept. Then the animals were killed, and the fresh weights of their thyroid glands determined using an analytical balance. Iodine in diets and in thyroid glands was determined by the method of Chaney(4).

Results. In Table 1, the weight gained by the rats fed the commercial chow may be taken as "normal." The Remington diet supported, as expected, about half the normal rate of body weight gain. The 2 semipurified diets YST and CAS, to the contrary, produced approximately normal rates of gain.

Goitrogenic effects may be judged by comparing thyroid gland/body weights, and also by comparing iodine contents of the pooled thyroid glands. The data shown for animals fed the Remington diet are concordant with prior publications(5), and may be taken as representative values for simple low iodine goiter in this species. The thyroid gland data from rats fed the commercial chow may be taken as "normal," since they agree with prior values for this sex and strain of rat fed diets adequate in all nutrients including iodine(6).

Thus all 3 low iodine diets produced enlarged thyroid glands with lowered iodine contents. Within the limitations of the iodine assay methods at this low level(7), diet CAS had about the same low iodine content as diet REM; but the animals fed diet CAS nevertheless had significantly smaller thyroids ($P = .025$), containing 3 times as much iodine, as rats fed diet REM. That this effect was due to the casein content of the diet CAS is suggested by numerous uncontroverted reports that ca-

TABLE I. Effects on Thyroid Parameters of Various Diets Fed Ad Libitum to Male Sprague-Dawley Strain Rats* for 7 Weeks Starting at 3 weeks of age. Average Values.

	DIET CODES†			
	YST	*REM*	*CAS*	*PUR*‡
No. of Rats	6	10	10	9
Iodine in Diet, μg/g	.03	.001	.009	2
Food Consumed, g	672	636	868	§
Wt Gained, g	213	117	245	227
Thyroid :Avg	25.2	19.3	15.3	7.6
Wt :	—	—	—	—
mg/100 g: St. Dev.	5.6	4.5	2.5	.8
Iodine in Pooled Thyroids, % of Dry wt	.0043	.0097	.0300	.2000

* Purchased from S & K Animal Co., Jamesburg, N. J.

† Ingredients of diets in % by weight: Diet *YST;* ground whole yellow corn 45.3, dry brewers type (Fleischmann's 50B) yeast 40, corn oil 8, salt mixture (USP XIII No. 2) 4, complete vitamin mixture triturated in dextrose (Nutritional Biochemicals Corp.) 2.2, DL-methionine 0.5. Diet *REM;* corn 75.8, wheat gluten 18, dry yeast 2, calcium carbonate 1, sodium chloride 1, vitamin mixture 2.2. Diet *CAS;* purified casein 20, corn starch 47.8, cellulose 14, corn oil 12, salt mixture 4, vitamin mixture 2.2.

‡ Purina Laboratory Chow, Ralston Purina Co., St. Louis Mo. § Not recorded.

sein has antigoitrogenic properties(8). Precisely the reverse may be seen for the data from rats fed diet YST. Their mean thyroid weight was significantly greater than those of rats fed diet REM ($P = .05$). Furthermore, their thyroid iodine content was only half as great as those of animals fed diet REM. Thus the low iodine 40% yeast diet, which had supported normal growth, did not exert an antigoitrogenic effect as do low iodine casein diets such as diet CAS. Indeed in this experiment diet YST had a significantly positive goitrogenic effect, over and above that to be expected from its low iodine content.

Discussion. Dry yeast has been used frequently in experimental animal diets, but rarely if ever at levels as high as the 40% employed in this study. This high level of yeast, together with supplementation with methionine, enabled diet YST in the present study to support a rate of gain in body weight similar to that supported by a standard laboratory rat chow or a semipurified diet based on casein. As the dry yeast had a low iodine content (0.06 μg/g), it was possible to use it in a low iodine diet. Furthermore, as seen in this study, the yeast did not have an "antigoitrogenic" effect aside from its iodine content, such as has been attributed to animal proteins like casein.

Hence diet YST, or similar ones, may prove useful in experimental goiter studies with the rat. The literature on dietary goitrogenesis does not clarify the apparent positive goitrogenic effect, over and above that attributable to low iodine content, seen with diet YST in this study.

Summary. By using 40% of brewers type dry yeast as the principal protein source, a low iodine diet has been designed that supports a good rate of body weight gain and also produces large goiters in rats. This diet appears to have a positive goitrogenic effect, over and above that attributable to its low iodine content.

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Effect of Dilantin Sodium on Various Cell Lines in Tissue Culture.* (27038)

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Previous studies from this laboratory(1,2) have clearly shown the dramatic stimulatory effects of sodium 5,5 diphenylhydantoin (Dilantin Sodium) and certain related analogues on the growth of a human gingival fibroblast-like cell in tissue culture. This property is consistent with the Dilantin-induced stimulation of wound healing in rats as judged by increased tensile strength also reported by this laboratory(3) and with well-known gingival hyperplasia occurring in epileptic patients under treatment with this drug. During these studies, it was found that the HeLa cell in tissue culture responded to Dilantin by a very limited stimulation of proliferation but there was no significant stimulation of cells isolated from rat fibrosarcoma. This variability of cell response suggested that this stimulatory effect of Dilantin might be quite cell-specific and, for this reason, a series of different cell lines carried in this laboratory have been tested.

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Materials and Methods. Two general types of cell lines have been tested: those isolated from 1) normal tissue and 2) tumor tissue (Table