allowed to stand at room temperature for 30 minutes. Two hundredths cubic centimeters of each mixture was then injected intracutaneously into the skin of the rabbit within the previously marked squares.

Interpretation of Neutralization Test. Human sera produced erythema in the rabbit's skin within 24 hours, but the zone of redness disappeared by the third or fourth day. The lesions produced by Toxoplasma appeared by the end of the fifth day and consisted of maculopapular eruptions surrounded by a zone of erythema. By the eighth day the lesions resulting from the larger concentrations of organisms underwent central necrosis and the results were determined on the ninth day. Each lesion was accurately measured, drawn on transparent paper and described. Careful records were kept of the time of disappearance of the erythema, the appearance of the toxoplasmic lesions and the interval to the production of necrosis, to evaluate any individual variations in the type of reaction on different rabbits. By the fourteenth day the lesions produced by the more dilute mixtures began to blanch and the necrotic lesions became encrusted. The animals usually died by the twenty-first day. Any reactions which could not be interpreted as conclusive were repeated on other animals.

Results. The serum of 2 individuals prevented the production of necrotic lesions in the skin of rabbits. These 2 persons were residents of the St. Louis area and had lived in this vicinity all their lives. Careful physical examinations were performed and were entirely negative. Examination of the eye grounds showed no pathologic lesions. A complete medical history was taken and no history of present or past illness was obtained that might be interpreted as a toxoplasmic infection. Both individuals were unmarried girls of 18 and 21 years respectively. No positive tests were obtained from the group of unmarried non-residents, the married women, or from any of the men tested in this series.

Conclusions. The sera of 2.7% of the individuals in the St. Louis area that were tested showed the presence of a definite inhibitory factor on the necrotizing action of Toxoplasma in the skin of rabbits.

14986 P

Human Thyrotoxicosis: Response to Para-Aminobenzoic Acid.

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The use of thiourea and especially of thiouracil in the treatment of hyperthyroidism was first suggested by Astwood.[1] Apparently, these compounds prevent thyroid hormone synthesis and numerous papers[2] have appeared showing that they are effective in mild or moderately severe cases of thyrotoxicosis and in the preoperative preparation of patients for thyroidectomy.[3] The disagreeable taste of thiourea makes thiouracil the preferred therapeutic agent, although the latter has been demonstrated clinically to give untoward reactions, including agranulocytosis,[1] myxedema,[4] skin eruptions, fever, and jaundice.[5,6] Indeed, according to a most recent report,[7] "Thiouracil is an effective drug for the treatment of thyrotoxicosis. It is also an unpredictable toxic drug which may produce serious and uncontrollable effects, especially on the bone marrow and liver."

In view of the ever increasing clinical appli-

1 Astwood, E. B., *J. A. M. A.*, 1943, **122**, 78.

2 Editorial, *J. A. M. A.*, 1944, **126**, 172.

3 Bartels, E. C., *J. A. M. A.*, 1944, **125**, 24.

4 Rawson, R. W., Evans, R. D., Means, J. H., Peacock, W. C., Lehman, J., and Coctell, R. E., *J. Clin. Endo.*, 1944, **4**, 1.

5 Gabrilove, J. L., and Kert, M. J., *J. A. M. A.*, 1944, **124**, 504.

6 St. Johnston, C. R., *Lancet*, 1944, **2**, 42.

7 Gargill, S. L., and Lesses, M. F., *J. A. M. A.*, 1945, **127**, 890.

TABLE I.
PABA Treated Hyperthyroid Cases.

Case No.	Age in years, sex	PABA treatment	Observation, Mo.	Weight (kg)	Pulse per min.	Blood pressure, mm	Basal metabolic rate	Serum cholesterol, mg/100 ml	Symptom-free after withdrawal of drug, Mo.
1	34 ♀	½ g every other day 1 week, then 1½ g 6 times weekly 6 mo.	0	50	110-140	150/90	+42	116	15
			1	55	95-110	140/90	+28	125	
			3	60	90-100	135/85	+12	142	
			6	65	80	125/80	— 5	180	
2	48 ♂	1 g 6 times weekly 2 mo., then 1½ g 6 times weekly 4 mo.	0	57	120	130/55	+32	120	11
			2	57	105	130/65	+20	186	
			4	65	85	125/70	+16	202	
			6	69	75	125/80	+ 8	252	
3	18 ♀	1½ g 6 times weekly 9 mo.	0	45	120-150	110/45	+48	95	6
			2	48	100-110	135/70	+25	132	
			4	53	95-105	130/75	+22	138	
			7	57	85-90	130/80	+15	150	
			9	63	80	120/80	+10	162	
4	28 ♀	1 g 6 times weekly 2 mo., then 1½ g 6 times weekly 3 mo.	0	49	120	140/65	+30	159	6
			2	54	100	140/70	+22	170	
			5	64	85	120/75	+ 8	225	
5	36 ♀	1 g 6 times weekly 3 mo., then 1½ g 6 times weekly 5 mo.	0	48	95-145	165/85	+45	170	4
			3	53	95-110	150/85	+32	195	
			5	60	95	145/85	+20	208	
			8	65	80	135/80	+10	252	
6	42 ♀	1 g 6 times weekly 2 mo., then 1½ g 6 times weekly 5 mo.	0	55	110-140	115/55	+36	158	6
			2	61	95-105	110/60	+22	175	
			4	69	85-95	115/70	+20	182	
			7	70	70	125/70	— 5	205	

cation of chemical substances in the treatment of toxic goiter, the results obtained with para-aminobenzoic acid (PABA) are deemed of value to the investigators and clinicians in the field. Although PABA had been investigated experimentally,[8] there have been no reports as to its use in human thyrotoxicosis. The present communication sketches 3 cases with some detail and gives numerical data obtained with 6 patients in tabular form.

My interest in the use of PABA for this purpose was aroused during the first half of 1943 when I began employing its sodium salt parenterally in large doses in the treatment of a case of vitiligo.[9] The patient was a 34-year-old woman (See Table I, Case 1-F.H.) who had lost about 10 kg in the course of a year. Because of a few small patches of vitiligo on her hands, she was given injections of ½ g of the sodium salt of PABA every other day for about one week and then 1½ g 6 times weekly. Her restlessness and nervousness subsided significantly after about 2 weeks of the daily therapy, then her sleeplessness improved with a concurrent gradual gain in weight. Her basal metabolic rate (BMR) had dropped from +42 to +28 by the end of the first month. It was +12 after 3 months and she had gained 10 kg in weight. At the end of ½ year of the treatment, the patient was discharged, her BMR was recorded as —5, her total weight gain was 15 kg and her serum cholesterol had risen from an initial 116 to 180 mg/100 ml. The patient was seen several times during the 15 months

[8] Astwood, E. B., *J. Pharm. and Exp. Therap.*, 1943, **78**, 79.

[9] Sieve, B. F., *Virg. Med. Mo.*, 1945, **72**, 6.

following withdrawal of PABA and no signs of recurrence of toxic goiter were observed.

Case 3 (M.R.) was first seen in October, 1943, complaining of swelling of the neck, extreme nervousness, heart palpitation, a peculiar feeling of constant, unmotivated anxiety and crying spells for a period of about a year. She showed a markedly enlarged thyroid with characteristic exophthalmos. Six months before, her BMR was +30 and thyroidectomy had been advised. She had refused surgery, but had taken intermittent rest cures, luminal, and iodine. Her weight had decreased gradually from 59 to 45 kg. Improvement in nervousness and sleep appeared after 3 weeks of PABA treatment, concurrent with a gradual gain in weight. After 9 months therapy, there was still some enlargement of the thyroid which had receded considerably. Nevertheless, the patient remained well and when seen again 6 months later, stated that she felt perfectly healthy and was working 8 hours daily as a secretary.

Case 5 (L.M.) was first seen in February, 1944. The patient stated that her illness had lasted about 8 months during which time she had lost 23 kg of weight, had attacks of palpitation and constant nervousness. She had been given daily injections of prostigmin in December, 1943, when her BMR had been found by a clinical laboratory to be +40. Subsequently, the palpitation and feeling of heart pounding had been somewhat relieved, but her general condition became even worse. Simultaneously with PABA therapy her weight increased and after 3 months the patient was able to go about her housework and to sleep well. At the end of 8 months treatment, the patient felt well and remained so for the following 4 months when she was last seen.

Table I summarizes the data obtained on the first 6 patients with thyrotoxicosis. PABA was always administered parenterally in form of its sodium salt and the effect of oral therapy is being determined. Seven additional hyperthyroid cases are at present under treatment. In none of the patients did untoward reactions ever occur, thus confirming the remarkably low toxicity of PABA observed in the treatment of typhus.[10]

It is not intended to offer any speculations as to the mode of action of PABA, but comparative experimental studies have been started with PABA, thiourea and thiouracil to demonstrate their respective roles in thyroid and pituitary activity. A change in intestinal flora, as a factor contributing to the beneficial results obtained, is a possibility in the light of Landy's analyses reported by Kornberg *et al.*[11] showing a 100-fold concentration of PABA in the cecum of rats treated parenterally with 50 mg of PABA per kg body weight, *i.e.*, approximately the same dosage given to the patients reported in the present communication.

Whatever the mode of action may be, PABA is a naturally occurring substance with a very favorable therapeutic index.[12] It was found to have definite beneficial effects in 6 cases of hyperthyroidism receiving its sodium salt parenterally.

[10] Yeomans, A., Snyder, J. C., Murray, E. S., Zarfonetis, C. J. D., and Ecke, R. S., *J. A. M. A.*, 1944, **126**, 349.

[11] Kornberg, A., Daft, F. H., and Sebrell, W. H., *J. Biol. Chem.*, 1944, **155**, 193.

[12] Ansbacher, S., *Vitamins and Hormones*, 1944, **2**, 215.