16310

Side Reactions to Pyribenzamine Medication.

SPENCER F. BROWN. (Introduced by W. R. Ingram.)

From the University of Iowa.

A number of recent publications have dealt with the use of the new anti-histaminic drugs, and more are appearing every month. Most of these articles mention various side effects encountered, but to date the author has seen no reports of controlled observations of such side effects. The following data regarding pyribenzamine may therefore be of interest.

All the patients who were studied were receiving injections of typhoid vaccine, and the effect of pyribenzamine upon their reactions to the vaccine will be reported elsewhere. At the time of administration of the vaccine, each patient was given either pyribenzamine (PBZ) tablets or indistinguishable placebos,* with instructions as to dosage. Forty-eight adults were on 100 occasions given five 50-mg PBZ tablets with instructions to take one tablet at once, one every 4 hours throughout the day, and one tablet the following morning. Forty-nine subjects were on 102 occasions given placebos with the same instructions. Thirty-seven subjects on 56 occasions were given ten 50-mg tablets of PBZ with instructions to take 2 tablets at a time instead of one. Each subject had a report sheet on which he was asked to indicate whether or not he had experienced any of the symptoms listed on the sheet. The accompanying table shows the percentage occurrence of the symptoms in the 3 groups of subjects.

TABLE I.
Percentage Occurrence of Side Effects.

Symptom	Five 50-mg PBZ tablets in 24 hr (N = 100)	Ten 50-mg PBZ tablets in 24 hr (N = 56)	Placebos, 5 in 24 hr (N = 102)
Drowsiness	37	48	30
Headache	26	36	42
Nausea	17	23	8
Dizziness	24	41	15
Nervousness	13	21	15
Dryness of mouth	29	45	30
Insomnia	12	23	6

* The pyribenzamine and placebos used were supplied by the Ciba Pharmaceutical Company, Summit, N.J.

These data indicate that the smaller dose of PBZ used here, which is the dose most frequently used in treating allergic conditions, has a negligible effect in producing the stated symptoms, all of which have been ascribed to PBZ medication. For example, drowsiness is the most commonly reported side reaction to PBZ, but the administration of 250 mg in 24 hours gave an incidence of drowsiness of only 37% as compared with 30% for placebo medication. The 2 patients who were bitter in their complaints of drowsiness both received placebos. Nausea, dizziness, and insomnia were somewhat more frequent in the 250 mg group as compared with the controls. Headache was less frequent, and nervousness and dryness of the mouth were apparently equally frequent in both groups. Doubling the dose of PBZ was accompanied by a definite increase in the incidence of symptoms, but headache was still less frequent than among the controls.

These data indicate the importance of using controlled studies in evaluating the side reactions, as well as the therapeutic effects, of a new drug.

Summary. A controlled study was made of side reactions to pyribenzamine. Five 50-mg tablets were given over a 24-hour period to 48 subjects; some subjects were used 2 or 3 times, and the total number of times the drug was given was 100. Placebos were given to 49 subjects a total of 102 times. The dosage of pyribenzamine was doubled in 37 other subjects on 56 occasions. Nervousness, dryness of the mouth, and headache were more frequent in the control group as compared with the smaller dose group of pyribenzamine. Drowsiness, nausea, dizzi-

ness and insomnia were less frequent in the control group. All side reactions mentioned occurred more frequently when the dose of pyribenzamine was doubled.

This study was prepared at Walter Reed General Hospital while the author was in the Army Medical Corps.

16311

Protective Action of Vitamins C and P Against Dichlorophenarsine Hydrochloride (Clorarsen).

FRANCES J. FRIEND AND A. C. IVY.

From the Department of Physiology, Northwestern University, and the Department of Clinical Science, University of Illinois, Chicago.

This study was undertaken specifically to ascertain whether the use of vitamins C and P in combination would protect against the acutely toxic effect of intravenously injected dichlorophenarsine hydrochloride in mice. It was thought that if these vitamins exerted a favorable effect on capillary fragility it might be demonstrated by the manifestation of a decrease in the acute toxicity of arsenic, since arsenic is a potent capillary poison.

The literature dealing with decreased capillary resistance as one of the toxic manifestations of antisyphilitic therapy has been reviewed by Horne and Scarborough.[1] The apparently protective action of vitamin C against the toxicity of arsenicals has been commented on by several groups of authors.[2,3,4] Scarborough and Stewart have reported that vitamin P (hesperidin) treatment increased capillary resistance in erythema and dermatitis due to arsenic and bismuth.[5]

Goldforb[6] suggested that the vitamin in the form of aqueous extracts of whole lemon might prevent arsenical encephalopathy in patients receiving intensive arsenical therapy. And, Goldstein, Stalman and Goldforb[7] found that treatment with the methyl chalcone of hesperidin decreased the mortality of a standard dose of mepharsen in rabbits from 90 to 57%, a difference that was of questionable significance ($X = 2.9$).

In a preliminary study on groups of control and treated mice (Table I), it was found that vitamin C alone (2.2 millimoles per millimole of dichlorophenophenarsine hydrochloride) had a favorable, but not statistically significant effect. The same was true when similar groups of mice were treated with hesperidin methyl chalcone alone (1 mg each daily for 9 days previous and 3 days following the injection of the arsenical).

For these reasons it was decided to investigate the protective effect of a combination of these two substances on the acute toxicity of a standard dose of intravenously administered dichlorophenarsine hydrochloride.

Method. Adult female white mice, weighing from 17 to 24 g (average weight, 21 g apiece in each group) maintained on a diet of Purina Checkers plus lettuce were used. Injections of dichlorophenarsine hydrochloride (clorarsen, Squibb) dissolved in saline were made into the tail vein, and all animals were observed for 3 days after injection, since those not

[1] Horne, G., and Scarborough, H., *Lancet*, 1940, **2**, 66.

[2] Sulzberger, M. B., and Oser, L. B., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 716.

[3] Bundesen, H. N., Aron, H. C. S., Greenbaum, R. S., Farmer, C. J., and Abt, A. F., *J. Am. Med. Assn.*, 1941, **117**, 1692.

[4] McChesney, E. W., Barlow, O. W., and Klinck, G. H., *J. Pharm. and Exp. Therap.*, 1944, **80**, 81.

[5] Scarborough, H., and Stewart, C. P., *Lancet*, 1938, **2**, 610.

[6] Goldforb, A. E., *Arch. Dermat. and Syph.*, 1941, **43**, 536.

[7] Goldstein, D. H., Stalman, A., and Goldforb, A. E., *Science*, 1943, **98**, 245.