THE YEAR BOOK *of* DRUG THERAPY

(1962-1963 YEAR BOOK *Series)*

WITH A SPECIAL SECTION ON

PRECAUTIONS

EDITED BY

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The designation *1962-1963 Series* is used in this volume to indicate publication during the "series year," which began in September, 1962.

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The designation *1962-1963 Series* is used in this volume to indicate publication during the "series year," which began in September, 1962.

INTRODUCTION

For the past several years there has appeared in the forward portion of this annual volume a "blue sheets" section entitled "New Drugs," in which were listed, with relevant comments, the recently introduced drugs likely to be promoted by their manufacturers to the majority of practitioners. There has been almost unanimous commendation of this section in formal reviews and private communications, but I have been dissatisfied with it nevertheless. Too many of the drugs listed were so new that little of a specifically helpful nature could be said of them; and in many instances space was occupied by consideration of agents unlikely to have widespread use, while many drugs, not so new but with important toxic potentialities, were not considered at all. So I decided to abandon the blue sheets and revamp the volume to present material hereafter in two different portions for two distinctly different services. One portion, to be titled "Drug Therapy," will bring to the reader's attention, in familiar abstract form as in the past, the therapeutic and prophylactic uses to which drugs have been put during the "series year." The other portion, to be titled "Precautions," will supply him with sketches, in quickly readable form, of accumulated experience regarding the toxic actualities and potentialities of *all* the drugs in current use. This, then, is what the book is to comprise henceforth, and why the forward blue sheets have been replaced by the rearward green sheets. Of course not "all" the available drugs are to be found in the "Precautions" section (good Lord! that excellent compendium, the *American Drug Index* for 1962, requires 831 packed pages merely to *list* them), but surely most of those employed for systemic action and likely to be of interest to any reader of the volume are there, and I shall add the important ones omitted as they are brought to my attention. Naturally, new drugs will be incorporated each year as they become available. Comment and criticism of what I am trying to accomplish in this new way are heartily invited.

HARRY BECKMAN

Use of Marax in Treatment of Bronchial Asthma was evaluated by Cecil M. Kohn[1] (Kansas City, Mo., Gen'l Hosp.). Of 616 patients with bronchial asthma treated with Marax, 298 were males and 558 were adults. Marax was used not only for relief in acute attacks but in many patients was administered 2 or 3 times daily to abort attacks. All patients were under hyposensitization therapy or had received emulsion repository therapy. Each tablet of Marax contained 25 mg. ephedrine sulfate, 130 mg. theophylline and 10 mg. hydroxyzine hydrochloride (Atarax). Marax syrup was also used, 5 ml. being the equivalent of ¼ tablet. Good results (complete or almost complete relief from asthmatic symptoms) were obtained in 462 (75%) patients; moderate results (substantial but incomplete control of symptoms) in 96 (15.6%) and poor results in 58 (9.4%). Side effects of mild nervousness, insomnia, tachycardia, epigastric distress, difficulty in micturition and drowsiness occurred in 76 patients. Nervousness, insomnia and tachycardia, which occurred in 48 patients, were considerably decreased by addition of 10 mg. hydroxyzine at the time of administration of Marax. Epigastric distress occurred in 16 patients and drowsiness in 12. In only 4 patients was the drug discontinued because of side effects. For relief from chronic asthma, the optimal dose of Marax was 1 tablet every 4 hours. Occasionally 2 tablets at one time was necessary. In patients with periodic attacks of asthma, administration of 1 tablet 2 or 3 times daily frequently prevented asthmatic attacks. Marax had more sustained action and fewer side effects than other combination drugs available for treatment of bronchial asthma that contain ephedrine, theophylline and a barbiturate. ► [This three-ingredient preparation contains hydroxyzine (Atarax) for its alleged tranquilizer, antispasmodic, anticholinergic and antiserotonin properties; ephedrine as sympathomimetic amine decongestant and, of course, stimulant; and theophylline as bronchodilator. Side effects from its use occurred in about 12% of the patients. May one not wonder whether juggling of the ingredients in written prescriptions would not have revealed which one was responsible for the undesirable effects in each instance and allowed therapy to be established on a more effective long-

(1) Ann. Allergy 20:252-256, April, 1962.

term basis? To be sure, the patient would have been put to greater drug-store expense in the beginning, but perhaps not in the end?—Ed.]

Clinical Evaluation of Bronkotabs: New Antiasthmatic Drug Combination. William H. Lipman[2] (Kenosha, Wis.) used Bronkotabs in 121 patients with acute bronchial asthma, 29 with chronic intermittent bronchial asthma or persistent bronchial asthma. Each Bronkotabs tablet contains 24 mg. ephedrine sulfate, 100 mg. theophylline, 10 mg. thenyldiamine hydrochloride, 100 mg. glyceryl guaiacolate and 8 mg. phenobarbital. The 11 patients aged 10 or under were given elixir of Bronkotab.

Specific antiallergic therapy was continued in 93 patients while they received Bronkotabs; 45 of these were given intermittent oral steroid therapy to supplement other treatment during episodes of acute "colds." A number of patients received antibiotics when indicated.

Response to Bronkotabs was most favorable in the younger patients. Ten of the 11 patients aged 10 or under had good to fair results. Side actions occurred in 2. Of 24 patients aged 10-25, 21 had good to fair results with side actions in 6. Good to fair relief from symptoms was observed in 69 of 86 patients aged 25 and over. Side actions occurred in 14. Side actions to Bronkotabs included nausea in 8 instances, nervousness in 5, weakness in 4, palpitation in 2 and headache and urinary retention in 1 each.

Fifty-two patients had received other efficient theophylline compounds previously. Of 31 who had taken Tedral, 26 had better relief with Bronkotabs; 5 were about the same or better with Tedral. Of 12 patients previously given Amesec, 7 felt better with Bronkotabs and 2 had similar results with the two drugs. Eight of 9 patients who had taken Amodrine were more comfortable with Bronkotabs. Side effects were somewhat more frequent with Tedral, Amesec or Amodrine than with Bronkotabs.

Bronkotabs are more effective than other ephedrine-theophylline combinations in treatment of asthma because of the addition of an expectorant (glyceryl guaiacolate) and an antihistamine (thenyldiamine hydrochloride).

► [Such evidence invites belief that use of this compounded, five-ingredient preparation is practical and worthwhile, and no doubt it is. Here are ephedrine for decongestion, theophylline for bronchodilatation, thenyldia-

(2) Ann. Allergy 19:1295-1299, November, 1961.

mine for antihistaminic action, phenobarbital for sedation and glyceryl guaiacolate for antitussive action. But this is shotgun therapy, and the possibility of adjustment in dosage of any one of the ingredients is lost. One is left with no leads to follow when the preparation begins to lose effectiveness in the individual case. Was it the ephedrine that was responsible for the initial relief, and could still be effective if stepped up in dosage, or the antihistaminic or the theophylline? The patient's fairly consistent response to antiallergic drugs is going to have to be determined the hard way through trial and error in each case if he stays in the practice long enough.—Ed.]

Clinical Evaluation of New Triple Drug Aerosol [Bronkometer] for Asthma was carried out by A. A. Goldfarb and A. Romañoff[3] (Lebanon Hosp., Bronx, N. Y.). The aerosol was a commercially available device that delivers 350 μg. isoetharine (Dilabron), 70 μg. phenylephrine and 30 μg. thenyldiamine per spray. Isoetharine is a bronchodilator, phenylephrine is a bronchodilator and vasoconstrictor and thenyldiamine is an antihistamine.

Of 76 patients (26 children) who used the aerosol, 63 obtained subjective relief from dyspnea due to severe chronic asthma within 7-10 minutes (table). All 76 showed objective improvement as measured by a timed vital capacity meter and physical examination.

Re-evaluation of the patients after they had used the product for 1 week revealed that 60 had followed instructions and used the aerosol properly. All 60 showed subjec-

RESPONSES TO TRIPLE DRUG AEROSOL

A. SUBJECTIVE: RELIEF OF ASTHMA WITH USE OF TRIPLE AEROSOL (AFTER 7 to 10 MINUTES)

Results	No. of Patients	Percentage
Marked	10	13%
Moderate	53	71%
No Relief	13	16%
Worse	0	0
	76	100%

B. OBJECTIVE: TIMED VITAL CAPACITY (TVC) IMPROVEMENT IN ONE SECOND

Results	TVC 1Sec. ml. increase	No. of Patients	Percentage
Marked	210-700	36	48%
Moderate	100-200	40	52%
No Change	....	0	0
Decrease	....	0	0
		76	100%

A. SUBJECTIVE: RELIEF OF ASTHMA WITH TRIPLE AEROSOL: (AFTER ONE WEEK'S USE)

Results	No. of Patients	Percentage
Marked	12	20%
Moderate	48	80%
No Relief	0	0
Worse	0	0
	60	100%

B. OBJECTIVE: TIMED VITAL CAPACITY (TVC) IMPROVEMENT IN ONE SECOND

Results	TVC 1Sec. ml. increase	No. of Patients	Percentage
Marked	210-700	15	25%
Moderate	100-200	45	75%
No Change	....	0	0
Decrease	....	0	0
		60	100%

(3) Ann. Allergy 20:307-314, May, 1962.

tive relief as well as objective improvement, as demonstrated by increased vital capacity (table) and decrease or absence of rales.

Side effects were absent in 72 of the 76 patients. Two patients found the taste objectionable. In 2 patients with coincidental hypertension, systolic and diastolic pressure was reduced after use of the aerosol. No significant cardiovascular effect and no central nervous system stimulation were observed in normotensive patients.

Double-blind study revealed that the commercial product was more effective than any of its individual ingredients or any combination of two of the three ingredients. This suggests a synergistic effect of the three drugs in combination. ► [Strange, isn't it, that only 4 of 76 patients had side effects from a preparation containing enough sympathomimetic amine and antihistaminic to be therapeutically effective?—Ed.]

Clinical Studies with Isoprophenamine, a New Bronchodilator, with and without the Antihistamine Methapyrilene, were conducted by Bennett Kraft and James G. Armstrong[4] (Marion Co. Gen'l Hosp., Indianapolis). In order to compare the efficacy of isoprophenamine with a mixture of isoprophenamine and antihistamine, 12 patients, aged 6-14, were treated by a double-blind method. The three medications used were the vehicle syrup (ethomoxane hydrochloride) alone, 1.5 mg./5 ml., vehicle syrup containing isoprophenamine, 10 mg./5 ml., and vehicle syrup containing isoprophenamine, 10 mg., and methapyrilene [Histadyl, etc.] 16 mg./5 ml. All three medications were given in the same dosage, 1 teaspoonful 3 times daily. Patients were instructed to increase dosage to 2-3 teaspoonfuls every 3 hours should wheezing occur. Each patient received each medication for 1 week on 2 occasions during the 6-week study period. All patients received weekly hyposensitization injections throughout the study.

Nasopharyngeal symptoms of sneezing and rhinorrhea occurred in 33 symptom-weeks of placebo therapy, 29 of isoprophenamine therapy, and 15 of combined isoprophenamine and methapyrilene therapy. In this regard, the bronchodilator was little better than placebo. Pulmonary symptoms of dyspnea, wheezing and coughing occurred in 43 symptom-

(4) Ann. Allergy 20:386-393, June, 1962.

weeks of placebo therapy, 33 of bronchodilator therapy, and 19 of combined bronchodilator and antihistamine therapy. Both bronchodilator and antihistamine therapy significantly reduced the number and duration of asthmatic attacks, but there was no statistically significant difference between the two active medications. Animal experiments, performed by others, warrant assumption that the enhanced antiasthmatic effect achieved when methapyrilene is used in combination with isoprophenamine depends mainly on an added bronchodilator effect and only secondarily on reduction in the secretion of mucus.

► [To my knowledge at press time, the mixture here used, Syrup Vortel, is not yet commercially available.—Ed.]

Dimethpyrindene [Forhistal]: Use in High-Dosage Hyposensitization Therapy; Prevention of Constitutional and Excessive Local Reactions are reported by Milton M. Hartman[5] (San Francisco). Dimethpyrindene was selected as the antihistamine for subcutaneous and oral use because of its antihistamine efficacy, adequacy of local anesthetic action, absence of toxicity and minimum of side actions. Of 100 patients treated (60 males), 41 had seasonal or perennial allergic rhinitis, 42 had combinations of one or the other with asthma and 17 had asthma alone. Multiple sensitivity to inhalants was the rule. House dust was a factor in 85, grass pollens in 84, feathers in 42, kapok in 25 and animal danders in 14. Other allergens were numerically less important. The routine adopted consisted of 1-2 sustained-action dimethpyrindene tablets taken 5-10 minutes before treatment. Each tablet had an outer layer of 0.75 mg. for immediate action and a core of 1.75 mg. for sustained release over 8-10 hours. Mixed with each subcutaneous dose of antigen or antigen mixture was 0.2 ml. of the following: 1 part 1:1000 epinephrine hydrochloride (0.1%); 1 part 4% ephedrine sulfate; and 2 parts 1:500 dimethpyrindene (0.2%). Among the 100 patients treated, clinical results were excellent in 91, good in 4, fair in 2 and poor in 3. Average number of treatments per year was 21.8. No evidence of hepatic, renal or bone marrow toxicity was noted. Slight drowsiness, the only side effect, occurred in 5% of patients. Ninety-four patients have

(5) California Med. 96:262-266, April, 1962.

continued maintenance treatment on their maximum tolerated doses.

For comparison, 100 patients matched for age, sex, clinical manifestations, sensitivities, residential areas and exposures were selected and given antigens without pre- or postinjection antihistamine medication. Similarly matched groups of 100 patients who had received vasoconstrictors in the antigen injection and who had the same admixture plus an oral antihistamine (usually tripelennamine, 100 mg.) were also compared. Analysis revealed that the present group, when compared with the untreated group, had one-eighth the incidence of constitutional reactions, one-third the incidence of local reactions, a 24% reduction in number of treatments and an appreciably higher proportion of excellent clinical results. The intermediate treatment groups were intermediate in results. They had fewer side effects than the group not treated by antihistamines, but the number of treatments was not reduced.

Prevention of Antihistamine Sedation with Amiphenazole [Daptazole]. Many patients who should be taking antihistamines refuse because of the drowsiness these agents induce. Amiphenazole is a partial antagonist of morphine, and has been noted to antagonize the sedative effects of antihistamines. D. W. Bruce[6] (Univ. of Melbourne) studied 33 subjects with standard, severe hay fever, who obtained relief from antihistamines normally available in clinical practice but were made sleepy by them. The most effective antihistamine was Benadryl. The most effective single dose of amiphenazole was 200 mg. by mouth. This was taken with each antihistamine tablet, except when another dose of antihistamine was required at bedtime. One to 3 antihistamine doses were required during the day. Thus the total daily dose range of amiphenazole was 200-600 mg.

Of the 33 patients, 30 (90%) found that combined amiphenazole and antihistamine gave complete symptomatic relief with no sedation. The other 3 stated they still became drowsy and noted no advantage. Amiphenazole is a slight central nervous system stimulant. If 200 mg. is taken at bedtime, insomnia is briefly induced.

► [If there is gross liver damage, amiphenazole too will have sedative effect.—Ed.]

(6) M. J. Australia 2:179-180, July 29, 1961.

Response to Bronchodilators in Intrinsic Asthma was studied by K. M. Hume and E. Rhys Jones[7] in 5 women and 2 men, aged 29-65, who were hospitalized in status asthmaticus. All failed to show improvement in lung function tests after 5 days of intensive bronchodilator therapy with intravenous and suppository aminophylline, subcutaneous epinephrine, frequent inhalations of 1% isoprenaline (Isuprel) and antibiotics. Pulmonary function was judged by the forced expiratory volume in the 1st second of the expiration ($F.E.V._{1.0}$) as measured by a spirogram.

METHOD.—After initial recordings, 0.25 Gm. aminophylline in 10 ml. distilled water was injected slowly into a vein. As a result of the pilot trial, estimation of $F.E.V._{1.0}$ was repeated in duplicate at 5, 10 and 15 minutes after the injection and the two lowest values discarded. After the last recording, 1% isoprenaline was administered for ½ minute through a Collison inhaler. Further recordings were made after 2 and 4 minutes. On occasions when the initial $F.E.V._{1.0}$ was similar to that for which the patient's response to aminophylline had already been tested, a different procedure was adopted. With a second inhaling apparatus, a 4% solution of atropine in distilled water was administered for 1 minute. The $F.E.V._{1.0}$ was recorded after 5, 10 and 15 minutes; after the last recording, isoprenaline was administered and the tests repeated. When an initial $F.E.V._{1.0}$ value was found for which the responses to both aminophylline and atropine had been estimated, aerosol isoprenaline was administered. Results were recorded as before; 0.25 Gm. aminophylline was then given intravenously and the tests repeated. On occasions all three drugs were administered in succession.

The trials were repeated daily. All patients were treated with prednisone acetate; the original dosage was 25 mg., given daily in 3 doses of 5 mg. during the day and 10 mg. before retiring at night; when the day-to-day value of $F.E.V._{1.0}$ showed no further improvement, dosage was reduced. One dram of magnesium trisilicate was given with each dose.

The effect of the three drugs singly and in combination was observed on 290 occasions. The initial values of $F.E.V._{1.0}$ were plotted as abscissas and the increases recorded after the drugs as ordinates.

Relatively small doses of isoprenaline and aminophylline produced the maximum response, and a higher dosage was of no advantage. When asthma was severe, response was poor. A combination of drugs of different bronchodilator groups was more effective than one drug. The improvement resulting in every patient from the most effective drug, isoprenaline, was enhanced when it was followed by aminophylline or atropine. When the drugs were administered in reverse

(7) Quart. J. Med. 30:189-199, April, 1961.

order, 5 patients had no greater improvement than when they inhaled isoprenaline alone. Isoprenaline was much more effective inhaled than when given sublingually.

► [So then, the recommended order of administration would be Isuprel inhalation first, followed by aminophylline intravenously. It is certainly fine to have available the results of this study, but of course the thing won't always work out this way clinically because some patients respond well to aminophylline though hardly affected by Isuprel at all as primary medicament. Only trial and error will be the determinant in the individual case. —Ed.]

Adrenaline and Status Asthmaticus. Epinephrine is a drug of choice in severe acute bronchial asthma and must be promptly administered. However, most textbooks advise caution in the speed of administration; usually a minim (0.06 ml.) a minute is recommended. Frequently, a vigorous therapeutic approach is necessary in status asthmaticus, and prompt administration of large doses might speedily avert a difficult situation. Bryan Broom[8] (Middlesex Hosp. Med. School) treated 24 patients with 1:1000 epinephrine, 2-5 ml. given in 5-15 minutes. Rapidity of response served as a guide to total dose. Three patients required a second injection. Two had to be hospitalized after 10 and 8 ml., respectively, failed to produce improvement. Side effects, often unpleasant, occurred in all but 6 patients and included tachycardia in 18, vomiting in 16, pallor, headache and sweating in 10, extrasystoles in 5 and tremors and anxiety in 2. These symptoms and the pain of the injection were willingly borne in the hope of quick and complete relief. After the acute attack was relieved, promethazine was given orally for the next 24 hours and penicillin by mouth for the next 5 days.

This experience indicates a need for a reorientation of epinephrine dosage in bronchial asthma to obtain rapid and complete relief from a severe attack. When an intramuscular injection is given, the rate should be comparatively slow, about 2-5 ml. in 5-15 minutes, and at minute intervals one must make sure the syringe is not in a vein.

► [Since I am honored by a listing among those textbook writers whose caution the author deplores, I take the liberty of addressing him as follows:

Dear Doctor Broom, I'll accord you the room
to chide me if that is your wish;
But do not presume to lower the boom
with adrenaline served up *by the dish!*—Ed.]

(8) Lancet 2:1174-1176, Nov. 25, 1961.

Clinical Evaluation of Theophylline Solution (Elixophyllin) in Children with Bronchial Asthma. Elixophyllin contains 80 mg. theophylline and 3 ml. ethyl alcohol in each 15 ml. of the water-alcohol solution. A. H. Eisen and H. L. Bacal[9] (Montreal) treated 35 children with acute bronchial asthma. The dose of Elixophyllin was 0.5 ml./lb. body weight every 8 hours.

Twelve patients (34%) showed a therapeutic response; the others did not improve. Of the 23 patients not responding, 12 were under age 2. Acute respiratory distress characterized by hyperinflation and wheezing is a frequent syndrome in infancy. Bronchiolar obstruction is the essential physiologic alteration. The bronchiole in infancy is small, with a narrow lumen and minimal muscle tissue. In this age group, it is thought that there is little or no muscular constriction contributing to the obstruction. Clinically, it is known that bronchodilators are usually ineffective in the wheezing and hyperinflation of infancy. Because of the ineffectiveness and the danger of toxicity, the authors believe that theophylline should be omitted from the treatment regimen of children under age 1, and between ages 1 and 2 years theophylline should be used cautiously in small doses.

If children under age 2 are omitted from the present trial of Elixophyllin, a favorable response was observed in 11 of 22 patients. Response was excellent in 6 patients and partial in 5.

The indirect maximum breathing capacity was measured in 10 patients with mild to moderate asthma who derived some symptomatic relief from Elixophyllin. Analysis of variance revealed no significant increase in maximum breathing capacity after treatment with the theophylline preparation. Epinephrine aerosol, however, did significantly increase this capacity.

Elixophyllin lends itself to highly accurate dosage of theophylline. Theophylline toxicity was not observed on the dosage schedule used. No adverse effects due to the alcohol content were noted clinically. The long-term effects of ethyl alcohol in this concentration in children are unknown.

► [It may be that rapid absorption of theophylline is promoted in this

(9) Canad. M. A. J. 86:444-446, Mar. 10, 1962.

preparation, but it should be borne in mind that the patient is also receiving alcohol, which often has a tranquilizing effect that is of considerable value in the asthmatic. In the days before the allergists developed their personal jitters at the mere thought of aspirin and threw a scare into all of us, an old remedy that often worked well was aspirin and whisky.—Ed.]

Use of New Elixir for Prophylaxis in Pediatric Bronchial Asthma is described by Gilbert Lanoff[1] (Children's Mem'l Hosp., Chicago). Bronkotab Elixir was used to treat 100 chronic asthmatic children (57 boys), aged 6 months to 14 years, for 6 months. Forty had undergone repository desensitization treatment, and the other 60 patients continued to receive multiple aqueous treatment. A teaspoonful of Bronkotab Elixir contains: glyceryl guaiacolate, 50 mg.; ephedrine sulfate, 12 mg.; theophylline, 15 mg.; phenobarbital, 4 mg.; and chlorpheniramine maleate, 1 mg. It is cherry flavored and palatable. Glyceryl guaiacolate is an effective oral expectorant. The dosage was ½ teaspoonful every 4 hours for children under age 2, 1 teaspoonful 2 or 3 times daily for children aged 2-7 and 2 teaspoonfuls every 4 hours for children aged 7-14 years. Excellent results, with complete relief from symptoms, were obtained in 24 patients; good results, with relief from symptoms for 2 or 3 hours, were obtained in 42; and fair results, with relief from symptoms for ½-2 hours, were achieved in 23. No beneficial effect was noted in the other 11. Side effects consisted of irritability in 1 patient, "choking" in 1 and lacrimation in 1. Bronkotab Elixir appears to be an effective symptomatic medication for treatment of bronchitis and chronic bronchial asthma in children.

► [This is a 30% alcoholic elixir. The older children, receiving 2 teaspoonfuls every 4 hours are taking something more than the equivalent of a teaspoonful of whisky at each dosing.—Ed.]

Rectal Aminophylline (Rectalad) was evaluated by Norman Traverse and Maurice S. Segal[2] (Tufts Univ.). Rectalad was used in the treatment of 206 patients, aged 6-76, with chronic bronchial asthma who required daily use of aminophylline for prevention of or relief from bronchospasm. Dosage ranged from 75 to 450 mg. and was given twice daily. Most patients used bronchodilator aerosols, and 42 required supplemental corticosteroids. The patients readily accepted Rectalad. Reduction in the need for and dependency

(1) Ann. Allergy 20:238 242, April, 1962.
(2) Ibid., pp. 182-188, March, 1962.

on bronchodilator aerosols was noted in over 75% of the patients. Reduction in the need for steroids was noted by 14 of the 42 on supplemental steroid therapy. In acute paroxysms, after administration of rectal treatment, relief was generally observed in 5-15 minutes, with freedom from cough and wheezing lasting for several hours. Gastrointestinal upset and nausea were noted by 12 patients and jitteriness by 6 who were taking the 450-mg. dose twice daily. Such reactions were not observed in these patients and others using 300-mg. doses. Six patients noted irritation or a burning sensation and omitted therapy. In 16 patients 1 hour after the administration of Rectalad, 450 mg., mean plasma theophylline concentration was 578 μg./100 ml. This was lower than the mean of 685 μg./100 ml. in 3 patients 1 hour after intravenous injection of 450 mg. Rectalad. After 2 hours, however, the mean plasma level was higher in the rectally treated group and remained so throughout the 6-hour study period. The suppository form yielded much lower plasma concentrations than the liquid form of Rectalad in 4 patients. Rectalad is a convenient and effective mode of treatment.

► [The findings of Prince *et al.* (1961-62 YEAR BOOK, p. 7) suggested that blood levels of 150-200 μg./100 ml. are effective for bronchospasmolysis in most asthmatics, a figure much lower than that achieved in the present study. I warn the reader again, as many times before, that the aminophylline dose for children under age 3 should not exceed one-fifth that of the adult, and that for older children this ratio should be only cautiously adjusted upward.—Ed.]

Long-Term Steroid Therapy in Chronic Intractable Asthma: Study of 317 Adult Asthmatics on Continuous Steroid Therapy for Average Period of 2½ Years is presented by Harry A. Rees and D. A. Williams[3] (Cardiff, Wales). In all patients, other therapeutic measures had been tried but had failed. Prednisone [Meticorten, etc.] was given to 279 patients (88%), triamcinolone [Aristocort] to 23, cortisone or hydrocortisone [Cortel, etc.] to 13 and dexamethasone [Decadron, etc.] to 2. In 96 patients, corticotropin [ACTH] was given in doses of 40-60 units intramuscularly every 1-6 weeks.

Patients were encouraged to use simpler and safer measures, such as ephedrine, aminophylline and/or inhalers, and were given the smallest dose of steroid that would keep them reasonably but not totally free from asthma; 58% re-

(3) Brit. M. J. 1:1575-1579, June 9, 1962.