Bulletin of the

University of Minnesota Hospitals
and
Minnesota Medical Foundation

Treatment of Hay Fever in the Adult

Volume XX | Friday, March 18, 1949 | Number 21

BULLETIN OF THE
UNIVERSITY OF MINNESOTA HOSPITALS
and
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I. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

March 20 - 26, 1949

No. 240

Sunday, March 20

9:00 - 10:30 Surgery Grand Rounds; Station 22, U. H.

10:30 - 11:00 Experimental Aspects of Hemoglobin Metabolism; Y. Sako; Rm. M-109, U. H.

Monday, March 21

8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General Hospital.

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:20 Pathology Seminar; Propylthiouracid and the Hamster; D. S. Mitchell; 104 I. A.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Class Room, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

4:00 - Pediatric Seminar; The Role of the Pediatrician in Preventing Speech Defects; Mr. Ellsworth Stensvick; 6th Floor, Child Psychiatry, U. H.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy and H. M. Stauffer and Staffs; M-109, U. H.

Tuesday, March 22

8:00 - 9:00 Fracture Conference; Auditorium; Ancker Hospital.

8:30 - 10:20 Surgery Seminar; Diaphragmatic Hernia; Dr. Dickman; Small Conference Room, Bldg. I, Veterans Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and Robert Hebbel; Veterans Hospital.

12:30 - Pediatric-Surgery Rounds; Sta. I, Minneapolis General Hospital; Drs. Bosma, Wyatt, Chisholm, McNelson and Dennis.

12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.

1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans Hospital.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; J. R. Aurelius and Staff, Ancker Hospital; Powell Hall Amphitheater.

Wednesday, March 23

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-515, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium, Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans; Room 1AW, Veterans Hospital.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker and Joe R. Brown; Veterans Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; O. H. Wangensteen, C. J. Watson and Staff; Todd Amphitheater, U. H.

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

Thursday, March 24

8:15 - 9:00 Roentgenology-Surgical-Pathology Conference; Craig Freeman and H. M. Stauffer; M-109, U. H.

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Class Room, Minneapolis General Hospital.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

2:00 - 3:00 Errors Conference; A. A. Zierold, C. Dennis and Staff; Large Class Room, Minneapolis General Hospital.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.

Friday, March 25

8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Staff; Veterans Hospital.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, O. S. Wyatt, A. V. Stoesser and Staffs; Minneapolis General Hospital.

11:30 - 12:50 University of Minnesota Hospitals General Staff Meeting; - No Meeting.

12:00 - 1:00 Surgery Clinical Pathological Conference; Clarence Dennis and Staff; Large Classroom, Minneapolis General Hospital.

1:00 - 1:50 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - 3:00 Pathology-Surgery Conference; Auditorium, Ancker Hospital.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

4:00 - 5:00 Electrocardiographic Conference; George N. Aagaard; 106 Temp. Bldg., Hospital Court, U. H.

Saturday, March 26

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 20, U. H.

8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.

8:00 - 9:00 Pediatric Psychiatric Rounds; Reynold Jensen; 6th Floor, West Wing, U. H.

8:00 - 9:00 Surgery Literature Conference; Clarence Dennis and Staff; Minneapolis General Hospital, Small Classroom.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-101, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 11:30 Surgery-Roentgenology Conference; Todd Amphitheater, U. H.

9:00 - 12:00 Psychiatry Conference; Powell Hall Amphitheater.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

II. TREATMENT OF HAY FEVER IN THE ADULT

J. S. Blumenthal

From the time that Hippocrates in the fifth Century B.C. described what is today recognized as a food allergy to cheese, the interest in all phases of allergy has been of great and of increasing importance. It was, however, not until 1565 that Botallus of Pavia[1] described seasonal vasomotor rhinitis elicited apparently by smelling roses. To this day hay fever is often called by the laity "rose fever". For the first time in medical literature John Bostock[2] in 1828 mentioned the term hay fever. He reported on twenty-eight patients suffering from "summer catarrh" and noted that the symptoms were elicited by hay. In 1831 Elliotston[3] called attention to the fact that patients had the idea, probably correct, that their catarrh was caused by grasses. Swett[4] in 1852 described both summer and autumnal types of hay fever in the United States. Outstanding above all others in the field of hay fever, however, is the figure of Charles H. Blackley[5]. It was he who in 1873 said that pollen catarrh was really a more appropriate term than hay fever and established the positive skin scratch tests with adequate controls.

In 1910 Barger and Dale[6] isolated histamine beta imidozolethylamino from ergot and in 1911[7] found histamine in the intestinal mucosa. Its precursor, histidine, is a common cell constituent. Best and McHenry[8] reported it is found most often in barrier tissue such as skin and intestinal mucosa. Histidine may be converted to histamine by the removal of carboxyl group not only by antigen antibody reaction but also by bacterial action[9]. Dr. R. Bieter notes that histamine tends to act on cells that are ennervated by the autonomic nervous system.

Histamine is known to produce constriction of smooth muscle, dilation and increased permeability of capillaries and to act as a secretagogue on the glands of exocrine secretion. It appears in the blood immediately after administration of an antigen, and in the guinea pig the phenomenon of anaphylaxis and the administration of histamine seem to be identical[10].

While as pointed out by Dragstedt[11] histamine release is at least a major factor in the causation of allergy symptoms, it is probably not the only factor. It is because of this that Sir Thomas Lewis[12] called the factor "H substance", and said, "I shall speak of an H substance, and in using it shall mean any substance or substances liberated by the tissue cells and exerts on the minute vessels and nerve ending an influence culminating in the "Triple Response". The relationship between the amount of histamine activity in the blood and the symptoms is not as direct as one would desire. The identification of histamine itself in the blood, Dragstedt has repeatedly pointed out, is always difficult. As Katz[13] has shown, there is always the problem of differentiation between histamine bound to cells and histamine in the free state. He[14] added horse serum in vitro to the blood of a rabbit sensitized with that serum and noted that the cell-free plasma showed a great increase of histamine. Rose and Brown[15] got essentially the same results and repeated the experiment with use of egg albumin added to the blood of egg sensitive rabbits with the same effect. While we thus have evidence from these experiments as well as others[16,17] that there is a transfer of the bound to the free state, we as yet do not have definite evidence that the reverse is also true. There are indications that it is.[16] This change in the state of histamine makes it hard to assay its exact role in allergy. In the main, however, the histamine theory is plausible.

In discussing the treatment of hay fever, it would seem appropriate here to give a concept of what takes place in the hay fever patient. As in all patients with allergic symptoms, we first must have the so-called "asthmatic state" -- a state defined by Rackemann[18,19] as

an inherited one in which a patient is more likely to develop these symptoms than do others in exactly the same environment. It is the condition which may be the background in which allergy in the usual sense can develop. We have, further, the capacity in these individuals to develop sensitiveness and to produce or react to H substance so as to cause a variety of symptoms of vasomotor origin. In hay fever pollens acting on such a person whose eyes, nose and throat are sensitized causes the production of antibodies of two types[20] - a thermostabile and a thermolabile antibody. The reaction, we can postulate, of the thermolabile antibody and the pollen allergen causes the release of histamine or H substance which in turn causes the symptoms of hay fever. In this concept, it is easy to see that the logical point of attack would be the fundamental asthmatic state. Unfortunately we know so very little about that beyond the important hereditary factor which makes attack here very difficult. Indeed, it would seem at times that hay fever victims seem to have an affinity for each other, for misery loves company. Allergics seem to tend to propagate their heredity. The next logical point of attack would be the allergen. Here again, though desirable, the economic and social factors make it frequently impossible to have the patient go where the pollen is not. Beyond that, the patient frequently becomes sensitized to other pollens. This factor was called forcibly to my attention on a recent visit to Mexico City. I met two Minnesota natives, doctors who had gone to live in Mexico City because of their severe hay fever. After a few years there, ragweed pollenosis had been replaced by an equally distressing pollenosis due to Bermuda grass pollens. Ragweed is present in the vicinity of Mexico City, but the amount is extremely small. Again, two years ago while visiting at the University of Havana, I met a native Iowa allergist who informed me that his hay fever of Iowa due to ragweed had been replaced by a pollenosis due to grass pollen which is found in the air of Cuba in varying amounts throughout the whole year. These people are taking hyposensitization with good results, but they could not get away from their primary allergic state by getting merely away from the original offending pollen.

In 1911 Noon[21] and Freeman[22] used specific active hyposensitization in hay fever by repeated injections of increasing amounts of allergen. In 1935 Cooke Bernard Hebald and Stull[20] first presented evidence for an antibody which could block the union of ragweed antigen with the ordinary neutralizing antibody, that is, there are really two antibodies in hay fever--the sensitizing thermolabile antibody destroyed by heat at 56 degrees Centigrade and the thermostabile antibody not so destroyed. Lovelace[23] states that the amount of blocking antibody is proportional to the symptomatic relief following treatment. Cooke[24], however, found that it is not, and it is true that frequently a high blocking antibody titre does not always accompany good clinical results. It is equally true, however, that adequate hyposensitization does give relief in a great percentage of hay fever patients. In our own experience, the larger the dosage used the better the clinical results.

There are two parts to the treatment of hay fever by hyposensitization--the particular extract used and the way it is used. The methods used in the series here reported is simple. Skin tests by the usual scratch methods are correlated with the history of onset of symptoms of the patient and a specific solution made for each. History is most important. A positive skin test to a pollen that gives rise to no significant symptoms when that pollen is present in the air can not be of too great clinical significance in spite of the positive skin test. At the present time, there are only two crude mthods of selection; one is the history to indicate the date of onset of symptoms as accurately as possible and to correlate this date with the onset of pollenation. The other is a field survey confirmed by pollen slides to make sure that a particular plant is capable of putting sufficient pollen in

the air where a particular patient is exposed to it. Where scratch tests did not confirm the impression of history and pollen survey, intradermal tests were carefully applied. When atypical in onset and duration or when conventional treatment had given unsatisfactory result, molds were incorporated in the extract. Molds, although not apparently as important in adults as in children and through a field wherein a tremendous amount of work remains to be done even as to identification, occasionally gave better results when used either together with the pollen extracts or by themselves usually in the form of alternaria, hormodendrum or aspergillus. The initial dose injected subcutaneously is usually 20 units using .00001 mg. of pollen nitrogen by the Kjeldahl method as the unit. The dosage was increased at 4 to 7 day intervals by fifty per cent, aiming at getting the 20,000 units or more before the patient's symptoms began. Dosage increases, of course, depend upon the reaction of the individual. The maximum dose was then continued throughout the pollen season unless reaction or symptoms so dictated otherwise. It was at times reduced when the season started. Where possible, treatment is continued throughout the year at reduced dosage, usually fifty per cent; i.e., usually 10,000 units.

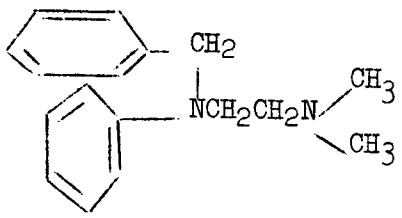
Since histamine or H substance has been designated as a common denominator for allergic manifestations, it is natural that many attempts should have been made to find some substance which could inhibit all anaphylactic and allergic reactions by counteracting or neutralizing histamine, the end product of the allergen antibody reaction. The second method of treatment, therefore, here reported is with the use of some of the so-called antihistamine drugs. Antihistamine drugs or histamine antagonists have been defined by Earl R. Loew[25] and as Dr. Bieter points out, as drugs which diminish or prevent several of the pharmacological actions of histamine by a mechanism other than by the production of pharmacological responses diametrically opposed to those produced by histamine. In other words, these drugs antagonize histamine and prevent its action without producing any pharmacological actions of their own. As Gilman[26] points out the antihistamines are really blocking agents, and the term histaminalytic would really be more appropriate. They prevent the histamine from gaining access to the receptor mechanism of the cell and exerting the characteristic effect. The incomplete results and varying results in allergic manifestations with treatment by the antihistamine drugs may be explained in part by the fact that histamine within the cell itself is not affected or the amount of histamine released is too great to be neutralized by the amount of drug given.

Hill and Martin[27] in 1932 listed 165 methods which have been used to attempt to inhibit anaphylaxis. Most were too toxic to use clinically. Among substances listed were atropine, barium, chloral, ether. Other substances used in the past decade - the amino acids - have been disappointing. Bovet[8] and Staub[28] in 1937 found two substances synthesized by E. Fourneau (hence the so-called F compounds) thymoxyethyldiethylamine and N:phenyl N ethyl N-diethylethylenediamine, called 929F and 1571F. These had marked antihistamine properties but were too toxic for clinical use. In 1942 Halpern[29] reported promising results with the new compound called antergan. Since then extensive research has resulted in the production of a great many of these drugs until their number seems legion. A list of the more prominent of the antihistamines with their chemical formulas are here listed. These are briefly: (1) phenulamines--antergan and antistine; (2) Pyridene amines--neoantergan, pyribenzamine and trimeton; (3) Thenyl, pyridine amines--Histadyl or thenylene, tagathen or chlorothen, diatrin, and bromothen; (4) Benzhydryl alkamine ethers--Benadryl and Decapryn; (5) Pyridindene--thephorin; (6) Pyrimidine amines--hetramine and neohetramine; (7) Phenothiazines--3015- Rhone-Poulene or 1627 Searle, 1721 Searle and Pyrrhoazote.

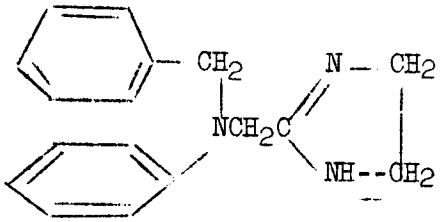
We have used these drugs both in hay

D. Chemistry

1. Phenylamines

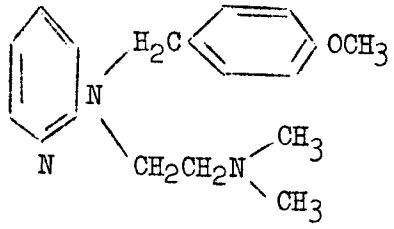


Antergan

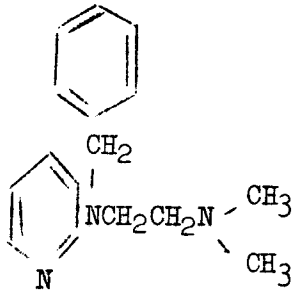


Antistine

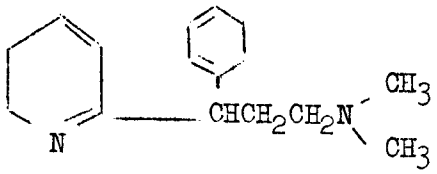
2. Pyridine amines



Neoantergan

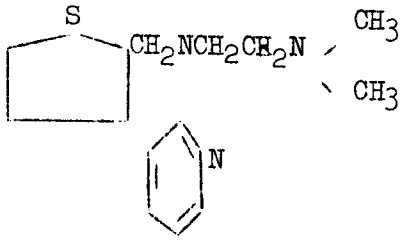


Pyribenzamine

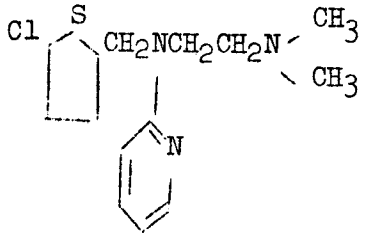


Trimeton

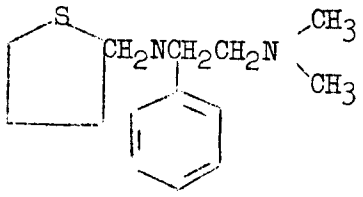
3. Thenyl, pyridine amines



Histadyl
Thenylene



Tagathen (Chlorothen)

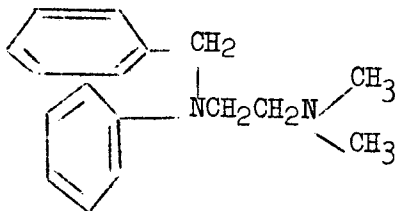


Diatrin

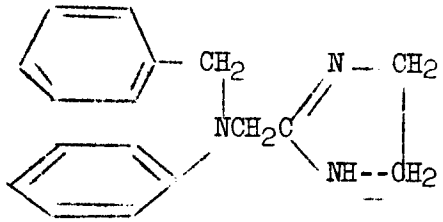
Bromothen is the
Br derivative.

D. Chemistry

1. Phenylamines

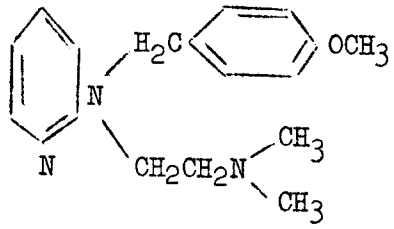


Antergan

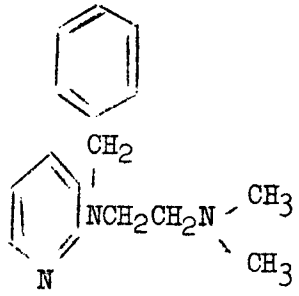


Antistine

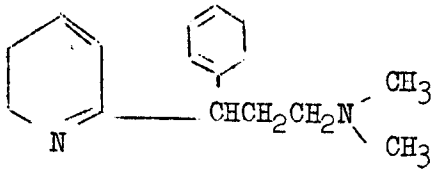
2. Pyridine amines



Neoantergan

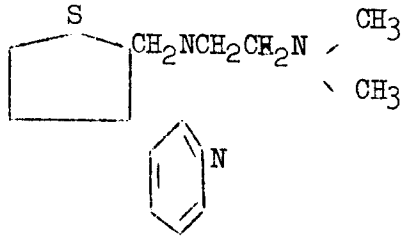


Pyribenzamine

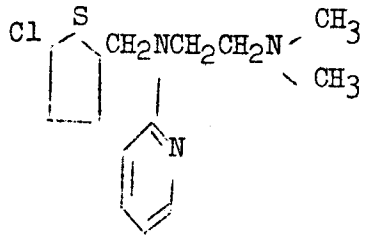


Trimeton

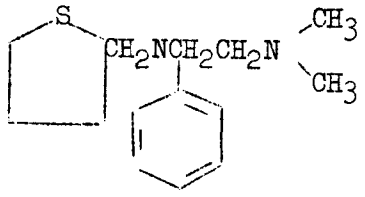
3. Thenyl, pyridine amines



Histadyl
Thenylene



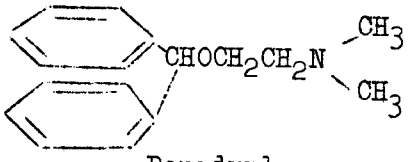
Tagathen (Chlorothen)



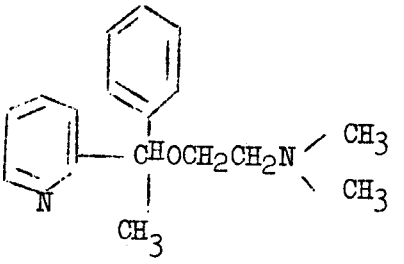
Diatrin

Bromothen is the Br derivative.

4. Benzhydryl alkamine ethers

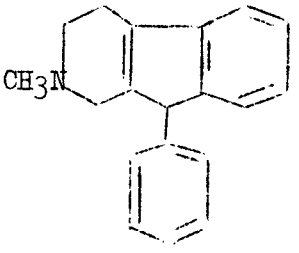


Benadryl



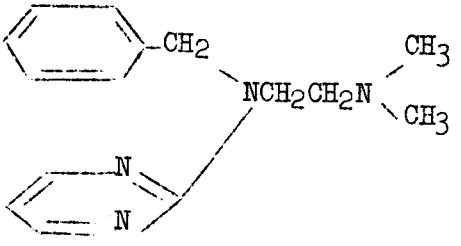
Decapryn

5. Pyridindene

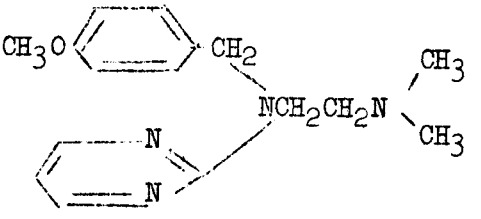


Thephorin

6. Pyrimidine amines

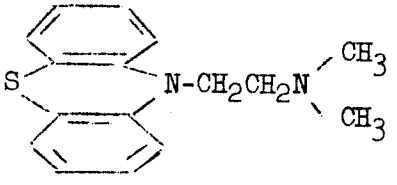


Hetramine

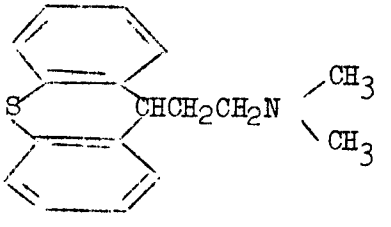


Neohetramine

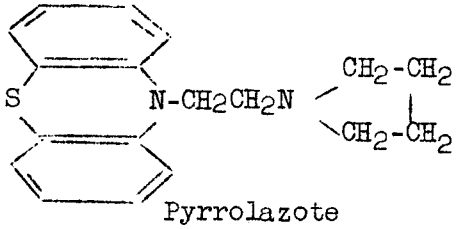
7. Phenothiazines



3015 R P (Rhone-Poulene)
1627 Searle



1721 Searle



Pyrrolazote

fever and in other allergic conditions. Results in conditions other than hay fever will be reported at a later date. On the whole results with the use of these drugs in hay fever has afforded, according to the literature, relief of up to 94 per cent. In reviewing some of the extensive literature, it is apparent that the drugs resemble one another in degree and duration of relief.[30-39] The effect persists four to six hours and results are apparent in one-half to one hour after oral administration.

Side effects[34,40-43] have been many, and though not usually serious are annoying. Among the most common are sleepiness, dizziness, skin eruptions, epigastric distress, headache, change of shock tissue. A very important and interesting report on the use of these drugs in their less obvious effects is that of Haltkamp and Hagerman and Whitehead[44]. They report on the effects on the mental ability, reaction time, and minimum distance of two point discrimination. They report definite alteration in fifty per cent of college students. Blasman and Hagens[45] report a case of exacerbation of asthma with fatal result in the use of Benadryl. Here again the exact role of Benadryl is very difficult to evaluate as is the case of any therapeutic agent in asthma. A humorous side light is afforded by an article appearing in the El Paso Herald Post and reported in the Journal of the American Medical Association on November 6, 1948.

> YOU GET SICK nowadays and what you got?--either a virus or an allergy.
>
> A virus is what you got when the doctors don't know what you got. An allergy is what you got when the doctors know what you got but don't know where you got it.
>
> The other morning I was awakened by a full-fledged, championship case of the hives.
>
> I really didn't have the hives, just a hive. One great big hive extending from scalp to toe and itching worse than Job's pleasant little boils ever hurt.
>
> It went away and I got up and dressed and then it came back. So I went back to bed so's I could scratch.
>
> Well, Mame, she calls the doc, and he sends out some pills.
>
> Good pills they were and they knocked me out colder than kraut and there was no more itching. In fact, you could have stuck hot needles in me and I wouldn't have know about that either.
>
> Next morning I got up to work and there are no more pills and if there was I couldn't have gone to work they would have knocked me so cold, and there was a lot more itching and I go on back to bed so I can scratch in peace and Mame telephones the office that I am not fit company for man or beast and they are very lucky that I can't come down that morning.
>
> Then she calls the doc again, and after a while here he comes and another doc with him.
>
> "Must be something you et," says the docs. "You got an allergy."

In the series of patients now being reported, all were seen once a week or oftener. Symptoms were recorded as were degree of relief and side effects. They were questioned as to nasal discharge, difficulty in breathing, itching, sneezing, increased flow of tears, smarting and redness of the eyes, wheezing, coughing and expectoration. New drugs were given as soon as evaluation was made. Dosage was prn and not at regular intervals. The results were evaluated according to the patients' own description and judgment and the overall picture including objective findings. Those who experienced fifty per cent relief or more

were considered to have fair results. Patients who had mild to practically no symptoms were considered to have had good results. It was evident that this is at best a very rough method of assaying conclusions, but as in most conditions in which the subjective symptoms are very important, we must use as nonprejudicial an attitude as possible and keep all aspects of the condition under consideration in judging the figures given. It has been well said that there are three kinds of lies--white lies, black lies and statistics. Certainly in no field of medicine do statistics lie and lie and lie as frequently and as profusely and as efficiently as they do even in so simple a field of allergy as hay fever. This is understandably so, for here is a condition in which the statistics of results of therapy are affected not only by the usual enthusiasm of the investigator, not only by the psychosomatic aspects of the patients, but even by the very furniture and people by which the patient is surrounded, the food he consumes and the very air that he breathes.

Table I

Hyposensitization	108 patients	
No Relief	Appreciable Relief	Good Relief
16 (14.8%)	32 (29.6%)	60 (56.6%)

108 patients were treated by hyposensitization by method described. Of these as seen in Table I, 16 or 14.8% had no or very slight improvement, 32 or 29.6% had appreciable relief where the patient thought treatment was worthwhile, and 60 or 56.6% had good relief.

Table II

Placebos	20 patients	
No Relief	Appreciable Relief	Good Relief
18 (90%)	1 (5%)	1 (5%)

Twenty patients were given placebos. It is interesting to note as emphasizing the psychosomatic aspects of any allergic condition that one or 5% had appreciable relief and one or 5% had marked relief though 18 or 90% had no relief whatever.

Table III

Benadryl	62 patients	
No Relief	Appreciable Relief	Good Relief
22 (35.5%)	12 (19.3%)	28 (45.2%)

Sixty-two patients were given Benadryl in doses of 50 to 100 mg. up to four times a day as needed. Of these, 22 or 35.5% had no relief, 12 or 19.3% had appreciable results and 28 or 45.2% had good relief of symptoms.

Table IV

Histadyl	22 patients	
No Relief	Appreciable Relief	Good Relief
7 (31.8%)	8 (36.4%)	7 (31.8%)

Histadyl was given in the same dosage as Benadryl. Of 22 patients 7 or 31.8% had no relief, 8 or 36.4% had appreciable relief and 7 or 31.8% had good relief.

Table V

Pyrabenzamine	55 patients	
No Relief	Appreciable Relief	Good Relief
17 (30.9%)	16 (29.1%)	22 (40%)

As noted in Table V Pyrabenzamine was prescribed to 55 patients. Of these, 17 or 30.9% had no relief of symptoms, 16 or 29.1% had appreciable relief and 22 or 40% had good relief of symptoms.

Table VI

Most Favorable Drug	72 Patients	
No Relief	Appreciable Relief	Good Relief
19 (26.4%)	19 (26.4%)	34 (47.2%)

It would seem from summaries so far given that the percentage of patients relieved by these drugs are essentially the same, but it was evident that some were relieved by one drug and some by another. There were differences in the amount and quality of the relief obtained. Therefore, 72 patients were given the opportunity to try different antihistamine drugs and use the one best suited to them. Of these, 19 or 26.4% had no relief with any of them, 19 or 26.4% had appreciable relief and 34 or 47.2% had good relief. Though hard to express in figures alone, it was evident that by changing to various drugs and using different ones when one drug had less benefit or gave undesirable side effects that better results could be obtained.

A very limiting factor in the use of antihistamine drugs since they were first used has been the toxic or side effects. While usually not too marked, they are often very annoying and limit their usefulness in clinical practice. The effects vary in different patients for the same drug and often in the same patient with the same drug. Usually the larger the dose the greater the side effects in degree and frequency. There is fortunately no correlation apparent between the symptomatic relief and the side effects except insofar as larger doses may be required. The side effects are tabulated.

Table VII

Side Effects

	Benadryl	Pyrabenzamine	Histadyl	Placebo
Drowziness	36	12	4	1
Weakness	32	8	2	
Hypnosis			1	
Dizziness	18	5		
Urticaria			1	
Nervousness	6	6		
Nausea	2	5	2	
Vomiting	1	3		
Asthma	1			

As noted in Table VII drowziness was the most prominent symptom noted. This was a prominent factor in 36 patients of 62 taking Benadryl, in twelve of 55 taking Pyrabenzamine, in 4 of 22 taking Histadyl and in 1 taking Placebo. Dizziness was a prominent action with Benadryl and Pyrabenzamine while six patients of both the Benadryl and Pyrabenzamine group complained of increased nervousness; weakness was noted particularly in the Benadryl group. Other side effects were hypnosis, urticaria, nausea and vomiting. We only had one patient in whom we felt that respiratory difficulty or asthma was apparently aggravated by Benadryl. Even here it is difficult to be certain as so frequently hay fever patients develop this complication who had never seen an antihistamine drug. I realize that change of shock tissue with development of asthma has been reported as a frequent side effect by some allergists, but this can not be too frequent. Certainly we have not had that experience in the adult patient. We must also realize that the antihistamines themselves may be antigens and cause allergic manifestations. The side effects were often combined in the same patient.

Table VIII

Hyposensitization plus Antihistamines		108 patients
No Results	Appreciable Results	Good Results
8 (7.4%)	12 (10.2%)	88 (82.4%)

The patients who had been hyposensitized were given the drugs to use as needed for symptomatic relief. In this group, much smaller and less frequent doses were required to control symptoms. The incidence of side effects was practically nil. The very hypnotic effect was at night very desirable. There seemed to be no marked preference for any of the drugs, and at times one would seem to work better than another, while often in the same patient the same drug would have different results as to efficacy in re-

lieving symptoms. In that case a change would have marked benefit. By combining the antihistamines with hyposensitization as noted in Table VIII, only eight patients were unable to obtain at least some degree of benefit. It is interesting to note that practically all of the patients found it desirable to use the drugs at some time during the season even those who had the best results with hyposensitization. In this group again as noted 8 or 7.4% had slight or no improvement, 12 or 10.2% had appreciable relief and 88 or 82.4% had good results which in these cases were such as to make them very comfortable even to completely free them of symptoms.

COMMENT: A study of the results here given would indicate that the antihistamine drugs are a great help in the control of hay fever patients and would certainly justify the conclusion that histamine must play some very definite role in the allergic reactions. It is very evident also that the drugs here reviewed are a long ways from ideal. The side effects are a very real and serious obstacle, and often the patient changes one set of symptoms for another. The itching, nasal discharge and eye symptoms are much more relieved than the nasal stuffiness and blockage. The patients very often object to taking drugs continually through a long period of time even though only seasonal. The results are purely palliative, and there is a recurrence of symptoms as soon as medication is stopped. They do not immunize the patient and protect him from the effects of an allergic reaction for any prolonged period. Beyond that, the effects are often very disappointing especially in the severe cases. We have many attempts at various times to use benzedrine, caffeine, ephedrine to counteract the drowziness of the large percentage of patients having this side effect but with no great success. In our experience, in instances where ephedrine was of benefit we found that the relief was better with no antihistamine at all.

The best results as noted are obtained not only in quantity but in quality which is difficult to express in figures, is by the combination of hyposensitization with the antihistamine drugs. The side effects, though not in direct ratio to the symptomatic relief, are very often in direct proportion to dosage used. It is, therefore, desirable to use a smaller dosage which is exactly the case when used in conjunction with hyposensitization. It must also be emphasized that while the antihistamine drugs seldom have marked benefit on the respiratory or seasonal asthmatic symptoms, hyposensitization frequently will give marked relief of asthma even when the symptoms referable to the nose and eyes are little affected. While it is evident that we will get better antihistamine drugs as regards potency and toxicity, it is also evident that it would be preferable to attack the problem in a more fundamental way at the beginning rather than by neutralizing the end product of the allergen-antibody reaction.

CONCLUSION: In conclusion it is probably justifiable to say that the antihistamine drugs used here are a very valuable addition to our methods of treatment of hay fever but are often not efficient and have serious side effects. A large percentage of patients will get relief with one or another in an appreciable degree. The preferred method, however, at present is the combined method of hyposensitization with the antihistamine drugs. Here the results are the best up to the present period.

I wish to thank Dr. R. Bieter, Chief of the Department of Pharmacology, for his help in obtaining and using these drugs. I also wish to express my appreciation to Dr. S. Hirsh and Dr. W. Peterson for their help in administering some of these drugs and tabulating some of the data.

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III. MEDICAL SCHOOL NEWS

Doctors Moore and Huseby Honored

Dr. George A. Moore, Clinical Instructor of Surgery in the Medical School, has been awarded a $25,000 medical scholarship grant from the John and Mary R. Markle Foundation of New York. The grant which will provide $5,000 annually for five years was made to the University for Dr. Moore in recognition of his work in cancer detection. Dr. Moore's work with fluorescein and radio-active fluorescein has won him world-wide recognition. He is one of 13 American medical scientists thus honored by the Markle Foundation in their program which is formed to assist young doctors to continue their work in medical teaching and research.

Dr. Robert A. Huseby was honored by the Junior Chamber of Commerce of Minneapolis when he was chosen as Minneapolis' outstanding young man of the year. Dr. Huseby, Assistant Professor of Cancer Biology on the Dr. William A. O'Brien cancer research professorship, was accorded this recognition because of his outstanding contributions to our knowledge of cancer. He has done research and published extensively in both fundamental and clinical spheres. Dr. Huseby has also been active as a teacher speaking to groups of physicians at medical societies and Continuation Center Courses.

* * *

New Minn. Medical Foundation Members

Chas. F. Medlin, M.D., Truman, Minn.
R. J. Wilkowske, M.D., Owatonna, Minn.
Herschel J. Kaufman, M.D., 5152 Upton Ave. S., Minneapolis, Minn.
Norman C. Carlson, M.D., Yellowstone Park, Wyoming
Donald E. Otten, M.D., Eugene, Oregon
Otto J. Seifert, M.D., New Ulm, Minn.
Julien V. Petit, M.D., 1111 Nicollet Ave., Minneapolis, Minn.

Biographical Briefs - Our Dean

Harold S. Diehl was born in Nittany, Pennsylvania, and spent most of his youth in that state, going to college in Gettysburg, and receiving his Bachelor of Arts degree there. He was active as an educator, although not a medical educator from 1912 to 1914 in Fulton, New York, where he was assistant principal and teacher of mathematics in the high school.

Dr. Diehl came to Minneapolis in 1914 to enter the Medical School at the University of Minnesota. At this same time, he taught chemistry at Augsburg College. During his later undergraduate years in Medical School, he was a teaching assistant in bacteriology and pathology. The closing years of World War I found Harold Diehl, now M.D., in France with the United States Army at Base Hospital 26.

Dr. Diehl's work in public health began in Europe where he served as Director of the American Red Cross Commission to Poland in 1919 and 1920. He returned to this country and to the University and served as pathologist to the University Hospitals in 1920-21.

In 1921 Dr. Diehl became Director of the Students' Health Service of the University. The University created a Department of Preventive Medicine and Public Health in the Medical School in 1922 with Dr. Diehl as its first head. He continued in both of these posts until 1935 when he was appointed by the Board of Regents as Dean of Medical Sciences. His interest in Preventive Medicine and Public Health has continued, and he is at present active as a professor in that department.

* * *

Editor's Note: A series of brief biographical sketches is begun this week to give friends of the Medical School background information on members of the Medical School faculty. No attempt will be made to give a complete account of accomplishments and honors.