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Drug Therapy in Parkinsonism

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I. DRUG THERAPY IN PARKINSONISM

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The treatment of parkinsonism represents a challenge to the physician--a challenge, which if successfully met, yields rich therapeutic rewards. It is not sufficient to give the patient a hastily written prescription and expect that he will do well. Each case is a problem unto itself, and what constitutes adequate treatment for one patient may be totally ineffectual for another. Perseverance and patience on the part of the physician are essential if the patient is to obtain the maximum benefit in the relief of his troublesome complaints. Often it is necessary to try the patient on many regimes and months may elapse before the best one is discovered.

The treatment of a patient with parkinsonism is a combination of intelligent use of drugs, emotional readjustment and exercise. A great number of drugs have been used at one time or another. Most of these medications are now only of historical interest and are documented in a number of excellent reviews[1,2,3,4]. However, definite improvement in the clinical picture has been produced by some medications, and encouraged by this, investigators are still in search of the ideal drug for the treatment of parkinsonism. In view of the large numbers of new drugs introduced in recent years in therapy of parkinsonism, a review of this phase of therapy seems timely. The medications currently in use or under investigation will be considered.

1. Belladonna derivatives: Excellent reviews on the belladonna drugs are available[4,5,6,7]. The belladonna drugs are widely distributed in nature, especially in the Solanaceae plants. Galenecal preparations of balladonna have been employed in medicine for many centuries and were known to the ancient Hindus. The professional poisoners of the middle ages often employed the deadly nightshade plant to produce a type of intoxication which was often prolonged and obscure. This prompted Linne' to name this shrub Atropa belladonna, after Atropos, the oldest of the three fates who severs the thread of life. The word "belladonna" itself is a reminder of the antiquity of these medicines in that it signifies "beautiful lady", the women of long ago being wont to instill a decoction of belladonna in their eyes to produce dilated pupils, a sign of comeliness. In the treatment of parkinsonism drugs of the belladonna group have been used since Ynauch in 1882 advocated the use of hyoscine. After that date, various alkaloids of belladonna, including atropine, hyoscyamine and scopolamine have been used extensively.

In 1926 Raeff[4], a plant collector, used extracts of Bulgarian belladonna root to treat parkinsonism. This form of therapy was taken up and extended by Panegrossi[4], who designated it the Bulgarian treatment. It was soon proved, however, that the Bulgarian belladonna root had no properties which made it superior as a therapeutic agent to the belladonna grown in other counties. Vollmer[8] considered that extracts of belladonna were too inconstant in the concentration of alkaloids and recommended the use of synthetic compounds, containing known concentrations of the various alkaloids. Extensive comparative studies[6,9] have shown that the alkaloids, root extracts and synthetic compounds have similar action and owe their activity to the alkaloids they contain. No one preparation is clearly superior to others. It is necessary to try the various drugs to find the one which is best for the individual patient. A change in medication may be necessary at a later date, and it is frequently necessary to shift from one drug to another for the maximum therapeutic benefit[10,11].

The active alkaloids of the belladonna group used in the treatment of parkinsonism are atropine, scopolamine (hyoscine) and hyoscyamine. Atropine and hyoscine are used independently in the treatment of parkinsonism. Atropine[9] is administered in a $\frac{1}{2}$ per cent solution commencing with 1 drop T.I.D. and increasing to 10 drops T.I.D. Hyoscine is administered as hyoscine hydrobromide in

tablets of gr. 1/100 and gr. 1/150. The amount of hyoscine hydrobromide given is that which produces the maximum benefit for the patient.

Tincture of stromonium contains atropine and hyoscyamine. The mode of administration of this drug recommended by Doshay[9] is to start with 20 drops T.I.D. and slowly build up to 60 drops T.I.D.

The remainder of the drugs of the belladonna group, bellabulgara, rabellon, and vinobel, are compounds, which contain varying proportions of atropine, scopolamine and hyoscyamine. Bellabulgara is a Lederle product. Each tablet of bellabulgara contains .4 mgm. of the total alkaloid of belladonna. Rabellon is a Sharpe and Dohme product and comes in .5 mgm. tablets. Each tablet contains .45 mg. of hyoscyamine, .037 mgm. of atropine and .012 mg. of scopolamine. Numerous publications[21,22,23,24,25,26,8] confirm the beneficial effect of this medication. Vinobel is a Merrill product. The tablets are of two sizes, .4 mgm. (red in color) and .8 mgm. tablet (orange in color). Numerous publications[24,9] confirm its therapeutic effect. The mode of administration of bellabulgara, vinobel and rabellon is to determine initially the maximum dosage of the drugs that the patient can tolerate and then to determine the minimum dosage which produces the maximum therapeutic effect. This is the maintenance dose of the drug.

The toxic symptoms encountered in the use of drugs of the belladonna series are dryness of the mouth; urinary retention; visual blurring; gastro-intestinal symptoms such as nausea, diarrhea and constipation; central nervous system symptoms such as headache, dizziness, and in some instances confusion, delirium and hallucinations.

2. Dihydro-beta-erythroidine: The clinical use of this drug was reported by Shapiro and Baker[12] in 1950. The drug is an alkaloid and the usual dosage is four of the 50 mgm. tablets per day. This drug is used as an adjunct to the atropine erivatives. It is indicated where rigidity is a feature. It has little effect on tremor or upon the oculogyric crises. The toxic symptoms are usually transient and consist of gastro-intestinal manifestation, visual disturbance and some dizziness.

3. Parpanit: In 1946 Grunthal[13] reported on the use of "parpanit", an antispasmodic related to "trasentine", in a number of extra-pyramidal disorders and found it more efficient and less toxic than the atropine-like substances. Hartmann[14,15] confirmed these observations in 1946 and in 1947, finding parpanit far more efficient in Parkinson's disease than the atropine-like drugs and reported briefly on its use in about 40 patients. Schwab and Leigh[16] studied its effects in 50 patients over a period of three months, and basing their views largely on the patient's ability to carry out the ordinary "chores of life," they considered that parpanit was more efficacious than the solanaceous drugs in 62 per cent of the cases, that it had an equal effect in 22 per cent, and that in 16 per cent the effect was not so good. Their dosage ranged from 90 to 600 mg. per day, given in divided doses, preferable every three hours, but at most every two hours. The average dose was found to be from 200 to 400 mg. per day, which represents one 50 mgm. tablet five times a day. Toxic effects were frequent and occurred in two-thirds of the patients, and it was necessary in one-fifth of the group to stop treatment on this account. The toxic symptoms encountered in order of frequency were, "giddiness", nausea and epigastric "burning", feeling of lightness of the legs and a sensation of floating. Dunham and Edwards[17] confirmed the lessening of rigidity in patients on parpanit and considered that its activity was comparable to that of the solanaceous alkaloids, but some patients found its side-effects, of which the most prominent is a sensation of dizziness, less upsetting.

Sciarra, Carter and Merritt[7] after using parpanit in twenty-eight patients with parkinsonism reported that none of them showed objective improvement, and in

only one patient was there subjective improvement. Toxic side effects were encountered in 86 per cent of the patients on whom the drug was used.

4. Artane (trihexphenidyl, or 3-(1-piperidyl)-1-phenyl-1-cyclohexyl-1-propanol hydrochloride): In general, the reactions of artane resemble those of atropine. However, it is entirely free of the toxic effects of atropine on the cardiac vagus, blood pressure and circulation[18]. Doshay and Constable[18] after investigating its use in 117 patients with parkinsonism concluded that artane was "the drug of choice in the arteriosclerotic and idiopathic cases, and should be tried regularly in postencephalitic cases in which atropine or other forms of medication prove disturbing or ineffectual". The usual dosage used was between 6 to 10 mgm. per day--with doses as high as 50 mgm. per day being used without deleterious effects. The toxic symptoms encountered included dryness of mouth, blurred vision, nausea or vomiting, dizziness or giddiness and drowsiness. Corbin[19] reported on its use and found that of 69 cases with idiopathic paralysis agitans 53 were benefited, and of 17 postencephalitics 12 obtained some relief. The drug appeared to act by relaxing rigid muscles and in some cases tremor also was improved. The side effects, usually slight, were, in order of frequency, dry mouth, nausea, "giddiness", blurring of vision, nervousness or "jitteriness", tinnitus, "tightness in the head" and soreness of the mouth. Four patients had severe and immediate toxic reactions; namely, mental confusion, dizziness with nausea, and marked agitation. The average daily dose used by Corbin was 8 mgm.

Schwab and Tillmann[20] treated 44 patients with artane for three months and found it improved the condition of 29, but in most of them it had its greatest effect when given in conjunction with parpanit, benadryl, or an atropine preparation.

5. Tolserol (Myanesin): (3-ortho-toloxy-1,2-propanediol): Favorable results following the use of this drug in the treatment of parkinsonism have been reported[27,28,29,30,31]. Toxic symptoms were rarely encountered and consist of 1. complaints of weakness, either in the arms or legs accompanied by a feeling of lassitude[28], 2. nausea in one case[31], 3. leucopoenia in two of eight cases[32a]. Early British investigators reported the presence of hematuria and hemoglobinuria but this has not been found by investigators in the United States. Tolserol is available in oral preparations, as suppositories, and in a 2 per cent solution for intravenous administration. Jeub[31] reports the effect of an oral dose as transitory, wearing off in forty minutes.

6. Antihistaminic Agents: Budnitz[33] reported a beneficial effect from benadryl in the treatment of eight cases of paralysis agitans of the arteriosclerotic group. Our results with the antihistamines as well as oral reports from other clinics have been less encouraging.

7. Diparcol: (diethylamino, 2, ethyl-N, dibenzo-para-thiazine hydrochloride): The use of diparcol in the symptomatic treatment of Parkinson's disease was described by Sigwald, Bovet and Dumont[34] in November, 1946, at a meeting of the French Society of Neurology. In a later paper[35] the same group of investigators reported on 168 patients who had been studied carefully. They claimed satisfactory and frequently dramatic results in 53 per cent, good results in 24 per cent, and fair in 17 per cent. Only 60 per cent of their patients represented therapeutic failures. They felt that the clinical response was substantially more gratifying than had been obtained previously with earlier drugs. Some improvement in symptoms has also been reported by other observers[36,37] but the side-effects of this drug will probably prevent its widespread usage: they include severe vertigo, paraesthesiae in the legs, somnolence, transient paralysis lasting about an hour[38], nausea, vomiting, hyperthermia, and leucopoenia.

8. Benzedrine: In 1935 Prinzmetal and Bloomberg[32] used benzedrine in treatment of narcolepsy. Since then it and

more recently dexedrine have been used in the treatment of oculogyric crises, psychic abnormalities and lethargy[4].

PART II

Because of the large numbers of drugs being made available for the treatment of parkinsonism, an objective method for assessing the efficacy of these medications is of prime importance. Reports of methods of assessing the therapeutic effect of new drugs in parkinsonism have failed to consider adequately the psychotherapeutic effect of the change in medication. Some have maintained that there is a direct relationship between the enthusiasm of the doctor and the therapeutic effect of the new medication. Others have raised the objection that the improvement of the patient following a change in medication is due to the psychic uplift, which the patient derives from such a change and not due to any pharmacological action of the drug itself. A method of objectifying the assessment of new drugs was devised in our clinic and is now routinely employed. It is felt that a detailed account of the original clinical study, in which the new method was first tried, might be of interest, as it not only demonstrates the procedure, but also provides some interesting information regarding the emotional factors encountered in assessing new drugs in parkinsonism.

Example of Clinical Study

Phenergan: Diparcol and a placebo were used in this study. Diparcol* is a synthetic compound (diethylamino, 2, . . ethyl-N, dibenzo-para-thiazine hydrochloride) was made available in 62.5 mgm. enteric coated tablets. Diparcol produces parasympatholytic effects and early reports indicated it might be of use in the treatment of parkinsonism. Phenergan* (diethyl-amino-2-methyl-1-ethyl)-N-dibenzoparathiaxine) belongs to the group of antihistamines and was provided in 25 mgm. tablets for this study. The enthusiastic report on the use of antihistamines in the treatment of parkinsonism[33] provided the rationale for the assessment of this drug.

Phenergan, diparcol and a placebo were delivered to the dispensary without ever having been seen by the examiner, so that he would not be familiar with t the physical characteristics of these compounds. The dispensary assigned the following numbers to each of the compounds: 2000-I, 2000-II, 2000-III. The key to the identity of the drugs was held only by the dispensary and not until this study was completed and the results tabulated was their composition revealed to the examiner. Throughout the course of this study, the patients were seen exclusively by the author and thus psychic factors contingent upon change of the patient-doctor relationship were kept constant for the whole group.

The patients were studies for a six-month period. It was felt that the initial psychic effect of a change in medication would be dissipated over this period of time. The patients were urged to continue with their new medication in spite of ill effects or in spite of any deterioration in their condition. Only when the patient refused to continue or their clinical condition made a change mandatory was other medication substituted. Six patients received one or more of the compounds--two patients receiving all three.

No effort was made to select the patients for this study and thirty consecutive patients attending the parkinsonism clinic were studied. To the first ten 2000-I, to the second ten 2000-II, and to the last ten 2000-III, was administered. The patient's previous medication was stopped and the new medication substituted. The patient's condition was assessed both objectively and subjectively at frequent intervals during the study. It was thus possible to compare the early responses of the patient to the medication to the response at the termination of that medication. The objective criteria by which the patients were judged are listed in table I.

*Made available for experimental study by Merck and Co., Rahway, New Jersey

TABLE I

OBJECTIVE CRITERIA FOR ASSESSING DRUG THERAPY IN PARKINSONISM

1. Time taken to dress
2. Ability to comb hair
3. Ability to wash
4. Ability to shave
5. Ability to clean teeth
6. Ability to get in and out of a chair
7. Distance the patient is able to walk
8. Ability to write
9. Time taken for an average meal
10. Ability to hold and read a newspaper
11. Other evidence of improvement

They concerned functional activities of the patient; primarily daily self-care and ambulation. A significant improvement in one or more of these activities was recorded as a good result. The subjective response of the patient was correlated with his objective performance and did not constitute the basis for assessment of the efficacy of the drug.

Results

Since two patients failed to return to the clinic, the remaining twenty-eight constitute the basis for this report. Eleven patients received 2000-I, thirteen patients received 2000-II, and thirteen patients received 2000-III, later identified as phenergan, placebo and diparcol respectively.

In all the patients receiving 2000-I (phenergan) the results were very poor. Their symptoms became so severe that only two were able to complete the six-month trial. Three of the patients complained of mild transient nausea, dryness of the mouth and dizziness. Similarly the condition of the patients receiving 2000-II (placebo) deteriorated and only two patients were able to complete the six months of treatment. Transient dizziness was mentioned by two of the patients receiving 2000-II (placebo.)

However, in the group of patients receiving 2000-III (diparcol), two patients (cases 17,23) achieved results superior to those obtained from all previous medications. In the remainder of the patients in this group, the results of 2000-III (diparcol) administration were poor. The high incidence of toxic symptoms was responsible for the large number of poor results. In two patients the toxic symptoms, consisting of nausea, vomiting, hyperthermia and leucopoenia, necessitated immediate discontinuance of the drug. In six additional patients nausea, vomiting and dizziness were encountered. One of these patients complained of tenesmus.

Of particular interest was the comparison in the group receiving the placebo (2000-II) between the initial and final assessments. Any improvement in the clinical condition of the patients in this group must of necessity be due to psychic factors. In three[8,27,9] of the thirteen patients in this group the initial assessment at the end of 30, 42 and 60 days respectively, revealed a favorable response. However, by the end of 110, 56 and 120 days respectively the results had become poor.

In twenty-two of the twenty-eight patients there was a direct correlation between the objective clinical response of the patient, as measured by the criteria outlined in Table I, and the subjective response of these patients to their change in medication. In the remaining six patients there was a marked discrepancy between the patient's favorable subjective response and the objective clinical picture.

Case #1, while receiving 2000-I (phenergan) and Case #22 while receiving 2000-I (phenergan) and 2000-II (placebo) reported definite subjective improvement, while their objective clinical picture remained unchanged. In Case #2 on 2000-I, in Case #10 and #27 on 2000-II, and in Case #28 on 2000-III (diparcol) there was a definite deterioration in the patient's condition while the patients continued to state that they felt improvement.

Comment

To our knowledge, this is the first study on drug therapy in parkinsonism in which the objectivity of the examiner was insured by the fact he did not know which of the patients were receiving placebos and which were receiving the active drugs. The fact that three of the patients receiving placebos achieved a good therapeutic effect for a period of one to four months stresses the importance of allowing a sufficient period of time to elapse before a report on a new drug is made. We feel that six months constitutes a mimimum period and that preferably a year should elapse. The danger of relying solely on the subjective statement of the patient as to the efficacy of his medication is pointed out by the fact that in six of the patients their clinical condition failed to show improvement or actually deteriorated, while subjectively they reported a good result.

Other investigators[16,19,36] have stressed the importance of the drug's effect on the functional activities of the patient as being a reliable index of the effectiveness of the drug. In our experience this index has been the best reflection of the patient's response to a new medication, and now constitutes the basis for assessment of new drugs in parkinsonism in this clinic. Objective laboratory tests such as electromyography, measurement of the rigidity of muscles by dropping standard weight on them and measuring the rebound, quantitation of the rate of voluntary movement by electrodes applied to thumb and index finger, comparison of samples of handwriting and testing patients ability to walk have proved in our experience unsatisfactory for assessing drug therapy. These laboratory tests only reflect the condition of the patient at the time of examination and we have found a discripancy between the patient's performance under these artificial conditions and his daily performance.

Summary

In this clinic, all drugs to be assessed in the treatment of parkinsonism are delivered to the dispensary without ever having been seen by the doctor, who is to conduct the study. Here numbers are assigned to the drug and to a placebo. The key to the identity of the drugs is not disclosed until the final assessment of the drugs is made at the end of a six-month period. One physician prescribes the numbered compounds to alternate patients, and he alone sees these patients during the period of study. A minimum of twenty cases is necessary for the study of a single new drug--ten receiving the placebo and ten the active compound.

By this method, the objectivity of the examiner is assured. In addition the effect of the new drug can be compared with that of the placebo, as well as with the previous medications the patient has received. We feel that this clinical method may be used to advantage in other chronic conditions in which the assessment of new remedies is desired.

PART III

During the past two years some two hundred patients have attended the parkinsonism clinic. Of these, fifty have been studied intensively by this author. During this period a variety of medications have been employed: rabellon, hyoscine, bellabulgara, vinobel, diparcol, benadryl, phenergan, tolserol (myanesin), dihydro-beta-erythroidine, meberal, phenobarbital, benzedrine and dexedrine. These drugs have been used alone or in various combinations.

The twenty-eight cases who were used in the clinical study discussed in Part II are representative of the patients studied intensively. The results of the medications which these patients received, since they have been treated by this examiner, are presented in detail in the charts at the end of this paper. It at once becomes obvious that no single drug or combination of drugs is the best. Nine different combinations were necessary to achieve the best therapeutic result in twenty-four of the twenty-eight patients studied. In the remaining four patients, three achieved

equally good results from two or more medications. The objective clinical picture of the fourth patient was not helped by any of the medications employed. Based on the results of the experimental clinical study outlined in Part II, it is obvious that in ten cases a longer period of study will be necessary before a final conclusion is made in these patients, as to which medication is superior. The following table shows which medications were superior and the number of patients obtaining maximum benefit from them:

Best Medication	No. of Patients	Time of Administration >6 months	Time of Administration <6 months
Artane	7	5	2
Rabellon	3		
Hyoscine	2	2	
Vinobel	2		2
Diparcol	2	1	1
Rabellon / Dihydro	3	3	
Artane / Dihydro	3		3
Vinobel / Dihydro	1		1
Rabellon / Benadryl	1	1	
Rabellon or Vinobel or Artane	1	1	
Vinobel or Artane	1		1
Rabellon or placebo or phenergan	1		

Another striking factor which emerges from a perusal of the attached charts is the long periods of time for which these patients must be followed and the number of combinations which have to be tried before the best medication for an individual case is found.

Conclusion

Finding the best medication for the individual patient with parkinsonism is a painstaking project, which frequently strains the equanimity of the physician. The final rewards are great, as these chronically ill patients are genuinely grateful for the additional improvement which results from employment of the medication best suited for each patient. A variety of drugs must be tried over a period of years, before the physician has discharged his obligation to the patient and is entitled to feel satisfied with a job well done.

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Case No.	Symptoms			Etiology	Drugs				Comment
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	
1.	65	++	++	Postencephalitic	Rabellon	330		Good	
					Rabellon, Dihydro	354		Good	
					Artane	60		Good	
					2000-I	124	Nausea	Poor	Rabellon + Dihydro
					Rabellon	90		Good	best combination.
					Artane	60		Poor	
2.	42	+	+	Postencephalitic	Vinobel	400		Good	
					2000-I	123		Poor	Vinobel
					Vinobel	60		Good	best medication
3.	56	+	+++	Postencephalitic	Rabellon	185		Good	
					Rabellon + Dihydro	440		Good	Artane + Dihydro
					2000-I	35		Poor	best combination.
					Artane	123		Good	
					Artane + Dihydro	160		Good	
4.	54	+++	++	Postencephalitic	Vinobel	185		Good	
					Vinobel + Dihydro	30		Good	Vinobel + Dihydro
					Vinobel	75		Good	best combination.
					Vinobel + Dihydro	42		Good	
					2000-I	185		Poor	
					Vinobel	62		Good	
5.	65	+++	++	Unknown	Vinobel + Dihydro	250		Poor	
					Vinobel	30		Poor	
					Hyoscine	90		Poor	
					Artane	190	Dizzy	Good	Artane best.
					2000-I	28		Poor	
					Artane	150		Good	
6.	63	++	+++	Unknown	Rabellon	21		Poor	
					Artane + Dihydro	62		Good	
					Vinobel	42		Poor	Artane + Dihydro
					Artane + Dihydro	14		Good	best medication.
					2000-I	5		Poor	
					Artane + Dihydro	30		Good	

Case No.	Symptoms			Etiology	Drugs				Comment
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	
7.	65	+	+++	Postencephalitic	Dihydro	31		Poor	
					Rabellon + Dihydro	93	Gastrointestinal Complaints	Poor	
					Rabellon	80		Poor	
					Benadryl	379		Poor	No medication altered the objective clinical picture.
					2000-II	72		Poor	
					Artane + Benadryl	21		Poor	
8.	43	+	++	Postencephalitic (Father died of Parkinsonism)	Vinobel, meberal	160	Nausea, dizziness, tingling sensation in legs	Good	
					Diparcol - (50 mgm. tablets)	93		Good	For 30 days 2000-II produced good results but by end of 110 days results poor.
					Rabellon	120		Good	
					2000-II	30		Good	Diparcol best medication.
					2000-II	110		Poor	
9.	61	+	++	Postencephalitic	Rabellon	180		Good	For first 60 days results good on 2000-II. By end of 120 days results poor on 2000-II. Rabellon best medicine.
					Diparcol (50 mgm.)	220	Nausea	Good	
					Rabellon	60		Good	
					2000-II	60		Good	
					2000-II	120		Poor	
10.	55	+	+	Postencephalitic	Rabellon	180		Good	
					Rabellon + Dihydro	75		Good	
					Rabellon	180		Good	Rabellon + Benadryl best combination.
					Rabellon + Benadryl	60		Good	
					Rabellon	42		Good	
					Artane	30		Poor	
					Rabellon + Benadryl	215		Good	
					2000-II	183	Dizzy	Poor	

Case No.	Symptoms			Etiology	Drugs				Comment
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	
11.	55	+	+++	Postencephalitic	Rabellon	31		Poor	
					Rabellon + Dihydro	75		Good	
					Rabellon	31		Poor	Rabellon + Dihydro best combination.
					Rabellon + Dihydro	235		Good	
					Artane	123	Dryness of mouth, blurring of vision	Poor	
					Vinobel	60		Poor	
					2000-II	45		Poor	
					Rabellon + Dihydro	185		Good	
12.	42	++ oculogyria	+	Postencephalitic	Hyoscine + Benzedrine	365		Good	
					Artane	70		Good	Artane better in controlling oculogyria than hyoscine and Benzedrine. Artane best medication.
					Hyoscine	63		Poor	
					Artane	31		Good	
					Hyoscine + Benzedrine	100		Good	
					Artane	37		Good	
					2000-II	21		Poor	
					Artane	56		Good	
					Hyoscine + Benzedrine	63		Good	
					Artane	123		Good	
13.	44	+ oculogyria		Postencephalitic	Rabellon	365		Good	
					Artane	42	Dizziness, difficulty controlling legs (took 4 pills at once)	Good	Artane best - caused marked decrease in oculogyria.
					2000-III	4		Poor	
					Artane	21		Good	
					2000-III	21		Poor	
					Artane	185		Good	

Case No.	Symptoms			Etiology	Drugs				Comment
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	
14.	48	+	++	Postencephalitic	Vinobel	34		Good	
					Vinobel + Dihydro	49		Good	Vinobel best medication.
					Rabellon + Benzedrine	62	Blurring of vision		(No additional
					Artane	290	Dryness of throat, pounding of heart	Good	gain from Dihydro.)
					2000-III	183	Dizziness, flatulence, tenesmus	Poor	
					Vinobel	60		Good	
15.	57	++ oculogyria	++	Postencephalitic	Rabellon + Benzedrine	180		Good	
					Rabellon + Benzedrine + Dihydro	31		Good	
					Rabellon + Benzedrine	90		Good	
					Artane	60		Poor	
					Rabellon	150		Good	Rabellon best
					2000-III	60		Poor	medication.
					Rabellon	180		Good	
16.	49	++	+++	Postencephalitic	Rabellon	180		Good	
					Rabellon + Benzedrine	140		Good	
					Rabellon	31		Good	
					Diparcol (50 mgm.)	14	Flushed numbness in hands and feet.	Poor	
					Rabellon + Dihydro	93		Good	Rabellon + Dihydro best medication.
					2000-III	1	Numbness, temp. 102°, leucopoenia, high sed. rate	Poor	
					Artane	14		Good	
					2000-III	1	Temp. 103°, arthralgia, leucopoenia	Poor	
					Rabellon	75		Good	
					Rabellon + Dihydro	60		Good	
					Artane	42		Good	

Case No.	Symptoms			Etiology	Drugs				Comment
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	
17.	54	++	++	Postencephalitic	Rabellon + Dihydro + Benzedrine	62		Good	
					Rabellon + Benzedrine	60		Poor	
					Rabellon + Dihydro + Benzedrine	93		Good	2000-III best medication (diparcol)
					Rabellon + Dihydro, Benzedrine + Benodryl	7	Epigastric burning, excessive salivation	Poor	
					Rabellon + Dihydro + Benzedrine	140		Good	
					2000-III	183	Dizzy, disturbed equilibrium.	Good	
					Rabellon	93		Poor	
18.	30	+	+	Postencephalitic	Rabellon	183		Good	Rabellon, Vinobel, Artane equal in effect.
					Vinobel	180		Good	
					2000-III	124	Headaches, Nausea, dizziness	Poor	
					Artane	123		Good	
19.	77		++	Arteriosclerotic	2000-III	93	Nausea	Poor	Rabellon best to date.
					Rabellon	70		Good	
20.	63	+	+++	Postencephalitic	Rabellon	180		Good	Dihydro essential for patient's welfare. Artane + dihydro best combination to date.
					Rabellon + Dihydro	550		Good	
					2000-III	19	Nausea, vomiting	Poor	
					Rabellon + Dihydro	42		Good	
					Artane + Dihydro	120		Good	
					Artane	60		Poor	
21.	48	++	+	Postencephalitic	Rabellon + Benzedrine	400		Good	
		oculogyria			Artane	105		Good	
					2000-II	21		Poor	Artane best.
					2000-III	30		Poor	
					Artane	60		Good	
					2000-I	60		Poor	
					Artane	60		Good	

Case No.	Symptoms			Etiology	Drugs				Comment
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	
22	71	/	-	Postencephalitic	Rabellon	180	Blurring of vision, dryness of mouth	Poor	Patient only slightly incapacitated. Noted improvement in sewings on all medications.
					2000-I	180	Dryness of mouth	Poor	
					2000-II	180		Poor	
23.	57	/	///	Unknown	Rabellon	185		Good	
					Rabellon / Dihydro	300		Good	Artane best.
					Rabellon	30		Good	
					Diparcol (50 mgm.)	75	Gastric distress, painless	Good	
					Rabellon / Dihydro	30		Good	
					Diparcol (50 mgm.)	95		Good	
					Rabellon / Dihydro	93		Good	
					2000-III	185		Good	
					2000-II	4		Poor	
					Artane	50		Good	
24.	69	/// oculogyria	/	Postencephalitic	Hyoscine	185		Good	
					2000-I	62	Dizzy	Poor	Hyoscine best.
					Artane	30		Good	
					2000-II	30		Poor	
					Hyoscine	123		Good	
25.	41	// oculogyria	//	Postencephalitic	Hyoscine / Benzedrine / Dihydro	150		Good	
					Benadryl	9		Poor	
					Hyoscine / Dihydro	62		Poor	
					Diparcol (125 mgm.)	7	Dizzy- dryness of mouth, sleepy, drowsy, nausea.	Poor	Hyoscine and Artane best. Patient preferred hyoscine.
					Diparcol, Hyoscine	6		Poor	
					Hyoscine	62		Good	
					Hyoscine / Benadryl	60		Good	
					2000-II	7	Dizzy	Poor	
					Hyoscine / Benadryl	14		Poor	
					2000-III	14	Dizzy, weak	Poor	
					Hyoscine	123		Good	
					Artane	123	Air hunger	Good	

Case No.	Symptoms			Etiology	Drugs				
	Age	Tremor	Rigidity		Name	Treatment (days)	Toxic Symptoms	Results	Comment
26.	56	//	//	Undetermined	Vinobel	180		Good	
					2000-II	3		Poor	Vinobel, Artane
					Vinobel	75		Good	equal.
					2000-I	3		Poor	
					Vinobel	60		Good	
					Artane	120		Good	
27.	61	/	///	Undetermined	Rabellon	30		Good	
					2000-II	42		Good	
					2000-II	56		Poor	Artane best. Good
					2000-III	7	Nausea, temp. 101.4°, leuco-poenia	Poor	response from 2000-II for 42 days.
					Vinobel	30	Nausea, vomiting	Poor	
					2000-II	14		Poor	
					Artane	123		Good	
28.	49	/	///	Postencephalitic	Rabellon	183		Good	
					Artane	183		Good	
					Rabellon	63		Good	Artane best
					Artane	42		Good	medication.
					2000-II	7		Poor	
					2000-III	42		Poor	
					2000-I	13		Poor	
					Rabellon	60		Good	

KEY

/ mild // moderate /// severe

2000-I - phenergan 2000-II - placebo
2000-III - enteric coated diparcol

Dihydro - dihydro-beta-erythroidine

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II. MEDICAL SCHOOL NEWS

Medical Alumni Hold Homecoming Clinic

Medical alumni returned to the University of Minnesota Hospitals on the morning of Homecoming Day, November 4, to renew their annual clinical fall meetings.

Dr. Herman E. Drill, President of the Medical Alumni Association, presided and brought the greetings of the alumni to the Medical School faculty and to the officers of the Minnesota Medical Foundation.

Alumni were greeted by Dean Harold S. Diehl on behalf of the Medical School and were welcomed to the University Hospitals by Mr. Ray Amberg, who also acted as host for mid-morning refreshments.

Dr. Irvine McQuarrie and Dr. Owen H. Wangensteen and their associates presented a Pediatric-Surgery Conference devoted to the diagnosis and treatment of congenital heart disease. Doctors Forrest Adams, Joseph Jorgens, and George Veasy discussed the "Diagnosis of Congenital Pulmonary Stenosis with a Patent Foramen Ovale." Dr. Richard Varco briefly discussed the results of surgery for this defect.

Doctors E. T. Bell and Leo G. Rigler joined in presenting a series of diagnostic problems as a part of a Clinical-Pathologic Conference. They were assisted by Dr. Samuel T. Nerenberg.

Alums were then taken on a brief tour of the Variety Club Heart Hospital and the Student Health Service Building following which they adjourned to the Coffman Memorial Union for a brief pregame luncheon.

Dr. Drill expressed his gratification over the attendance at this renewal of the Homecoming Clinics and expressed the hope that it might once more become an annual occasion.

* * *

Host to Western Surgical Society

The Department of Surgery at the Veterans Administration Hospital will be host to the Western Surgical Society on November 30. Clinical and scientific sessions will be presented.

Mayo Physician Named President of Medical Group

Dr. Henry W. Meyerding, emeritus member of the Mayo Clinic staff and professor of orthopedic surgery in the Mayo Foundation, has taken over his duties as president of the United States Chapter of the International College of Surgeons at its annual meeting in Cleveland, Ohio.

University physicians who presented papers at the four-day assembly were: Thomas J. Kinsella, John S. Lundy, and Gershom J. Thompson.

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Interstate Postgraduate Medical Association

Dr. Richard V. Ebert, Veterans Administration Hospital, spoke before the 34th assembly of the Interstate Postgraduate Medical Association on Wednesday, November 8, in Chicago.

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Occupational Therapy Holds Open House

Open house was recently held at the Occupational Therapy Unit for psychiatry on the sixth floor of the Elliot wing of the University of Minnesota Hospitals.

The new facilities, which include printing press, mimeographing equipment, looms, facilities for painting, lathe, and beautiful sets of hand wood-working tools, are housed in a colorfully decorated room just east of the operating room balcony and will be used by psychiatric in-patients from stations 60 and 61.

Miss Borghild Hansen, director of the course in Occupational Therapy, announced that Miss Mary Nelson will be the occupational therapist in charge of the occupational and recreational activities.

Working closely with physicians and nurses, the occupational therapists hope to assist the patients both as an immediate therapeutic measure and in discovering and developing long term occupational and recreational interests which will be of importance to the patients after they have been discharged from the hospital.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

Visitors Welcome
November 12 - 18, 1950
- - - -

Sunday, November 12

University Hospitals

9:00 - 10:00 Surgery Grand Rounds; Station 22.

10:30 - Surgical Conference, Todd Amphitheater.

Monday, November 13

Medical School and University Hospitals

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 Physical Medicine Seminar; Etiology: Scoliosis due to Bony Deformities--Metabolic and Congenital; F. J. Kottke; E-101, U. H.

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

12:00 - 12:50 Physiology Seminar; Certain Vascular Responses to Large Doses of Epinephrine; Hiram Essex; 214 Millard Hall.

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

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

4:00 - 5:00 Pediatric Seminar; Demyelating Disease; Lewis Thomas; 6th Floor West, U. H.

4:00 - Public Health Seminar; 113 Medical Sciences.

4:30 - 5:30 Dermatological Seminar; M-436, U. H.

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

5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss, and Staffs; Powell Hall Amphitheater.

7:30 p.m. History of Surgery Seminar; History of Blood Transfusions; Arnold J. Kremen; Todd Amphitheater, U. H.

Minneapolis General Hospital

9:00 - 10:00 Pediatric Rounds; Dr. Lowry; 5th Floor.

Monday, November 13 (Cont.)

Minneapolis General Hospital (Cont.)

1:00 - 2:00 Staff Meeting; Classroom, 4th Floor.

2:00 - 3:00 Journal Club; Classroom, Station I.

Veterans Administration Hospital

9:00 - G. I. Rounds; R. V. Ebert, J. A. Wilson, Norman Shrifter; Bldg. I.

11:30 - X-ray Conference; Conference Room; Bldg. I.

1:00 - Metabolic Disease Rounds; N. E. Jacobson and G. V. Loomis; Bldg. I.

4:00 - Medical Surgical Conference; Conference Room, Bldg. I.

Tuesday, November 14

Medical School and University Hospitals

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

9:00 - 12:00 Cardiovascular Rounds; Station 30, U. H.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.

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

4:00 - 5:00 Physiology-Surgery Conference; Hyperglycemia Factor in the Pancreas; Bernard Zimmerman; Todd Amphitheater, U. H.

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

5:00 - 6:00 X-ray Conference; Presentation of Cases by University Hospital Staff; Eustis Amphitheater, U. H.

8:00 - Journal Club; E-101, U. H.

Ancker Hospital

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

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

Minneapolis General Hospital

8:00 - 9:00 Pediatric Rounds; Dr. Adams; 4th Floor.

8:30 - Pediatrics Allergy Rounds; Dr. Nelson; 4th Floor.

9:00 - 10:00 Pediatric Rounds; F. H. Top; 7th Floor.

Veterans Administration Hospital

8:45 - Surgery Journal Club; Conference Room; Bldg. I.

8:30 - 10:20 Surgery Conference; Seminar Conference Room, Bldg. I.

9:00 - Infectious Disease Rounds; W. Hall.

Tuesday, November 14 (Cont.)

Veterans Administration Hospital (Cont.)

9:30 - Surgery-Pathology Conference; Conference Room, Bldg. I.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and E. T. Bell.

10:30 - Surgery Tumor Conference; Conference Room, Bldg. I.

1:00 - Chest Surgery Conference; J. Kinsella and Wm. Tucker; Conference Room, Bldg. I.

1:30 - Liver Rounds; Samuel Nesbitt.

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

3:30 - 4:20 Autopsy Conference; E. T. Bell and Donald Gleason; Conference Room, Bldg. I.

Wednesday, November 15

Medical School and University Hospitals

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.

8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; Allen Judd and L. G. Rigler; Todd Amphitheater, U. H.

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

11:50 - 12:50 Radio-Isotope Seminar; Sensitivity of the Geiger Counter; James F. Marvin; 113 Medical Sciences.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Powell Hall Amphitheater.

5:00 - 7:00 Dermatology Clinical Seminar; Dining Room, U. H.

8:00 p.m. Dermatological Pathology Conference; Todd Amphitheater, U. H.

Ancker Hospital

8:30 - 9:30 Clinico-Pathological Conference; Auditorium.

3:30 - 4;30 Journal Club; Surgery Office.

Minneapolis General Hospital

9:00 - 10:00 Pediatric Rounds; Dr. Lowry; 5th Floor.

12:15 - Staff Meeting; Classroom, 4th Floor.

2:00 - 4:00 Infectious Disease Rounds; 8th Floor.

3:00 - 4:00 Pediatric Rounds; E. J. Huenekens; 4th Floor.

Wednesday, November 15 (Cont.)

Veterans Administration Hospital

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans and Bernard O'Loughlin; Conference Room, Bldg. I.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker.

11:00 - EKG Conference; Conduction Defects; Ernst Simonson; Conference Room, Bldg. I.

2:00 - 4:00 Infectious Disease Rounds; Main Conference Room, Bldg. I.

4:00 - 5:00 Infectious Disease Conference; Wesley Spink; Main Conference Room, Bldg. I.

7:00 p.m. Lectures in Basic Science of Orthopedics; Conference Room, Bldg. I.

Thursday, November 16

Medical School and University Hospitals

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.

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

12:00 - 1:00 Physiological Chemistry Seminar; Serum Lipo-proteins; Lee Wattenberg, 214 Millard Hall.

4:00 - 5:00 Physiology Seminar on Circulation; Substrate Utilization; 116 Millard Hall.

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

5:00 - Bacteriology Seminar; The Use of Ionizing Radiation as a Tool in Immunological Research; J. Friedman; 214 Millard Hall.

5:00 - 6:00 X-ray Seminar; Methods and Experiences in Standardizing X-ray Machines; James Marvin; Eustis Amphitheater, U. H.

7:30 - 9:30 Pediatrics Cardiology Conference and Journal Club; Review of Current Literature 1st hour and Review of Patients 2nd hour; 206 Temporary West Hospital.

Minneapolis General Hospital

8:00 - Pediatric Rounds; Forrest Adams; 4th Floor.

9:00 - 10:00 Pediatric Rounds; F. H. Top; 7th Floor.

10:00 - Pediatric Rounds; Adult Contagion.

11:00 - 12:00 Clinical Pathology Conference; Large Classroom.

11:30 - Pediatric Conference; Main Classroom.

1:00 - 2:00 EKG and X-ray Conference; Classroom, 4th Floor.

2:00 - EKG and X-ray Conference; Classroom, Station I.

Thursday, November 16 (Cont.)

Veterans Administration Hospital

8:00 - Surgery Ward Rounds; Lyle Hay and Staff.

9:15 - Surgery Grand Rounds; Conference Room; Bldg. I.

11:00 - Surgery Roentgen Conference; Conference Room, Bldg. I.

1:00 - Chest Rounds; William Stead.

Friday, November 17

Medical School and University Hospitals

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

11:45 - 12:50 University of Minnesota Hospitals Staff Meeting; Porphyria; Clinical Manifestations in Relation to Clinical Findings; Paul Lowry, Rudi Schmid, Violet Hawkinson, Samuel Schwartz, and C. J. Watson; Powell Hall Amphitheater.

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

2:00 - 3:00 Dermatology and Syphilology Conference; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

2:00 - 4:00 Physiology Conference; Cardiovascular Demonstration Course; Rodney Harvey; 214 Millard Hall.

3:00 - 4:00 Neuropathology Conference; F. Tichy; Todd Amphitheater, U. H.

4:00 - 5:00 Clinical Pathological Conference; A. B. Baker; Todd Amphitheater, U.H.

4:15 - 5:15 Electrocardiographic Conference; 106 Temp. Bldg., Hospital Court, U.H.

5:00 - 6:00 Urology Seminar; Interstitial Cystitis in the Male; Robert Evert; Powell Hall Amphitheater.

Ancker Hospital

1:00 - 3:00 Pathology-Surgery Conference; Auditorium.

Minneapolis General Hospital

9:00 - 10:00 Pediatric Rounds; Dr. Lowry; 5th Floor.

9:30 - Surgery-Pediatric Conference; O. S. Wyatt and T. C. Chisholm; 4th Floor.

Friday, November 17 (Cont.)

Veterans Administration Hospital

10:30 - 11:20 Medicine Grand Rounds; Conference Room, Bldg. I.

1:00 - Microscopic-Pathology Conference; E. T. Bell; Conference Room, Bldg.I.

1:30 - Chest Conference; Wm. Tucker and J. A. Myers; Ward 62, Day Room.

3:00 - Renal Pathology; E. T. Bell; Conference Room, Bldg. I.

Saturday, November 18

Medical School and University Hospitals

7:45 - 8:50 Orthopedic X-ray Conference; Wallace H. Cole and Staff; M-109, U. H.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.

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

9:15 - 10:00 Surgery-Roentgenology Conference; J. Friedman, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

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.

11:00 - 12:00 Anatomy Seminar; The Histology of Antibody Production, Berry Campbell; Effects of Beta Rays on Nerve Conduction, Edgar L. Gasteiger; 226 I. A.

Ancker Hospital

8:30 - 9:30 Surgery Conference; Auditorium,

Minneapolis General Hospital

8:00 - Pediatric Rounds; Forrest Adams; 4th Floor.

9:00 - 10:00 Pediatric Rounds; F. H. Top; 7th Floor.

11:00 - 12:00 Pediatric Clinic; Charles May; Classroom, 4th Floor.

Veterans Administration Hospital

8:30 - Hematology Rounds; P. Hagen and E. F. Englund.