EADIE: All patients were followed up for at least six months, the longest for 11. At this stage the data were analysed. It is now difficult to avoid patient pressure to receive L-dopa, no matter how well the patient is doing on other therapies.

Dr. K. HEATHFIELD (Whipps Cross Hospital, London): With regard to long-term management, we followed the 12 patients in our original trial on 200 mg daily for a year, and found that the improvement was maintained in eight of them. Two were considerably better than at the end of the first month's trial, and two were worse—but no worse than at the beginning of the trial, before they went on the amantadine.

PARKES: What happened to the oculogyric crises in the patients with post-encephalitic Parkinsonism?

EADIE: These people have not had oculogyric crises in recent years. I cannot remember seeing, in Australia in the past five years, a patient with post-encephalitic Parkinsonism who still has oculogyric crises. They seem to have died out.

GILLIGAN: We had two patients still having oculogyric crises. One lost them on continued Symmetrel treatment.

Dr. VERA DALLOS (Whipps Cross Hospital, London): I am interested in the patient whom you referred back to the psychiatrist, because we have had four patients with exacerbations of psychiatric disorder. All were stable when they started amantadine treatment, in that they were not on tranquillisers and none of them was under psychiatric treatment at the time. While on amantadine, all four relapsed very badly and had to be referred back to the psychiatrist; one of them was admitted. I wondered about the full history of your patient.

EADIE: The lady had had a psychosis for some time. She was functioning reasonably in her family environment and not receiving any phenothiazines. The psychosis did not alter, but the attrition got her family to a stage where they wanted psychiatric help, and to provide this it was necessary to lose her from the trial. One could not say that the amantadine caused deterioration in the psychosis in this instance.





CHAIRMAN: Dr. Dallos, what kind of psychiatric disturbances did your patients have?

DALLOS: Severe depression, one with a homicidal episode three years before we started him on amantadine. After two weeks on 200 mg he had a complete relapse. The other three had had anxiety and depression and had previously been under psychiatric out-patient care. All four had to discontinue amantadine because of relapse; this occurred mostly on the higher dose. They were taken out of the trial.

## AUSTRIAN EXPERIENCE

GERSTENBRAND: In the neuropsychiatric clinic in Vienna we now have experience with 54 cases. Out of 10 cases with a mild form of the Parkinson syndrome, treated first with Symmetrel, the akinesia was significantly improved in five cases, much the same result as in Dr. Gilligan's series.

Again in 34 cases pretreated with conventional antiparkinsonism drugs, the results were almost the same as in Dr. Gilligan's series.

### PSYCHOLOGICAL TESTING

To prove the results of Symmetrel treatment, we are using psychological test methods. The first is to test motor activity. In this, the patient puts dots in each of a number of small squares, first with the right and then with the left hand, within 60 seconds. When one patient was tested before starting Symmetrel and again after 12 days' treatment, the score improved from 47 to 66 dots within 60 seconds. In the total series of 24 patients, mean scores were 71 with the right hand and 72 with the left hand (70 together), and they increased to 74 and 81 (75 together) during Symmetrel treatment.

Th second test was a digit symbol test to demonstrate associative ability, visual capacity and memory. Certain digits have to be associated with other symbols. After treatment there was an increase in the rate of filling in symbols from 5.9 to 6.7. In a group of 24 patients, the results of the first and the second tests were significant at the 5% level.

The third test method examines the patient's powers of concentration. The number of crossed out letters and the total number of errors are converted to a standard value. Here also there was improvement with Symmetrel treatment.

The fourth test is designed to establish memorising ability, and the fifth test involves the crossing out of letters. We also used Rorschach tests and found in 75% of the patients an increase in mental activity independent of clinical improvement.

Our results with these test methods seem to demonstrate improvement with Symmetrel treatment, especially in idiopathic Parkinsonism. We are now using these tests in most of our treated cases.

CHAIRMAN: Dr. Gerstenbrand, you are clearly finding tests of value in assessing the effects of Symmetrel. Have you any observations about the response to the different types of Parkinsonism?

GERSTENBRAND: Our cases are mostly idiopathic. In this study no post-traumatic cases were included and only 10 had post-encephalitic Parkinsonism. We cannot see any difference between the idiopathic and the post-encephalitic groups, but in the group tested specially only idiopathic Parkinsonism patients were included. About 70% of them showed improvement in mental capacity.

## SWISS CLINICAL STUDY

Prof. G. WEBER (St. Gallen, Switzerland): My experience is a very modest one, limited to a clinical study of the therapeutic effect of Symmetrel in Parkinsonism. (This is to be published by my colleagues, Dr. H. Hacohen and Dr. B. Gurtner.) We have had experience with 27 patients, 21 of them in the age group 60 to 82. Sixteen were men, 11 women. Five had very severe damage in regard to self-care activity. Only one patient had post-encephalitic Parkinsonism; 26 showed the idiopathic form, six probably together with arteriosclerotic brain damage. We gave a dosage of 100 to 300 mg Symmetrel.

We got good or very good results in about two-thirds of the 27 cases and no effect in one-third. Thus, 18 of the 27 showed a clinically good response, but we did not make any double-blind studies. We saw these good responses in the first few days of treatment, and they have been sustained over a period of three to 13 months, with some fluctuations such as one also sees in Parkinsonism patients without treatment.

Dr. P. LEVIN (Basle): May I ask whether any of these patients had been operated on previously, and if Prof. Weber would care to comment on his experience with stereotactic surgery and Symmetrel?





WEBER: Eight patients had been operated on. The hypokinesia in operated patients was improved in the same way as that in the non-operated patients. I have the clinical impression that hypokinesia is more improved than tremor and rigidity in our patients.

CHAIRMAN: Were your patients already on anticholinergic therapy?

WEBER: Yes, before starting Symmetrel, and many of them throughout the trial. We also tried Symmetrel in patients with post-traumatic akinetic mutism (apallic syndrome) but obtained no noteworthy results.

## NEW ZEALAND M.R.C. TRIAL

Dr. P. B. JØRGENSEN (formerly of Dunedin): I would like to give a résumé of the New Zealand Medical Research Council trial of Symmetrel in Parkinson's disease, carried out in mid-1970. Three main New Zealand centres took part, and there were 149 patients, 85 males and 64 females, aged 35 to 82 years with a duration of disease from one to 42 years. Based on the Webster scale of scoring, 38 were mild cases, 94 moderate and 17 severe. One hundred and forty patients were classed as idiopathic and five as post-encephalitic; in four cases the condition was associated with cerebrovascular disease. Twenty-six patients had received stereotactic surgery at some stage.

### METHODS

The design of the trial was double-blind, with amantadine and placebo each given for three weeks; 100 mg amantadine was given daily for one week, then 200 mg daily for two weeks. Anticholinergic drug therapy, which most patients were already receiving, remained unchanged. Table 1 shows the features that were assessed and given a score of 0 to 3 according to Webster's scale.

We also did some timed function tests: circle tracing tests, handwriting and a walking test, in which the patient rose from a chair, walked 15 ft, turned about, came back and sat down. In addition we did some tests with a machine that measured rigidity and tremor. Patients were asked to fill in a questionnaire of 30 daily activities

# Parkinson's Disease

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