NOTES FROM THE LOG-BOOK OF A PSYCHOPHARMACOLOGICAL RESEARCH UNIT II*

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This is a report on another series of systematic observations conducted by our research department. As in the first series of similar observations reported, these data were previously collected in a methodical manner and under competent clinical control conditions. However, the strict experimental design for some of the studies reported here, was deliberately compromised (placebo control, sample size, etc.) in order to obtain tentative short-cut answers to clinical questions without running into the expense of time, man-power and money which more elaborate experiments would demand. We feel that our results have sufficient informative value to warrant publication without claiming definitive validity for them.

MP-809 — A new Antidepressant

In 1962 Azima *et al.* reported a placebo-controlled study of MP-809, a tryptamine derivative on 50 depressed patients. Their study showed a significant antidepressant activity in 52% of all patients and in 71.4% of neurotic depressions ($P > 0.001$). Our clinical trial was carried out over a six-week period with fifteen patients selected from the different chronic units of the hospital. Patients chosen were characterized by withdrawal, depressive mood change and/or apathy as their most prominent clinical symptoms. The compound was administered, from 15 to 60 mgm. daily, in gradually increasing doses.

As criteria of the drug effects, we utilized our Depression Rating Scale and Target Symptom Rating Scale (Lehmann, Cahn and DeVerteuil). Improvement was seen in four out of the five items of the Depression Rating Scale in the following order: mood, facial expression, retardation, depressive ideation. The means of the total Depression Scale in this experimental population decreased in the course of the drug trial from 4.39 to 3.64.

In analysis of the individual cases; out of 15 patients, ten (66.6%) showed improvement (slight: four, moderate: four, marked: two). One showed no change and four became worse. The behavioural toxicity of the drug was mild and was manifested in these four cases on the increased scores on the Target Symptom Rating scale in symptoms of increased excitement and suspiciousness. None of the 15 patients were taken off medication because of clinical side effects. No physical toxicity was observed.

Our clinical trial confirmed the findings of Azima *et al* on the antidepressant properties of the drug, although in a smaller number of cases and with a less elaborate technique. It should also be noted that in some of our chronic patients (four) the antidepressant effect of the drug was felt to be superior to previously applied treatments.

The Effect of Methandrostenolone and Nursing Care on Incontinence

A double-blind placebo - controlled study was designed to evaluate the therapeutic effect of methandrostenolone on 30 psychiatric patients suffering from urinary incontinence of different origins. The trial lasted three months and followed a crossover design. There was an overall improvement noted through the three months, expressed in monthly means of incontinence ratings, for the two groups, i.e. the drug-treated and the placebo-treated: Group A: 1.81 — 1.71 — 1.39 and Group B: 2.22 — 1.91 — 1.54. It should be noted that the first and third months'

*The drugs for this study were supplied by the following Pharmaceutical firms—
MP-809 — Sandoz
Methandrostenolone — Danabol — Ciba
Dextroamphetamine — Dexedrine — Smith Kline & French
Methylphenidate — Ritalin — Ciba
Opipromal — Ensidon — Geigy
Perphenazine — Trilafon — Schering
Trimepropamine — Surmontil — Poulenc
Imipramine — Tofranil — Geigy
Levomepromazine — Nozinan — Poulenc
Diazepam — Valium — Hoffmann-La Roche

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results showed a somewhat greater reduction of incontinence in the group who were on the active medication. However, these findings did not reach statistical significance. This would suggest the simultaneous presence and effectiveness of an "indirect training" method deriving from the experiment itself, in the sense that some patients might have become gradually "toilet-trained" due to the regular control observations without, of course, receiving any directive instructions.

The Effects of Stimulants on Chronic Psychotic Patients

A comparative four-week clinical study was conducted on 45 chronic hospitalized psychiatric patients, with the primary aim of studying psychoactive and/or psychotogenic properties of three chemically - different known psychotropic compounds: trimethylxantine, dextroamphetamine and methylphenidate. The dosage schedule of drug administration was from 400 to 1,200 mgm. of Caffeine Citrate daily and from 10 to 30 mgm., daily for both the methylphenidate and dextroamphetamine groups over a period of four weeks.

We observed that all three drugs had an euphorizing effect. This effect was combined with an increase in motor-activity, attentive functioning, work performance and social behaviour in the trimethylxantine group. On the other hand, the euphoria and increased motor-activity in the dextroamphetamine group was associated with an increase in thought disturbance, delusions, regressed social behaviour, seclusiveness and an inclination to aggression.

Subjectively the patients experienced trimethylxantine and methylphenidate effects as pleasant and the dextroamphetamine as unpleasant, when the drugs were given for several weeks.

On the basis of these findings it would appear that while all three compounds had stimulating properties, therapeutically valuable psychological stimulation was effected both by methylphenidate and trimethylxantine, while dextroamphetamine appeared to achieve more of a psychotogenic action.

The Psychotropic Properties of Opipramol

Opipramol is an iminostilbene related to imipramine and the attached side chain is a piperazine group, identical to that of perphenazine. Our preliminary studies on the influence of this drug on dextran-induced edema on rats suggested that it would have both tranquillizing and antidepressant properties. On the basis of psychophysical testing of human subjects it was found to produce mild sedation after single dose administration. Our first clinical trial indicated that it had mild tranquillizing and antidepressant properties. Our clinical trial on ten patients established that it could be safely administered over a twelve-week period in a dosage of 200 mgm., daily, without producing significant clinical side effects or organ toxicity.

It should be noted that the drug was administered to chronic schizophrenics who were apathetic but not depressed and it did not reveal any psychotogenic properties but temporarily produced a state of increased socialization and activity.

The Effect of Trimepropamine on Geriatric Psychiatric Patients

Trimepropamine is a new antidepressant which was derived from chemical synthesis of the iminodibenzyl, imipramine and the phenothiazine levomepromazine.

Our study with trimepropamine was conducted with ten female patients over 65 years of age whose prominent symptoms were: inactivity, depression and apathy. The patients were continued on whatever previous medication they were receiving (digitalis; vitamins, etc.) to which trimepropamine was added in the dosage of 50 mgm. daily in two divided doses, for a period of six weeks. The ten patients included in this study belonged to different diagnostic categories: schizophrenia, paranoid – five; chronic brain syndrome due to chronic alcoholism – one, due to syphilis – one, due to cere-

bral arteriosclerosis: – one; involutional psychosis – one, senile psychosis – one. Their ages ranged from 63 to 82 years, giving a median age of 70 years. Their length of hospitalization ranged from six months to 32 years with a median of 11 years.

The data from three psychiatric rating scales were evaluated with two non-parametric tests of significance, the Wilcoxon matched-pair signed-ranks test and the Sign test. The following significant patterns were noted: the total symptomatology, as rated on the Target Symptoms rating scale, tended to improve during the last five weeks of the trial period. Changes were slight, but more marked in the following symptoms: hostility, lowered ($p = .03$), depression, slightly alleviated ($p = .03$), attention, less impaired ($p = .03$). From the third week until the end of the trial the total Target Symptoms ratings showed a relatively consistent improvement over the pre-trial ratings ($p = .048$).

Changes on the Depression Rating Scale were slight and irregular but by the seventh week there had been a drop in the severity of the depressive symptoms, significant at the .02 level of confidence.

The most definite trends in the clinical data were found in those symptoms related to general interest, participation in conversation, and socialization. Improvement in the social behaviour of the subjects, as judged by the total scores on a sociability rating scale, began during the third week, and was maintained throughout the trial ($p = .028$).

No organ toxicity was observed in any patient. Among the clinical side effects, transient drowsiness was noted in four cases, and dry mouth in three, accompanied in one by coated tongue and stuffed nose. Skin rash, itching and dyspnea occurred in the first week of drug administration and they were transient in nature. The dyspnea occurred in a patient with a cardiac condition at the end of the drug trial.

Our findings indicated that trimepropamine may be safely used in the treatment of geriatric patients, even in combination with other medication. The drug's beneficial effect is seen mainly in the improvement of the affective psychic parameter (depression, hostility, etc.) and in the arousal parameter on the attention-function. Note should be made that, in spite of the transient clinical side effects, no serious organ toxicity was revealed and in no case was medication discontinued because of adverse effects.

The Effect of Diazepam on Newly Admitted Schizophrenic Patients

Diazepam was administered to 15 newly admitted schizophrenic patients, chosen randomly on admission. The dosage ranged from 30 to 90 mgm. daily. The trial was originally designed for eight weeks, but ten of the patients had to be taken off the drug within three weeks and one in the fourth week of the trial because of inadequate behavioural control and the absence of any therapeutic effect on the psychotic manifestations. On the basis of these results diazepam would appear to be relatively ineffective in acute schizophrenics; however, the finer statistical analysis of our findings indicated that the drug did have some beneficial effect in reducing anxiety.

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Résumé

II. – Cet article est le deuxième d'une série de observations cliniques faites au Verdun Protestant Hospital. Les sujets suivants ont été discutés:

1. MP 809 – une nouvelle médication antidépressive.
2. L'effet de la methandrostenolone sur l'incontinence.
3. L'effet des stimulants sur les psychoses chroniques.
4. L'effet psychoactif de l'opipramol
5. L'effet de la trimepropamine sur des cas de psychoses séniles.
6. L'effet de la diazepam sur des patients psychiatriques récemment admis.