A phenothiazine derivative recently introduced to Thailand in this era of chemotherapy is pericyazine, the formula of which is 2-cyano-10 (3,4 hydroxy piperidino-propyl phenothia-
zine), and the structural formula is:

![Chemical Structure of Pericyazine](image)

**General Pharmacology**

It has been reported to be ten times more active than chlorpromazine in sedative action. The anti-adrenergic effect is comparable to that of chlorpromazine, but the anticholinergic effect is nearly twice as much as that of chlorpromazine. Its psycho-correc-
tive properties are more active than those of prochlorperazine.

Pericyazine, like chlorpromazine, has only weak antihistaminic activity, but its anti-apomorphine activity is as much as ten times greater than that of chlorpromazine.

**Therapeutic Effects**

A number of trials of pericyazine in clinical usage have been performed and reported by various authors in the United Kingdom, Scandinavia, Canada, France, and India. The results indicate the main action of the drug to produce combined tranquilizing and stimulating effects. The patients involved in these trials belonged to groups of different ages with a variability of diagnostic categories.

Chanoit et al reported favorable results in treating schizophrenic and other chronic psychotic patients with pericyazine, especially in the area of character disorders and behaviour disturbances.

Power treated a short series of adult male schizophrenics, who had previously failed to respond to large doses of potent phenothiazine deriva-
tives, with pericyazine alone for five months and reported a satisfactory result.

Nimb stressed the beneficial therapeutic effect on behaviour disorders in 137 patients at a Welfare Home in Copenhagen.

Bartlet, who tried the drug on hard-core schizophrenics, found that pericyazine was a very useful drug in aggressive chronic schizophrenics.

Sivadon treated 27 males and 28 females suffering from various psychi-
atriac disorders and found that pericyazine was a valuable maintenance psychosedative, whereas no serious side-effects were encountered.

Heller emphasized the advantage of pericyazine over other phenothia-
zines in the control of behaviour disorders in chronic schizophrenics.

* Somdet Chaopraya Hospital.
Oules reported his experience with pericyazine in 50 chronic psychotic patients. Twenty two of them were chronic schizophrenics whose behaviour and delusions were improved after the drug trial with adaptation in impulsiveness and aggressiveness.

Rasch et al. determined the effect of adding pericyazine to existing drug treatments in mixed groups of chronic institutionalized patients with severe behaviour disorders, and reported favourable results in the area of severe behaviour disorders.

**Mode of Administration and Dosage**

Pericyazine can be administered both orally and intramuscularly, the latter in the form of aqueous solution. In trials performed by early authors with clinical experience of the drug, the therapeutic dosage ranged from 30-120 mg. per day. Deshaies claimed that 280 mg. per day was given without untoward effects. In instances where daytime sedation is undesirable, it is suggested that two-thirds of the daily dosage be given in the evening.

**Side-effects**

As described by many authors, the drug is less toxic and produces fewer side-effects than other major neuroleptics. At the start of the treatment, drowsiness is not uncommon, but this effect should disappear within a few days. Numerous investigators have reported infrequent occurrences of mild extra-pyramidal symptoms; orthostatic hypotension, especially in elderly patients and in children, which did not necessitate any special treatment; gastro-intestinal disturbances, particularly nausea, vomiting and diarrhoea. Autonomic disturbances such as sweating and sialorrhoea are also infrequent. Photosensitization has not been observed by previous investigators, and allergic skin reactions have rarely been observed.

In psychopathic patients, dizziness, voracious appetite, and consequent weight gain were also encountered.

The work done so far has revealed no complications pertaining to the haemopoietic system, liver or renal impairment.

As pericyazine enhances the therapeutic effects of other phenothiazine derivatives, care should be taken when the drug is prescribed in conjunction with other phenothiazine derivatives or with central nervous system depressants, such as barbiturates or opiates. Reduction of pericyazine dosage is recommended in combined chemotherapy, depending upon individual response.

**Methodology**

The study was carried out in the Female Section of the In-patient Department of Somdet Chaopraya Hospital, Dhonburi for a period of four months.

A careful selection was made of 20 female chronic schizophrenic patients, who had been hospitalized for years but still remained symptomatically unimproved exhibiting the following symptoms:

1. disorganization
2. disturbances of behaviour, particularly aggressiveness, severe hostility, or socially unacceptable habits, such as playing with faeces, disclosing genitalia, excessive greediness with extreme loss of control.
Clinical Trial with Pericyazine

3. Persistent hallucinations and delusions.

These patients all had a history of treatment in large dosages with the phenothiazines available in the hospital, namely chlorpromazine, promazine, trifluoperazine, perphenazine, prochlorperazine, reserpine, and thioridazine. In the majority of cases (all but one) E.C.T. had been given. Regardless of such previous intensive treatment, psychotic symptoms were apparent in all cases to a certain degree.

The ages varied between 19-60 years, with 16 of the cases ranging between 25-40 years. The duration of the admissions varied from 3 to 19 years. Fourteen of the group had been hospitalized for over 10 years.

Since most of the patients were beligerent and many of them had had a violent reaction to drug administration, it was difficult to manage oral medication regularly at accurate dosages. Because of this the trial was started in a relatively unusual way by the intramuscular administration of pericyazine ("Neulactil" of May & Baker) in all cases.

The intramuscular dosages given varied from 20 mg. to 40 mg. per day, divided into two injections. The size of individual dosage depended upon the severity of psychotic symptoms, and the weight of the individual. After a fortnight, parenteral administration was discontinued in every case and the oral preparation of pericyazine ("Neulactil" of May & Baker) was substituted. The dosages varied from patient, to patient, running between 40-120 mg. per day. Two weeks after the initial oral dose it was necessary to increase the daily dosage in some cases, although they still remained in the range of 40-120 mgm per day.

Apart from physical and mental status examination, the patients underwent laboratory tests for routine blood, urine, and liver function before the commencement of the trial. The physical and psychiatric examination, and the laboratory tests were repeated at one and two months respectively. The rating scale was scored fortnightly by the head nurse, nurse-aids, and attendants.

Chlorpromazine via the intramuscular route was the only additional phenothiazine, used on rare occasions and in a very few cases throughout the trial.

In regard to the rating scale used in this study, that of Fergus Fall State Hospital in Minnesota, U.S.A., modified by Lucero and Mayer, was chosen; it was the most convenient and accurate one which suited the patients in this category. The raters were the head nurse, nurse-aids, and attendants of the chronic ward. Most of them had seen these patients for years.

There were 3 main types of behaviour for scoring; i.e. behaviour towards others, behaviour towards self, and behaviour towards activities and therapy. Some of these were degrees of co-operative attitude towards therapist, nurse, attendants, social workers, other patients, and towards medication, insight, hostility, mobility, productivity, interest in external world, hygienic care, eating and eliminating habits, initiative power for routine activities, occupational therapy, and rehabilitation.
RESULTS

It might be advantageous to future investigators if the assessment of this trial is described in detail. Starting from the first day of treatment, it is interesting to observe the highly effective sedative action of pericyazine right from the first injection. The ward atmosphere was unusually serene. 18 out of the 20 patients were absolutely quiet in a heavy lethargic state, lasting from 4-6 hours, not even caring about meals. These patients had never been as quiet before, even after intramuscular injection of chlorpromazine.

The lethargy subsided within a few days, but patients still remained quieter. Psychomotor activity was gradually decreased in the hyperactive ones but aggressive behaviours were observed to have a considerable reduction in frequency and in severity.

Two weeks after the start every patient was able to take tablets of pericyazine either voluntarily or by encouragement and persuasion by the nurse. Before this, only four would accept oral medication without problems, three by persuasion, and the rest almost always refused and so had to receive treatment by parenteral route.

Two months after the treatment six patients were observed to be improved by the mental status and fifteen by the rating scale, but at the end of the trial, there was no such differences. This is simply explained by the fact that mental status includes not only behaviour, but also thinking processes and ideation of the patients, whereas the rating scale is almost totally concerned with behaviour. It is easily understood that a thinking disorder takes a longer time than a disturbed behaviour to be corrected.

The results were illustrated in table I.

<table>
<thead>
<tr>
<th>Degree of improvement</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markedly improved</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Moderately improved</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>slightly improved</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>unchanged</td>
<td>5</td>
<td>25</td>
</tr>
</tbody>
</table>

The determining grades of responses in the evaluation of the clinical results are based on objective symptoms of the patients. The highest grade of response is "markedly improved" which implies the subsidence of socially unacceptable behaviour particularly the aggressive ones, elimination of hallucinations and/or delusions, nor-

malizing of psychomotor activity, increasing of productivity, restoration of adaptive power and sociability, and better insight. "moderately improved" is one whose behaviour and ideation have been improved to a great extent, but whose productivity and sociability are still beyond his potency. "Un-
changed" needs no explanation. A
Clinical Trial with Pericyazine

"slightly improved" patient is one between "moderately improved" and "unchanged".

It is noteworthy that physical and psychiatric examination before the study were done with difficulty in many patients. In eight cases, had intramuscular chlorpromazine not been given, the examination would not have been possible. A couple of patients were so agitated and fearful that one had to be re-examined on the following day, due to severe hostility and resistance. At the end of the trial only one patient, who for a long time had been in a deteriorating condition, refused to be examined and ran away. All the rest were calm and co-operative.

From an objective standpoint, different symptoms show varying degrees of responsiveness to pericyazine as assessed by clinical evaluation, which may more or less reflect the indications for the drug usage. The results on selected symptoms are elaborated in Table II.

<table>
<thead>
<tr>
<th>Chief Symptoms</th>
<th>No. of cases with such symptoms</th>
<th>No. of cases relieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe autism</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Aggressive behaviour</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Regressive behaviour</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Bizarre behaviour</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Severe hostility</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Abnormal psychomotor activity</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Agitation</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Persistent hallucinations:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. auditory</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>b. visual</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Persistent delusions:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. systematized, persecutory</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>b. non-systematized</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Underproductivity</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>
Side-effects

Throughout the trial, the drug revealed no serious toxicity or side-effects of clinical or laboratory significance, either in incidence or in severity. Only one patient (aged 60) developed postural hypotension once on the first day of parenteral pericyazine, which required no particular treatment and who spontaneously recovered. This patient tolerated a high dosage of oral medication throughout the course of the trial.

After four months of pericyazine treatment, a slight fall in blood pressure was detected in the routine physical examination. Systolic B.P. in 13 patients was 10-20 mmHg below their control levels, which is not uncommon in the prolonged used of major tranquilizing drugs. These patients remained asymptomatic.

In spite of the high daily dosage of 120 mg., only two patients developed Parkinsonism-like syndromes, characterized by a moderate degree of rigidity of neck muscles and extremities; one on the 10th day and the other on the 15th day, easily relieved by parenteral antihistaminic drugs with subsequent control by low dosage of an antiparkinsonian drug. In both cases similar syndromes had previously occurred with every phenothiazine given.

Laboratory tests showed that the haemopoietic system and liver function were not affected by the drug.

Discussion

In is possible to note discrepancies in this study of such a small group of twenty patients, if not contemplating the fact that these very patients had been tried without success on nearly all available major tranquilizers and only one of them had not yet been treated with E.C.T.

Considering the status of the patients, this study had the gratifying result of 75 percent of varying degrees of improvement in chronic schizophrenics, irrespective of subgroup of types. This supports the experiences of Aules, Astrup and Clemm, and Bhaskaran and Antony.

It is of interest to note that the eight cases of dramatic response had a wide range of differences in age (19-60 years), in duration of hospitalization (3-16 years), and in degree of deterioration. It is also remarkable that four out of the five unchanged had formerly been severely deteriorated, while two of them were hebephrenics.

In regard to relieved symptoms, not much can be discussed in percentage in such a small number of patients. However, the result tends to point towards the different degrees of efficiency of the drug against the different symptoms. Conclusively, the drug appears to be valuable for the treatment of patients in areas of:

1. correction of behaviour, especially the aggressive ones
2. normalizing of psychomotor activity
3. devitalization or elimination of hallucinations and delusion.

Simultaneously, the drug is relatively less effective in improving severe autism and restoring productivity.

In regard to the risk of side-effects, pericyazine is highly tolerated which gives it an advantage over other phenothiazines.

It is of paramount importance that these chronic schizophrenics should
receive maintenance therapy. Seven improved patients developed symptoms again after approximately four weeks of the termination of the trial. The symptoms periodically appeared mostly in the form of hostility, aggressiveness and disturbed behaviour. Two of them who, up until present, have been maintained on the drug (8 months on pericyazine), still remain clear of symptoms with favorable progress in sociability and voluntary participation in Occupational Therapy, inspite of their previous agitation, conspicuous incoherence paranoid delusions, and inability to socialize. One of these had been seclusive, collecting rubbish and hiding it around her waist for years, and painting her face and exposed body area with pressed cooked rice.

Among the five unchanged cases, two have markedly bun deteriorated, disorganized, depersonalized and are still nowhere reaching their potentiality to restore their social functioning to even the lowest level. One patient used to lock herself in a cell all day and night for many years. At times she would manipulate her faeces and was noticed at one time to attempt to murder a cat by violently pulling his legs apart. None of these showed any response to pericyazine.

**Summary**

A short series of recalcitrant types of 20 female chronic schizophrenics, who previously had failed to respond to numerous phenothiazines and ECT, were treated in the clinical trial with pericyazine. After four months, an evaluation was made and revealed satisfying results in percentage of improvement. The drug was highly tolerated with minimal side-effects in comparison with other major neuroleptic drugs. By conclusion, the drug is more effective in correction of behaviour, normalizing of psychomotor activity, and diminution or elimination of hallucinations and delusions, but is less effective in severe autism and underproductivity. It is also highly recommended that maintenance therapy be extended at a minimal dosage for a certain period. Discontinuation of the drug requires careful control and gradual reduction in dosage.

**Acknowledgements**

May I express my appreciation to Messrs. May & Baker Ltd. for the generous supply of "Neulactil", brand of pericyazine in both parenteral and oral forms of preparation for the whole four months period of the trial; to the nurse, nurseaids, and attendants of the chronic ward of the Female Section for their willing help in rating the patients under close observation; and to Dr. Somsawat Yasarawan and Dr. Chira Sitasuwan, whose encouraging support and advice have been of so much value to my work.

**References**


อาการทั่วไปของ Postural hypotension คืออาการจิตพัก ออกทางก้านความประพฤติ เช่น ความก้าวร้าวกัน และต้องการประสาทหลอน หรือเหงา แตกต่างน้อยกว่าในรายที่มีอาการเดินทางแยกด้านขึ้น หรือช่วยเหลือ และในผู้ป่วยที่เสียหายมากแล้ว ถ้ามีช่วยให้อากการทางจิตภัณฑ์ชีวิตยิ่งมาก