# UNEVENTFUL TRIFLUOPERAZINE (STELAZINE) THERAPY AFTER PREVIOUS GRANULOCYTIC DEPRESSION

By

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THERE are many reports referring to incidence of agranulocytosis in patients receiving phenothiazines. This and the potential hepatotoxic effect of this group of drugs have been the greatest drawback in their usage.

For this reason it is felt worth while reporting the following case, not only because it is to the author's knowledge the first case of white cell depression concomitant with administration of trifluoperazine, but also because it demonstrates the usefulness of routine haematology, particularly in the initial stages of treatment with a new medication. In addition the reinstitution of therapy with trifluoperazine resulting in much improved mental status with no toxic bone marrow effects is of interest.

G.C., a 34-year-old catatonic schizophrenic, extremely regressed, mute, refusing to wear clothes and incontinent, was placed on perphenazine (Trilafon (Schering, perphentazin)), eventually reaching a dosage of 48 mg. per day (he received perphenazine for 20 weeks with some slight improvement only). On 3 March, perphenazine was discontinued and he was put on trifluoperazine, 10 mg. t.i.d. Within three days some improvement was noted and at the end of a week he was fully dressed, talking and able to feed himself. However, by 16 March, a diminished granulocyte count was evident (see accompanying table). Because of the frequency of low white cell count on patients receiving medication, he was carefully watched and the medication continued. However, by 31 March a serious white cell depression was evident and he was withdrawn from the medication and for prophylactic purposes procaine penicillin, 1 million units daily, instituted for eight days. Blood counts were taken daily and within five days the haematological picture was normal for this patient. His mental state again relapsed, he was no longer clothed, feeding himself nor continent. He was then placed on reserpine, 10 mg. per day, by injection (he refused oral medication). One week later this was reduced to 5 mg. per day, combined with 2 mg., b.i.d. Cogentin. He improved to the stage of remaining dressed, but was bizarre, silly, grimacing and with inappropriate affect. He was sexually aggressive and quite uninhibited. The reserpine-induced salivation resulted in his continually spitting, occasionally in the faces of the nurses and doctor. On 24 April, it was decided to withdraw the reserpine and again administer trifluoperazine, 30 mg. per day as previously. This decision was made because of his poor response to medications other than trifluoperazine. Daily white cell counts were taken and the patient closely observed. The patient slowly improved and after three weeks of treatment was no longer bizarre, aggressive nor inappropriate, was fully clothed and ate well. After ten weeks of treatment he was accepted for



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a home visit and although this visit was unsuccessful this did represent his first time out of the hospital in twenty months.

TABLE I

| Date | W.C.C. | P. | E. | L. | M. | |
|---|---|---|---|---|---|---|
| 2.3.60 | 5,400 | 71 | 4 | 23 | 2 | |
| | | | | | | Trifluoperazine commenced |
| 9.3.60 | 6,400 | 65 | 2 | 32 | 1 | |
| 16.3.60 | 3,800 | 57 | 2 | 39 | 2 | |
| 24.3.60 | 4,000 | 56 | 6 | 35 | 3 | |
| 31.3.60 | 2,800 | 53 | 2 | 42 | 3 | |
| | | | | | | Trifluoperazine withdrawn |
| 1.4.60 | 3,600 | 55 | 3 | 38 | 4 | |
| 2.4.60 | 3,200 | 52 | 6 | 42 | – | |
| 3.4.60 | 4,700 | 70 | 3 | 26 | – | |
| 4.4.60 | 3,800 | 58 | 6 | 34 | 2 | |
| 5.4.60 | 4,400 | 57 | 7 | 34 | 2 | |
| 6.4.60 | 6,700 | 72 | 2 | 24 | 3 | |
| 7.4.60 | 4,500 | 56 | 2 | 38 | 4 | |
| 8.4.60 | 7,200 | 64 | 4 | 31 | 1 | |
| 11.4.60 | 5,600 | 69 | 3 | 27 | 1 | |
| 13.4.60 | 6,500 | 64 | 4 | 30 | 2 | |
| 19.4.60 | 6,400 | 71 | 1 | 28 | 1 | |

W.C.C.—Total white cell count.
P.—Polymorph leucocytes.
E.—Eosinophils.
L.—Lymphocytes.
M.—Monocytes.

All bloods were taken at the same time each day, the only exception being the one on 8.4.60.

## DISCUSSION

Phenothiazines are potent, extremely useful therapeutic agents in the management of many conditions. The presence of the nitrogen-benzene linkage places it in Damshek's category of "white cell granulocyte reactors" (1). The occurrence of a depressed white cell count whilst receiving trifluoperazine is, therefore, not surprising. The failure to reproduce a leukopenic reaction on reinstitution of the drug does not at all exclude this as a causative agent, Yules *et al.* (2), Platter *et al.* (3), Jacoby (4), Pisciotta *et al.* (5), have all reported cases of agranulocytosis resulting from chlorpromazine therapy, which did not recur on re-administration of chlorpromazine.

On the other hand, Pisciotta reports cases where agranulocytosis did recur whilst in Jacoby's reported case the patient had had two attacks of agranulocytosis before receiving 6,400 mg. daily of chlorpromazine for four months without any ill effect.

The frequency of occurrence of agranulocytosis during chlorpromazine therapy is estimated at 0·001 to 0·002 per cent. (6). The widespread usage and low toxicity of this agent has made the use of routine blood counts fall into disfavour. The importance of infection as a danger signal seems to be likewise ignored; this latter seems an unnecessarily dangerous situation. Particularly in a new medication it is felt that the former is a careful choice, the latter obligatory. Pisciotta, in discussing eighteen cases of agranulocytosis due to chlorpromazine, states that nine were detected on routine blood checks and nine because of infection.

The question of dosage, time and rapidity of onset of agranulocytosis

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is frequently raised. The Pisciotta article claims that phenothiazines produce a toxic effect similar to antithyroid drugs, that is, rarely before the tenth day of administration; the onset is gradual and only after large dosages are given. This, they assume, is due to an increasing concentration of the drug in the bone marrow. This latter statement seems doubtful and is based mainly on the fact that most cases of agranulocytosis have been reported in psychiatric patients where higher dosages are usually employed (in effect mental hospitals). The case here reported received the same high dosage on both occasions and Jacoby's case received enormous quantities of chlorpromazine after previously exhibiting white cell depletion on two occasions. It seems equally possible that a metabolic factor could be involved either due to poor nutrition or associated with schizophrenia. If this were so, one could hypothesize that in the case reported here the initial good response to trifluoperazine, resulting in normalized activity, including dietetic, may have had a protective role when the drug was readministered.

## Summary

1. A case is presented of granulocytic depression reaching serious proportions in a patient receiving trifluoperazine, which subsequently reached normal levels when the drug was discontinued.

2. Readministering the drug at a later date again resulted in improvement of the patient's condition but no evidence of toxic effect on the bone marrow was noted.

3. The value of routine white cell counts on patients receiving phenothiazines is again emphasized.

4. Possible factors in causing agranulocytosis are briefly discussed.

5. Even in a single case, the therapeutic efficacy of trifluoperazine is demonstrated.

## References

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