

of myeloid tissue, sufficient for a normal defence reaction. Her proneness to infections cannot therefore be explained by a lack of myeloid tissue. If one assumes that it has some connexion with the leukaemia one has to look for another explanation. It may be that the formation of antibodies was altered in some way, if it is assumed that these are formed by lymphocytes. However, this is unproved. Hickling and Sutcliffe (1928) report a case of pneumonia in chronic lymphocytic leukaemia in which they found a moderate amount of protective antibodies in the serum after recovery.

The question of a remission of leukaemic signs through intercurrent infections has been summed up by Wintrobe and Hasenbush (1939). They come to the conclusion that there is little evidence for this even in the literature. In the case here presented it does not seem that the frequent infections have contributed to the remission. The recovery has taken place throughout unaffected by the infections.

Summary

A case is presented of ten years' clinical and haematological recovery from chronic lymphocytic leukaemia.

The clinical history of the patient, with blood pictures extending over eleven years, is given.

The literature is reviewed and one similar and one doubtful case are quoted and discussed.

The present case is discussed as regards diagnosis, frequency of intercurrent infections, and the influence of infection on leukaemia.

It is a great pleasure to thank Dr. C. J. Young, head of the Pathological Department, Bradford Royal Infirmary, for his constant encouragement, without which this paper would not have been written, and for kindly going through the manuscript. He has also given me considerable help with the laboratory investigations and advice in the management of the patient. I also wish to thank Dr. F. E. Chester-Williams for treating the patient and for permission to quote details of the x-ray treatment.

REFERENCES

- Forkner, C. E. (1938). *Leukaemia and Allied Disorders*. Macmillan, London.
- Gloor, W. (1930). *Munch. med. Wschr.*, 77, 1, 1096.
- Heilmeyer, L., and Begemann, H. (1951). "Blut und Blutkrankheiten." In *Handbuch der inneren Medizin*, edited by G. von Bergmann *et al.*, vol. 2. Springer, Berlin.
- Hickling, R. A., and Sutcliffe, W. D. (1928). *Amer. J. med. Sci.*, 175, 224.
- Jaffé, R. H. (1932). *Arch. Path. (Chicago)*, 14, 177.
- Kolmer, John A. (1949). *Clinical Diagnosis by Laboratory Examinations*, 2nd ed., p. 675. Appleton, New York.
- Naegeli, O. (1931). *Blutkrankheiten und Blutdiagnostik*, 5th ed., pp. 478, 493. Springer, Berlin.
- Schiassi, F. (1933). *Boll. Sci. med.*, 105, 289.
- Wintrobe, M. M. (1951). *Clinical Haematology*, 3rd ed., p. 856. Kimpton, London.
- and Hasenbush, L. L. (1939). *Arch. intern. Med.*, 64, 701.

The number of fatal accidents in the home is rising every year, according to the figures quoted by C. A. Boucher in the March issue of the *Monthly Bulletin of the Ministry of Health*. Whereas there were 4,904 fatal accidents in 1949, in 1953 there were 5,895. During the last ten years 57,413 people have died as a result of home accidents, and of these approximately 10,000 were children aged under 5; children under 5 and old people of over 65 accounted for four-fifths of the total figure, the peak risk period for a child being in the third year of life. Although 1953 saw a drop in the figures of children killed accidentally, the number of old people affected increased, about 60% of the accidents in this group being due to falls. It was hoped that the regulations introduced under the Heating Appliances (Fireguards) Act of 1952 would reduce the fatalities due to burns, but the provisional figures for 1954 indicate that the situation has worsened. The regulations apply only to heating appliances on sale and not to those already in the home. To counteract the large number of these fatal accidents the Home Safety Department of the Royal Society for the Prevention of Accidents has set up 70 local committees and hopes to set up more. A Home Safety Group has also been inaugurated, which will supply posters and propaganda.

USES OF CHLORPROMAZINE IN MENTAL HOSPITAL PATIENTS

BY

J. LOMAS, M.B., D.P.M.

Assistant Psychiatrist, Springfield Hospital, London, S.W.17

Since its original use by Laborit and Huguenard (1951) in anaesthetic practice chlorpromazine hydrochloride ("largactil") has found a steadily increasing application first in the anaesthetic sphere and later in psychiatry.

Courvoisier *et al.* (1953) have investigated the pharmacology of the drug in animals, and from the psychiatric standpoint its most important properties appear to be its depressant effect on central nervous and autonomic activity and its potentiation of narcotic and analgesic drugs.

Early investigation into the psychiatric uses of the drug by Delay and his collaborators, reported in a series of papers (see References), has subsequently been confirmed and enlarged upon by a number of workers on the Continent, particularly by Sigwald and Bouttier (1953a, 1953b), Staehelin and Kielholz (1953), Flügel (1953a), and more recently in this country by Anton-Stephens (1954). All authors are agreed that its most striking effect is its sedative action in all states of tension, agitation, or excitement of whatever origin, but that this sedative effect is entirely different from that produced by the barbiturates or other hypnotics in that the patient is able to take a normal interest in his environment and perform his ordinary duties without, except in the early stages, any undue sleepiness.

Even when a soporific state arises, the patient is as easily roused as from normal sleep and tends to fall asleep only if he has no external interests at the time. Furthermore, Flügel (1953b) has shown that there is no falling off in mental capacity as measured by psychological tests—in some cases there is even an increase—and that the E.E.G. is not altered in the same way as with ordinary hypnotics. This unique sedative action of the drug has been variously described as a "chemical leucotomy" (Delay and Deniker), "a harmonizing of the personality" (Flügel), and "a state of psychic indifference" (Anton-Stephens).

The drug has been used in a wide variety of psychiatric conditions, and some success has been reported in almost all these conditions, but the most generally accepted indications are excitements of all kinds (manic, schizophrenic, or organic), agitated depression, neurotic tension states, and drug intoxications. Opinion about its effect on chronic psychotic states is more divided, but these conditions have been less extensively investigated.

Chlorpromazine has been in use at Springfield Hospital since November, 1953, and between then and the end of July, 1954, just under 500 patients have received the drug for periods varying from a few days to six months.

This paper reports the findings on the 205 patients (55 male and 150 female) who received treatment between November, 1953, and the end of March, 1954.

Selection of Material and Assessment of Results

The earliest cases treated were seriously disturbed chronic psychotics, but as the efficacy of the drug became more apparent the field of application steadily widened to include every type of case catered for by a large mental hospital.

Acute and chronic disturbed psychotics, however, are by far the largest class of patients in the series.

Patients whose treatment had to be stopped for any reason before they had received it for a week, and the few who had E.C.T. concurrently, are excluded from the results, otherwise the series includes all patients starting treatment during the stated period.

Results were assessed either when treatment was stopped or, in cases in which treatment was prolonged, at a time not less than eight weeks after the start.

The following criteria of improvement were used :

1. Not improved.—Slight or no change either in symptoms or in behaviour.
2. Slightly improved.—Decrease in symptoms and disappearance of gross behaviour disturbance.
3. Moderately improved.—Improvement in adjustment at hospital level or to the outside world at a dependent level, as shown by taking an interest in environment and in ward social activities and employability within the hospital.
4. Much improved.—Improved in adjustment to the outside world at an independent level, as shown by increase in initiative, reliability, and responsibility.
5. Recovered.—Symptom-free, with insight and capacity for adjustment to the outside world at the same level extant before the breakdown.

Where there was any doubt about the correct assessment the less favourable was chosen.

Dosage and Management of Cases

The early cases received a commencing daily dosage of 25 mg. t.d.s. intramuscularly, increasing to 50 mg. t.d.s. after the first three days. At the end of a week they were given the same dose orally. Despite reports that the drug is fully and rapidly absorbed from the intestinal tract, it was soon realized that a larger oral dose was required to produce the same effect. The oral dose was therefore increased to 75 mg. t.d.s. Later the intramuscular route was abandoned except in those who were too resistive to take drugs readily by mouth, as there seemed no special advantage in starting treatment by injection. This, however, is contrary to the findings of most other workers, who advocate starting treatment by injection except in very mild cases. Subsequent attempts to confirm the finding that treatment is more effectively initiated by intramuscular injection have failed to reveal any advantage. Improvement when it occurred was gradual whether the drug was administered orally or by injection, and the dramatic effects produced in the first 24 hours that are quoted by most authors were absent in this series.

Although there were many individual variations, the most generally adopted scheme of dosage in the later cases was to give 50 mg. t.d.s. orally in the first week, 75 mg. t.d.s. in the second week, and 100 mg. t.d.s. in the third and subsequent weeks. Very few patients failed to tolerate this dosage, and these were mainly among the neurotics and mildly disturbed psychotics.

Some patients received higher dosages than 300 mg. daily, but in general the impression gained was that most patients who improved with the drug did so on 150 mg. daily. Of those who failed to improve on 150 mg. a large number improved when the dose was increased to 225 mg. daily, and of those who still failed to improve at this level a few did so on 300 mg. Little further improvement could be expected with higher doses.

The more disturbed and chronic psychotic patients both tolerated higher dosages and required more drug to produce betterment. Improvement was noticed in some cases within a few days of starting treatment but in others not for several weeks. In only one case did improvement start after the patient had been on treatment for more than two months, and in the great majority of cases the maximum benefits of the drug had been achieved in three months. Treatment was therefore not abandoned as useless in under two months and was not as a rule prolonged beyond three. It was

terminated abruptly without any withdrawal effects being noticed in any case.

Almost all cases treated were ambulant from the start, the only exceptions being those whose mental state necessitated a period in bed, and all elderly people or those with cardiovascular dysfunction. Although a few patients complained of slight giddiness, particularly during the first few days of treatment or immediately following an increase in dosage, no marked hypotensive effects were observed except in those with arteriosclerosis or some other cardiovascular disease and in one other case.

In the early cases all sedatives were withdrawn and only later prescribed with great caution owing to the possible risk of potentiation. Experience, however, showed that this risk was negligible in normal dosage, most patients not only tolerating but also at first requiring whatever sedatives they had been having before the start of chlorpromazine treatment. The potentiating effect of chlorpromazine was noticeable only in those in whom continual narcosis was produced, when it was possible to do so with much smaller doses of barbiturates in association with chlorpromazine than would have been possible with barbiturates alone.

Unless, therefore, individual needs suggested some modification, it was customary to treat ambulant patients with an initial dosage of 150 mg. daily; to increase this to 300 mg. in the course of three weeks; and to maintain it at this level for three months, when treatment was abruptly terminated. But as opinion about the most suitable dosage and duration of treatment was changing throughout the period under review there is no doubt it will continue to evolve in the light of further experience.

Results

Table I shows the results in the different diagnostic groups in 196 cases. The remaining nine patients died while under treatment. They were all elderly patients and seriously ill physically before chlorpromazine was started. None were

TABLE I.—Results in Different Diagnostic Groups

Diagnosis	Recovered		Much Improved		Moderately Improved		Slightly Improved		Not Improved		Total No. of Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
Schizophrenic group of diseases	4	3	17	12	39	29	39	29	37	27	136
Endogenous depression ..	2	11	4	21	4	21	2	11	7	37	19
Neuroses and psychopathic states	2	11	6	33	2	11	1	6	7	39	18
Organic states ..	—	—	—	—	6	38	5	31	5	31	16
Mania and hypomania ..	1	14	—	—	2	29	2	29	2	29	7
Total ..	9	5	27	14	53	27	49	25	58	29	196

expected to live. The cause of death, which was in each case ascertained by post-mortem examination, was pulmonary embolus from femoral thrombosis in one case, and in the rest either bronchopneumonia or the cardiovascular changes associated with senility. It was not thought that chlorpromazine could in any way be incriminated.

Schizophrenics comprise the largest single group, and a sufficient number have been treated to form a rather more definite impression of the value of the drug than in any other diagnostic group. But although 136 cases have been treated, no very definite prognostic criteria have emerged, both remarkable successes and equally unexpected failures being quite common. In the more acutely disturbed patients, the drug has a quieting effect in a few days, but the dramatic change described by other authors within 24 hours has not been noticeable in this series. In fact, where excitement has been intense it has invariably been necessary to give barbiturates in large doses in addition to chlorpromazine. It is, however, in just these acutely disturbed patients that the prognosis in schizophrenia is best, and it is doubtful whether chlorpromazine in any way improves

the outlook, although it is certainly a very effective sedative when used either alone or in conjunction with barbiturates.

On the other hand, in schizophrenics of poor prognosis—that is, in chronic cases and in the paranoid group—the value of the drug is much less ambiguous. Of the 136 schizophrenics treated, 55 had been in hospital continuously for two years or longer; their average age was 41 ± 1.8 years and the average stay in hospital prior to treatment 8.5 ± 0.9 years. All of them were seriously disturbed patients, but in this extremely unpromising group the following results were obtained: much improved, 2 (4%); moderately improved, 15 (27%); slightly improved, 21 (38%); not improved, 17 (31%).

The two patients who were much improved had both been in hospital for four years and both had previously had insulin, E.C.T., and prefrontal leucotomy without any improvement at all. They were both very difficult turbulent patients. One of them has now been out of hospital for three months and is earning her living, and the other is expecting to leave shortly.

The effect of the drug in these cases is somewhat similar to that of leucotomy but without its disadvantages. There is first a stage which Anton-Stephens well describes as one of psychic indifference in which delusions and hallucinations persist but no longer have the same emotional significance, and consequently there is considerable improvement in behaviour. Later the delusions and hallucinations themselves fade and in some few patients an unexpected degree of insight has developed.

In some patients the effects are clearly symptomatic only, as relapse occurred shortly after withdrawing the drug. But, although the long-term results of chlorpromazine treatment are as yet unknown, immediate relapse is surprisingly rare even in chronic patients if the drug is not withdrawn too soon. And improvement, once started, often continues for many weeks after the drug has been discontinued. It is felt, therefore, that an important effect of chlorpromazine is to make possible the rehabilitation of patients who were formerly too disturbed for this to be accomplished. In this respect it can again be compared to leucotomy.

In endogenous depression the results shown in Table I are unimpressive. This can largely be attributed to the fact that patients who failed to respond quickly to chlorpromazine were taken off the drug and given E.C.T. It is therefore possible that if treatment had been prolonged results would have been better. In general it was felt that E.C.T. is a more effective treatment for depression than chlorpromazine. On the other hand, in two cases of chronic retarded depression of nearly two years' duration which had either failed to respond or had responded but briefly to E.C.T., given on more than one occasion in the past, the results were excellent, a far more satisfactory remission being achieved with chlorpromazine, and one which has so far lasted in the first instance for four months, and in the second for two. Chlorpromazine may therefore prove a useful line of treatment in cases of depression which fail to respond to E.C.T.

In the 16 patients suffering from organic dementia improvement was largely symptomatic and relapse was frequent when treatment was stopped.

The findings in neurotic patients were in agreement with those of other workers in suggesting that states of anxiety or emotional tension were the most likely to respond to chlorpromazine. On the other hand, one chronic hysteric, whose principal complaint was irritation of the ear, completely lost her symptom. That this was a direct response to chlorpromazine and not due to suggestion was demonstrated by substituting identical neutral tablets, unknown to the patient, when her symptoms returned, to disappear once more when chlorpromazine treatment was resumed.

Psychopathic states behaved in a similar way to neuroses, the best results occurring when there was considerable associated anxiety. In one class of patients, the aggressive psychopaths, chlorpromazine appeared definitely to be con-

traindicated. Not only did it not produce any improvement, but it often increased the tendency to explosive outbursts of violence. While the number of cases in the series is too few to be more than suggestive, this experience has been repeated in cases treated subsequently.

Of the seven cases of mania and hypomania treated, only one was better than moderately improved. This man, who recovered, was the only case of acute manic excitement treated, and the effect of chlorpromazine was very impressive. Barbiturates had controlled his excitement only very ineffectively and he had developed pneumonia, so that both his physical and his mental conditions were causing grave concern. Within 48 hours of starting chlorpromazine he was overactive and euphoric, but was co-operating well and was no longer a nursing problem of any sort. The other six cases were all chronic hypomanics, and a good hospital adjustment was the best that could be achieved.

All patients were classified as acute, subacute, or chronic cases, according to the time they had been in hospital before treatment was started. Those who had been in less than six months were regarded as acute cases, from six months to two years as subacute, and over two years as chronic. This method of classification has the merit of being unambiguous. On the other hand, it does not take into account previous breakdowns, or the duration of the illness prior to admission. As information on this score was too often missing, it was felt to be the most satisfactory classification in the circumstances, but it is obviously biased towards the acute end of the scale.

In general, most of the acute cases were receiving chlorpromazine as the first line of treatment, the subacute group had recently failed to respond to some other form of therapy, and the chronic group had already received all appropriate treatment for their condition without improvement. There was no difference in the average age of the three groups, which was just over 40, nor in the dosage they received, and the mean durations of illness were 6 weeks, 13 months, and 9 years respectively.

Table II shows the results.

TABLE II.—Results Analysed According to Duration of Stay in Hospital Before Treatment

Time in Hospital Before Treatment	Recov-ered		Much Im-proved		Moder-ately Im-proved		Slightly Im-proved		Not Im-proved		Total No. of Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
1-6 months ..	9	10	20	21	23	25	19	20	22	24	93
6-24 ..	—	—	5	13	15	39	6	16	12	32	38
Over 2 years ..	—	—	2	3	15	23	24	37	24	37	65
Total ..	9	5	27	14	53	27	49	25	58	29	196

As might be expected, the best results were achieved in the acute cases. But there are too many imponderables concerned in assessing the results in acute psychiatric cases for any definite assertions to be made about a new line of treatment unless carefully controlled trials are made, and this the present survey does not pretend to be. The preliminary impression gained is that chlorpromazine has a part to play in the treatment of acute psychiatric conditions of all sorts, but the detailed indications for its use remain to be worked out. In the subacute group, the part played by extraneous factors in any improvement produced becomes less important, and in the chronic cases any change can even more certainly be attributed to the drug. It is in these two groups that the value of chlorpromazine is felt to be beyond doubt.

It will be noted that 37 out of the 103 subacute and chronic patients (36%) reached a level of good hospital adjustment or better. All the patients in these two groups were previously making a poor adjustment and the great majority were seriously disturbed.

The indications for chlorpromazine have been considered by most authorities to be largely symptomatic—that is, in

states of excitement, agitation, or emotional tension. All patients were classified, therefore, according to their psychomotor state. In the overactive group were classed excited, aggressive, or emotionally unstable schizophrenics, manics, agitated depressives and seniles, and anxious neurotics, while the inhibited group contained catatonic stupors and detached schizophrenics, retarded depressives, and apathetic neurotics. Detached schizophrenics who became periodically impulsive were placed in a separate category.

The results shown in Table III are somewhat surprising. Although more patients recovered in the overactive group and more inhibited patients did not improve, if the recovered

TABLE III.—Results Analysed According to Psychomotor State

Psychomotor State	Recoy-ered		Much Im-proved		Moder-ately Im-proved		Slightly Im-proved		Not Im-proved		Total No. of Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
Overactive ..	8	6	17	13	31	25	35	28	35	28	126
Inhibited ..	1	2	9	17	15	29	6	12	21	40	52
Inhibited with im-pulsive outbursts	—	—	1	6	7	39	8	44	2	11	18
Total ..	9	5	27	14	53	27	49	25	58	29	196

and much improved are grouped together on the one hand and the slightly improved and not improved on the other, the results are almost identical in both inhibited and overactive patients. This suggests that some revision is needed in the conception of chlorpromazine as being mainly a symptomatic treatment for excited states.

Chlorpromazine and Leucotomy

The effects of chlorpromazine have often been compared to those of leucotomy. It might therefore be supposed that patients in whom leucotomy had failed would equally fail to respond to chlorpromazine, and, conversely, that chlorpromazine might prove a useful prognostic indicator for leucotomy. Neither of these suppositions is borne out by the results in this series.

The results in 28 patients in the series who had previously been leucotomized were as follows: much improved, 3 (11%); moderately improved, 6 (21%); slightly improved, 11 (39%); not improved, 8 (29%). These results do not vary significantly from those in the series as a whole, and lend further support to the view that chlorpromazine can be of value in prognostically poor cases.

On the other hand, four patients who failed to respond in any way to chlorpromazine have made a very good immediate response to leucotomy, though it remains to be seen whether this will be maintained.

Side-Effects and Toxic Reactions

The various side-effects and toxic reactions recorded in the literature were noted in this series, but, as their occurrence in a much larger number of cases is the subject of a separate communication, no details are mentioned here.

Summary and Conclusions

The results in 205 patients treated with chlorpromazine are examined.

A tentative scheme of dosage and duration of treatment is discussed. It is not felt that the intramuscular route offers any advantages over the oral.

Results in the different diagnostic categories suggest that chlorpromazine may play a useful part in the treatment of acute states of excitement of all sorts, in neurotics in whom tension or anxiety is a prominent symptom, and in some depressive patients in whom E.C.T. has proved ineffective.

The most striking results, however, were obtained in chronic psychotic patients in whom the prognosis would

normally be very bad. It enabled a few of these patients to be discharged and many more to make a good hospital adjustment.

In chronic patients it was felt that the chief part played by chlorpromazine was to make possible the rehabilitation of those in whom this was formerly impossible and that, while in some relapse occurred immediately treatment was stopped, in others improvement still continued.

There seemed to be little difference between its effect on overactive and inhibited patients.

As good results were found after leucotomy as in other chronic patients.

I wish to thank Messrs. May & Baker for kindly making supplies of chlorpromazine available for this trial; Dr. Robert Forgan, of May & Baker, for his very valuable help and advice; and Dr. H. C. Beccle, medical superintendent of Springfield Hospital, for much helpful criticism in the preparation of this paper.

REFERENCES

- Anton-Stephens, D. (1954). *J. ment. Sci.*, **100**, 543.
 Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M., and Koetschet, P. (1953). *Arch. int. Pharmacodyn.*, **92**, 305.
 Delay, J., and Deniker, P. (1952a). *Congr. Méd. alién. Neurol. Franc.*, p. 7.
 ——— (1952b). *Ibid.*, p. 19.
 ——— (1953). *Thérapie*, **8**, 347.
 ——— and Harl, J. M. (1952a). *Ann. méd.-psychol.*, **110**, 112.
 ——— (1952b). *Ibid.*, **110**, 267.
 ——— and Grasset, A. (1952). *Ibid.*, **110**, 398.
 ——— and Tardieu, Y. (1953). *Presse méd.*, **61**, 1165.
 Flügel, F. (1953a). *Med. Klin.*, **48**, 1027.
 ——— (1953b). Paper read to the German Pharmacological Congress, October 4-7, 1953.
 Laborit, H., and Huguenard, P. (1951). *Presse méd.*, **59**, 1329.
 Sigwald, J., and Bouttier, D. (1953a). *Ann. Méd.*, **54**, 150.
 ——— (1953b). *Presse méd.*, **61**, 607.
 Staehelin, J. E., and Kielholz, P. (1953). *Schweiz. med. Wschr.*, **83**, 581.

CHLORPROMAZINE IN TREATMENT OF ELDERLY PSYCHOTIC WOMEN

BY

C. P. SEAGER, M.B., B.Ch., D.P.M.

Registrar, Bristol Mental Hospitals

One of the difficult nursing problems in a mental hospital concerns the group of elderly long-stay patients who suffer from periods of restlessness, confusion, and disorientation or who are continually in a state of agitation, with stereotyped speech and activity. The Board of Control (1954) stated that, "on January 1, 1953, 28.8% of the mental hospital population were over the age of 65 and two-thirds of these were women."

A related problem is the shortage of nursing staff, owing to which large wards of noisy, difficult patients have to be in the care of too few nurses, or patients have to be left at night with inadequate supervision. It is hoped to show that chlorpromazine ("largactil") may play a part in the solution of these problems.

Since interest in the psychiatric use of chlorpromazine was roused by Sigwald and Bouttier (1953), who summarize the literature, and by Ey and Bérard (1952), who used it as a method of prolonged sleep treatment (*cure de sommeil*) in psychiatric patients, various authors in this country have published series of cases suggesting its value when tension and agitation predominate—Anton-Stephens (1954) on psychiatric patients with varying diagnoses, Garmany *et al.* (1954) in psychoneurosis, Elkes and Elkes (1954) in psychosis, and Howell *et al.* (1954) in geriatrics.

The present series is a group of elderly psychotic women with varying diagnoses but having in common