recorded in the present series particularly when the blood had been centrifuged and resuspended before use. This 'technical fault' contributed in large measure to the high incidence of false negative results obtained by the laboratory technician. Storing of blood in EDTA for short periods (less than 4 hours), however, had no adverse effect on the interpretation of the result. Bearing in mind that Azostix is used primarily for screening purposes or for obtaining urgent blood urea results at the bed-side, the problems related to the storage of blood can be discounted. If specimens can wait that long, more accurate quantitative laboratory methods may as well be used!

No difference in the interpretation of simultaneously obtained capillary (finger-prick) and venous blood (venepuncture) samples was noted. This therefore confirmed the suitability of Azostix as a true 'bedside' diagnostic medium. Azostix has been used to advantage and found to be valuable in general practice, radiology and in general hospitals. The determination of urea by conventional methods involves special laboratory equipment, and is frequently time-consuming. Provided that Azostix is used correctly, most authors agree that it is a reliable method of determining blood urea values by the bedside, in clinics and consulting rooms, as a means of screening normal from abnormal groups. It must be emphasized that all abnormal or suspect results should be sent for definitive chemical analysis.

SUMMARY
A study was undertaken to assess the reliability and efficacy of Azostix (Ames) as a means of screening for abnormal blood urea concentration. The results were compared with the automatic method and were based on the interpretation of 1,066 individual blood samples. Five observers participated in the trial. Azostix was found to be satisfactory for purposes of classifying patients into normal and abnormal categories, but was liable to a variable observer error, particularly in the higher ranges of abnormality. This error was largely due to excessive washing of the strip, indecision and delay in deciding upon the colour change, and an inability to interpret this change.

Centrifuging and prolonged storage of the blood specimen in EDTA frequently resulted in false negative results. No difference in the interpretation of simultaneously tested venous and capillary blood samples was noted.

Provided that the minutiae of the advocated technique were observed, Azostix was found to be a useful method of screening patients into normal, suspect and abnormal ranges of blood urea. All patients in the last two categories must be referred for definitive study.

We should like to thank Mrs A. Ellis, Miss A. Juggan, Mr A. Mamambola, Drs E. Vermaak and Van Niekerk, and the medical and nursing staff of the Obstetric Units at King Edward VIII and Addington Hospitals, Durban, for their assistance. We also wish to thank Mr G. Peploe and Mr K. Wilson of Ames Laboratories Limited for financial support for this study and the supply of test material.

REFERENCES

TREATMENT OF THE DEPRESSIVE REACTION: A CLINICAL EVALUATION OF A NEW PSYCHOTHERAPEUTIC DRUG, DOXEPIN (SINEQUAN)*

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O that this too, too solid flesh would melt,
Thaw and resolve itself into a dew!
Or that the Everlasting had not fix'd
His canon 'gainst self slaughter! O God! God!
How weary, stale, flat and unprofitable
Seem to me all the uses of this world!

Shakespeare: Hamlet.

Hamlet's depression, precipitated by his father's sudden death and his mother's blatant expression of sexuality, was already full-blown by the time his father's ghost revealed to him the far more disturbing facts of murder and adultery which he alone was called upon to avenge. How could this youthful prince restore the honour and kingdom lay betrayed to the enemy and ravaged through all its territories by the obscure power of 'bad dreams'? Does the modern physician or psychiatrist believe that, by relieving Hamlet's crippling sense of despair, futility and disgust, one could have averted the whole tragic train of destruction whereby his dilemma was finally to be worked out? To be precise, can a course of psychotropic pills restore to health a mind which has been infected at its source by 'a father killed' and 'a mother stained'? Such a question highlights some of the controversial and even philosophic issues related to the evaluation of the many psychotherapeutic preparations developed in recent years to assist in the treatment of depression. It is not my intention to examine these issues here, but to acknowledge their existence and to record the opinion that they can on no account be ignored.

It goes without saying that the evaluation of new psychotropic drugs is influenced by subjective factors such as the clinical assessment of the patient's condition and progress and the observer's orientation towards psychoanalytic or organic methods of treatment. Results may also be affected by such objective factors as the particular patients selected for treatment and whether they are institutionalized or treated as outpatients. With due regard for these considerations, the present study represents an attempt to evaluate yet another antidepressant, doxepin. Although I am normally conservative in the prescription of drugs, being inclined towards a psychoanalytic approach, I was encouraged to embark upon the trial of

*Date received: 27 July 1970.
The observe its effect. Ideally, the administration dosage amicou:ld deliverance upon psychotropic agents in the control and relief of acute cases only were to be admitted and it was anticipated that some emphasis would fall upon physical methods of treatment. At the same time, clinical duties at an extremely busy outpatient clinic conducted by the local Mental Health Society would necessitate considerable reliance upon psychotropic agents in the control and relief of anxiety and depression. It was felt that these circumstances provided a suitable opportunity to assess the efficacy of a new preparation reputed to be of value in relieving the symptoms of neurotic and psychotic depressants, the best known of which are imipramine and amitryptiline. The chemical structures of doxepin, imipramine and amitryptiline are shown in Fig. 1.

![Chemical structures of doxepin, imipramine, and amitryptiline](image)

Doxepin hydrochloride is a dibenzoxepin derivative and therefore not, strictly speaking, chemically related to known psychotherapeutic agents. It does, however, share some structural features with certain tricyclic antidepressants, the best known of which are imipramine and amitryptiline. The chemical structures of doxepin, imipramine and amitryptiline are shown in Fig. 1.

**TRIAL PROCEDURE**

It was regarded as extremely important to establish a diagnosis of each patient's condition in accordance with accepted clinical syndromes, in so far as this was possible. The reason for this was twofold: firstly, to permit one to determine in what specific conditions, if any, the preparation may be expected to prove most effective, and, secondly, to guard against any masking of the clinical picture which may arise once treatment has commenced.

The initial diagnosis was established with reference to accepted clinical concepts. First of these is the distinction between normal and pathological depression. Depressive feelings may be appropriate to and commensurate with the situation eliciting the reaction, as in the normal grief response. Such experiences are usually relatively short lived and are not accompanied by any severe loss of self-esteem. In pathological depression, however, the reaction is of an intensity or duration generally considered inappropriate to the occasion even when a precipitating factor is present. Depression may also be secondary to a more fundamental disorder as, for example, in the case of an obsessive-compulsive neurotic who becomes depressed when he fails to achieve his goals. We are all familiar with the distinction between reactive and endogenous depression, with the depressive phase of manic-depressive psychosis and with the painful condition of involutional melancholia, which is a depression of psychotic intensity occurring at the climacteric in individuals without a previous history of manic-depressive reaction but with a tendency to a highly compulsive life pattern. Again, while it is recognized that the stress of parturition and motherhood can precipitate a basic endogenous depression or manic-depressive disorder, it may also produce a functional illness characterized by panic, depression and feelings of inadequacy. It must be admitted, however, that it is not always possible to arrive at a clear-cut diagnosis, especially in the case of outpatients.

Fifty patients suffering from various forms of pathological depression were treated with doxepin during the period February - June 1970. Twenty-two were hospitalized and 28 were treated at the outpatient clinic. The hospitalized patients were seen at least twice weekly at the outset and a global assessment of improvement was recorded. In addition, the Hamilton Anxiety Rating Scale was completed for each of these patients before and after treatment. Outpatients were assessed weekly or fortnightly.

Patients suffering from psychotic depression (either endogenous or manic depressive) were treated with a dosage varying between 75 and 200 mg daily. Those with neurotic depression were treated with a smaller dosage of 30-50 mg daily, including a double dosage at night to eliminate the necessity for a soporific. Where possible, the first dose was taken after arriving home so that the patient could observe its effect. Ideally, the administration of the drug should be commenced over the weekend to allow the outpatient to become familiar with its effects before beginning a new working week.

**RESULTS**

The results in Tables I and II indicate that doxepin is useful in treating endogenous depression, the depressed phase of manic-depressive psychosis, and, to a lesser extent, involutional melancholia. In smaller doses, it may...
be a useful adjunct to psychotherapy in the treatment of anxiety states, especially in busy outpatient clinics. Among the severe cases of psychotic depression treated with doxepin were several that many clinicians would have preferred to treat with electroplexy. In such cases, any initial failure to respond was usually found to be due to underdosage. In manic-depressive psychosis, doxepin was successfully combined with lithium carbonate, the dosage of doxepin being gradually reduced as the depression lifted. Only 1 of 4 cases of involutional melancholia required electroplexy to produce a satisfactory remission of symptoms.

It was observed that the antidepressant effect of doxepin takes approximately 10 days to develop, while the anxiolytic effect is immediate; thus, agitated suicidal patients can be brought under rapid control. Side-effects, as dry mouth, blurred vision, sweating, tachycardia, constipation and urinary retention, are usually mild and transient and subside with adaptation to treatment or reduction of the dose.

CONCLUSION

In the management of severe psychotic depression, where the practitioner is usually forced to rely on physical methods of treatment, doxepin was found to be effective in relieving both despondency and agitation, and may therefore be used in place of a combination of imipramine and chloridiazepoxide where such symptoms coexist. It may also replace electroconvulsive therapy in suitable cases, reducing the indications for such a distressing procedure to a minimum. In the treatment of psychoneurotic depression, on the other hand, it is my opinion that alleviation of symptoms alone is a very poor substitute for a constructive attempt to relieve the basic maladaptation from which the symptoms arise. Here, much depends on the orientation of the therapist. The organically oriented practitioner relies heavily on chemotherapy, while the traditional analyst may steadfastly refuse to make use of any drugs whatsoever. Neither attitude is wholly fair to the ordinary neurotic sufferer who benefits most from sympathetic support and understanding, aided by a judicious use of chemotherapy when his defences falter under the crippling onslaughts of anxiety. In all cases, the practitioner should constantly bear in mind that psychotropic drugs cannot cure. They can only ease the distress accompanying the underlying depression, which continues to take its course behind the mask provided by the pill. Those who see the agony of mind experienced by sufferers from severe depression, however, will not despise the means of easing its worst manifestations.

SUMMARY

Doxepin was used in the treatment of pathological depression in 22 hospitalized patients and 28 outpatients. Results were assessed in terms of clinical impressions, patients' reports, and, in the case of the hospital patients, the Hamilton Anxiety Rating Scale. It was found that the drug was effective in relieving endogenous and agitated forms of depression and was a useful adjunct to the management of anxiety neurosis.

I should like to thank Pfizer Laboratories (Pty) Limited for the supply of doxepin (Sinequan) for the purposes of this trial; and the Secretary for Health, for permission to publish.

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**BOOKS RECEIVED : BOEKE ONTVANG**


