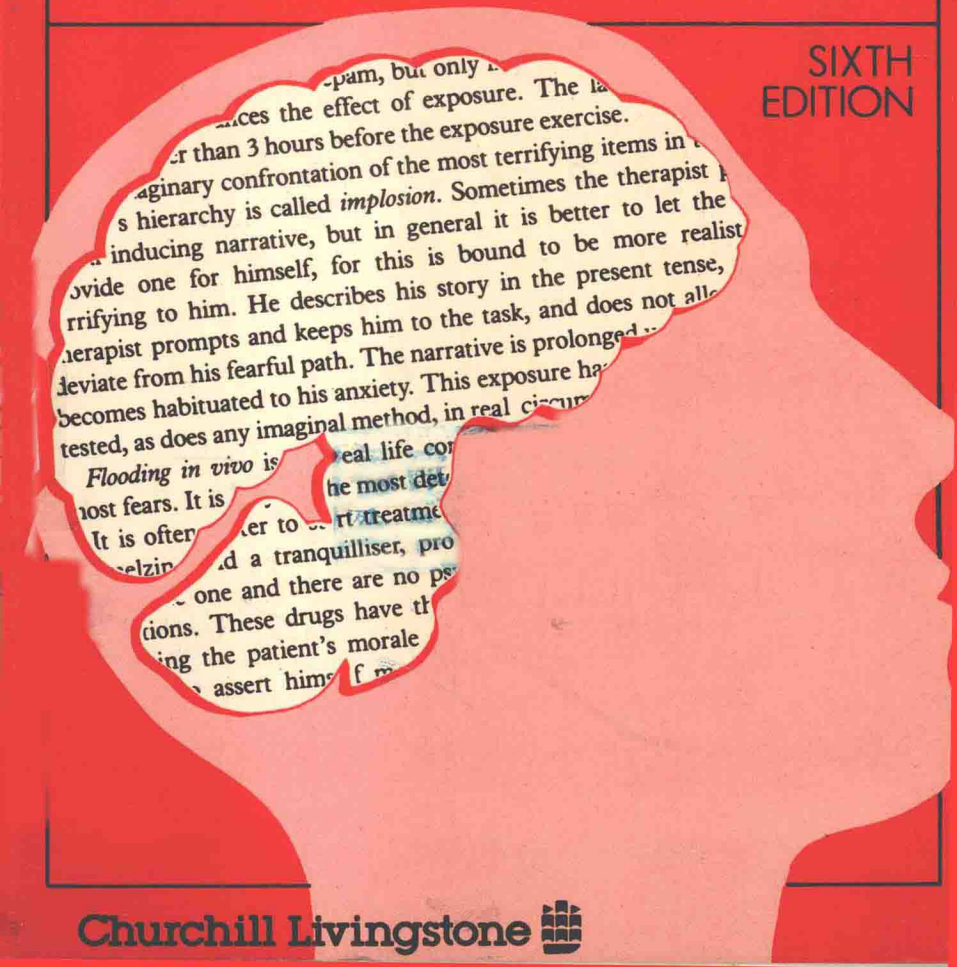
An Introduction To
PHYSICAL METHODS OF TREATMENT IN PSYCHIATRY

Peter Dally & Joseph Connolly

SIXTH EDITION



Churchill Livingstone

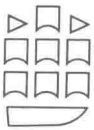
An Introduction to Physical Methods of Treatment in Psychiatry

Peter Dally
MB, FRCP, FRCPsych, DPM
Consultant Psychiatrist, Department of Psychological Medicine, Westminster Hospital, London

Joseph Connolly
MB, MPhil, MRCP, MRCPsych, DPM
Senior Lecturer in Psychiatry, Westminster Hospital Medical School, London; Honorary Consultant in Psychiatry, Westminster Hospital and Queen Mary's Hospital, London

SIXTH EDITION

Fifth and previous editions by
William Sargant and *Eliot Slater*



CHURCHILL LIVINGSTONE
EDINBURGH LONDON MELBOURNE AND NEW YORK 1981

CHURCHILL LIVINGSTONE
Medical Division of Longman Group Limited

Distributed in the United States of America by Churchill Livingstone Inc., 19 West 44th Street, New York, N.Y. 10036, and by associated companies, branches and representatives throughout the world.

Sixth edition 1981

Fifth and previous editions by
William Sargant and *Eliot Slater*

ISBN 0 443 02019 1

British Library Cataloguing in Publication Data
Dally, Peter
An introduction to physical methods of treatment in psychiatry. – 6th ed.
1. physical therapy 2. Psychiatry
I. Title II. Connolly, Joseph
III. Sargant, William
616.89'13 RC482 80–41298

Printed in Singapore by Kyodo Shing Loong Printing Industries Pte Ltd

An Introduction to Physical Methods of Treatment in Psychiatry

Preface

There has been a steady improvement of treatment in psychiatry during the past 8 years, since the last edition of the book appeared. This has also been a period of reassessment. The overenthusiastic claims for this or that drug or treatment have been exposed and replaced in some instances by nihilistic, 'anti-psychiatry' attitudes. Even so well established a treatment as e.c.t. has met with considerable criticisms, and not only from the ill-informed. Yet this has produced at least one useful result for practising psychiatrists. They have had to re-examine carefully their techniques, assess the value of their treatments, strip away the nonspecific placebo effects and see anew the specific nature of what their treatments actually achieve, and how useful these really are.

It is clear that psychotropic drugs, e.c.t., and psychosurgery all have specific therapeutic effects and disadvantages. It is apparent that these treatments are sometimes misused, prescribed unnecessarily, or for the wrong conditions, or withheld when the patient's symptoms might be rapidly lifted. There have been great changes in our detailed knowledge of this over the past 15 years. Antidepressant drugs, to take an example, have removed much of the past need for e.c.t., but they have not totally replaced it. E.c.t. is still needed in severe depression and in cases otherwise refractory to treatment. We still meet patients who have been given e.c.t. when they would have responded better, say, to a MAOI, and who now complain bitterly of memory upset. But even more common is the patient who has partially recovered with antidepressant drugs, and is allowed to drift for months, when a few e.c.t. would lift him into full recovery.

As a result of reassessing individual treatments we now have increased understanding and greater acceptance of the synergistic effect of treatments. Psychotherapists now recognise that a drug may allow them to make contact with patients otherwise inaccessible to them, and enable patients to make greater use of their psychotherapeutic insights. Behaviour therapy may not begin to show results until drugs have reduced a patient's anxiety to a tolerable level. Psychotherapists and behaviour therapists have begun to recognise that there are factors

common to both their techniques, and that one is not altogether dissimilar from the other.

Although this book is essentially a description of physical methods of treatment, we hope that no one will overlook the need to take a broad view of treatment, to remove causes when these are removable, and to encourage a patient to develop wider, more resilient attitudes. Because of the emphasis in recent years on behaviour therapy, we have thought it politic to include a short chapter on this subject. We have also added chapters on sexual dysfunction and deviations, and on psychiatric disorders of women and of old age.

We have omitted the chapter on epilepsy. The subject may have merited a place in the earlier editions, especially as e.c.t. was then sometimes given in an attempt to regulate the epileptic's fits, and allow him to have them under ideal conditions. Modern antiepileptic treatment has outmoded such methods. Temporal lobe epilepsy is occasionally associated with schizophrenic-like behaviour, or with aggressive outbursts. Post-e.c.t. automatism may occasionally intrude in a differential diagnosis. Nonetheless, the treatment of such conditions is generally best left to neurologists and physicians more experienced in epilepsy than the average psychiatrist.

We have also left out the previous editions' chapters on insulin, both deep and modified. Deep insulin therapy no longer has any place in the treatment of schizophrenia. Modified insulin is rarely used, and then largely for its nonspecific effects. Weight can be increased more readily by means of other safer drugs, especially chlorpromazine.

In other respects we have generally followed the path of the earlier editions. Above all, we hope that we have conveyed in this edition the enthusiasm and dedication of the original authors, and especially their principle of 'therapeutic persistence'.

1981

P.D.
J.C.

Acknowledgements

We are grateful to Dr Joan Gomez for her advice and criticism, particularly on the subject of alcoholism, to Dr Ann Dally and, most of all, to Anne Lingham for the work she put into typing the book, and her ability to keep us sane.

We also wish to thank William Heinemann Medical Books Ltd. for permission to reproduce material from *Anorexia Nervosa* by Dally, Gomez and Isaacs, 1979.

1981

P.D.
J.C.

Contents

1

Psychotropic drugs

PART 1. PRINCIPLES

Just as e.c.t., introduced in 1939, revolutionised the treatment of endogenous depressive illness, so the arrival of psychotropic drugs from the 1950s onwards profoundly changed the treatment of psychiatric disorders. Reserpine appeared in 1952, to be almost at once superseded by chlorpromazine, the first of the phenothiazine derivatives. Within a few years chlorpromazine became the standard treatment of schizophrenia, making deep insulin therapy (DIT) a matter of historical interest. Antidepressant drugs were introduced in 1957; they were found to alleviate depressive symptoms, unlike the amphetamines which merely produce a short-lived and sometimes uncomfortable arousal. Chlordiazepoxide, quickly followed by other benzodiazepine derivatives, became available in 1960. Understandably, in view of their safety and low dependence potential, these tranquillisers have largely replaced barbiturates and meprobamate in the treatment of anxiety states.

In addition to their direct therapeutic effects, psychotropic drugs have had other influences. Mental illness, now that it is more amenable to treatment, is more comprehensible, and therefore more acceptable to the general public. Patients in the UK are less likely to be incarcerated in vast, isolated mental hospitals. Today they are treated as outpatients, in day hospitals and centres, or if needing admission, in psychiatric units attached to general hospitals located near their families and friends. Locked hospital wards—except in special security units—are virtually a phenomenon of the past. Institutionalisation is less common. Patients are now part of a therapeutic community; they participate in group meetings, discuss their problems openly and realistically, engage in occupational therapy (OT), and steadily rebuild their self confidence in preparation for returning to the everyday world.

It is true that the concept of the therapeutic community was taking shape even before psychotropic drugs came on the scene. But it was their beneficial effects on patients, particularly in reducing disruptive and often destructive behaviour, that allowed these humane ideas to be put so widely into practice. On an individual level, many other treatments

became effective as drugs broke the vicious circle created by anxiety and depression. Psychotherapy, individual or group, which previously had been ineffectual because of the patient's crippling tension and impulsive acting out, could now be utilised by him. Thus, by enlarging the therapeutic armamentarium, psychotropic drugs and physical treatments also created an atmosphere which enhanced their own efficacy.

Inevitably, psychotropic drugs have been abused. It has taken many years to begin to understand how these drugs work, when they should be prescribed and why, their effective dosage, and for how long they should be given. This applies especially to the tranquillisers, both minor and major varieties, and antidepressant drugs. By no means all schizophrenic patients for example, need a maintenance dose of a phenothiazine; yet many are still unnecessarily, even harmfully, prescribed them. Anxious and depressed patients are often given drugs routinely, when they should in fact be advised to face and deal with their problems. By all means give a tranquilliser when anxiety is such that the patient is incapable of tackling his problems, but never forget or ignore the underlying causes. Very few psychiatric disorders arise that are not the result of adverse external events interacting with a patient's constitutional make up. Of course, many patients may be unable to alter their circumstances; in which case a drug is necessary to help them adapt to or accept their unhappy situations.

It is plain therefore that every doctor prescribing a psychotropic drug must know why he is doing so, and what he expects. So too should a patient know the reasoning behind his treatment. Clearly a doctor cannot prescribe rationally until he has made a diagnosis and understood the main causes of his patient's distress. Only then can he assess the need for treatment, its nature, and for how long it may be required.

As well as the therapeutic effect of any drug he employs, he must know the likely side effects, dangers from idiosyncratic reactions, and ways in which it may interact with other drugs. He must always balance the probable good against the possible dangers of a treatment. Once a drug is prescribed, the doctor must be perceptive about his patient's reactions, be prepared to vary the dosage up or down, or to stop the drug if need be; for instance, if the patient becomes pregnant or develops heart, renal or liver failure, with consequent impairment of the drug's metabolism and excretion.

Today, armed with drugs that are therapeutically potent, it is apparent to doctors that many treatments given in the past had no specific effects. Rather, they worked because of their placebo and nonspecific qualities, because the doctor wanted them to help, and because the patient needed to believe in them. Placebo effects have long been recognised and utilised; shape, size and colour of a drug, and dosage schedule, are all

important factors. Even more so is the nature of the doctor–patient relationship, the degree to which a patient trusts his doctor, likes, admires and even loves him, or dislikes him. Some of the reactions of a patient depend on his intelligence and social sophistication, on his cultural background, how he looks on a drug and its likely effects. And even the most well informed of us still have a need for magic, are still, beneath our cultivated exteriors, irrational.

Today we are inundated with controlled trials of new drugs. Most of them contribute almost nothing to clinical understanding and wisdom. Indeed, since their results and conclusions are so often contradictory, the effect is confusing. The reason for this is that the patients making up most drug trials are clinically heterogenous; depression for instance is a protean term and there is no uniform agreement about terminology. Drugs are given for comparatively short periods, the dosage is often inadequate, and the results of such trials depend more on arbitrary rating scales than on clinical perceptiveness.

When a drug really works it is obvious to everyone, doctor and patient. That impramine and amitriptyline are most useful in endogenous types of depression, and the MAOIs particularly effective in reactive depression, became apparent to most clinical psychiatrists within 1 or 2 years of these drugs being introduced. It hardly required laborious double blind controlled trials to prove this point, any more than did streptomycin's efficacy in tuberculous meningitis.

Double blind trials in psychiatry are, on the whole, valueless; their instigators all too often pretend to be 'scientific', and rely on questionnaires rather than clinical ability. The essential requirements for useful research into psychotropic drugs are, understanding the natural history of the condition under investigation, the patience to undertake a painstaking selection of patients, and the ability to analyse the responses of patients to the treatment under study. In many instances, uncontrolled drug trials have yielded more information than double blind controlled studies.

Polypharmacy is, regrettably, often needed in psychiatry. Depression is frequently accompanied by anxiety or agitation of such intensity that an antidepressant drug alone is not enough; a tranquilliser must then be added. An anti-Parkinsonian drug may have to be given concomitantly with a neuroleptic to counteract its extrapyramidal effects. An antidepressant drug may have to be prescribed to a depressed schizophrenic receiving monthly injections of fluphenazine or flupenthixol.

Many drugs interact and have antagonistic, synergistic or additive effects, which can occasionally be fatal. One drug may prevent the absorption of another, compete for binding sites on plasma proteins or receptors, inhibit or stimulate catabolising enzymes, enhance or

diminish renal clearance. It is essential to recognise such possible interactions before prescribing a second or third drug to a patient.

Pharmacokinetic studies are still young, but suggest that genetic factors are responsible for individual differences in the rate at which a drug is metabolised, and the extraordinary wide variation in effective drug dosage that exists. Depending on the drug, absorption occurs from the stomach, and later from the intestine. The degree and rapidity of absorption are affected by various factors: content of the gastric juice, motility, diet, and the presence of other drugs. Once absorbed, drugs pass to the liver and are metabolised, sometimes into therapeutically active metabolites; for instance amitriptyline to nortriptyline, diazepam to medazepam. From there the drug, its concentration by now reduced, passes to the brain. Giving a drug by injection allows it direct access to the brain, without alteration in the liver.

The activity of the microsomal enzymes of the liver, responsible for drug metabolism, is stimulated by some drugs, inhibited by others. The most important from a clinician's point of view are alcohol, barbiturates, phenytoin, and possibly phenothiazine derivatives. A heavy drinker who continues to drink may well need a bigger dose of an antidepressant drug than a nondrinker. So also may the patient who regularly takes a barbiturate at bedtime. A few drugs, notably the MAOIs and progesterone, inhibit liver enzymes and thereby lessen drug metabolism. A woman taking one of the progesterone-containing contraceptive pills may therefore need a smaller dose than otherwise of an antidepressant or tranquilliser; and if she stops the contraceptive pill, the dosage of the drug, to remain effective, may need to be increased. Needless to say, extreme caution is necessary if psychotropic drugs have to be given to anyone with serious liver damage.

In the blood stream most psychotropic drugs, with the exception of lithium, are bound to plasma proteins, in which form they are inactive. Only 10 to 20 per cent of a drug is free and therefore active. Measurement of the concentration of a drug is still largely a matter of research interest. However, it may well have a useful part to play in the future in the treatment of intractable depression.

Lithium exists free and active in the plasma, and it is important that its concentration in the blood should lie between 0·6 and 1·2 mmol/l for it to be effective in controlling most cases of manic depression.

Reports that antidepressant drugs, such as nortriptyline, are ineffective below 50 ng/ml are understandably consistent. But that levels above 250 ng/ml are also ineffective is difficult to accept, particularly when reports are contradictory Clinically there are patients who respond only when very large doses of an antidepressant drug are given. Of course such patients may absorb only part of the dosage, or the drug may be meta-

bolised excessively rapidly, or virtually all of it be bound to plasma proteins. Much more work is needed on the subject before we can afford to be dogmatic about dosage. It is important for the clinican to recognise that each patient is unique, and has his own optimum drug dosage.

Excretion takes place largely through the kidneys. Renal damage or conditions such as cardiac failure which impair excretion invariably reduce the rate at which drugs are removed from the body. Apart from lithium, only a small proportion of any psychotropic drug is excreted unchanged in the urine; for instance, less than 30 per cent of imipramine. How often a drug needs to be given to maintain an effective concentration in the blood obviously depends largely on the speed at which it is metabolised, and if metabolites are active. Some drugs must be taken three or four times a day, for instance, nomifensine, others, like amitriptyline, once a day. And a drug such as penfluridol, which has an extremely slow rate of excretion, once a week.

Pharmacogenetics have proved of increasing if limited usefulness. A depressed patient with say a first-degree relative who responded to a particular antidepressant in the past, is more likely to be helped by that drug or its close analogue than one of a different class. Of course, to have had a close relative who responded well to drug which is then prescribed for oneself may well heighten its placebo effect. A genetic explanation is not necessarily the only one possible.

Lastly, it is always important to question the possible reasons for a patient not responding to drug treatment after reasonable length of time. Is the dosage too low? Is the patient really taking the drug regularly? Are the effects of the drug being countered by alcohol or another drug? Are unsuspected organic factors playing a part? Or is the diagnosis wrong? All these matters should be considered before new treatment is instigated.

PART 2. ANTIDEPRESSANTS

In the past depression was treated in a variety of ways, by isolation and rest, shocks, mesmerism and so on. Particularly when accompanied by much anxiety, opium or one or more of a large range of sedatives were employed; the most popular of which, just before the advent of the psychotropic drugs, were bromides and barbiturates. In the 1930s the amphetamines were introduced, and they and related compounds were virtually the only drugs available for the treatment of depression until 1957. But their euphoric effect was short-lived, and their disadvantages were considerable; their usefulness in fact, in the vast majority of depressed patients, was negligible. E.c.t., introduced in 1937, was the

only treatment that truly relieved depression. But by no means all patients responded to e.c.t., or if they did they were liable to relapse within a few weeks; and side effects, particularly disturbance of memory, were sometimes upsetting.

In 1952 iproniazid was used in the treatment of tuberculosis and seen to have a remarkable if unexpected stimulating effect on patients. It was shown to be an inhibitor of MAO, but interest in the drug lapsed until the introduction of reserpine. Reserpine and chlorpromazine were given for the treatment of depression in the early 1950s, but results were not encouraging. However, interest in reserpine increased when it was discovered that it was itself liable to produce depression in about 15 per cent of patients treated with the drug, either for psychiatric purposes or hypertension. This depressant action was believed to be mediated through depletion of the storage and concentration of monoamines in the brain. New interest was now taken in iproniazid, which was indeed found to relieve some states of depression. It seemed possible that the antidepressive effect of iproniazid was due to its ability to inhibit MAO, and so increase the concentration of monoamines in the brain. Confirmation followed when it was found that iproniazid could abolish the depressive syndrome produced by reserpine in laboratory animals.

Iproniazid began to be used clinically in 1957. Almost at once another compound, imipramine, was discovered, again by accident, to be an effective antidepressant. Its structure and properties were unlike those of iproniazid; it did not inhibit MAO. But like iproniazid it was capable of increasing the concentration of monoamines at receptor sites in the brain. It did this not by inhibiting MAO, but by blocking the reuptake of monoamines released in the synaptic cleft.

Suddenly then, in 1957, two potent antidepressant drugs became available to clinicians and an exciting field of research into the biochemical basis of depression appeared. Inevitably there was clinical confusion at first, and exaggerated claims for each drug or group of drugs were made. Gradually, with increasing experience, the picture has cleared, although by no means completely.

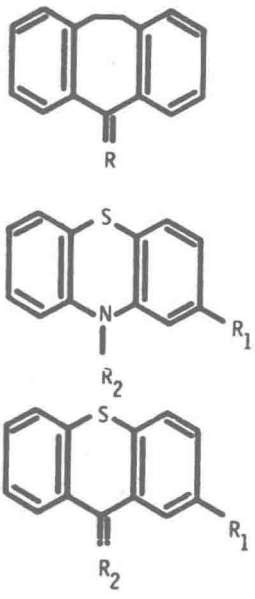
We know that the MAOIs are particularly useful in reactive types of depression and anxiety states, and that endogenous depression responds much better to imipramine and the other tricyclic analogues. However, not only is this classification still controversial, but it is admittedly often difficult to decide whether a depression is reactive or endogenous. All too often the clinical state is a mixed one, with reactive and endogenous features. The idea that a reactive depression always has clear cut external causes, while an endogenous depression has none, or insufficient to account for such depression, is of course misleading; a minority of patients conform to textbook stereotypes. For the most part, clinicians

must depend on signs and symptoms, the length and course of the illness, the family history of affective disorder and its response to treatment, the patient's personality and life style. The need to make a diagnosis is no longer simply an academic exercise; the type of treatment prescribed, whether a MAOI, tricyclic, or other drug or combination of drugs, is dependent on this. It requires not only the most careful scrutiny of the patient and his symptoms, but also the use of that subtle intuitive sense which develops (and which is all too often suppressed today) with experience. To judge by the remarks of some practitioners, treating a depressed patient is a simple clockwork exercise; you prescribe the 'safest' and latest antidepressant and gradually work your way along the drug line, often bypassing the MAOIs because of their 'dangers', often using unsuitable dosages, until eventually e.c.t. is suggested as a last resort. This of course makes a mockery of psychiatry. We may still be a long way from becoming scientists, but we do have effective tools at our disposal now, and they demand expertise. Just as the poor workman blames his tools for bad work, so today the poor psychiatrist blames his failures on his drugs. Only by understanding to the full the effects of the antidepressant drugs now available, and the differing ways in which they interact with individual patients, and among themselves, can clinical psychiatrists expect their treatment to succeed.

Tricyclic antidepressants

The molecules of all these substances include three joined rings, differing from the phenothiazine nucleus in having seven atoms instead of six in the central ring (Fig. 1.1). It is this ring structure which gives the drug its antidepressant quality. Variations in the side chain attached to the central ring (R2), and in the atom at R1, account for differences in potency and sedative action between individual tricyclics. (Table. 1.1)

Imipramine and amitriptyline are the oldest and best established members of the tricyclic group. Today there are more than 12 potent derivatives of this molecular structure. Biochemically they vary. Some predominantly inhibit the reuptake of noradrenaline (NA)—for instance nortriptyline, desipramine, and the quadricyclic maprotiline. Others inhibit 5HT reuptake, especially clomipramine. Most of the others inhibit the reuptake of both 5HT and catecholamines in differing degrees. Some, such as trimipramine, appear not to influence the reuptake of either substance. This knowledge is not simply of academic interest, for it can sometimes be usefully applied clinically, albeit clumsily. Catecholamine reuptake inhibitors are best when reactive elements are prominent; 5HT reuptake inhibitors with biopolar depressions.



TRICYCLIC ANTIDEPRESSANTS

PHENOTHIAZINES

THIOXANTHENES

Fig. 1.1

Depression is protean, and it is easy for the unwary to overlook the possibility of depressive illness. Many patients present with anxiety and worry, especially about their health. Physical symptoms are common, abdominal pain, headache, back pain, and muscle discomfort. Unusual, irresponsible behaviour may mask depression.

The tricyclic antidepressants not only elevate mood, restore energy and

Table 1.1 Classification of thymoleptics (From Dally, P.J. 1978. Drug therapy. In *Therapy Options in Psychiatry*. Ed. Connolly, J. Pitman Medical)

1.	**Tricyclic antidepressants**	
	Amitriptyline	Butriptyline
	Imipramine	Desipramine
	Nortriptyline	Clomipramine
	Trimipramine	Protriptyline
2.	**Tricyclic-based compounds**	
	Dothiepin	Nomifensine
	Dibenzepin	Doxepin
3.	**Tetracyclic antidepressants**	
	Maprotiline	Mianserin
4.	**Oxazines**	
	Viloxazine	

drive, lift depression and lessen tension, they also sedate, in some cases excessively. Their usefulness, by and large, is in the treatment of endogenous states of depression; with broken sleep and early morning waking, lack of appetite, sometimes with severe weight loss, anergia, absent libido, self blame and guilt, depression at times serious enough for suicide to be contemplated, improving towards evening, and varying degrees of retardation and agitation. In the most severe cases psychotic symptoms develop.

The reactive depressions which respond so well to MAOIs are more akin to anxiety states; depression is not so deep, autonomic functions not so seriously upset, and the patient often angrily blames others for his misfortunes, seeing himself the victim rather than the cause of his troubles. Imipramine and amitryptyline have been consistently shown to be superior to MAOIs such as phenelzine and tranylcypromine, in endogenous depression. Seventy to 80 per cent of mildly depressed patients respond within a fortnight to amitriptyline; often with a comparatively small dose of around 75 mg at night. Even smaller doses are effective in the elderly. But when depression is severe the tricyclic antidepressants may not be adequate. Certainly, if suicide is a risk, then e.c.t. should never be delayed, particularly in view of the comparatively long interval between starting an antidepressant and its therapeutic effect.

However, a tricyclic can be safely combined with e.c.t., and by the time several e.c.t. have been given its antidepressant effects are emerging. Not only does this reduce the number of treatments needed, but the risk of subsequent relapse is greatly reduced.

There are clinicians who maintain that there is little to choose between the antidepressant effectiveness of the various tricyclics, and it is only the patient's intolerance to different side effects which makes one drug seem preferable or superior to another. The same used to be said of the neuroleptics. Certainly the unpleasantness of side effects may make it impossible to give an adequate dose. But there are good clinical reasons for thinking that clomipramine is better in depression associated with obsessional/compulsive symptoms, and in some cases of manic depression, while nortriptyline and the quadricyclic maprotiline often seem most effective when stressful reactive factors are prominent.

Of course the ability of a drug to sedate is also a reason why one tricyclic is preferred to another (Table. 1.2). Amitriptyline is more sedating than imipramine or clomipramine, and is the first choice when dealing with an agitated depression. Trimipramine is most sedating of all the tricyclics and is ideal for treating very tense anxious patients, constantly complaining of broken sleep and early morning anxiety. On the other hand, its antidepressant qualities are low and, on its own, it is no substitute for amitriptyline in serious depression.