Basic Notes in Psychopharmacology is a concise summary, in the form of notes, which gives the reader a quick and easy-to-use overview of the subject. This greatly expanded fourth edition now covers all the major classes of drugs, and for each individual drug the principal mode of action, indications and adverse effects are provided. In addition, it now includes 35 peer-reviewed clinical vignettes, focusing on psychopharmacological treatments which play a major part in management.

As a short and practical guide it will be invaluable for junior hospital psychiatrists, general practitioners and medical students. Others, including psychiatric nurses, psychiatric social workers, psychiatric occupational therapists and clinical psychologists, will also find it extremely useful.

Levi’s latest edition of his already popular book provides the busy clinician with a reliable access point to key essential facts. Invaluable for all training grades within psychiatry, the discerning medical student and mental health nurses. Consultants involved in training will also find it of assistance in planning teaching sessions. This new edition of Mike Levi’s book restores the publication to the cutting edge of psychopharmacology and he is to be congratulated on his commitment to the field of psychiatric education.” GARETH VINCENTI, IN THE FOREWORD

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Foreword to the Fourth Edition

For many years the field of psychopharmacology barely changed, but the last 15 years have witnessed a revolution, with new drugs and new treatment strategies following one another in bewildering succession. We now live in the world of guidelines and meta-analyses, and it can sometimes be difficult to see the wood for the trees. Mike Levi's latest edition of his already popular book once again provides the busy clinician with a reliable access point to key essential facts about psychopharmacology.

This fourth edition of *Basic Notes in Psychopharmacology* incorporates a new approach, and contains a large and varied amount of case vignettes and discussion. These illuminate the basic factual text, and provide a useful insight into the clinical approach of an experienced and able clinician. As such, this book will remain invaluable for all training grades within psychiatry, the discerning medical student and our mental health nurse colleagues. Consultants involved in training will also find it of assistance in planning teaching sessions.

This new edition of Mike Levi's book restores the publication to the cutting edge of psychopharmacology and he is to be congratulated on his commitment to the field of psychiatric education.

Dr Gareth Vincenti MB BS LLB FRCPsych
Consultant Psychiatrist & Medical Director
Cygnet Hospital, Harrogate
August 2007
Preface to the Fourth Edition

Following the popularity of the third edition, I was encouraged to write this new edition for junior hospital psychiatrists, general practitioners and medical students.

I have completely updated the book to include new psychotropic drugs that have been launched in the UK since the appearance of the third edition in 2004. I have also reviewed all the drugs covered in the third edition and updated these entries, where appropriate, in the light of current knowledge.

The fourth edition also includes 35 clinical vignettes in the area of general adult psychiatry with suggested psychopharmacological management plans.

MIL
August 2007
Introduction

The purpose of writing this book is twofold: Section One provides a concise summary of psychopharmacology in the form of notes. The drugs discussed in this section of the book are those considered by the author to be the most important drugs that the practising physician needs to know about. The aim is to provide the principal mode of action, indications and adverse effects of the drugs covered. I have based these notes on what is generally regarded to be the most comprehensive textbook\(^1\) for the MRCPsych examination. These notes represent my own view of current clinical practice.

Section Two provides the reader with 35 clinical vignettes in the area of general adult psychiatry with suggested psychopharmacological management plans. I clearly acknowledge the importance of psychosocial treatments in mental illness. However, for the purpose of this book, I am unashamedly focusing on psychopharmacological treatments which play a major part in management.

The reader should study each clinical vignette, consider their answer, then turn the page and see how they got on. Of course, they will not always agree with my suggested psychopharmacological management plan. However, agreement or not is unimportant, as in disagreeing one is forced to justify one’s own line of thinking. This can only help to firm up one’s own ideas regarding psychopharmacological management.

The book is intended to have wide readership — particularly among junior hospital psychiatrists, general practitioners and medical students. In addition, the book will also be useful to psychiatric nurses, psychiatric social workers, psychiatric occupational therapists and clinical psychologists.

Reference

Acknowledgements

The author is indebted to Ms Deborah Barron for her invaluable help in producing the manuscript.

Many thanks also to Dr Gareth Vincenti for his helpful comments and for providing the Foreword to the book.
SECTION ONE

Basic Psychopharmacology
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CHAPTER 1

Hypnotic and Anxiolytic Drugs

I BENZODIAZEPINES

(a) Mode of action
1 GABA (γ-aminobutyric acid) agonists; act at benzodiazepine BZ₁- and BZ₂-receptors which are located postsynaptically throughout the brain at GABA-ergic synapses.
2 There are three subtypes of benzodiazepine receptors:
   (i) Omega-1 – mediates hypnotic effect of drug
   (ii) Omega-2 – mediates anxiolytic effect of drug
   (iii) Omega-3 – mediates myorelaxant effect of drug.
Benzodiazepines act on all three receptor subtypes and therefore have muscle relaxant, anxiolytic and hypnotic effects.

(b) Indications
1 Transient insomnia in those who normally sleep well – if a benzodiazepine is indicated, use one that has a short half-life with little or no hangover effect and only prescribe 1 or 2 doses of the drug, e.g. lormetazepam; dose range 0.5 mg nocte to 1.5 mg nocte.
2 Anxiety disorders (generalised anxiety disorder and panic disorder) – provide symptomatic relief of severe anxiety in the short term (should not be prescribed for more than 2–4 weeks), e.g. diazepam; dose range 2 mg tds increased if necessary to 15–30 mg daily in divided doses. The use of an antidepressant drug should also be considered in this situation (see later).
3 Phobic anxiety disorders – provide some immediate relief of phobic symptoms in the short term.
4 Obsessive compulsive disorders – provide some short-term symp-
4 Basic notes in psychopharmacology

tomatic relief (should not be prescribed for more than 2–4 weeks’ duration).

5 Acute organic disorder:
(i) May be used during the night-time to help the patient sleep.
(ii) In the special case of hepatic failure – may be used during the day-time to calm the patient despite their sedative effects, since they are less likely to precipitate coma – cf haloperidol (which is the usual drug of choice to calm such patients).
(iii) In the special case of alcohol withdrawal – chlordiazepoxide is the most suitable drug.

6 Chronic organic disorder – may be used to alleviate anxiety.

7 Barbiturate dependence – used to cover the withdrawal symptoms from barbiturates.

8 Acutely disturbed behaviour – if an antipsychotic drug alone fails to bring the situation under control, they may be given in addition a slow intramuscular injection of 2 mg of lorazepam,* if necessary repeated 2 hours later.

9 Akathisia.

(c) Adverse effects

1 Both psychic and physical dependence occur.

2 Chronic benzodiazepine dependence – often manifests features of benzodiazepine intoxication, which are:
   (i) Unsteadiness of gait.
   (ii) Dysarthria.
   (iii) Drowsiness.
   (iv) Nystagmus.

3 Withdrawal effects from benzodiazepines:
   (i) Rebound insomnia.
   (ii) Tremor.
   (iii) Anxiety.
   (iv) Restlessness.
   (v) Appetite disturbance.
   (vi) Weight loss.
   (vii) Sweating.
   (viii) Convulsions.
   (ix) Confusion.
   (x) Toxic psychosis.

* Used but this indication is not currently licensed in the UK.
(xi) A condition resembling delirium tremens.

4 Benzodiazepines – cf barbiturates. Advantages of benzodiazepines:
   (i) Milder side-effects – including less risk of respiratory depression.
   (ii) Less severe physical dependence.
   (iii) Less dangerous in overdosage.
   (iv) Less likely to interact with other drugs – as induction of hepatic microsomal enzymes does not occur to the same extent.

II BARBITURATES

(a) Mode of action
GABA potentiators; do not act at benzodiazepine receptors; may have specific binding sites elsewhere on the neuronal membrane.

(b) Indications
1 Severe intractable insomnia in patients already taking barbiturates – even in such patients, an attempt to slowly withdraw the barbiturate should be considered, covering the withdrawal syndrome with a benzodiazepine.
2 Dissociative (conversion) disorders – classically, abreaction was brought about by an intravenous injection of small amounts of amylobarbitone sodium. In the resulting state, the patient is encouraged to relive the stressful events that provoked the hysteria, and to express the accompanying emotions. Now, such abreaction can be initiated more safely by a slow intravenous injection of 10 mg of diazepam.

(c) Adverse effects
1 Both psychic and physical dependence occur.
2 Chronic barbiturate dependence – often manifests features of barbiturate intoxication, which are:
   (i) Slurred speech.
   (ii) Incoherence.
   (iii) Dullness.
   (iv) Drowsiness.
   (v) Nystagmus.
   (vi) Depression.
3 Withdrawal effects from barbiturates:
(i) Clouding of consciousness.
(ii) Disorientation.
(iii) Hallucinations.
(iv) Major seizures.
(v) Anxiety.
(vi) Restlessness.
(vii) Pyrexia.
(viii) Tremulousness.
(ix) Insomnia.
(x) Hypotension.
(xi) Nausea.
(xii) Vomiting.
(xiii) Anorexia.
(xiv) Twitching.
(xv) A condition resembling delirium tremens.

4 Drug interactions – induction of hepatic microsomal enzymes leads to increased metabolism of:
   (i) The oral contraceptive pill.
   (ii) Corticosteroids.
   (iii) Warfarin.
   (iv) Tricyclic antidepressants.
   (v) Most antipsychotic drugs.
   (vi) Cyclosporin.
   (vii) Theophylline.

III CHLORAL DERIVATIVES

(a) Mode of action
   GABA potentiators.

(b) Indications
   Short-term treatment of insomnia, e.g. chloral betaine; rarely used now.

(c) Adverse effects
   Abuse potential – therefore should not be prescribed for more than 1–2 weeks’ duration.
IV OTHERS

1 CHLORMETHIAZOLE

(a) Mode of action
GABA potentiator.

(b) Indications
In the management of alcohol withdrawal for inpatients only, chlormethiazole may be prescribed in either of two ways:

1. On an as-required basis, i.e. flexibly according to the patient’s symptoms.
2. On a reducing regimen basis, i.e. on a fixed 6-hourly regimen of gradually decreasing dosage over 6–9 days.

NB: The patient must stop drinking when taking chlormethiazole. If chlormethiazole is taken in combination with alcohol, each potentiates the CNS depressant action of the other, and overdosage is frequently fatal; thus nowadays chlordiazepoxide is preferred as an alternative to chlormethiazole in the management of alcohol withdrawal – chlordiazepoxide has the advantage over chlormethiazole of being less addictive and being less dangerous if taken in combination with alcohol.

(c) Adverse effect
May cause acute cardiac arrest or acute respiratory arrest if taken in combination with alcohol.

2 β-BLOCKERS

(a) Mode of action
Block β-adrenoceptors in the heart, peripheral vasculature, bronchi, liver and pancreas and brain (although CNS penetration is poor).

(b) Indications
Limited use in treating anxiety disorders in which palpitations, sweating or tremor are the most troublesome symptoms, i.e. those anxiety disorders with predominantly somatic symptoms, e.g. propranolol; dose range 40 mg bd (or 80 mg SR) to 40 mg tds.

NB: β-Blockers have little effect on subjective feelings of anxiety.
(c) Adverse effects
Contraindicated in patients with:

1. Asthma.
4. Second- or third-degree heart block.

3 BUSPIRONE

(a) Mode of action
1. Thought to act at specific serotonin (5HT1A) presynaptic autoreceptors – as a partial agonist.
2. Response to treatment may take up to 2 weeks – similar to antidepressant drugs.

(b) Indications
1. Short-term treatment (up to several months) of generalised anxiety disorder; usual dose range 5 mg tds to 10 mg tds; maximum dose of 15 mg tds; long-term efficacy is untested.
2. May be useful in the treatment of resistant depression* – as an augmenting agent to SSRIs (by enhancing serotonin accumulation within the synapse).
3. May be useful in the treatment of obsessive compulsive disorder* – as an augmenting agent to SSRIs.

(c) Adverse effects
1. Physical dependence and abuse liability low.
2. Non-toxic augmenting agent, cf lithium carbonate.
3. Does not potentiate the effects of alcohol, cf benzodiazepines, which do.
4. Lacks sedative and myorelaxant properties of benzodiazepines.
5. Contraindicated in pregnancy and epilepsy.

4 ZOPICLONE

(a) Mode of action
1. The first cyclopyrrolone.
2. GABA potentiator – although not a benzodiazepine, it acts on

*Used but these indications are not currently licensed in the UK.
benzodiazepine receptors, which are located postsynaptically throughout the brain at GABA-ergic synapses.
3 Acts on Omega-1 and Omega-2 receptor subtypes and therefore has anxiolytic and hypnotic effects.

(b) Indications
1 Transient insomnia in those who normally sleep well – as an alternative to a benzodiazepine; dosage 7.5 mg nocte in adults.
2 For short-term use only (preferably only 1 or 2 doses).

(c) Adverse effects
Since it acts on benzodiazepine receptors, it may give rise to the problems of physical dependence as observed in benzodiazepines if used for long-term treatment.

5 ZOLPIDEM

(a) Mode of action
1 The first imidazopyridine.
2 GABA potentiator – although not a benzodiazepine, it acts on benzodiazepine receptors, which are located postsynaptically throughout the brain at GABA-ergic synapses.
3 Acts on Omega-1 receptor subtype only and therefore has a pure hypnotic effect.

(b) Indications
1 Transient insomnia in those who normally sleep well – as an alternative to a benzodiazepine; dosage 10 mg nocte in adults.
2 For short-term use only (preferably only 1 or 2 doses).

(c) Adverse effect
1 Since it acts on one of the same receptor subtypes as benzodiazepines, it may give rise to the problems of physical dependence as observed in benzodiazepines if used for long-term treatment.
2 May have less abuse potential because it spares the Omega-2 receptor subtype, cf zopiclone.

6 ZALEPLON

(a) Mode of action
Acts on the Omega-1 subtype of the central benzodiazepine's receptor – and therefore has a pure hypnotic effect.
(b) Indications

1 Insomnia (short-term use).
2 Dosage 10 mg at bedtime or after going to bed if difficulty falling asleep; the latter is accounted for by the very short half-life (duration of action) of Zaleplon.

(c) Adverse effect

May have less abuse potential because it spares the Omega-2 receptor subtype, cf zopiclone.

7 PREGABALIN

(a) Mode of action

1 Antiepileptic.
2 Binds to an auxiliary subunit (\(\alpha_2-\delta\) protein) of voltage-gated calcium channels in the central nervous system, potentially displacing \([\text{H}^3]\)-gabapentin.

(b) Indications

1 Licensed in 2006 for the treatment of generalised anxiety disorder (GAD) in adults.
2 It has been shown to be effective in reducing both the psychological and somatic symptoms of GAD.
3 The dose range is 150 to 600 mg per day given as two or three divided doses. The need for treatment should be reassessed regularly.

(c) Adverse effects

1 Very common side-effects include dizziness and somnolence.
2 Common side-effects include dry mouth, constipation, vomiting and flatulence.