If no CD is here, please call 0141 223 1600

Introduction to Pharmaceutical Care in Mental Health

NHS Education for Scotland (Pharmacy)
3rd Floor, 2 Central Quay
89 Hydepark Street
Glasgow
G3 8BW

Telephone 0141 223 1600
Fax 0141 223 1651
E-mail pharmacy@nes.scot.nhs.uk
Website www.nes.scot.nhs.uk/pharmacy
Introduction to Pharmaceutical Care in Mental Health
Acknowledgements
This pack has been developed, with permission, using the majority of the material from a CPPE Open learning course `Presentation and Management of Common Mental Disorders` published in 2005. NES wishes to greatly thank CPPE as well as the contributors, editors and reviewers of the CPPE pack.

However, members of the group of Scottish Pharmacy in Mental Health (SPMH) have been involved in editing and reviewing the CPPE open learning course in order that we could develop this NES pack which has a specific focus on legislation, guidance and issues relevant in Scotland.

Specialist Editors – Scotland (SPMH)
We gratefully acknowledge and thank the following specialist editors of this pack:

Liz Kelly and Joan Hoek, Senior Clinical Pharmacists (Mental Health) NHS Ayrshire and Arran and Gazala Akram, Senior Clinical Pharmacist (Child Psychiatry) NHS Greater Glasgow and Clyde / Lecturer, University of Strathclyde, Glasgow.

Specialist Reviewers – Scotland (SPMH)
We gratefully acknowledge and thank the following reviewers of this pack:

Alyson Henderson, Senior Clinical Pharmacist (Mental Health), NHS Fife
Barrat Luft, Senior Clinical Pharmacist (Mental Health), NHS Greater Glasgow and Clyde.

Design and print
Shandwick Design, Glasgow
Meigle Print, Galashiels.

Disclaimer
While every precaution has been taken in the preparation of these materials, neither NHS Education for Scotland nor external contributors shall have any liability to any person or entity with respect to liability, loss or damage caused or alleged to be caused directly or indirectly by the information therein.
Contents

About this pack 6

Chapter 1 Introduction to mental health and mental illness 11
1.1 Background 13
1.2 History of mental healthcare 14
1.3 Development of mental health law and social care 16
1.4 Definitions and controversy 24
1.5 Classification systems for mental and behavioural disorders 27
1.6 Mental health rating scales 29
1.7 Guidance on care in Mental Health 32

Chapter 2 Neurochemistry and neuroanatomy 39
2.1 Introduction 41
2.2 Revision points 41
2.3 Neurotransmitters 42
2.4 Receptors 43

Chapter 3 Schizophrenia 45
3.1 Introduction 47
3.2 History of schizophrenia 47
3.3 Epidemiology 48
3.4 Symptoms of schizophrenia 49
3.5 Course of schizophrenia 51
3.6 Aetiology of schizophrenia 52
3.7 Treatment of schizophrenia 57
3.8 Side-effects of antipsychotics 59

Chapter 4 Depression 71
4.1 Introduction 73
4.2 Epidemiology 73
4.3 Symptoms of depression 73
4.4 Aetiology of depression 75
4.5 Treatment of depression 78
4.6 Counselling points on depression 86
## Chapter 5  Bipolar affective disorder

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1 Introduction</td>
<td>91</td>
</tr>
<tr>
<td>5.2 Epidemiology</td>
<td>93</td>
</tr>
<tr>
<td>5.3 Symptoms of bipolar affective disorder</td>
<td>94</td>
</tr>
<tr>
<td>5.4 Course of bipolar affective disorder</td>
<td>95</td>
</tr>
<tr>
<td>5.5 Aetiology of bipolar affective disorder</td>
<td>96</td>
</tr>
<tr>
<td>5.6 Treatment of bipolar affective disorder</td>
<td>97</td>
</tr>
<tr>
<td>5.7 Adverse effects of medications used in bipolar disorder</td>
<td>101</td>
</tr>
<tr>
<td>5.8 Common drug interactions</td>
<td>105</td>
</tr>
</tbody>
</table>

## Chapter 6  Anxiety disorders

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1 Introduction</td>
<td>111</td>
</tr>
<tr>
<td>6.2 Prevalence of anxiety disorders</td>
<td>113</td>
</tr>
<tr>
<td>6.3 Symptoms</td>
<td>113</td>
</tr>
<tr>
<td>6.4 The neurobiological basis of fear and anxiety</td>
<td>114</td>
</tr>
<tr>
<td>6.5 Presentation of anxiety disorders</td>
<td>115</td>
</tr>
<tr>
<td>6.6 Management of anxiety</td>
<td>118</td>
</tr>
</tbody>
</table>

## Chapter 7  Sleep disorders

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.1 Sleep</td>
<td>135</td>
</tr>
<tr>
<td>7.2 Insomnia</td>
<td>137</td>
</tr>
<tr>
<td>7.3 Management of insomnia</td>
<td>139</td>
</tr>
<tr>
<td>7.4 The presentation and management of other sleep disorders</td>
<td>141</td>
</tr>
</tbody>
</table>

## Chapter 8  Dementias

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1 Introduction</td>
<td>153</td>
</tr>
<tr>
<td>8.2 Epidemiology</td>
<td>155</td>
</tr>
<tr>
<td>8.3 Symptoms</td>
<td>155</td>
</tr>
<tr>
<td>8.4 Diagnosing dementia</td>
<td>157</td>
</tr>
<tr>
<td>8.5 Classification of the dementias</td>
<td>159</td>
</tr>
<tr>
<td>8.6 Assessment tools in dementia</td>
<td>164</td>
</tr>
<tr>
<td>8.7 Management of cognitive features of dementia</td>
<td>165</td>
</tr>
<tr>
<td>8.8 Management of non-cognitive symptoms</td>
<td>170</td>
</tr>
<tr>
<td>8.9 Older people and their medicines</td>
<td>173</td>
</tr>
<tr>
<td>8.10 Communicating with patients</td>
<td>174</td>
</tr>
</tbody>
</table>
### Chapter 9  Multiple pathology, multiple problems

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.1 Introduction</td>
<td>181</td>
</tr>
<tr>
<td>9.2 Psychotropic medication and physical illness</td>
<td>181</td>
</tr>
<tr>
<td>9.3 Dual diagnosis</td>
<td>183</td>
</tr>
<tr>
<td>9.4 Polypharmacy</td>
<td>185</td>
</tr>
<tr>
<td>9.5 Drug Interactions</td>
<td>190</td>
</tr>
<tr>
<td>9.6 Stopping medication</td>
<td>192</td>
</tr>
<tr>
<td>9.7 Changing medication</td>
<td>193</td>
</tr>
</tbody>
</table>

### Chapter 10  The role of the pharmacist in managing mental health

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1 Introduction</td>
<td>205</td>
</tr>
<tr>
<td>10.2 Setting the scene</td>
<td>205</td>
</tr>
<tr>
<td>10.3 Information needs of patients and their carers</td>
<td>210</td>
</tr>
<tr>
<td>10.4 Patients at special risk</td>
<td>212</td>
</tr>
<tr>
<td>10.5 Concordance with medication</td>
<td>213</td>
</tr>
<tr>
<td>10.6 Stopping the medication</td>
<td>215</td>
</tr>
<tr>
<td>10.7 Prodromes for mental illness</td>
<td>216</td>
</tr>
<tr>
<td>10.8 An advocacy role for pharmacists</td>
<td>217</td>
</tr>
<tr>
<td>10.9 The specialist mental health pharmacist</td>
<td>218</td>
</tr>
<tr>
<td>10.10 What do users think?</td>
<td>219</td>
</tr>
</tbody>
</table>

### Glossary and appendices

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glossary</td>
<td>229</td>
</tr>
<tr>
<td>Appendix 1 – Mental healthcare through the ages</td>
<td>234</td>
</tr>
<tr>
<td>Appendix 2 – Psychological treatments of mental illness</td>
<td>238</td>
</tr>
<tr>
<td>Appendix 3 – Support agencies, self-help groups and useful websites</td>
<td>241</td>
</tr>
</tbody>
</table>

### Multiple choice questions

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>255</td>
</tr>
</tbody>
</table>
About this pack

Welcome to this distance learning pack, which provides an introduction to the pharmaceutical care of people in Scotland who have mental health problems.

Mental health is a significant issue in Scotland for individuals, for communities and for services. The Scottish Executive Health Department stated in their key document on NHS reforms *Delivering for Health*, that they would develop a national Mental Health Delivery Plan by December 2006 in order to accelerate improvements in mental health services. As a result, *Delivering for Mental Health*, was published in December 2006 with the ultimate aim of improving the prevention and treatment of any mental health problems, for everyone living in Scotland. The pharmacist in providing pharmaceutical care and public health services, have a key role to play in this agenda.

Within this pack we have focused on the most common forms of mental health. As you work through the pack, you will learn something about its incidence and impact and how, as a pharmacist, you can make a significant contribution to tackling some of the problems that these create.

This course is aimed at any pharmacist, whether working in the community, primary care or in a hospital, interested in updating and extending their knowledge about mental disorders and their treatment. You may be newly qualified, a veteran in your field, or somewhere in the middle!

Successful completion will not qualify you to become an expert in mental health, but may confirm your interest and point you in that direction. If you do want to take your learning further, the Certificate or Diploma in Psychiatric Therapeutics, run by Aston University, may be your next project. Alternatively you may want to seek accreditation from the College of Mental Health Pharmacists (CMHP) [www.ukppg.org.uk/cmhp.html](http://www.ukppg.org.uk/cmhp.html)

In addition there is a NES Core Course pack on ‘Pharmaceutical Care of People with Depression’ which provides background knowledge on depression and allows the pharmacist to implement a Pharmaceutical Care Needs Assessment Tool with the use of an Aide Memoire. This can be obtained from NES on the website at [www.nes.scot.nhs.uk/pharmacy/resources](http://www.nes.scot.nhs.uk/pharmacy/resources)

You can find a lot of information about the pharmacist’s role in mental health both within this package (particularly Chapter 10) and from Scottish Pharmacy in Mental Health [www.spmh.co.uk](http://www.spmh.co.uk) (a specialist interest group for pharmacy staff), and the UK Psychiatric Pharmacy Group [www.ukppg.org.uk](http://www.ukppg.org.uk)
Format
The pack is organised into ten chapters.

The initial two chapters focus on the background to mental health problems and the neuroanatomy/neurophysiology of mental health disorders. The next seven chapters individually tackle the most common specific mental health disorders, with the final chapter focusing on the role of the pharmacist in mental health.

Aim
The overall aim of this pack is to help you develop your knowledge and skills in relation to pharmacy services, and in particular pharmaceutical care, in relation to mental health.

The package is designed to equip you to deliver care that is evidence based and up-to-date, while providing you with many additional sources of useful information.

To prepare and support pharmacists, prescribing advisors and pharmacist prescribers working in primary care, charged with providing pharmaceutical care to those suffering from the common mental disorders.

Objectives of the pack
The objectives of this pack are to support:

1. Appreciation of the presentation and prognosis of the common mental disorders.
2. Appreciation of the management of the common mental disorders.
3. An understanding of the proposed mode of action of the commonly-used psychotropic agents, including their potential for ADRs and interactions.
4. Knowledge of national guidance on the management of common mental disorders and the use of psychotropic agents.
5. An understanding of the various methods of service delivery.
6. Awareness of national targets/issues surrounding the pharmaceutical care of people with mental illness.
7. Appreciation of the potential role of the pharmacist in providing pharmaceutical care for this group.
8. Appreciation of the service user perspective.
9. Appreciation of the importance of monitoring physical health in those with a mental disorder and receiving psychotropic agents.
Learning Outcomes
Completing this course will enable pharmacists to:

1. Recognise the presentation and prognosis of some common mental disorders and advise or refer as appropriate.
2. Initiate preparatory tasks for the management of the common mental disorders.
3. Understand the proposed mode of action of the commonly used psychotropic agents including their potential for ADR and interaction.
4. Apply knowledge of national guidance on the management of common mental disorders and the use of psychotropic agents.
5. Assist development of the various methods of service delivery.
6. Promote awareness of national targets/issues surrounding pharmaceutical care and people with mental illness.
7. Initiate and promote pharmaceutical care for people with common mental health disorders in the local area.
8. Empathise with the service user perspective.
9. Take appropriate steps to monitor the physical health in those with a mental disorder and receiving psychotropic agents.

Activities
There are various activities detailed throughout the pack which are indicated by the following icons in the margin:

- Activity
- Key Facts
- Suggested Answers
- Case Studies
- Learning Outcomes
- Assessment

Case studies
Case studies are used to demonstrate the context in which mental health problems are experienced in practice. Cases are developed to prompt you to consider making queries, developing plans and working with the inter-professional team. They are designed to offer preparation for similar or related cases that you may face in your practice. Clinical governance issues are integrated with the case studies and self-assessment activities.

Exercises
Throughout the sections you will come across exercises, which are intended to reinforce learning and give you an opportunity to reflect on what you have read. They will also help you to meet the objectives for this course.

Complete the exercises as fully as possible before comparing what you have written with the answers at the end of the sections. You may wish to discuss your responses to the exercises with a colleague. This can be an extremely useful way of consolidating your learning and expertise.
Practice points
You will be prompted at various points throughout the text to consider whether you have uncovered a learning need to be translated into a CPD record. This will help you to look for ways of improving your practice once you have completed the pack. Use your CPD record sheets to plan and record actions you have taken.

Multiple choice questionnaire
On completion of the package, the multiple choice questionnaire should then be attempted and returned to the NES Pharmacy office, either as a paper copy or can be submitted electronically online (see instructions on page 256).

Feedback
We hope that you find this pack a useful background and/or update for you to provide pharmacy services in relation to patients with mental health disorders and as a useful reference point for the main aspects of mental illness. Please help us to assess the value and effectiveness of the pack by adding any comments in the relevant section of the MCQ answer sheet provided at the end of the pack.

This course has been adapted for use in Scotland from the CPPE distance learning package. It will take you approximately 10 hours to work through depending on your learning style and experience. It is best to work your way through the chapters from the beginning to the end in a logical order, completing the activities for each chapter as you go. However you may wish to focus on particular chapters that are relevant to your practice. Some of the other distance learning packages available from NHS Education for Scotland (Pharmacy) will complement this package. A full list of these packages are available on the NES website www.nes.scot.nhs.uk/pharmacy, or by telephoning 0141 223 1603.

How this package can assist your CPD
At the beginning of each chapter the objectives describe what you should be able to do when you complete the particular chapter. This is designed to help you monitor how you are progressing through the pack and to identify any further learning needs that you may have in relation to each aspect. You should use your personal CPD record to record your learning, future learning needs and changes to practice that you have implemented as a result of your learning. If the information is not detailed in the pack we have also listed many useful reference websites which may provide you with the relevant information.

Keeping up to date
Although the information is as up-to-date as possible at the time of publication there is always new information, statistics, policy directives and research evidence becoming available. In addition there is always information available which is pertinent to your local situation in relation to services for patients with mental health problems – you should contact your local Mental Health Specialist Pharmacist for local guidance. You should also endeavour to continue to review recommended websites for further study. The CD ROM supplied with this programme also contains helpful references for further study.
Chapter 1
Introduction to mental health and mental illness
Objectives

This chapter will enable you to:

- describe the relative contribution of various mental disorders to the global burden of disease
- describe some of the practices which characterise mental healthcare
- identify key events in the development of mental health law and social care
- debate the definitions used in the field of mental health
- recognise the different classification systems and rating scales used to diagnose, assess and monitor mental health disorders
- discuss the expectations of mental healthcare described in NHS QIS standards, as well as in published SIGN and NICE guidance
1.1 Background

Mental disorders are universal, affecting people of all countries and societies, individuals at all ages, women and men, the rich and the poor, from urban and rural environments. They have an economic impact on societies and on the quality of life of individuals and families.

At any point in time one in ten of the adult population is affected by a mental disorder and one in four people will be affected at some time during their lives.

Around one in five of all patients seen by primary healthcare professionals have one or more mental disorders.

Further reading: Office for National Statistics Website
www.statistics.gov.uk/cci/nugget.asp?id=1333

One in four families is likely to have at least one member with a mental disorder.

The World Health Organisation (WHO) measures the burden of disease in terms of years of life lost (YLL), i.e. premature death, years of life lived with disability (YLD) and the composite measure, disability-adjusted life years (DALY). One DALY is one year of ‘healthy’ life lost.

In 2000 the WHO estimated that mental and neurological disorders accounted for 12% of the total DALYs lost due to all diseases and injuries and an estimate of 15% is projected for 2020. More DALYs are lost to depression than to heart disease or stroke.

Suicide is common in many mental disorders, not just depression, and is a leading cause of premature death. Unipolar depression is the leading cause of disability for men and women of all ages, accounting for a staggering 12% of YLDs for all diseases and injuries.

Alcohol abuse, bipolar disorder and schizophrenia are in the top ten leading causes of disability for both sexes of any age and together with unipolar depression they represent the four leading causes of YLDs in younger men (aged 15 – 44 years).

Alzheimer’s disease is one of the top 20 causes of disability for men and women of all ages, together with drug use disorders, panic disorders and obsessive compulsive disorders in the 15 – 44 age group.

1.2 History of mental healthcare

Most histories of mental healthcare concentrate on the gruesome, featuring medieval witch hunts, overcrowded wards in Victorian asylums, lobotomies and insulin coma therapy, but the history of mental healthcare is by no means all bad. Practitioners from as long ago as 2000 BC clearly demonstrate that there is very little in our present day ‘enlightened’ approach that hasn’t been said or done before!

A brief overview of mental healthcare through the ages and a summary of the development of psychological therapies are included as Appendices 1 and 2 respectively. What is clear is that throughout history, theories and beliefs about the cause of mental illness and how it should be treated have been variably influenced by ignorance, fear, compassion and enlightenment. Even today, personal perception about the nature of mental illness and the behaviours and management of people suffering mental distress varies greatly.

The statements in Exercise 1 are an extract from *Attitudes to Mental Illness* 2007. Compare your responses to the public responses documented in the report. This survey is commissioned by the Department of Health and is currently conducted every three years. The report can be found at dh.gov.uk/en/Publicationsandstatistics/Publications/DH_076516

The National Scottish Survey of Public Attitudes to Mental Health is conducted every two years and is commissioned by the Scottish Executive Health Department (SEHD). The survey in 2002 informed the work of the National Programme and provided relevant baseline data. Against this backdrop a number of initiatives and campaigns were introduced including ‘See Me’ and ‘Choose Life’. The survey measures the effects of actions taken to change public attitudes and covers:

- general health and lifestyle
- mental health and well-being
- experiences and attitudes to mental health problems
- sources of information about mental health issues and awareness of relevant promotional activities across Scotland.

There were significant, positive changes in attitude towards people with mental health problems between 2002 and 2004, particularly relating to perceived dangerousness and issues associated with the protection of the general public. While it is difficult to be certain what brought about these changes it may be that the National Programme work has helped to reduce the stigma surrounding mental ill-health. The 2004 report can be viewed at www.wellscotland.info/public-attitudes-survey.html or the summary at www.wellscotland.info/uploads/file.php?serve=1133627307-public-attitudes-survey-summary-2004.pdf&action=download

Unfortunately, this positive picture is not matched by the experiences of service users. One explanation for this discrepancy is that there is a difference between people’s declared attitudes and how they in fact behave.
**Exercise 1**

Examine your own thoughts about mental illness and the way it should be treated by considering how strongly you agree or disagree with the following statements.

Score your responses as follows:

- **Agree strongly** +2
- **Agree slightly** +1
- **Neither agree nor disagree** 0
- **Disagree slightly** – 1
- **Disagree strongly** – 2

<table>
<thead>
<tr>
<th>Statement</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>We need to adopt a far more tolerant attitude to people with mental illness in our society</td>
<td></td>
</tr>
<tr>
<td>We have a responsibility to provide the best possible care for people with mental illness</td>
<td></td>
</tr>
<tr>
<td>People with mental illness don’t deserve our sympathy</td>
<td></td>
</tr>
<tr>
<td>People with mental illness are a burden on society</td>
<td></td>
</tr>
<tr>
<td>Virtually anyone can become mentally ill</td>
<td></td>
</tr>
<tr>
<td>Mental illness is an illness like any other</td>
<td></td>
</tr>
<tr>
<td>There is something about people with mental illness that makes it easy to tell them from normal people</td>
<td></td>
</tr>
<tr>
<td>One of the main causes of mental illness is a lack of self-discipline and will-power</td>
<td></td>
</tr>
<tr>
<td>People with mental illness should not be given any responsibility</td>
<td></td>
</tr>
<tr>
<td>Most women who were once patients in a mental hospital can be trusted as babysitters</td>
<td></td>
</tr>
<tr>
<td>As soon as a person shows signs of mental disturbance they should be hospitalised</td>
<td></td>
</tr>
<tr>
<td>The best therapy for many people with mental illness is to be part of a normal community</td>
<td></td>
</tr>
<tr>
<td>Less emphasis should be placed on protecting the public from people with mental illness</td>
<td></td>
</tr>
<tr>
<td>As far as possible, mental health services should be provided through community-based facilities</td>
<td></td>
</tr>
<tr>
<td>It is frightening to think of people with mental problems living in residential neighbourhoods</td>
<td></td>
</tr>
<tr>
<td>There are sufficient existing services for people with mental illness</td>
<td></td>
</tr>
</tbody>
</table>
Mental health professionals also hold negative attitudes to people with mental health problems. Attitudes to self-harm, eating disorders and substance misuse are often particularly negative. Tackling the role that health professionals play in maintaining stigma is one of the themes of the Royal College of Psychiatrists’ ‘Changing Minds’ campaign. For more information, see their website at www.changingminds.co.uk

In Scotland the ‘See Me’ campaign, was launched in October 2002 to challenge stigma and discrimination around mental ill-health. www.seemescotland.org.uk. A survey conducted in 2006 explored people’s changing experience of stigma and their views on the contribution of the ‘See Me’ campaign. The public has become more aware and accepting of mental health problems, but the report exposed continuing problems with stigma and discriminations particularly among friends and family, the community, in employment and when accessing services. Worries and fears about experiencing stigma continue to damage people’s confidences, life chances and recovery prospects. The report A Fairer Future: Building Understanding – Moving Forward Together can be accessed at www.seemescotland.org.uk/media/include/downloads/16823%20Hear%20Me%20report.pdf

Concerns have also been raised about the misleading and stigmatising nature of advertisements for antipsychotic medication in professional journals. See Haley C J, ‘The “Hitchcock factor” in advertising’. Psychiatric Bulletin (2000) 24: 315–316. Downloadable at pb.rcpsych.org/cgi/content/full/24/8/315-b

1.3 Development of mental health law and social care

Public and professional opinions have a considerable impact on how mental illness is perceived and managed, but law determines the framework for delivery. Legislation in health and social care has evolved over time to reflect changing attitudes, enabling the restructuring of mental healthcare provision and increasing social support for people with mental illness. Although mental health law and social care are probably of less interest to pharmacists than psychotropic drugs, they have all played an important role in the transition from overpopulated asylums to community-based care.

Check out the history of mental health provision in your area online by accessing The Index of Lunatic Asylums and Mental Hospitals at www.mdx.ac.uk/WWW/STUDY/4Asylums.htm#Dundee

In 1579 the basis of the system of poor relief in Scotland for the following three centuries was laid by an act of the Scottish Parliament ‘for Punishment of Strange and Idle Beggars, and Relief of the Pure and Impotent’. A further act in 1597 shifted the administration of poor relief to the church authorities in each parish, the Kirk Session. An act of 1672 ordered magistrates to erect ‘correction houses’ or workhouses in which beggars could be detained and made to work. These were funded by a variety of means including collections at church doors, incomes from rents, private donations, hiring of hearses and benefit plays at theatres.
The asylums and beyond

In the 18th century people with mental health problems were cared for in a number of ways: within their own families, looked after within their own homes by minders or ‘keepers’, boarded out with another family, placed in the custody of men and women who operated private ‘madhouses’, or incarcerated in an infirmary, poor relief institution, asylum or prison. The first public asylum in Scotland was opened in 1782 in Melrose.

An important landmark in the care of the mentally ill was the 1815 ‘act to regulate madhouses in Scotland’ which required annual licensing of private asylums with twice yearly inspections by the Sheriff-Depute and medical practitioners. New legal structures were put in place to ensure that people were not confined without a reception order from a sheriff and that this was: ‘by the certificate or report of medical persons, and otherwise as the circumstances of the case may seem to require’.

By the 1840s the demand for relief exceeded supply. The systems of administration were variable and, following the Disruption in 1843 when 40% of the clergy of the Church of Scotland left to form the Free Church, no longer effective. A Commission of Enquiry was set up in 1843 to review the system of poor relief in Scotland and to suggest improvements. The Commission’s report in 1844 noted that poor relief in Scotland was generally confined to the old, infirm, disabled and mentally ill. The recommendations were put into effect in the 1845 Act for ‘The Amendment and better Administration of the Law Relating to the relief of the Poor in Scotland’. Around 70 poorhouses were eventually in operation, but the majority of paupers continued to receive out-relief. Poorhouses provided medical and nursing care for the elderly and sick when there were few hospitals and private medical treatment was beyond the means of the poor.

The terms ‘lunatic’ and ‘insane’ were used to describe people suffering from various degrees of mental disturbance. In 1857, the Lunacy (Scotland) Act was passed by Parliament, which established the General Board of Commissioners in Lunacy, who became responsible for the care and treatment of lunatics and provision, maintenance and regulation of lunatic asylums. These hospitals were provided and paid for out of local rates. People considered insane were quickly removed from society and shut away behind locked doors – ‘out of sight, out of mind’. The Act laid down conditions for certification and provided powers to keep a patient under observation for six months without certification and to board out harmless lunatics with private persons. Carers received payment for their services, which became known as ‘guardianship’ by 1913.

The Board survived until 1913 when the Mental Deficiency and Lunacy (Scotland) Act replaced it by the General Board of Control for Scotland and voluntary admissions were simplified. Care of the ‘mentally handicapped’ was provided separately from the asylums which henceforth concentrated on the treatment of the mentally ill. Parish councils were abolished in 1930, thereafter poor law authorities were the county councils, large burghs and the four cities acting through Departments of Public Assistance or Public Welfare. The 1930s saw the introduction of physical treatments, such as electroconvulsive therapy (ECT), lobotomy and insulin coma treatment, allowing the discharge of some people back to the community. ECT was developed in Italy and was first introduced in the UK in Dundee in 1939.

A number of poorhouses were used during the First World War for the treatment of military casualties or for military accommodation. In 1946 many former poorhouses were assessed in preparation for the setting up of the National Health Service and consequently refurbished or upgraded, or condemned, sold off or demolished.
The Poor Law was entirely abolished in 1948 and replaced by the National System (National Insurance Act 1948). By then hospitals had largely replaced the medical function of poorhouses, however, various welfare functions including care of the mentally and physically handicapped remained with local authorities. In 1949 Dingleton Hospital, Melrose was the first hospital worldwide to fully implement an open-door policy. Integration of the ‘mental hospitals’ into the NHS was one of the main factors, which led to a general move away from institution care policies in the 1950s.

From 1955 onwards, psychiatric inpatient numbers began to slowly decrease due to the introduction of social methods of rehabilitation and resettlement in the community, and the availability of welfare benefits, as well as the introduction of effective treatment with antipsychotic and antidepressant medication.

The Mental Health (Scotland) Act 1960 set up a Mental Welfare Commission (MWC) as an independent body appointed by the Crown to exercise protective functions in regard to patients; encouraged community care; reduced powers of compulsory detention but retained the role of sheriffs; and repealed the 1857 and 1913 acts. When the MWC was established the existing General Board of Control for Scotland ceased and its property passed to the MWC and its rights, liabilities and obligations passed to the Secretary of State.

In 1984 the Mental Health (Amendment) (Scotland) Act required that mental health officers who were experienced, trained and accredited personnel were involved in the compulsory detention of people with mental disorders. The powers of the Mental Welfare Commission were also strengthened.

The Framework for Mental Health Services in Scotland (Scottish Office, 1997) set out the vision for comprehensive community-based services, shaped to meet identified local needs. This policy was an important landmark in requiring local health and social work planning partners to develop joint strategies for mental health and accelerating the shift from hospital to community based care.

A White Paper Towards a Healthier Scotland (1999) proposed a sustained attack on inequality, social exclusion and poverty by investing in housing, education and employment opportunities; and particular initiatives were to be directed at the detection and prevention of disease, improving nutrition and increasing physical activity.

Audit Scotland’s report: A shared approach – developing adult mental health services in Scotland (October 1999) provided an overview of the needs of service users and their carers, and analysed the expenditure on mental health services by local authorities and the NHS. It also looked at how existing resources were being used and targeted, and ways that joint working was involved in the planning and provision of services. www.audit-scotland.gov.uk/publications/pdf/1999/99hs_08.pdf

**Outpatients, day-care and after-care**

The National Association for Mental Health (NAMH, now MIND) was formed in 1946 and lobbied for better services for people with mental health problems, set up day centres and hostels and provided training services for social workers and residential care staff. During the 1950s day hospitals began to be established, increasing flexibility in psychiatric services and reducing the use of hospital beds. Hostels and therapeutic social clubs were set up to provide support for discharged patients. In 1954 the first outpatient nurses were appointed at Warlingham Park Hospital, Croydon. Their duties included visiting outpatients, supporting inpatients who
had been discharged, helping find jobs and accommodation for them, and being available to give advice at outpatient clinics or therapeutic social clubs. By the 1960s such work was commonplace. The introduction of depot antipsychotic injections in the 1960s and 1970s further encouraged the development of community psychiatric nursing. Multidisciplinary teams (Community Mental Health Teams) began to emerge in the 1980s with other disciplines offering services which complimented, or sometimes, duplicated those of Community Psychiatric Nurses (CPNs).

Social policy and community care

In December 1942, the Government published the report on Social Insurance and Allied Services, better known as the Beveridge Report. This watershed publication would shape Government social policy for the rest of the century.

In 1946 Parliament passed the National Health Service Acts, by which the Minister of Health and the Secretary of State for Scotland were to promote a comprehensive health service for the physical and mental health of the people of England, Wales and Scotland, and for the prevention, diagnosis and treatment of illness. The NHS in Scotland is a separate and distinct body and was founded by the National Health Service (Scotland) Act 1947. The National Assistance Act of 1948 stated that;

‘it shall be the duty of every local authority to provide residential accommodation for persons who, by reason of age, illness, disability or any other circumstances are in need of care and attention which is not otherwise available to them’.

This, together with the introduction of welfare benefits, encouraged the beginning of the move from institutional to community-based care.

By 1968 the progress in modernising the organisation of mental health services was lagging behind progress in applying modern methods of treatment. In 1970 the Chronically Sick and Disabled Person’s Act required local authorities to find out the needs of people in their local populations and to provide certain services for them and the Local Authority Social Services Act created social services departments as we now know them. This Act was extended to Scotland by the Chronically Sick and Disabled Persons (Scotland) Act 1972.

In 1985 the Scottish Office Report ‘Mental Health in Focus’ acknowledged that there was a shortfall in community alternatives to enable the development of locally-based mental health services and care in the community to become a reality. Closure of beds proceeded at a slower rate in Scotland than in England.

The Care Programme Approach (CPA) was introduced in Scotland in 1991 and aims to ensure that people with severe and enduring mental illness, including dementia, who also have complex social needs, are provided with co-ordinated care and supervision.

Developing the policy for community care for those with mental health problems in Scotland

The Framework for Mental Health Services in Scotland (Scottish Office, 1997) was produced following the Scottish Affair’s Committee Report on the closure of psychiatric hospitals in Scotland (1995). It was intended as an aid to health, social work and housing agencies for improving joint working and promoting the implementation of existing policy. Service users,
their carers and staff involved in voluntary and other agencies were recognised as partners and stakeholders. The framework sets out in a tiered system, the essential features of a local mental health strategy for people with severe and/or enduring mental health problems, including those with dementia. However, it does not address the needs of those with learning disabilities, or alcohol and/or substance misuse, unless there are concomitant mental health problems. Supporting initiatives were introduced to promote the implementation of existing policy and the development of mental health services in Scotland: Scottish Development Centre for Mental Health (providing training, information sharing and learning, research and evaluation), Mental Health Development Fund, Local Care Partnerships, Scottish Needs Assessment Programme Reports and Making it Happen (a working guide).

*Our National Health: a plan for action, a plan for change (2000)* endorsed the Framework for Mental Health Services in Scotland, setting new objectives including in the areas of person centred care, reducing stigma, liaison psychiatry, investment in improvement through grant schemes and investment in crisis services. [www.show.nhs.uk/sehd/onh/onh-00.htm](http://www.show.nhs.uk/sehd/onh/onh-00.htm)

**The National Programme for Improving Mental Health and Well-being**, launched in October 2001, is the key catalyst as part of the Scottish Executive’s commitment to health improvement and social justice, aiming in 2003–06 to:

- Raise awareness and promote mental health and well-being
- Eliminate stigma and discrimination around mental ill health
- Prevent suicide and support people bereaved by suicide
- Promote and support recovery from mental health problems.

In collaboration with Scotland’s major mental health charities (including Highland Users Group, National Schizophrenia Fellowship (Scotland), and Penumbra), the Royal College of Psychiatrists (Scottish Division) and public health bodies, a range of campaign organisations have been created and supported which address the priority areas. The initiatives include:

**See Me**
‘See Me’ was set up in 2002 to eliminate the stigma and discrimination associated with mental ill health by running a national campaign to improve public attitudes. The campaign provides posters and postcards for distribution or display, and along with the website offers resources, information and personal stories around stigma. [www.seemescotland.org](http://www.seemescotland.org)

**Choose Life**
The ‘Choose Life’ strategy was launched in 2002 and is a 10-year plan aimed at reducing suicide in Scotland by 20% by 2013. It draws on the experience and expertise of a broad range of partners including the family members of people who had attempted or completed suicide, health and social care workers, teachers, young people, suicide survivors, public health specialists, voluntary and community agencies. Research and training (including ASIST and STORM) is available via the Choose Life website. [www.chooselife.net](http://www.chooselife.net)

**Breathing Space**
Breathing Space is a free and confidential phoneline service available from 6pm to 2am daily for any individual who is experiencing low mood or depression, or is unusually worried and in need of someone to talk to (Telephone 0800 838 587). It was launched in Glasgow in 2002 and extended nationally in 2004. Breathing Space is aimed specifically, but not exclusively, at young men between 16–40 years – a particularly vulnerable at-risk of suicide group within Scottish
society. The service is operationally managed by NHS 24 and delivered from its contact centre in Clydebank. www.breathingspacescotland.co.uk

Scotland’s Mental Health First Aid
Scotland’s Mental Health First Aid (SMHFA) course was launched in 2004 and improves people’s confidence, knowledge, ability to help others, and also reduces negative and stigmatising attitudes. The course helps people recognise the signs and symptoms of mental health problems and how to offer initial assistance, support and guidance. www.smhfa.com and www.healthscotland.com

The Scottish Recovery Network
The Scottish Recovery Network was launched in 2004 and aims to raise awareness that people can and do recover from long-term and serious mental health problems, and to support recovery. The website includes information about recovery including personal testimony, research and international models of recovery. www.scottishrecovery.net

HeadsUpScotland
HeadsUpScotland and Scottish Development Centre organises training courses for frontline staff working with children and young people, aiming to develop an understanding of the mental health needs of children and young people. www.headsupscotland.com

Well Scotland
Positive mental health is essential if Scotland is to enjoy a healthier future. Well?, a magazine distributed to approximately 80,000 people in Scotland twice a year, highlights mental health improvement work, contacts and news. WellScotland have a website for mental health improvement work in Scotland and acts as a main source of news, research and information. www.wellscotland.info

National Resource Centre for Ethnic Minority Health
National Resource Centre for Ethnic Minority Health, a network of agencies across Scotland, is concerned with improving the mental health of people within black and minority ethnic communities. It is aimed at community groups, frontline mental health staff, planners, BME communities and service users. www.nrcemh.nhsscotland.com

Mind the gaps
Meeting the needs of people with co-occurring substance misuse and mental health problems. Report of the joint working group, Scottish Executive, 2003 can be found at www.scotland.gov.uk/library5/health/mtgd-00.asp
The Mental Health (Care and Treatment) (Scotland) Act 2003

The Mental Health (Care and Treatment) (Scotland) Act 2003, was passed by the Scottish Parliament in March 2003. It came into effect in October 2005.

The new Act is based on a set of 10 principles (the ‘Millan Principles’) which are:

1. Non-Discrimination
2. Equality
3. Respect for Diversity
4. Reciprocity
5. Informal care
6. Participation
7. Respect for Carers
8. Least Restrictive Alternative
9. Benefit

In keeping with the above principles several main changes have resulted. The biggest change is the replacement of Sheriff Courts by Mental Health Tribunals. Under the previous Mental Health (Scotland) Act 1984, any detention hearings were made in a sheriff court under the direction of a sheriff. It is hoped that the new tribunals will be less intimidating and encourage service users to engage with tribunal members. The tribunal will consist of three members: a legally qualified person, a doctor with experience in mental health and a relevant third person with skills and experience of the subject such as a service user or carer.

The Act also puts into place the concept of a Named Person. Any individual aged over 16 years has the right to choose a ‘named person’ to support them and their rights. This named person can attend tribunal hearings and represent the wishes of the individual service user.

Advance statements are also a new concept introduced under the Act. An advance statement is basically a written statement containing details of the nature of treatment an individual wished to receive or not receive in the event they become mentally unwell. Particular types of medication; psychology interventions etc. can be cited.

The new legislation also supersedes the previous Act which regards to powers of detention and subsequent treatment plans. These have been altered in light of changes that have occurred in the NHS since the early 1980s. The authority of the new Act is intrinsically concerned with three types of compulsory treatment.

- Emergency detention
- Short term detention
- Compulsory Treatment Order (CTO).

Emergency detention

Allows an individual to be detained in hospital for assessment up to a maximum period of 72 hours. Detention is dependent on the recommendation of a doctor and (if possible) a Mental Health Officer (usually a social worker trained in mental health issues). (Under this detention, an individual cannot be treated without their consent, unless there is an urgent requirement or they are being treated under the Adults with Incapacity Act).
Short term detention
An individual can be detained for a maximum period of 28 days for the assessment and treatment of a mental disorder. This detention can only be recommended by a psychiatrist and agreed by a Mental Health Officer (MHO)

Compulsory Treatment Order (CTO)
As the name suggests this is a treatment order which stipulates the details of an individual’s treatment plan. It is usually put into place to allow discharge into the community. The plan will lay out details such as: where the individual must live, where and what time they must attend particular services; or attend a particular place for treatment. (It is envisaged that this may include details of community pharmacies who agree to instalment or supervised dispensing of psychotropic medication e.g. antidepressants or antipsychotics.)

The CTO can only be approved by a Tribunal, which must be applied for by a MHO. The CTO initially lasts for 6 months but can be extended for another 6 month period. After this time and if it is considered necessary, a CTO can be extended for another 12 months at a time.

Other significant amendments include: duration an individual can be given pharmacological treatment without their consent. Previously an individual detained under the MHA (Scotland) (1984) could be given treatment for a period of 90 days. After this time, all treatment had to be written down in a detailed ‘treatment plan’ which if the individual consented to would be detailed in a Form 9 and if they did not, would be detailed in a Form 10. In order for treatment to be given without consent, a second opinion doctor from the Mental Welfare Commission would have to agree with the prescribed plan and hence sign off the form 10.

In the new act, the period of non consensual treatment has been shortened to 56 days and the forms are now referred to as T2 (previous Form 9) and T3 (previous Form10). Again a second opinion doctor from the Mental Welfare Commission must agree and be prepared to sign off the prescribed treatment plan.

Further detailed information about the new Act can be found at www.scotland.gov.uk/health/mentalhealthlaw and www.mwcscot.org.uk/web/site/home
1.4 Definitions and controversy

‘Mental disorder’ according to the Mental Health (Care and Treatment) (Scotland) Act 2003 means any mental illness, personality disorder, or learning disability, however caused or manifested. The Act specifically states that a person is not mentally disordered by reason only of any of the following:

- sexual orientation; sexual deviancy; trans-sexualism; transvestism
- dependence on, or use of, alcohol or drugs
- behaviour that causes, or is likely to cause, harassment, alarm or distress to any other person; or by acting as no prudent person would act.

The positive dimension of mental health is stressed in WHO’s definition of health:

‘Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Mental health is a state of well-being in which the individual realises his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community.’

There is no universally agreed cut-off point between normal behaviour and that described as mental illness.

What is considered abnormal behaviour or an abnormal reaction to circumstances differs between cultures, social groups within the same culture, and even different social situations.

Use of the term mental illness may be misleading if it is taken to imply that all mental health problems are solely caused by medical or biological factors. In fact, most mental health problems result from a complex interaction of biological, social and personal factors. For example, some people may be biologically vulnerable to experiencing depression, yet strong social support during difficult times can reduce their risk of becoming severely depressed. Similarly, in people genetically predisposed to schizophrenia, a particular psychotic episode may be triggered by stressful life events and circumstances.

For many people the existing systems of categorising illnesses do not relate closely enough to their experiences. Some people, including some professionals, prefer not to accept diagnoses that may be misleading or stigmatising, for example ‘personality disorder’ or ‘schizophrenia’. They find these terms unhelpful and prefer to talk about ‘psychotic experiences’.

The label mental illness is highly stigmatising. It encourages people to think of ‘the mentally ill’ as an entirely separate category from ‘people like us’, rather than as ordinary people who have, for whatever reason, severe emotional or psychological difficulties to cope with. Popular misconceptions, fuelled by the media, depict mentally ill people as violent and dangerous. These stereotypes are not representative of ordinary people’s experiences of mental health problems affecting themselves, their family members, friends or work colleagues.

Some psychiatrists attribute mental illness to organic/neurochemical causes that can be treated with psychiatric medication, psychotherapy, lifestyle adjustments and other supportive measures. However, it is important to note that the existence of mental illness and the legitimacy of the psychiatric profession are not universally accepted. For many years some professionals, notably Doctor Thomas Szasz, Professor Emeritus of Psychiatry at Syracuse, have been profoundly
opposed to the practice of labelling ‘mental illness’ as such. Szasz’s first book *Mythical Mental Illness* was published in 1960. The movement, known as anti-psychiatry, argues against a biological origin for mental disorders, suggesting that all human experience has a biological origin and so no pattern of behaviour can be classified as an illness *per se*. Unfortunately it is often essential to have a diagnosis as a precondition for access to services, treatment and benefits.

Advocacy organisations have been trying to change the common perception of psychiatric disorders as a sign of personal weakness and something to be ashamed of to one of an illness with a physical cause, like arthritis or a stomach ulcer. However, even if one excludes the views of ‘anti-psychiatry’, the subject remains controversial. For example, homosexuality was once considered a mental illness and this perception varies with cultural bias and theory of conduct.

At the start of the 20th century there were only a dozen recognised mental illnesses. By 1952 there were 192, and the *Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition* (DSM-IV) (see Section 1.5) today lists 374. Depending on an individual’s perspective, this could be seen to be the result of:

- A century of research resulting in more effective diagnosis and better characterisation of mental illness.

- Increased incidence of mental illness, due to some causative agent such as diet or the ever-increasing stress of everyday life.

- Over-medicalisation of human thought processes, and an increasing tendency on the part of mental health experts to label individual ‘quirks and foibles’ as illness.

- Healthcare systems where a disorder has to be characterised before treatment can be funded.

- The influence of the pharmaceutical industry in finding new indications for their products, e.g. paroxetine in social phobia.
Exercise 2

For each of the following vignettes try to decide whether the behaviour represented:

- deviates from statistical norms
- deviates from social norms
- displays dysfunctional behaviour
- displays personal distress
- displays unpredictable behaviour
- displays irrational behaviour
- causes observer discomfort
- constitutes mental illness

**John** once walked from John O’Groats to Land’s End together with his dog, and in his bare feet, wearing pyjamas. He later lived mostly in a cave for ten years, saying he enjoyed the ‘cathedral-like silence, which helps me to think’.

**Simon**, happily married to Ann, suddenly started to make random life-changing decisions about meeting new partners and travelling abroad, and claimed to see religious visions that other people do not.

**Caroline** describes depression as ‘like falling into a deep, dark hole that you cannot climb out of. You scream, but it seems like no-one hears you’. She shies away from personal relationships, including family and friends and has attempted suicide.

**Note your thoughts below before reading on.**

*Turn to the end of the chapter for suggested answers*
1.5 Classification systems for mental and behavioural disorders

Two major classification systems dominate the field of psychiatry:

- **DSM-IV**
  Mental Illness: Criteria and Treatment, DSM-IV Diagnostic and Statistical Manual of Mental Disorders.

- **ICD-10**
  Tenth Revision of the International Classification of Diseases.

**DSM-IV**

The *Diagnostic and Statistical Manual of Mental Disorders*, published by the American Psychiatric Association (APA), is the classification system used most often in diagnosing mental disorders in the United States and other countries.

While widely accepted among psychologists and psychiatrists, the manual has, at times, proved controversial in its listing of certain characteristics as mental disorders. The most notorious example being the listing in the DSM-II of homosexuality as a mental disorder, a classification that was removed in 1973. Controversy aside, DSM-IV remains an internationally accepted gold standard in psychiatric diagnosis.

The first edition (DSM-I) was published in 1952, with about 60 different disorders. DSM-II was published in 1968. Both of these editions were strongly influenced by the psychodynamic approach – the interaction of various conscious and unconscious mental or emotional processes, especially as they influence personality, behaviour, and attitudes. There was no sharp distinction between normal and abnormal, and all disorders were considered reactions to environmental events. Mental disorders existed on a continuum of behaviour. That way, everyone was considered more or less abnormal. People with more severe abnormalities have more severe difficulties with functioning.

DSM-III was published in 1980, when the psychodynamic view was abandoned in favour of the medical model and a clear distinction between normal and abnormal was introduced. The DSM effectively became ‘atheoretical’, since it had no preferred aetiology for mental disorders. In 1987 DSM-III-R appeared as a revision of DSM III and finally evolved into DSM-IV in 1994, currently in its fourth edition. The most recent version is the ‘Text Revision’ of the DSM-IV, also known as the DSM-IV-TR, published in 2000. This text revision (TR) includes very few changes in diagnostic criteria, and mainly corrects what were perceived as errors in the original text.

There are thirteen different categories in DSM-IV. Some categories contain many illnesses and others only a few.
Introduction to pharmaceutical care in mental health

Table 1

<table>
<thead>
<tr>
<th>DSM Group</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorders usually first diagnosed in infancy, childhood or adolescence</td>
<td>Mental retardation, autism, ADHD</td>
</tr>
<tr>
<td>Delirium, dementia, and amnestic and other cognitive disorders</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td>Mental disorders due to a general medical condition</td>
<td>AIDS-related psychosis</td>
</tr>
<tr>
<td>Substance-related disorders</td>
<td>Alcohol abuse</td>
</tr>
<tr>
<td>Schizophrenia and other psychotic disorders</td>
<td>Delusional disorder</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>Clinical depression</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>Generalised anxiety disorder</td>
</tr>
<tr>
<td>Somatoform disorders</td>
<td>Somatisation disorder</td>
</tr>
<tr>
<td>Factitious disorders</td>
<td>Munchausen syndrome</td>
</tr>
<tr>
<td>Dissociative disorders</td>
<td>Dissociative identity disorder</td>
</tr>
<tr>
<td>Sexual and gender identity disorders</td>
<td>Dyspareunia, gender identity disorder</td>
</tr>
<tr>
<td>Eating disorders</td>
<td>Anorexia nervosa</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Impulse-control disorders not elsewhere classified</td>
<td>Kleptomania</td>
</tr>
<tr>
<td>Adjustment disorders</td>
<td>Adjustment disorder</td>
</tr>
<tr>
<td>Personality disorders</td>
<td>Narcissistic personality disorder</td>
</tr>
<tr>
<td>Other conditions that may be a focus of clinical attention</td>
<td>Tardive dyskinesia, child abuse</td>
</tr>
</tbody>
</table>

Note
DSM-V is scheduled for publication in 2010.

ICD-10

ICD-10 is the classification system used routinely in the UK. The Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems, published by the World Health Organisation, is the latest in a series that was formalised in 1893 as the Bertillon Classification or International List of Causes of Death. While the title has been amended to make clearer the content and purpose and to reflect the progressive extension of the scope of the classification beyond diseases and injuries, the familiar abbreviation ‘ICD’ has been retained.

Chapter 5 of ICD-10 is exclusively devoted to mental and behavioural disorders. As well as giving the names of diseases and disorders, Chapter 5 has been further developed to give clinical
descriptions and diagnostic guidelines as well as diagnostic criteria for research. The broad categories of mental and behavioural disorders covered in ICD-10 are as follows:

Table 2

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organic, including symptomatic, mental disorders</td>
<td>Dementia in Alzheimer’s disease, delirium</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to psychoactive substance use</td>
<td>Harmful use of alcohol, opioid dependence syndrome</td>
</tr>
<tr>
<td>Schizophrenia, schizotypal and delusional disorders</td>
<td>Paranoid schizophrenia, delusional disorders, acute and transient psychotic disorders</td>
</tr>
<tr>
<td>Mood (affective) disorders</td>
<td>Bipolar affective disorder, depressive episode</td>
</tr>
<tr>
<td>Neurotic, stress-related and somatoform disorders</td>
<td>Generalised anxiety disorders, obsessive-compulsive disorders</td>
</tr>
<tr>
<td>Behavioural syndromes associated with physiological disturbances and physical factors</td>
<td>Eating disorders, non-organic sleep disorders</td>
</tr>
<tr>
<td>Disorders of adult personality and behaviour</td>
<td>Paranoid personality disorder, transsexualism</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>Mild mental retardation</td>
</tr>
<tr>
<td>Disorders of psychological development</td>
<td>Specific development disorders of scholastic skills, childhood autism</td>
</tr>
<tr>
<td>Behavioural and emotional disorders with onset usually occurring in childhood and adolescence</td>
<td>Hyperkinetic disorders, conduct disorders, tic disorders</td>
</tr>
<tr>
<td>Unspecified mental disorder</td>
<td></td>
</tr>
</tbody>
</table>

Diagnoses that proceed from these classification systems are not merely symptom-based, but rely on a combination of course and syndrome, and knowledge of differential diagnoses. These systems have had an enormous impact on improving diagnostic accuracy and consistency. Accurate diagnosis is important. It is the gateway to both appropriate treatment and services and benefits.

1.6 Mental health rating scales

DSM-IV and ICD-10 define diagnostic criteria. Rating scales measure changes in the severity of mental illnesses. Rating scales are not diagnostic tools. Their main use is in research to evaluate the effectiveness of treatments. Many are seldom used in clinical practice because they take too long to work through. However, they can serve as checklists, allowing clinicians to be certain that all items addressed by the scale have been covered in the clinical interaction. In structured or semi-structured interviews, their use allows some certainty that items will be addressed in a consistent way in successive interviews. Finally, when used over time, scales may provide information about the longitudinal course of a patient’s illness.

There are an increasing number of scales being introduced to the clinician with resulting confusion as to which rating scale(s) to use in which clinical situation. Ratings scales in psychiatry
feature several items with directions on how to score each item, together with anchor points to enable differentiation between severity scores and basic information on what the score(s) returned means in a clinical context.

The most commonly used scales are shown in Table 2.

**Table 3 The most commonly used rating scales**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Most commonly used rating scales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Hamilton Depression Rating Scale (HAM-D)¹</td>
</tr>
<tr>
<td></td>
<td>Montgomery–Asberg Depression Rating Scale (MADRS)²</td>
</tr>
<tr>
<td></td>
<td>Geriatric Depression Scale (GDS)³</td>
</tr>
<tr>
<td></td>
<td>Hospital Anxiety and Depression Rating Scale (HAD)⁴</td>
</tr>
<tr>
<td></td>
<td>Edinburgh Post-natal Depression Scale (EPDS)⁵</td>
</tr>
<tr>
<td>Mania</td>
<td>Young Mania Rating Scale (YMRS)⁶</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Hamilton Anxiety Rating (HAM-A) Scale⁷</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Positive and Negative Syndrome Scale (PANSS)⁸</td>
</tr>
<tr>
<td></td>
<td>Brief Psychiatric Rating Scale (BPRS)⁹</td>
</tr>
<tr>
<td></td>
<td>Calgary Depression Scale for Schizophrenia (CDSS)¹⁰</td>
</tr>
<tr>
<td>Dementia/Alzheimer’s</td>
<td>Mini Mental State Examination (MMSE)¹¹</td>
</tr>
<tr>
<td>Disease</td>
<td>Alzheimer’s disease assessment scale – cognitive subscale (ADAS-cog)</td>
</tr>
<tr>
<td>General rating Scales</td>
<td>Global Assessment of Functioning (GAF)¹²</td>
</tr>
<tr>
<td></td>
<td>Clinical Global Impression (CGI)¹³</td>
</tr>
<tr>
<td>Side-effects (dyskinesias)</td>
<td>Abnormal Involuntary Movement Scale (AIMS) 标记</td>
</tr>
<tr>
<td></td>
<td>Barnes Akathisia Scale (BAS)¹⁴</td>
</tr>
<tr>
<td></td>
<td>Simpson-Angus Scale (SAS)¹⁵</td>
</tr>
</tbody>
</table>

**References for Table 2**

1 Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960; 23: 56–62.


Unlike the rating scales detailed above, the Health of the Nation Outcome Scales (HoNOS) was developed to measure outcomes of mental healthcare within the NHS.

In 1993 the UK Department of Health commissioned the Royal College of Psychiatrists’ Research Unit (CRU) to develop scales to measure the health and social functioning of people with severe mental illness. The initial aim was to provide a means of recording progress towards the Health of the Nation target ‘to improve significantly the health and social functioning of mentally ill people’. The twelve item scale is completed after routine clinical assessments in any setting and has a variety of uses for clinicians, researchers and administrators, in particular healthcare commissioners and providers.

The scales were developed using stringent testing for acceptability, usability, sensitivity, reliability and validity, and have been accepted by the NHS Executive Committee for Regulating Information Requirements for entry in the NHS Data Dictionary.

The scales also form part of the English Minimum Data Set for Mental Health. HoNOS is probably the outcome measure most widely used by English mental health services. A survey commissioned by the NHS Executive (October 1997–May 1998) found that about two-thirds of trusts currently use it in one or more settings, or have active plans to do so. The use of HoNOS is recommended by the English National Service Framework for Mental Health and by the working group to the Department of Health on outcome indicators for severe mental illnesses.

Examples of rating scales and their applications can be viewed at [www.cnsforum.com/resources/ratingpsychiatry](http://www.cnsforum.com/resources/ratingpsychiatry)

In Scotland there is currently no national consensus on the assessment to follow an individual service user’s progress. HoNOS, FACE/CORE or AVON are used in different parts of Scotland.

The Scottish Executive’s National Programme for Improving Mental Health and Well-being has commissioned NHS Scotland to establish a core set of national, sustainable, mental health and
well-being indicators for Scotland. It is expected that an indicator set for adults will be identified by 2007. The progress can be viewed at www.phis.org.uk/info/mental.asp?p+bg

1.7 Guidance on care in Mental Health

Delivering for Mental Health

The Scottish Executive Health Department (SEHD) stated in Delivering for Health that they would ‘develop a national Mental Health Delivery Plan by the end of December 2006 and in so doing, accelerate improvements in mental health service’. The document Delivering for Mental Health published in December 2006 by the SEHD, fulfils the first part of this commitment.

It applied the general principles of Delivering for Health to Mental Health – to deliver NHS services as locally as possible, provide systematic support for people with long-term conditions, reduce the health inequality gap and actively manage admissions to, and discharges from, hospital.

Although much of the document

‘…relates to NHS services, it is also about what happens in non-health settings and can only be delivered by partnerships between the NHS and local authorities, between the statutory and voluntary sectors and between service providers and users and carers’.

The vision for the document relates to the following:

● Good mental health is important to everyone living in Scotland. It underpins the Executive’s vision for a healthier, more successful Scotland.

● We must work to promote health and prevent illness and where illness occurs, to treat it or minimise the damage that it causes.

● It is not just about severe and enduring mental illnesses such as schizophrenia, bipolar disorder and dementia, but also about a wider range of disorders and illnesses including depression and anxiety.

● Population and social inclusion approaches are important in reducing the number of people who develop mental illnesses and in addressing inequalities in mental health.

● The need to continue to address the stigma still attached to mental illness and ensure that patients, their carers and all who work with them are treated with dignity and respect.

● Delivery on SEHD commitments in respect of equality, social inclusion, recovery and rights as central to SEHD vision and success of the plan.

● Use and build on evidence in order to produce better outcomes in relation to what works in the delivery and organisation of care, the treatment available to those suffering from mental illness and the importance of other interventions and supports such as exercise, good diet, better physical health and good relationships in promoting mental health and recovery.

Within the document, the SEHD makes 14 key recommendations and three targets for improvement in care. These can be reviewed in detail in the document found at www.scotland.gov.uk/Resource/Doc/157157/0042281.pdf
Through these key commitments (along with other subsidiary commitments) and targets in Delivering for Mental Health it is hoped that this will provide the direction to improve mental health in Scotland. Both hospital and community pharmacists have a role to play in these commitments and targets for the coming years, for example in relation to the target to reduce the annual rate of increase of defined daily dose per capita of antidepressants to zero by 2009–10.

Integrated Care Pathways: Assessment of Quality of Care and Treatment – NHS QIS

The Clinical Standards Board for Scotland (CSBS) was established in 1999 and in 2001 published the Clinical Standards for Schizophrenia to assess the quality of clinical services in community and hospital settings throughout Scotland for people with schizophrenia. CSBS has now come under the umbrella of the special health board NHS Quality Improvement Scotland (NHS QIS) www.nhshealthquality.org/nhsqis/files/Schizophrenia%20jan%2001.pdf

NHS QIS was set up in 2003 to take the lead in improving the quality of healthcare and treatment delivered by NHSScotland by:

- Providing guidance and advice on effective clinical practice
- Setting clinical and non-clinical standards of care
- Reviewing and monitoring performance of NHS services
- Supporting patient safety and implementation of clinical governance.

NHS QIS have been tasked with developing Integrated Care Pathways (ICPs) for schizophrenia, bipolar disorder, depression, dementia and personality disorder. They are taking this work forward in conjunction with clinicians, social care professionals, service users and others. www.nhshealthquality.org

An ICP sets out the process of assessment, care and treatment for service users with similar diagnoses or symptoms, as well as let service users know what they should expect from services.

NHS QIS Integrated Care Pathways will describe the functions of the services and set standards which individual boards will need to meet to be accredited. The standards will address the process of developing and implementing an ICP, handling information, treatment and outcomes, based on research evidence and good practice in relation to the condition specific ICPs.

Each profession will be involved in identifying their role within the individual ICPs and agree implementation plans. Pharmacists in all sectors of care should be aware of their role and that of the other healthcare professionals they need to link with in order that these can be delivered at a local level.

Guidelines

An important recent trend has been the advent of guidelines to provide evidence-based direction to clinical decision-making. These guidelines are drawn up by a number of organisations - the most influential of which are the Scottish Intercollegiate Guidelines Network (SIGN) providing guidance for Scotland and the National Institute for Clinical Excellence (NICE). The SIGN guidelines which are relevant to Mental Health can be found at www.sign.ac.uk

NICE is part of the NHS. It is the organisation responsible for providing national guidance on the clinical- and cost-effectiveness of treatments for those using the NHS in England and Wales. NICE
Introduction to pharmaceutical care in mental health

Guidance is for healthcare professionals and patients and their carers to help them make decisions about treatment and healthcare. The Institute supports the work of those who make the complex treatment decisions – doctors, nurses, and other health professionals. The needs of the patient are central to NICE’s work, and the Institute has forged strong links with patient groups and representatives of service users. Their website is www.nice.org.uk.

NICE Guidance is issued in Scotland with advice on the implications for Scotland given by NHS Quality Improvement in Scotland (NHS QIS). The contextual differences between Scotland and England and Wales which are considered include:

- Principles and values of NHSScotland
- Epidemiology (frequency, distribution and stage at presentation)
- Structure and provision of services in Scotland
- Other implications to NHSScotland e.g. rural issues, predicted uptake, existing advice from the Scottish Medicines Consortium.

NICE produces guidance in three domains:

- **Technology appraisals**
  The use of new and existing medicines and treatments within the NHS in England and Wales.

- **Clinical guidelines**
  The appropriate treatment and care of patients with specific diseases and conditions within the NHS in England and Wales.

- **Interventional procedures**
  The safety and usefulness of an interventional procedure, for example a new type of surgery.

Topics for the NICE work programme are selected by the Department of Health and the National Assembly for Wales. NICE advises the NHS on how these technologies can best be used. It is also responsible for the production of national clinical guidelines, promoting best practice throughout the NHS. To support and assess the implementation of such guidelines, audit tools are produced for use in the clinical setting.

Health professionals are expected to consider NICE guidance when exercising their clinical judgement for individual patients. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

**Practice point**

- Consider any learning needs you have identified to do with the work of NICE and SIGN
- Make the appropriate notes in your RPSGB CPD portfolio.
Table 4  NICE and SIGN guidance in psychiatry

<table>
<thead>
<tr>
<th>Title, Published technology appraisals (TA)</th>
<th>Completed</th>
<th>Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s Disease – Donepezil, galantamine, rivastigmine (review) (TA111)</td>
<td>Nov 2006</td>
<td>Sept 2009</td>
</tr>
<tr>
<td>Bipolar disorder – new drugs (TA66) (replaced by Clinical Guideline 38)</td>
<td>Sep 2003</td>
<td>Aug 2006</td>
</tr>
<tr>
<td>Depression and anxiety – computerised cognitive behaviour therapy (CCBT) (TA97)</td>
<td>Feb 2006</td>
<td>Sept 2008</td>
</tr>
<tr>
<td>Electroconvulsive therapy (ECT) (TA59)</td>
<td>Apr 2003</td>
<td>Nov 2005</td>
</tr>
<tr>
<td>Insomnia – newer hypnotic drugs (TA77)</td>
<td>Apr 2004</td>
<td>Apr 2007</td>
</tr>
<tr>
<td>Schizophrenia – atypical antipsychotics (TA43)</td>
<td>Jun 2002</td>
<td>May 2005</td>
</tr>
</tbody>
</table>

Published NICE clinical guidelines

<table>
<thead>
<tr>
<th>Published NICE clinical guidelines</th>
<th>Published</th>
<th>Updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety (CG22)</td>
<td>Dec 2004</td>
<td>Dec 2008</td>
</tr>
<tr>
<td>Depression (CG23)</td>
<td>Dec 2004</td>
<td>Apr 2007 (amended)</td>
</tr>
<tr>
<td>Eating disorders (CG9)</td>
<td>Jan 2004</td>
<td>Jan 2008</td>
</tr>
<tr>
<td>Schizophrenia (CG1)</td>
<td>Dec 2002</td>
<td>Dec 2006</td>
</tr>
<tr>
<td>Violence (CG25)</td>
<td>Feb 2005</td>
<td>Feb 2009</td>
</tr>
<tr>
<td>Depression in children and young adults (CG28)</td>
<td>Sep 2005</td>
<td>Sept 2009</td>
</tr>
<tr>
<td>Bipolar disorder (CG 38)</td>
<td>Jul 2006</td>
<td></td>
</tr>
<tr>
<td>Obsessive compulsive disorder (OCD)</td>
<td>Nov 2005</td>
<td>Nov 2009</td>
</tr>
<tr>
<td>Antenatal and postnatal mental health</td>
<td>Feb 2007</td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>Nov 2006</td>
<td>Nov 2010</td>
</tr>
</tbody>
</table>
Table 4 (continued) NICE and SIGN guidance in psychiatry

<table>
<thead>
<tr>
<th>Published SIGN guidelines</th>
<th>Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of patients with dementia</td>
<td>Feb 2006</td>
</tr>
<tr>
<td>Bipolar affective disorder</td>
<td>May 2005 (updated July 2005)</td>
</tr>
<tr>
<td>The management of harmful drinking and alcohol dependence in Primary Care</td>
<td>Sept 2003 (updated Dec 2004)</td>
</tr>
<tr>
<td>Postnatal depression and puerperal psychosis</td>
<td>June 2002</td>
</tr>
<tr>
<td>Attention Deficit and Hyperkinetic disorders in young people</td>
<td>June 2001 (updated Aug 2005)</td>
</tr>
<tr>
<td>Interventions in the management of behavioural and psychological aspects of dementia</td>
<td>Feb 1998 (under review, recommendations being updated)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Technology appraisals (in development)</th>
<th>Anticipated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia (non-Alzheimer) – new pharmaceutical treatments</td>
<td>(currently suspended)</td>
</tr>
<tr>
<td>Idiopathic and drug induced Parkinson’s disease in adults</td>
<td>(scheduled 2007–08)</td>
</tr>
</tbody>
</table>

**National Service Framework**

There is also a National Service Framework for Mental Health with seven key standards, however these standards are only really applicable for England. It was developed in 1999 and includes a 10-year programme to address the mental health needs of working age adults up to age 65. The seven standards have been set involving the following areas:

- Mental Health promotion
- Primary care and access to services
- Effective services for people with severe mental illness
- Caring about carers
- Preventing suicide.

The executive summary can be downloaded from the Department of Health website.
Summary

The burden of mental illness is substantial in both personal and global terms. Despite this, many mental disorders remain poorly understood and sufferers are often stigmatised and marginalised. Historically treatment of the mentally ill has variously demonstrated ignorance and enlightenment, cruelty and compassion, structure and chaos and changes in mental healthcare provision were often driven by political and social agendas, with little regard for the needs of the individual.

In order to provide high quality care for people suffering from mental disorders, it is essential to understand the nature and characteristics of their disorders, the burden of their illness, the value of treatments and the most appropriate methods of service delivery.

The history of mental healthcare outlines the evolutionary processes that have brought us to the present day and teaches some valuable lessons while documents such as the National Service Framework for Mental Health (in England and Wales) and Clinical Standards (in Scotland) offer guidance for the future.

Learning Outcomes

On completion of this chapter you should be able to:

1. Describe the relative contribution of various mental disorders to the global burden of disease.
2. Describe some of the practices which characterise mental healthcare.
3. Identify key events in the development of mental health law and social care.
4. Understand and use the definitions used in the field of mental health.
5. Recognise the different classification systems and rating scales used to diagnose, assess and monitor mental health disorders.
6. Adapt practice to meet expectations of mental healthcare described in the Clinical Standards and in published NICE and SIGN guidance.

Further reading


**Suggested answers**

**Exercise 2 (page 26)**

**John** is an ‘eccentric’. Eccentric behaviour deviates from established patterns, ie: from social and statistical norms and by its very nature is unpredictable. Although eccentric behaviour may appear irrational to the observer, and possibly even cause them distress, it is usually quite rational to the eccentric who would probably not pursue it if it caused them personal distress. Eccentrics usually function adequately, if a little differently, and are generally mentally well.

**Simon** suffers from schizophrenia. Loss of a reality that is common to the rest of society may lead to deviation from social and statistical norms. Disrupted thinking and blunted emotions can lead to unpredictable, irrational and dysfunctional behaviour – though it is often rational to the sufferer. The extent of personal or observer distress is variable. Most aspects of schizophrenia compromise mental health.

**Caroline.** Depression is common and it is the extent of the suffering that determines whether an individual deviates from statistical or societal norms. In severe depression behaviour is often dysfunctional and, depending on the view of the observer, it may be irrational and unpredictable, particularly if they cannot identify a ‘cause’ for the depression. Observer distress is variable, but personal distress is usually substantial and severely compromises mental health.

Hopefully you will appreciate that someone who is different, unpredictable, even seemingly irrational and who makes others feel uncomfortable is not necessarily mentally ill.

Mental illness is about individuals, their inability to function adequately in a normal environment and their level of personal distress.
Chapter 2 Neurochemistry and neuroanatomy
Objectives

This chapter will enable you to:

- discuss the mechanisms of synaptic transmission
- relate clinical actions of psychoactive drugs to cellular mechanisms
- describe the extent to which mechanisms of drug action inform our understanding of the causes of mental illness
Chapter 2
Neurochemistry and neuroanatomy

2.1 Introduction

Psychopharmacology is complex and sometimes contentious. A basic understanding of the structure and function of neurons and synapses is essential if one is to understand the mechanism of action of psychotropic drugs.

This chapter assumes a basic knowledge of the processes of communication in the nervous system and offers some revision points. Detailed neurochemistry, specific to individual agents, is discussed in the context of each chapter.

The CD ROM enclosed in the front pocket of this pack contains the CPPE course, ‘Neurochemistry and Neuroanatomy’ which offers excellent revision of synaptic transmission.

Further reading


The Lundbeck Institute provides an excellent online neurochemistry and neuroanatomy resource, free from any company or product promotional material, at www.brainexplorer.org

2.2 Revision points

The action potential

- The action potential is self-propagating and does not diminish as it travels along the neuron.
- The mechanisms responsible for the action potential are essentially the same in all nerves. This means that drug effects exerted by interference with action potentials are likely to be non-specific, e.g. anaesthetics; local action is only achieved by local administration.

Synaptic transmission

- Neurotransmitters are stored in vesicles at the nerve terminals.
- Arrival of a sequence of action potentials causes influx of calcium ions (Ca²⁺) into the nerve terminal.
- Vesicles bound to the presynaptic membrane release their contents by a process called exocytosis.
- Released transmitter diffuses across the synaptic cleft and binds to post-synaptic receptors.
Neurotransmitters are inactivated either by enzymatic breakdown outside the cell (acetylcholine and all peptide transmitters) or by active transport back into the presynaptic neuron (serotonin [5HT], dopamine, glutamate, gamma-aminobutyric acid [GABA] and noradrenaline.

For an excellent online animation of this sequence of events see www.brainexplorer.org/anim/anim1.html

### 2.3 Neurotransmitters

Most psychoactive drugs affect synaptic mechanisms involving one or more of the small molecule transmitters in the CNS. The important small molecule transmitters are:

- 5-hydroxytryptamine (5-HT, serotonin)
- Acetylcholine (ACh)
- Dopamine (DA)
- Noradrenaline (NA, norepinephrine)
- Glutamic acid (glutamate)
- Gamma-aminobutyric acid (GABA).

In addition to these small molecule neurotransmitters, a range of larger peptide molecules also function as neurotransmitters. More than 80 peptide transmitters have so far been identified. Prominent among them are:

- Opioid peptides (enkephalins, endorphins, dynorphins)
- Vasoactive intestinal polypeptide (VIP)
- Somatostatin
- Cholecystokinin (CCK)
- Substance P and other tachykinins
- Vasopressin
- Neuropeptide Y.

### Comparison of small molecules and peptides in neurotransmission

The similarities between the small molecules and peptide neurotransmission outweigh the differences. Many neurons simultaneously release more than one neurotransmitter (co-transmission). In the most common form of co-transmission a small molecule transmitter and a peptide transmitter are released together. Peptide transmission is generally slower than that mediated by small molecules. Peptides tend to act as neuromodulators, altering the background activity against which the more rapid effects of the small molecule transmitters are seen.

### The clinical potential of peptide transmitters

The clinical potential of peptide transmitters and co-transmission has not yet been realised; currently available psychoactive drugs affect only small molecule neurotransmission.

An example of the possible involvement of peptides in mental illness and its treatment is cholecystokinin (CCK) and anxiety. There is good evidence that in many areas of the brain CCK
is co-released with 5-HT and it is known that synthetic analogues of CCK induce panic attacks, particularly in susceptible individuals. CCK antagonists are anxiolytic in animal models, but are not yet available clinically.

In a similar way, interest has been shown in neurotensin, a peptide co-released with dopamine, as a possible target in psychosis.

### 2.4 Receptors

Receptors are the key to specificity in the nervous system. Different cells respond differently to the same neurotransmitter because there are different populations of receptors on their cell surfaces. This specificity provides a valuable target for developing pharmacological selectivity. Much of the effort involved in the search for new psychotropic drugs is directed at producing selective agonists and antagonists for specific types of receptor.

Because of the recent advances in molecular biology, the structure of many receptors is now known. Often the receptors have been cloned and can be replicated in vitro. Unfortunately there are many instances where receptor types and subtypes have been identified by the molecular biologists without any corresponding physiological differentiation. The true significance of these findings will only emerge if, and when, functional differences are demonstrated.

Another factor that defines the specificity of a population of receptors is the sequence of events triggered by the binding of the neurotransmitter to the receptors. There are two kinds of mechanism involved:

- receptors linked to ion channels in the cell membrane (ionotropic)
- receptors linked to G-proteins in the cell membrane (metabotropic).

#### Receptors linked to ion channels

The receptors may be linked to ion channels that penetrate the postsynaptic cell membrane. Activation of the receptor opens the ion channels allowing specific ions into or out of the cell. This is a very rapid process and provides the fastest form of neurotransmission. Receptors linked to sodium or calcium ion channels are excitatory; opening these channels allows the positively charged ions to rush into the postsynaptic cell down the concentration gradient, thus depolarising the cell. An example of an excitatory receptor type linked to a positively charged ion (or ‘positive ionophore’) is the nicotinic acetylcholine receptor.

Conversely, movement of the negatively charged chloride ion into the neuron will hyperpolarise the cell. The GABA receptor is an example of a receptor linked to Cl-channels.

#### Receptors linked to G-proteins

Receptors may activate a biochemical cascade that sends a signal through the cell membrane into the internal environment of the neuron. The essential links between the receptor and the inside of the cell are membrane-bound G-proteins, so called because of their interactions with guanine nucleotides. G-proteins, in turn, interact with specific protein targets or ‘second messengers’.

The two most common second messengers are:
Adenylate cyclase An enzyme producing cAMP from ATP. cAMP can, in turn, activate a multitude of intracellular pathways. Dopamine D₁ and D₅ receptors are linked to G-proteins that activate adenylate cyclase whereas D₂, D₃, and D₄ receptors inhibit adenylate cyclase.

Phospholipase C An enzyme that acts on phosphatidylinositol (PI) within the cell membrane, generating diacylglycerol (DAG) within the membrane and inositol 1,4,5-triphosphate (IP3) within the cell. IP3 in turn controls release of intracellular calcium. Lithium blocks IP3 turnover and there is evidence that this may contribute to its clinical effectiveness in mania. 5-HT₂ receptor subtypes activate IP3 turnover.

Autoreceptors
Most receptors are located on the dendrites or cell bodies of postsynaptic cells, but receptors are also found on the cell membranes of presynaptic nerve terminals. Often, these receptors respond to the neurotransmitter released from the same presynaptic nerve terminal. Since they serve a self-regulatory function they are called autoreceptors. Usually this feedback is inhibitory in nature, serving to turn off further synthesis and release of the neurotransmitter when the concentration in the synaptic cleft reaches a critical level. However, some presynaptic autoreceptors are excitatory; for example acetylcholine nicotinic receptors on cholinergic neurons.

Autoreceptors are important in regulating synaptic transmission and are therefore a potential target for drug action. See, for example the discussion about enhancing cholinergic transmission in the treatment of Alzheimer’s disease.

Summary
The study of the effect of psychotropic drugs on neurotransmission informs our understanding of the pathophysiology underpinning some mental disorders. It also enables us to appreciate the complexities of neuromodulation and better understand the limitations of current therapies.

Learning Outcomes
On completion of this chapter you should be able to:
1. Discuss and describe the mechanisms of synaptic transmission.
2. Relate clinical actions of psychoactive drugs to cellular mechanisms.
3. Appreciate the extent to which mechanisms of drug action inform your understanding of the causes of mental illness.
Chapter 3 Schizophrenia
Objectives

This chapter will enable you to:

- describe the key symptoms of schizophrenia
- discuss the proposed mechanisms of action of antipsychotic medication
- differentiate between typical and atypical antipsychotics
- state the side-effects of antipsychotic medication and options for their management
- discuss the NHS Quality Improvement Scotland Clinical Standards for Schizophrenia
Chapter 3
Schizophrenia

3.1 Introduction

Psychosis is a broad term used for forms of mental illness where psychotic symptoms such as hallucinations and delusions occur.

The umbrella term, psychotic disorders, is not particularly useful as it includes conditions that have little in common, e.g. schizophrenia and acute mania. The term psychotic episode is more appropriate as it relates to a group of symptoms rather than a specific illness. Almost anyone can have a brief psychotic episode. It may result from a lack of sleep (through severe jet lag, perhaps), illnesses and high fevers (including malaria, pneumonia, ‘flu and other viral infections) or substance misuse (alcohol, street drugs and prescription medication, including steroids).

This section focuses specifically on schizophrenia, but the use of antipsychotics obviously extends to the treatment of non-schizophrenic psychotic episodes.

3.2 History of schizophrenia

Clinical descriptions first became apparent at the beginning of the 19th century. However, the modern conceptualisation of schizophrenia dates from the end of the nineteenth century with the description of ‘dementia praecox’, i.e. precocious or early onset dementia, by Emil Kraepelin.

Kraepelin attempted to classify diseases according to aetiology, symptoms, course and outcome. He was the first person to distinguish between the psychotic disorders, dementia praecox and manic-depressive disorder, based on differing symptoms and course. Characteristic symptoms of dementia praecox included delusions, hallucinations, disordered thinking and behaviour, and affective flattening. A chronic course and a poor outcome were thought to be important features of the illness.

Eugen Bleuler realised that dementia praecox was neither a dementia, nor did it necessarily occur at a young age. While Bleuler acknowledged Kraepelin’s contribution to the identification of individual symptoms and grouping them together to form the disease entity, he emphasised the fragmentation of mental functioning, particularly loosening of associations, as the essential characteristic of the illness. He observed that the person with schizophrenia lost the capacity for their thought processes to follow concepts that were properly linked together; hence he coined the name, schizophrenia, from the Greek ‘schizo’ – split and ‘phrene’ – mind. Bleuler described a chronic, remitting and exacerbating illness that, although it may improve, would never fully resolve.

In the 1950s, Kurt Schneider emphasised the importance of distinct phenomenological features that were later to provide the framework for diagnostic classification systems such as the ICD and DSM. Schneider was concerned with improving the method of diagnosis in psychiatry. He particularly championed diagnoses based on the form, rather than the content of a sign or
symptom, e.g. a delusion should not be diagnosed by the content of the belief, but by the way in which a belief is held. Schneider was also concerned with differentiating schizophrenia from other forms of psychotic illness, by listing the psychotic symptoms particularly characteristic of schizophrenia. These became known as ‘Schneiderian First Rank Symptoms’ or simply, ‘first rank symptoms’. They are:

- auditory hallucinations of a specific type
- audible thoughts (thought echo)
- voices heard arguing
- voices heard commenting on one’s actions
- experience of influences playing on the body (passivity phenomena)
- thought alienation
- delusional perception.

Other symptoms such as other disorders of perception, mood changes, and emotional impoverishment were described as ‘second-rank’ symptoms. The reliability of ‘first rank symptoms’ for the diagnosis of schizophrenia has been questioned, but the term is still used descriptively.

### 3.3 Epidemiology\(^1\text{-}^3\)

- Point prevalence is 0.5%.
- The lifetime risk of developing schizophrenia is 1%.
- There is roughly an equal incidence in both sexes (but onset is earlier in males – see Figure 1).
- It often manifests in the second and third decade, but can occur at any age.

Increased rates are found in deprived socially isolated areas of large cities. This may be due to social drift, i.e. the sufferer drifts to these areas as a result of their illness.

**Figure 1** Ages of onset of schizophrenia

![Age of onset of schizophrenia](Figure_1.png)

- Male and female
- Male onset median age 25 years
- Female onset median age 28 years

*Source: www.abpi.org.uk*
3.4 Symptoms of schizophrenia

Although symptoms can be broadly divided into positive and negative psychotic symptoms, it is important to consider cognitive and affective symptoms too, as these are common in schizophrenia and can be particularly disabling.

It is relatively easy to discuss the burden of side-effects of anti-psychotic drugs, but it is often much more difficult to convey the benefits of treatment. To fully appreciate the therapeutic value of anti-psychotic drugs it is essential to appreciate the intense distress that schizophrenia causes; distress of such magnitude that 50% of sufferers attempt suicide and one in ten sufferers’ lives end in completed suicide.

Positive symptoms – the presence of abnormal behaviour

Hallucinations
Most commonly auditory, which may take the form of a running commentary on the individual’s actions, a dialogue about the person or hearing their own thoughts spoken out loud, but may occasionally be visual, tactile, olfactory (smell) or gustatory (taste).

Delusions
False beliefs which persist in spite of incontrovertible evidence to the contrary and which are out of keeping with the individual’s cultural and religious background. Delusions may be primary, i.e. ‘out of the blue’, or secondary, i.e. arising from some other psychotic event such as hallucinations or thought disorder. Delusions of reference occur when sufferers connect external events to themselves in a way that is not real. Although some sufferers have grandiose delusions of divine powers, many more experience persecutory delusions that leave them terrified.

Thought disorder
Examples include feelings that thoughts are being inserted, withdrawn or broadcast (collectively called thought alienation) or the train of thought is broken. Thought alienation is often validated by a secondary delusion and was described by Schneider as passivity phenomena. A common example is the insertion or withdrawal of thoughts being attributed to aliens.

Disorganised speech
Jumbled words may be spoken with normal intonation (word salad) and new words invented (neologism) resulting in incoherent speech. Thought dissociation is often evident in disorganised speech when conversation meanders pointlessly or constantly changes direction.

Catatonic behaviour
Psychomotor activity is either grossly exaggerated or retarded. Sufferers may appear unresponsive to normal stimuli or highly excitable.

Negative symptoms – the absence of normal behaviour

Avolition
An inability to initiate and persist in goal-directed activities. When severe enough to be considered pathological, avolition is pervasive and prevents the person from completing many different types of activities, e.g. work, intellectual pursuits, self-care.
Blunted affect
A flattening of mood or feelings that makes it difficult to interact with others. Facial expression is often minimal or absent. Inappropriate affect, i.e. laughing at something sad, is also a common symptom, particularly in hebephrenic schizophrenia.

Anhedonia
A failure or inability to feel pleasure. Depression is a common feature of schizophrenia either as a co-morbid condition or a residual symptom.

Alogia
An impoverishment in thinking that is inferred from speech and language behaviour. There may be little spontaneous speech (poverty of speech) or an adequate amount of speech that conveys little information because it is too abstract, too concrete, repetitive, or stereotyped (poverty of content).

Negative symptoms are often present at onset but only become prominent when the florid, positive symptoms of acute illness are relieved by treatment. With the benefit of hindsight, negative symptoms can often be identified as features of a prodromal illness before onset of the first acute episode. Many sufferers have residual negative symptoms between acute psychotic episodes and they are associated with a high level of functional disability.

Cognitive symptoms
Although intellect is generally preserved in schizophrenia, cognitive deficits often occur, particularly in the areas of executive function (higher level cognitive functions such as attention, decision-making, planning, sequencing and problem-solving), working and long-term memory.

Affective symptoms
Blunted or inappropriate affect is a commonly-occurring negative symptom in schizophrenia, but sufferers can experience clinical depression and mania. If symptoms sufficient to meet the diagnostic criteria for schizophrenia occur concurrently with an uninterrupted period of depression, mania or mixed state then a diagnosis of schizo-affective disorder is appropriate.

Loss of insight
Insight is the ability to recognise, understand and accept that one is suffering from a particular condition. Loss of insight is a feature of any psychotic episode where delusional symptoms are present, be it psychotic depression, acute mania or schizophrenia. Clearly this can be a significant barrier to successful treatment.

All patients diagnosed with schizophrenia fulfil the basic diagnostic criteria, but the condition is further subdivided on the basis of the most prominent symptom(s). For example, paranoid schizophrenia is characterised by delusions of perception, i.e. persecution or grandeur, but there is often little evidence of disorganised thinking. On the other hand, hebephrenic schizophrenia is characterised by grossly disorganised thinking, silly behaviour and inappropriate affect, e.g. laughing at bad news.
3.5 Course of schizophrenia

Schizophrenia does not follow the same course in everyone. In schizophrenia, there are many courses. The commonest patterns are illustrated in Figure 2.

In the five longest studies reported in the literature, no researcher found fewer than eight individual courses.

**Figure 2** Patterns of schizophrenia

<table>
<thead>
<tr>
<th>Onset</th>
<th>Course</th>
<th>Outcome</th>
<th>Percentage with this pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>acute</td>
<td>episodic</td>
<td>mild or recovered</td>
</tr>
<tr>
<td>B</td>
<td>acute</td>
<td>continuous</td>
<td>moderate or severe</td>
</tr>
<tr>
<td>C</td>
<td>gradual</td>
<td>episodic</td>
<td>mild or recovered</td>
</tr>
<tr>
<td>D</td>
<td>gradual</td>
<td>continuous</td>
<td>mild or recovered</td>
</tr>
<tr>
<td>E</td>
<td>gradual</td>
<td>continuous</td>
<td>moderate or severe</td>
</tr>
<tr>
<td>F</td>
<td>Other patterns</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Source: www.abpi.org.uk*

Onset in women is generally later than in men and they tend to have fewer hospitalisations, respond better to antipsychotics and have a more favourable prognosis.

In either sex, onset may be acute or gradual and the course of symptoms episodic or continuous. The degree of functional impairment can range from mild to severe and recovery can vary from complete, partial or minimal.
3.6 Aetiology of schizophrenia\textsuperscript{1–3}

**Psychological factors**

Schizophrenia is a complex disorder, and probably results from a combination of genetic, behavioural, developmental and other factors. The exact cause is not known but stress, trauma and viral infection at an early age are factors thought to be involved. The onset of illness is often associated with a stressful period in life and it may be that stress can trigger the onset of illness in those people with a genetic predisposition to the disease.

**Genetic factors**

A genetic predisposition to schizophrenia exists and the prevalence rates depend on the genetic relationship to the sufferer.

- one schizophrenic parent – 12%
- two schizophrenic parents – 46%
- sibling – 8%.

In twin studies the concordance rates are:

- dizygotic twins 9%
- monozygotic twins 42%.

**Monoamine hypothesis\textsuperscript{4–9}**

The areas of the brain implicated in schizophrenia are the forebrain, hindbrain and limbic system. It is thought that schizophrenia may be caused by a disruption in some of the functional circuits in the brain, rather than a single abnormality in a discrete part of the brain. Although the brain areas involved in this circuit have not been defined, the frontal lobe, temporal lobe, limbic system, (specifically the cingulate gyrus, the amygdala and the hippocampus) and the thalamus are thought to be involved. The cerebellum, which forms part of the hindbrain, also appears to be affected.

The dopamine hypothesis of schizophrenia postulates that schizophrenia is caused by an overactive dopaminergic system; excessive dopamine and reduced striatal activity can disrupt all aspects of motor, cognitive and emotional functioning and can result in acute psychosis. An excessive dopamine concentration in the brains of people with schizophrenia was originally thought to be associated with increased activity of the D\textsubscript{2} dopamine receptors in the prefrontal cortex. Recent studies indicate that reduced numbers of the D\textsubscript{1} dopamine receptors may contribute to the rise in dopamine concentration.

Other neurotransmitters, including serotonin (SHT), glutamate, GABA and acetylcholine may also be involved in the pathogenesis of schizophrenia, not as causal agents, but as modulators of dopaminergic activity.
Dopaminergic pathways

There are four major dopaminergic pathways in the brain, see Figure 3.

**Figure 3** Dopaminergic pathways in the CNS

Neurons in the nigrostriatal pathway connect the substantia nigra to the caudate nucleus and putamen of the basal ganglia (also known as the corpus striatum). The nigrostriatal pathway is an integral part of the motor pathways responsible for initiation and control of voluntary movement. These pathways have been traditionally divided on anatomical grounds into pyramidal and extrapyramidal tracts. The nigrostriatal tract is part of the extrapyramidal system. Although the division is no longer sustainable on functional grounds, the term extrapyramidal is still used to describe the motor side-effects of psychotropic drugs.

Loss of the dopaminergic neurons of the nigrostriatal pathway gives rise to the symptoms of Parkinson’s disease. Blockade of the dopamine receptors in the striatum effectively mimics the degenerative changes of Parkinson’s disease. The extrapyramidal side-effects associated with typical antipsychotic drugs are therefore totally predictable.

The cell bodies of the mesolimbic and mesocortical dopaminergic pathways lie in the midbrain close to, but distinct from the cell bodies of the nigrostriatal pathway. Their axons run to some of the basal ganglia (the amygdala and nucleus accumbens) that form part of the limbic system and to the cerebral cortex (the outer layer of the cerebral hemispheres) respectively. The limbic system generates emotional responses while the cerebral cortex is responsible for higher thought processes. It is generally believed that the clinical efficacy of antipsychotic drugs is related to blockade of dopamine receptors of the mesolimbic pathways.

The dopaminergic neurons of the tuberofundibular pathway lie entirely within the hypothalamus. Dopamine released from these cells acts on the anterior pituitary gland as prolactin inhibitory
factor (PIF). Blocking dopamine receptors here leads to enhanced prolactin secretion, causing a number of distressing symptoms in men and women.

In addition to these four major pathways, dopamine receptors are also found in the chemoreceptor trigger zone (CTZ). The CTZ lies on the floor of the IVth ventricle in the area postrema, a part of the pons. The blood–brain barrier in this region is particularly weak. The emetic properties of dopamine receptor agonists, such as apomorphine and levodopa and the anti-emetic properties of metoclopramide and antipsychotics are caused by action at D₂ receptors in the CTZ.

**Dopamine (DA) receptors**

There are five distinct dopamine receptors grouped into two ‘families’, the ‘D₁-like’ receptors (D₁ and D₅) and the ‘D₂-like’ receptors (D₂, D₃ and D₄) – see Figures 4 and 5. The functional significance of these different receptors is not fully understood.

**Figure 4** Dopaminergic transmission

![Dopaminergic transmission](image)

**Figure 5** Dopamine receptor characteristics

<table>
<thead>
<tr>
<th>Receptor coupling</th>
<th>D₁ Like</th>
<th>D₂ Like</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor activation</td>
<td>Positive coupling to cAMP</td>
<td>Negative coupling cAMP</td>
</tr>
<tr>
<td></td>
<td><em>Receptor activation increasing cAMP formation</em></td>
<td><em>Positive coupling to IP₃</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Main synaptic function</th>
<th>Post-synaptic inhibition</th>
<th>Pre- and post-synaptic inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>D₁</td>
<td>D₃</td>
<td>D₂</td>
</tr>
<tr>
<td>Mesolimbic stereotypy and psychosis</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Mesocortical arousal</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Nigrostriatal motor</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Tuberofundibular pituitary</td>
<td>+++</td>
<td></td>
</tr>
</tbody>
</table>

DOPA dihydroxyphenylalanine  
DA dopamine  
HVA homovanillic acid  
E₁ dopa decarboxylase  
E₂ monoamine oxidase
Clinically effective psychotropic drugs act predominantly by blocking inhibitory D\textsubscript{2} receptors. D\textsubscript{2} receptors also function as presynaptic inhibitory autoreceptors.

There is good evidence that blocking postsynaptic D\textsubscript{2} receptors in the mesolimbic system is responsible for the reduction in positive symptoms of schizophrenia by typical and atypical antipsychotic drugs. Whilst it is predictable that blocking D\textsubscript{2} receptors in the nigrostriatal pathway will give rise to extrapyramidal symptoms (EPS), not all patients experience them.

More controversial is the role of the mesocortical dopamine pathway. It is likely that D\textsubscript{2} receptor blockade in the cortex aggravates or even precipitates negative symptoms of emotional blunting and cognitive deficits. The atypical antipsychotics are so called because they generally produce fewer of the side-effects typical of the older antipsychotics. They may be more effective at reducing negative symptoms, but evidence is mixed and it is possible that they merely aggravate negative symptoms less than older antipsychotics.

Early work with clozapine indicated that the drug preferentially blocked the D\textsubscript{4} receptor. This was encouraging because there is evidence that the density of D\textsubscript{4} receptors is relatively high in the mesolimbic pathway, and because of reports of higher density of D\textsubscript{4} receptors in brain tissue obtained post mortem from patients with schizophrenia, compared with normal controls. Unfortunately it has also been demonstrated that some potent D\textsubscript{4} receptor antagonists lack antipsychotic activity.

More recent work has concentrated on the relationship between serotonin and dopamine in the different areas of the brain innervated by dopaminergic neurons. This interest has stemmed largely from the observation that a common feature of the newer atypical antipsychotic agents is a mixed pharmacology involving antagonism of D\textsubscript{2} and S-HT\textsubscript{2} receptors. The relationship between serotonin and dopamine is complex, but in general serotonergic neurons inhibit dopamine release.

To make sense of the clinical findings it is necessary to assume that the ratio of D\textsubscript{2} and S-HT\textsubscript{2A} receptors varies in the regions of the brain that give rise to the beneficial and unwanted effects of the drug.

The hypothesis assumes there are relatively few S-HT\textsubscript{2A} receptors in areas controlled by the mesolimbic pathway. Blockade of what few receptors there are will have little effect on local dopamine concentrations and will not diminish the beneficial effect of D\textsubscript{2} receptor blockade. The hypothesis also assumes there is a higher density of S-HT\textsubscript{2A} receptors in the nigrostriatal pathway and blockade of these receptors will enhance dopamine release, thus overcoming the detrimental effect of postsynaptic D\textsubscript{2} receptor blockade on motor function. Similarly, a high density of S-HT\textsubscript{2A} receptors in the cerebral cortex means that atypical antipsychotics will enhance dopamine release and nullify the detrimental effects of postsynaptic D\textsubscript{2} receptor blockade on executive function.

The latest refinement to the dopamine hypothesis (the ‘fast-of’ hypothesis) suggests that it is how antipsychotics bind to D\textsubscript{2} receptors that predicts an atypical profile. The hypothesis proposes that 65% binding to the D\textsubscript{2} receptor is necessary for efficacy, but if a drug binds tightly to over 80% of D\textsubscript{2} receptors extrapyramidal side-effects will occur. It is also suggests that binding to D\textsubscript{2} receptors in excess of 72% predicts hyperprolactinaemia. Older antipsychotics bind tightly to a higher
proportion of D₂ receptors, whilst atypical antipsychotics bind loosely and to a lower proportion of D₂ receptors.

Loose binding allows atypical antipsychotics to dissociate quickly from the receptor allowing stimulation by endogenous dopamine itself, and a more rapid response to natural surges in dopamine concentration.

There are anomalies to this hypothesis: both risperidone and olanzapine are tightly bound to D₂ receptors. While clozapine and quetiapine have fast on-off properties and are associated with placebo levels of EPS and prolactin, other atypicals cause EPS in a dose-dependent way. Olanzapine causes moderate rises in prolactin and risperidone and amisulpiride raise prolactin to the same extent as older antipsychotics.

Aripiprazole introduces yet another dimension. It is a partial dopamine agonist with a high affinity for D₂ receptors and an antagonist at 5-HT₂A receptors. As an agonist, aripiprazole is less potent than endogenous dopamine. If all D₂ receptors are occupied by aripiprazole the net effect is a 30% reduction in activity compared to dopamine. In areas of the brain where there is excess dopamine, aripiprazole will attenuate activity and conversely in areas where there is too little dopamine activity aripiprazole will augment it.

Glutamate and schizophrenia

Glutamate (Glu) is the principal excitatory neurotransmitter in the CNS. It also plays an important metabolic role and concentrations are high throughout the central nervous system. Glutamate is synthesised from glucose or glutamine, predominantly in glial cells. Many receptors have been identified for glutamate, both ionotropic (linked to Na⁺ and Ca²⁺ ion channels) and metabotropic (linked to G proteins).

Most attention has focused on the N-methyl-d-aspartate (NMDA) receptors as possible sites for clinically useful drug action. As well as a glutamate binding site, the NMDA receptor complex includes facilitator sites for glycine, polyamines and zinc ions (Zn²⁺), and further binding sites within the ion channel for magnesium ions (Mg²⁺) and compounds like ketamine and phencyclidine.

The observation that drugs that block the NMDA receptor, such as phencyclidine and ketamine, induce hallucinations and other positive symptoms of schizophrenia, sparked interest in the possible involvement of glutamate in the aetiology of schizophrenia.

We know that not all the sensory information that constantly bombards the nervous system actually reaches the higher levels of the brain. The thalamus performs an essential function in filtering out unwanted, inappropriate information. One hypothesis links many of the positive symptoms of schizophrenia to an abnormality in this filtering or gating process.

Normal sensory filtering by the thalamus is inhibited by dopamine and promoted by glutamate. According to the hypothesis, enhanced dopamine activity and/or reduced glutamate activity leads to impaired filtering resulting in psychotic symptoms. The clinical evidence is contradictory and far from complete, but it has been reported that glutamate concentrations are lower in post mortem brain tissue from schizophrenics compared to controls.

According to this hypothesis, direct stimulation of NMDA receptors should be associated with an antipsychotic effect. In practice this is difficult to achieve because overstimulation of NMDA
receptors can cause cell death (excitotoxicity). Some reports suggest that a more successful approach is to enhance activity at NMDA receptors by targeting their facilitator sites such as the glycine binding sites.

3.7 Treatment of schizophrenia\textsuperscript{10–17}

The management of schizophrenia involves a comprehensive package of care with the aim of addressing all of the person’s clinical, emotional and social needs. The \textit{Clinical Standards for Schizophrenia} (2001) published by NHS Quality Improvement Scotland are intended to promote best practice in information gathering, diagnosis, assessment and care planning, transferring care, information and support for carers, prescription of antipsychotic drugs (Standards 8 and 9), social and psychological approaches to care, and misuse of alcohol and illicit drugs. Partnership working is a central theme with mutual understanding and respect between people who use services and their carers, and those people who provide services. Guidelines and algorithms will be in place locally for prescribing antipsychotic drugs for people who have a diagnosis of schizophrenia. For further information contact your local specialist mental health pharmacy team.


Pharmacological management centres on antipsychotic drugs, although drug therapy currently accounts for less than 5% of total healthcare costs for schizophrenia.

Psychological interventions are also employed in the management of schizophrenia. Cognitive behavioural therapy (CBT) can aid the development of coping strategies for managing resistant psychotic symptoms and together with family interventions should be available as a treatment option. See: SIGN Guideline 30, \textit{Psychological Interventions in the Management of Schizophrenia} (1998) [www.sign.ac.uk/guidelines/published/index.html](www.sign.ac.uk/guidelines/published/index.html)

Antipsychotic drugs have been available to treat symptoms of schizophrenia since the introduction of chlorpromazine in 1952. All are equally effective in the treatment of positive symptoms, with the exception of clozapine, which is effective in treatment-resistant schizophrenia. The more recently introduced ‘atypical’ antipsychotics (amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, risperidone, sertindole and zotepine) generally have a more favourable side-effect profile with respect to EPS and raised prolactin levels but there is still considerable variability (see Sections 3.6 and Section 3.8 for further information).

Exercise 3

Read the NICE summary guidance on the use of atypical antipsychotics. [www.nice.org.uk/pdf/43_Antipsychotics_summary.pdf](www.nice.org.uk/pdf/43_Antipsychotics_summary.pdf)

- When should an atypical antipsychotic be offered?
- How is treatment-resistant schizophrenia (TRS) defined?

Turn to the end of the chapter for suggested answers.
Antipsychotic drugs may take several weeks to control acute psychotic symptoms, although some drugs such as haloperidol and olanzapine injection are effective for rapid tranquillisation of seriously disturbed patients. Six weeks' treatment at a therapeutic dose is considered a reasonable trial for efficacy against psychotic symptoms.

Antipsychotics are of value in the alleviation of positive symptoms during an acute psychotic episode and in the prevention of relapse. Efficacy in the acute phase is objectively assessed using appropriate rating scales (Section 1.6). Chronic illness generally predicts a poorer response to antipsychotics but careful drug selection may relieve some negative symptoms.

About 50% of patients with schizophrenia do not comply fully with treatment. This is similar to compliance levels for other chronic illnesses such as hypertension and diabetes. Concordance is generally better if the treatment is perceived to be effective, lacking in distressing side-effects, and tailored to the needs of the individual. The involvement of the patient in the choice of medication, based on an understanding of potential benefits, risks and differences in side-effect profiles of antipsychotics is of vital importance.

NICE guidance recommends depot antipsychotics as a treatment option if the patient prefers an injection, or if it is a clinical priority to avoid covert non-compliance with therapy. However patients can still default from treatment by failing to turn up or refusing administration. Until recently, only typical antipsychotics were available as a depot formulation. These usually consist of esters of the drug dissolved in thin vegetable oil, allowing release of the active constituent over a period of several weeks. Initial release from all depot preparations is slow and it is therefore necessary to cover the initial treatment period with additional antipsychotic medication. Risperidone is now available as a long-acting injection, containing microspheres that degrade to release the drug after about three weeks. Patients should have a trial of oral risperidone before the long-acting injection is prescribed, and should be continued for at least three weeks after the first injection.

It is important that patients of all ethnic backgrounds and cultures are offered equal access to treatment and information about medication and that their preferences for treatment are taken into account. Consideration should be given to potential differences in drug metabolism due to ethnic variations in cytochrome P450 enzymes.

Choice of antipsychotic is obviously governed by a number of factors including efficacy, tolerability, patient acceptability, route of administration, co-morbid conditions, e.g. epilepsy (antipsychotics lower convulsive threshold) and concurrent therapy. There are many clinically important drug interactions associated with antipsychotics; some examples are listed below.

- Any drug that increases QT interval, e.g. anti-arrhythmics, erythromycin, tricyclic antidepressants, selective serotonin reuptake inhibitors, or any drug that decreases potassium levels (e.g. diuretics) increases the risk of ventricular arrhythmias with antipsychotics.

- Drugs that induce cytochrome P450 enzyme, e.g. carbamazepine accelerate the metabolism of many antipsychotics.

- Drugs that inhibit cytochrome P450 1A2 can increase clozapine levels. Examples include some selective serotonin reuptake inhibitors (particularly fluvoxamine which can increase clozapine levels 4-10 fold), erythromycin and some antiviral agents.

- Drugs which carry a significant risk of neutropenia should not be used with clozapine, e.g. carbamazepine, penicillamine, co-trimoxazole and cytotoxics.
The use of benzodiazepines with clozapine requires care because of rare reports of postural hypotension, respiratory depression and respiratory arrest with the combination.

### 3.8 Side-effects of antipsychotics

#### Extrapyramidal side-effects

These are a common feature of the older antipsychotics and variably occur with the newer atypical antipsychotics.

**Exercise 4**

Use the BNF to determine the relative likelihood of extrapyramidal side-effects for the following antipsychotics:

- chlorpromazine, haloperidol, pericyazine, flupentixol, trifluoperazine

**most likely**

**moderately likely**

**least likely**

*Turn to the end of the chapter for suggested answers*

Movement disorders are characterised in four domains:

- Parkinsonism
- Akathisia
- Dystonias
- Tardive dyskinesias.

**Parkinsonism**

Approximately 20% of patients treated with typical antipsychotics will develop the parkinsonian side-effects of rigidity, tremor, akinesia (lack of movement) and bradykinesia (slowness of movement). Onset is usually early in treatment (within days or weeks) and options for management include reducing the dose of antipsychotic, prescribing an anticholinergic drug or switching to an atypical antipsychotic.

**Akathisia**

Commonly occurs in patients treated with conventional antipsychotic medication (over a quarter of patients). It manifests as an irresistible urge to perform a repetitive movement, e.g. pacing up
and down or crossing and uncrossing legs. It may be misinterpreted as psychotic agitation, leading to an inappropriate increase in the dose of the offending drug. Akathisia has been linked to both suicide and aggressive behaviour. It responds poorly to anticholinergic medication and treatment options are generally limited to dose reduction or change to an atypical antipsychotic, although small studies suggest propranolol, benzodiazepines and cyproheptadine may be helpful.

Dystonias

Acute dystonic reactions occur when a group of muscles go into spasm, e.g. torticollis (neck), oculogyria (eyes). They are sudden in onset (90% occur within the first five days of treatment), terrifying for the patient and may constitute a medical emergency if, for example, respiratory muscles are affected. Up to 10% of patients treated with typical antipsychotics will develop a dystonia of one form or another. Risk factors include young age, male, high dose or high potency preparations and use of the intramuscular route. Immediate treatment is with an anticholinergic, usually given intramuscularly, followed then by changing to an atypical antipsychotic.

Tardive dyskinesias

Tardive dyskinesias develop over months or even years following chronic exposure to antipsychotics. They are characterised by the involuntary orofacial movements such as chewing, lip smacking or pursing and tongue movements. Occasionally there is limb involvement, which can result in rocking, pelvic thrusting, and ‘guitar-playing’ movements of the fingers. They are not responsive to anticholinergics and may in fact be unmasked. Tardive dyskinesias may resolve on stopping the drug. However this can take up to six months, but in some cases it is irreversible.

There is some evidence to suggest a lower risk of tardive dyskinesias with atypical antipsychotics. However, clinical data on the use of clozapine and some other atypicals has indicated no proven case of tardive dyskinesia and there is evidence to support the use of clozapine to diminish involuntary movements in patients with severe tardive dyskinesia. Clozapine is only indicated for the management of schizophrenia in patients who fail to respond to an adequate trial of two antipsychotics or who are neuroleptic intolerant, so is not a first-line treatment for tardive dyskinesia.

Hormonal side-effects

Typical antipsychotics cause increased levels of the hormone prolactin. Hyperprolactinaemia is also a dose-related and transient side-effect of the atypical antipsychotics amisulpiride, olanzapine, risperidone and zotepine. Hyperprolactinaemia can cause gynaecomastia (breast enlargement) and galactorrhoea (securing breast milk), ovarian dysfunction, infertility, reduced libido, atrophic changes in the urethra and vaginal mucosa, reduced vaginal lubrication and dyspareunia (pain on intercourse). Acne and mild hirsutism can develop, due to the relative increase of androgenic compared with oestrogenic activity.

Women with prolonged premenopausal oestrogen deficiency secondary to hyperprolactinaemia may be at increased risk of osteoporosis. In addition, chronically elevated prolactin levels may have a number of as yet unknown effects. Binding sites for prolactin are widely distributed in the body and several hundred different actions have been described in animals, e.g. prolactin is a known immunomodulator and has been linked to tumour growth.

Hyperprolactinaemic symptoms in patients treated with antipsychotic drugs are poorly researched, reflecting the low priority given to this phenomenon. Many treatment trials simply
regard hyperprolactinaemia as a biochemical anomaly and do not comment on whether there were associated symptoms.

The short duration of randomised controlled trials (several weeks) means that it is an impossibility to identify amenorrhoea (absence of periods) or oligomenorrhoea (scanty periods), as these are usually defined as occurring over a period of at least three months. Existing cross-sectional studies of women on long-term medication can only identify an association between raised prolactin level and symptoms. Proving a causal relationship requires a follow-up study to determine whether reversal of hyperprolactinaemia is accompanied by symptom resolution. There are no formal studies, only case reports of amenorrhoeic women with schizophrenia who resumed menstruation after antipsychotic medication was discontinued or switched to a prolactin-sparing atypical.

Counselling point
Women of childbearing age may need contraceptive advice when switching from a typical to an atypical antipsychotic.

In women treated with conventional antipsychotic agents spontaneous galactorrhoea of varying severity has been reported to have a prevalence of 10–57%. It is more likely to occur in premenopausal women who have had children.

Sexual dysfunction is difficult to investigate in patients with schizophrenia, as there are so many interrelated factors, not least the illness. However, the impact on self-esteem and personal relationships is yet another factor to consider when addressing issues of concordance.

Cardiovascular side-effects
The QT interval on an ECG represents the time between the start of ventricular depolarisation and the end of ventricular repolarization. It is useful as a measure of the duration of repolarisation. Prolongation of the QT interval may lead to Torsade de Pointes, an unusual ventricular arrhythmia associated with ventricular fibrillation and sudden death. High dose antipsychotics and antipsychotic polypharmacy increase the risk of a prolonged QT interval and is therefore not advised. Prolonged QT interval has also been linked to specific antipsychotics and was the basis for withdrawal of droperidol, and the restrictions on thioridazine and sertindole; regular monitoring is essential for both these drugs.

Postural hypotension can occur with antipsychotics due to alpha-receptors blockade. Clozapine, risperidone, quetiapine and sertindole all require dose titration to minimise risks of postural hypotension.

Tachycardia is a dose-related side-effect of clozapine managed by slower titration, dose reduction or introduction of a beta-blocker. Myocarditis and cardiomyopathy have been reported with clozapine and are the subject of a CSM warning. Symptoms that resemble those of a myocardial infarction are of particular concern, as are unexplained symptoms of heart failure such as breathlessness or ankle oedema. ECG changes can also occur. If clozapine-induced myocarditis or cardiomyopathy is suspected, treatment must stop immediately and the patient jointly re-evaluated by a cardiologist and a psychiatrist.
Introduction to pharmaceutical care in mental health

Haematological effects

Clozapine – neutropenia and agranulocytosis

Clozapine is associated with a greater risk of neutropenia (incidence of 2.9%) and agranulocytosis (incidence of 0.8%). This side-effect is not dose-related, and although it can occur at any time, the first 18 weeks are considered the period of highest risk. Mortality rates due to agranulocytosis have fallen from 1% to 0.01% due to regular blood monitoring. Other blood dyscrasias associated with the use of clozapine include eosinophilia, leucopenia, leucocytosis, thrombocytopenia and thrombocytosis. Monitoring is essential and a condition of treatment. A full blood count must be performed weekly for 18 weeks, fortnightly up to 52 weeks and 4-weekly thereafter.

Particular attention must be paid to flu-like symptoms, sore throat, temperature and unexplained bruising as they may indicate a blood dyscrasia. A full blood count should be checked immediately if patients present with such symptoms.

The risk of developing agranulocytosis with typical antipsychotics is estimated between 0.01% and 0.14%, with the highest risk associated with use of chlorpromazine. There have been isolated reports of blood dyscrasias such as agranulocytosis, neutropenia and thrombocytopenia with atypical antipsychotics such as risperidone, olanzapine and quetiapine.

Hyperlipidaemia, diabetes and weight gain

Hyperlipidaemia can occur with any antipsychotic. High potency conventional antipsychotics and the atypical antipsychotics risperidone, amisulpride and aripiprazole are associated with a lower risk of hyperlipidaemia. Low potency conventional antipsychotics and the atypical antipsychotics clozapine, olanzapine and quetiapine are associated with a higher risk of hyperlipidaemia. Possible mechanisms include weight gain and the development of glucose intolerance.

People suffering from schizophrenia are at increased risk of developing diabetes. A review of untreated patients with schizophrenia showed that more than 15% of patients had impaired glucose tolerance, compared to controls that did not have schizophrenia. It is unclear whether this is directly linked to schizophrenia or lifestyle factors associated with the illness, e.g. poor diet.

Typical antipsychotics have long been associated with an increased risk of hyperglycaemia and development of diabetes. Recent attention has focussed on the emergence of diabetes in patients treated with atypical antipsychotics and relative risk of developing diabetes follows a similar pattern to that observed for hyperlipidaemia, i.e. low relative risk of diabetes with risperidone and a high relative risk with clozapine and olanzapine.

The mechanism by which atypical antipsychotics induce diabetes is not clear. Reports suggest that it may be related to increased insulin levels, insulin resistance, effects on 5-HT1A receptors or effects on insulin sensitive glucose transport.

Careful consideration should be given to the choice of atypical antipsychotic in patients who already have diabetes. If patients develop diabetes whilst on treatment, consideration should be given to changing the antipsychotic. If this is not practical, e.g. if the patient is taking clozapine for treatment-resistant illness, the diabetes should be treated with hypoglycaemic agents.
Weight gain is associated with all antipsychotic medications, particularly the atypicals, although this is not the case with aripiprazole. Weight monitoring is an integral part of antipsychotic treatment monitoring. Mechanisms underlying weight gain are unclear, although many have been suggested:

- Sedative effects reducing physical activity.
- Direct action at a receptor level in appetite control systems – dopamine, histamine and serotonin receptors have all been implicated increase in leptin levels.
- Increased prolactin levels affecting gonadal-adrenal steroids and insulin sensitivity.

Again atypical antipsychotics follow a similar pattern for relative risk of weight gain to that for hyperlipidaemia and diabetes. Clozapine and olanzapine present the greatest risk with weight gains in excess of 10 kg over a year in some people. Risperidone, amisulpride and aripiprazole are associated with a much lower level of risk.

There is limited evidence on the impact of diet, exercise and drug treatment in the management of antipsychotic-induced weight gain. A moderate level of physical activity should be recommended and dietary advice given, preferably before or early in treatment. Pharmacological interventions should not be routinely used; sibutramine in particular should not be given to patients taking any antipsychotic. Counselling on lifestyle, calorie-restriction in a controlled setting and structured counselling, combined with cognitive behavioural therapy may be helpful.

Other side-effects

Constipation
Secondary to use of clozapine, there has been a Committee on Safety of Medicines warning following cases of gastrointestinal obstruction, including three fatalities. Prompt recognition and management of constipation is vital.

Hypersalivation
This can occur with clozapine and, if problematic, may be managed by drugs such as hyoscine hydrobromide e.g. sucking or chewing Kwells® (off-label use).

Photosensitivity
This commonly occurs with chlorpromazine, so patients need to be advised about using high protection sunscreens.

Neuroleptic Malignant Syndrome (NMS)
NMS is a rare but serious side-effect of all antipsychotics and can be fatal if not recognised early. It is thought to occur in approximately 1% of patients treated with antipsychotics.

The syndrome occurs when dopamine blockade in the hypothalamus interferes with temperature regulation, and is most likely to occur after an increase or change of medication. The primary symptom is raised temperature together with severe muscle rigidity, possibly with labile blood pressure and/or pulse, incontinence, confusion and sweating. Factors such as dehydration, current infection and lithium treatment increase the risk of NMS. Management requires prompt recognition, immediate withdrawal of antipsychotic medication and supportive treatment. Hospitalisation is usually necessary.
Exercise 5

Case study 1

Alan
Alan is 18 years old and he and his family have been coming into the pharmacy since he was a toddler. His mother has recently taken him to see his GP as she has become increasingly worried about him. He has become more isolated, though is still managing to attend his college course. He is locking himself in his room feeling that he is not safe and has accused his mum of poisoning his food. Consequently he has lost a significant amount of weight. She hears him shouting things like ‘stop talking to me’ and ‘stop tormenting me’ when he is alone in his bedroom. The GP has said that he may be suffering from a psychotic illness, possibly schizophrenia, and has prescribed haloperidol 10 mg three times daily. Alan suffers from asthma, smokes and drinks alcohol socially. He has never taken illicit substances.

1. How appropriate is the prescription for haloperidol?

His mother comes into your pharmacy and explains that he took the haloperidol for about eight weeks but stopped it last week as he had a tremor and was finding it very hard to sit still through an entire lecture. The GP referred him to the local hospital and he has an urgent appointment with a psychiatrist the following day. She wants to know whether there is any other medication that would be more suited to him.

2. What advice would you give about alternative options?

Many months later Alan comes to the pharmacy to get his inhalers. He asks to speak to the pharmacist in private. In the course of the conversation he explains that after the haloperidol he was given risperidone, which was increased to 6 mg daily. Six months later this was swapped to quetiapine as the side-effects of risperidone were affecting his relationship with his girlfriend. He has been taking quetiapine 750 mg daily for about four months now but things are still difficult and he is finding it hard to come to terms with the fact that the doctors are saying
he has schizophrenia. He feels that neither risperidone nor quetiapine have been particularly helpful. At his last appointment, the doctor mentioned the option of clozapine in passing and has arranged for him to see the consultant about this. He wants more information about it as he has heard it ‘kills blood cells’ and causes other nasty side-effects.

3. Comment on the mechanisms by which risperidone may cause sexual dysfunction. Was quetiapine a reasonable alternative?

4. What information would you give Alan about clozapine?

Six months later, Alan’s mum presents a prescription for erythromycin for Alan. She says that overall he is much better since starting the clozapine although he feels lousy at the moment as he has a sore throat, temperature and chest infection.

5. What action would you take on hearing this information and seeing the prescription?

Turn to the end of the chapter for suggested answers

Summary

Schizophrenia is a complex disorder primarily characterised by well-defined patterns of psychotic behaviours.

Current therapies are most effective in relieving positive symptoms of psychosis. However negative, cognitive and affective symptoms contribute significantly to the burden of illness in many sufferers and are often challenging to manage.

Atypical antipsychotics reduce the risk of antipsychotic-induced movement disorders but are associated with an increased risk of developing other long-term health problems such as diabetes and coronary heart disease.
Learning Outcomes

On completion of this chapter you should be able to:

1. Describe the key symptoms of schizophrenia.
2. Discuss and evaluate the proposed mechanisms of action of antipsychotic medication.
3. Differentiate between typical and atypical antipsychotics.
4. Describe the side-effects of antipsychotic medication and appreciate options for their management.

Further reading


References


Suggested answers

Exercise 3 (page 57)
When should an atypical antipsychotic be offered?

- First choice treatment for newly diagnosed schizophrenia.
- As an option for individuals currently receiving typical antipsychotic drugs who, despite adequate symptom control, are experiencing unacceptable side-effects, and for those in relapse who have previously experienced unsatisfactory management or unacceptable side-effects with typical antipsychotic drugs.
- It is not recommended that, in routine clinical practice, individuals change to one of the oral atypical antipsychotic drugs if they are currently achieving good control of their condition without unacceptable side-effects with typical antipsychotic drugs.

How is treatment-resistant schizophrenia (TRS) defined?

TRS is suggested by a lack of satisfactory clinical improvement despite the sequential use of the recommended doses for six to eight weeks of at least two antipsychotics, at least one of which should be an atypical.

Exercise 4 (page 59)
Use the BNF to determine the relative likelihood of extrapyramidal side-effects for the following antipsychotics:

Most likely haloperidol, flupentixol, trifluoperazine
Moderately likely chlorpromazine
Least likely pericyazine

Case study 1 – Alan (page 64-65)

1. Haloperidol is no longer advocated as a first-line antipsychotic. NHS QIS Clinical Standards and NICE Guidance advocate the use of an atypical antipsychotic for people newly diagnosed with schizophrenia. The dose of 30 mg is also much too high and puts him at increased risk of extrapyramidal side-effects. The BNF states that whilst 30 mg can be employed in treatment resistant schizophrenia, initial doses should be 1.5–3 mg two or three times daily or 3–5 mg two or three times daily in severely affected patients. There is evidence to suggest that there is no additional benefit in using doses above 12 mg for the treatment of psychosis, and that in newly diagnosed patients doses as low as 4 mg daily may be as effective as higher doses.

2. Alan has obviously experienced extrapyramidal side-effects secondary to the use of haloperidol. An atypical antipsychotic would be the preferred option and you should inform his mother of their advantages and side-effects, the medications available and some of the differences between them. Appropriate printed information could be given to Alan’s mother.

3. Risperidone can cause hyperprolactinaemia, particularly at higher doses, and this is one mechanism by which it may induce sexual dysfunction. Hypotension can also be a
contributory factor. Was he experiencing any other side-effects related to increased prolactin levels e.g. gynaeacomastia, that he has not mentioned? Quetiapine does not raise prolactin levels at any dose and so is a suitable alternative.

4. It is obvious that Alan requires more information about clozapine. Explain that clozapine can reduce the number of white blood cells in the body, therefore affecting its ability to fight infection. Stress that this is why regular blood tests are taken to pick up signs of a problem early. Explain that with blood test monitoring only about 3 per 100 patients develop this side-effect, and if it happened it would be picked up at the earliest possible opportunity. Reinforce that he has a part to play, in making sure that he reports any signs of infection, temperature, and sore throat so that an additional blood test can be done.

Tell Alan about some of the other possible side-effects and how they are managed, e.g. weight gain, sedation, hypersalivation, tachycardia, and constipation.

5. Alan is displaying some signs suggestive of neutropenia, although they could also be purely secondary to a chest infection. It is important to check whether a blood test has been taken and if not, advise that one is needed. The prescription for erythromycin should also be queried as this may increase clozapine levels and induce adverse effects such as seizures. Suitable alternatives would be a penicillin or clarithromycin (lower risk than erythromycin).
Chapter 4  Depression
Objectives

This chapter will enable you to:

- describe the major symptoms associated with depression in adults
- discuss the NICE guideline on treatment of depression in adults
- discuss the SIGN guideline on the treatment of postnatal depression and puerperal psychosis
- discuss the non-pharmacological management of depression in adults
- describe the mode of action and side-effects of the antidepressants.

This chapter does not cover the symptoms or management of depression in children and adolescents under the age of 18 years.
4.1 Introduction

Defining depression as simply being low or unhappy is inappropriate as it negates the emotional depths that sufferers feel. Everybody has their own way of describing what their depression is like, but this description gives some insight into how it feels:

“When I am depressed it is like I am stuck at the bottom of a deep dark well. The sides of the well are slippery, almost glass like. I am unable to claw my way back up the well as when I try I just slide back down to the bottom again.”

4.2 Epidemiology

In the UK it is estimated that at any one time 21 out of 1000 individuals aged between 16 and 65 years are suffering with depression (17 males, 25 females). If a broader diagnosis of depression with anxiety is used, these figures rise to 98 in 1000 (71 males, 124 females).

These figures highlight the gender differences in depression rates, with pre-menopausal women having an increased likelihood of developing depression. However after the age of 55 the gender difference is reversed, with widowed men showing a higher incidence.

Depressive disorders are ranked as the fourth leading cause of disability and disease burden among all diseases worldwide. It is expected that the trend will continue to rise and that by 2020 depressive disorders are expected to become the second most important. One in four women and one in ten men will have depression serious enough to require treatment at some point in their lives. About two-thirds of adults will experience depressed mood severe enough to interfere with their normal activities at some time.

Depression is the third most common reason for consultation in general practice and is more common in people with chronic medical conditions such as diabetes, chronic obstructive pulmonary disease and cardiovascular disease. Socio-economic factors such as unemployment, divorce or separation, poor housing and poverty are strongly associated with depression.

4.3 Symptoms of depression

The clinical diagnosis of depression recognises the wide range of symptoms that can be present.

The core symptoms are:

- depressed mood
- anhedonia (lack of interest or pleasure in normal activities)
- lack of energy.
Other symptoms are:

- changes in weight and appetite
- sleep disturbance
- low self-esteem
- psychomotor agitation or retardation
- guilt or self-reproach
- poor concentration
- suicidal thoughts or plans.

Just as there is a wide range of depressive symptoms, there is also a broad range of disease severity. It is now common practice to define depression as mild, moderate or severe. The classification of severity depends upon the number of symptoms that an individual presents with.

- For mild depression to be diagnosed, four symptoms must be detectable, two of which are core symptoms.
- For moderate depression to be diagnosed, six symptoms must be detectable, two of which are core symptoms.
- For severe depression to be diagnosed, eight symptoms must be detectable, including all three core symptoms.

In all cases the symptoms should have been present for at least two weeks, and there must be a clear difference between current and pre-morbid functioning.

Despite these clear diagnostic guidelines, it can still be difficult to distinguish the mood changes between depressive illness and those occurring ‘normally’. Persistence, severity and the degree of social or functional impairment can aid diagnosis. Frequently, in depression, mood will remain unaffected by daily circumstances, i.e. it will remain low throughout the day. In some people there may be a diurnal variation in their mood; typically a gradual improvement during the day with a return to low mood the next morning.

Dysthymia is a milder, but more persistent mood disorder term, involving long periods over many years during which the individual experiences depressive symptoms but not of sufficient intensity to satisfy a diagnosis of major depression. Low mood or loss of interest must be present and delusions and hallucinations are absent. The individual could almost be regarded as having a depressive ‘personality style’.

While this disorder may interfere with social or occupational functioning, the disturbance is not severe enough to qualify for a diagnosis of major depressive disorder. Nevertheless, some individuals with dysthymia can experience co-morbid major depressive episodes during the course of the dysthymic disorder, although DSM-IV, (see Chapter 1) requires that there have been no major depressive episodes during the initial two years of the disorder.
Case study 2a

Penny
Penny Gunn is a 26-year-old insurance claims assessor. Over the last few weeks her colleagues have noticed a change in her appearance. She used to be immaculately turned out but now looks distinctly unkempt. Her boss has noticed a deterioration in her work. When he approaches her about this, she says that she just feels so tired and run down at the moment. No matter what time she goes to bed in the evening, she never seems to get more than a couple of hours sleep. During the discussion Penny becomes quite tearful and apologetic. She says she is really trying hard but cannot get things together at the moment.

List the symptoms of depression that Penny is demonstrating.

Turn to the end of the chapter for suggested answers

4.4 Aetiology of depression

Untoward events can frequently be a trigger for depression in somebody’s life, e.g. bereavement, separation, redundancy or physical ill-health. Precisely why different people will respond differently to each situation is not clear. However, the likelihood of developing depression will, to some extent, depend upon how psychological and biological factors interrelate. In turn it allows them to move forward and stop seeking a simple reason for their depression.

Overall the causes of depression are probably multifactorial. This provides reassurance to patients as it is impossible to blame a single factor.

Psychological factors
Adverse circumstances that can increase the likelihood of developing depression include:

- Developmental experiences, such as abuse, separation from one or both parents or failure of the parents’ relationship.
- Psychological stressors, such as relationship problems or problems at work.
- The lack of a confiding, supportive friendship.
- A number of major life events, particularly in the months before the depressive episode, e.g. bereavement, loss, separation, illness, marriage or a new baby.
Getting through these events and stresses requires good coping mechanisms. Some people offload their worries or concerns by confiding in a friend. Others have close relationships with parents or partners. Watching a good role model cope well with life issues can reduce the impact of life events.

**Genetic factors**

It is increasingly accepted that there is a genetic link to an individual’s depressive illness. Studies involving identical and non-identical twins find that the likelihood of a twin developing depression when the other is affected is substantially greater for identical twins. These sorts of studies help to rule out the effect of social environment on the development of depression. Sometimes it may seem that depression runs in a family, but this could be due to the family having a similar, poorly adapted, coping mechanism for stress.

How genetic loading contributes to an increased risk of developing depression is not clear, but it may involve an increased sensitivity or greater production of cortisol. The body’s natural reaction to stressful events is to produce cortisol (the major stress hormone). Depressed patients have been found to have higher than normal cortisol levels. In turn cortisol can alter the expression of many genes, which may lead to altered levels of circulating neurotransmitters.

The monoamine theory is based on an observation which fits with accepted ideas about the possible effect of cortisol but does not account for the impact of psychological experience.

**Monoamine hypothesis**

For many years, it has been assumed that because antidepressant drugs enhance the functional levels of the neurotransmitters noradrenaline and serotonin in the brain, depression results from a deficiency of one or other of these monoamines. Clinical evidence to back up this hypothesis is still far from clear cut, although the weight of evidence now suggests that the primary deficit is at serotonergic synapses.

**Serotonergic pathways**

Cell bodies of serotonergic neurons are found in clusters lying close to the midline (or raphe) in the pons and lower midbrain. Unlike dopaminergic neurons (see Section 3.5) the axons from these raphe nuclei are not discretely localised. Serotonergic terminals are widely distributed throughout the brain and spinal cord.

Serotonin is involved in a variety of physiological functions, including control of food intake, sexual activity, mood, pain control and blood pressure. Blocking reuptake of the neurotransmitter back into the presynaptic nerve terminal is not a selective mechanism and the action of 5-HT will be enhanced throughout the brain wherever serotonergic terminals are found. It is therefore not surprising that enhancing serotonergic transmission, by blocking reuptake of 5-HT, results in side-effects which include changes in appetite and body weight, nausea and vomiting, sleep disturbance and sexual dysfunction.

Efforts to identify the region(s) of the brain where augmentation of serotonergic transmission leads to an antidepressant effect have not yet been conclusive, but most theories have concentrated on the hippocampus and the amygdala. Both of these structures are part of the limbic system.
The amygdala is a dense complex of nuclei embedded in the white matter of the temporal lobe of the cerebral hemispheres. Overactivity in pathways involving the amygdala probably generates anxiety. There is a significant serotonergic input to the amygdala and blockade of 5-HT receptors in the amygdala may be anxiolytic; for instance, the anxiolytic properties of buspirone are probably related to the fact that it is a partial agonist at 5-HT\(_{1A}\) receptors.

The hippocampus is part of the cortex of the temporal lobe of the cerebral hemispheres. It rolls inwards, so that much of its surface abuts the lower parts of the lateral ventricle. The hippocampus is involved in many complex functions, including memory. It is important for motivation and for so-called ‘coping mechanisms’. It has been suggested that depression results from a failure of these coping mechanisms. This failure may be related to a deficiency in the serotonergic input to the hippocampus.

**Noradrenergic pathways**

The cell bodies of nerves that release noradrenaline as a neurotransmitter are found in clusters in the pons and medulla. The most prominent of these is the locus coeruleus. Terminals of noradrenergic neurons are found throughout the cortex, hippocampus and cerebellum. In the CNS the mechanisms of transmission – synthesis, storage, release and inactivation of noradrenaline is essentially the same as in the autonomic nerves of the peripheral nervous system. Both a and b adrenoreceptors are found in the CNS. The effects of noradrenaline are predominantly inhibitory via activation of b-adrenoreceptors.

Given the hypothesis that depression is related to serotonergic deficiency, it is important to account for the efficacy of drugs that do not significantly affect the 5-HT reuptake transporter. These drugs include reboxetine, which selectively blocks noradrenaline reuptake and mirtazapine which has no effect on either noradrenaline or serotonin receptors nor does it inhibit re-uptake of either.

Current hypotheses suggest that these agents act indirectly to increase 5-HT release. Increasing levels of noradrenaline (by re-uptake inhibition, e.g. reboxetine, high dose venlafaxine and some TCAs) results in increased stimulation of \(\alpha_1\) noradrenergic receptors on the cell bodies of serotonergic neurons, enhancing serotonergic activity. Blocking inhibitory \(\alpha_2\) noradrenergic receptors on the terminals of noradrenergic and serotonergic neurons (mirtazapine) increases the release of 5-HT which will act directly and noradrenaline which will act indirectly via the mechanism already described.

**Serotonin (5-HT) receptors**

There are seven subtypes of serotonin receptor, 5-HT\(_{1-7}\) and several subsets, e.g. 5-HT\(_{1A-1D}\). The distribution and function of some of these receptor subtypes explains the delay in onset of the clinical effects of SSRIs and other antidepressant drugs.

It is assumed that depression is linked to a functional deficiency of 5-HT at serotonergic synapses in the hippocampus. The rationale for using an SSRI is that blocking reuptake of 5-HT at the terminal will increase 5-HT concentration in the synaptic cleft, resulting in increased stimulation of post-synaptic 5-HT\(_{1A}\) receptors and correct the functional deficiency.

If an SSRI also blocks reuptake in the cell body region, the resulting increase in extracellular 5-HT will increase stimulation of the 5-HT\(_{1A}\) cell body autoreceptors. As these receptors are inhibitory, the firing rate of the serotonergic neuron will be decreased, resulting in less 5-HT released into the synaptic cleft – effectively making things worse, not better!
However, the theory supposes that with time cell body autoreceptors become desensitised (downregulated) and the normal firing rate of the serotonergic neuron is restored. Thus 5-HT release returns to normal, is potentiated by inhibition of post-synaptic reuptake and the therapeutic effect is finally evident.

There is evidence from animal studies that blocking 5-HT\textsubscript{1A} autoreceptors accelerates the onset of antidepressant action. However clinical evidence is more equivocal. Human studies have relied mainly on pindolol, which is a non-selective 5-HT\textsubscript{1A} receptor antagonist. The definitive answer may have to await the availability of more selective antagonists.

4.5 Treatment of depression\textsuperscript{3}

Guidance on the management of depression has been issued by NICE. Psychological therapies are receiving increasing prominence as options for the treatment of depression, but the use of anti-depressant medication remains important.

NICE guidance – CG23 Depression: the management of depression in primary and secondary care was amended and published in April 2007. However due to revised prescribing advice by the Medicines Healthcare Regulatory Authority (MHRA) in May 2007 on Venlafaxine, the guideline has been updated in relation to this drug. A full update will be discussed later in 2007. www.guidance.nice.org.uk/CG23

The guideline on depression recognises that whilst medication has an important role to play in treating depression, there are also many effective alternatives. It recommends that for mild and moderate depression, psychological treatments specifically focused on depression (such as cognitive behaviour therapy (CBT), computerised CBT (CCBT) and counselling) can be as effective as drug treatments and should be offered as treatment options.

The guideline also recommends that:

- Antidepressants should not be used for the initial treatment of mild depression, because the risk-benefit ratio is poor.
- Where antidepressants are prescribed for moderate or severe depression it should be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are as effective as tricyclic antidepressants and their use is less likely to be discontinued because of side-effects.
- All patients prescribed antidepressants should be informed that, although the drugs are not associated with tolerance and craving, discontinuation/withdrawal symptoms may occur on stopping or missing doses or, occasionally, on reducing the dose of the drug.
- There should be screening for all high risk groups – for example, those with a past history of depression, significant physical illnesses causing disability, or other mental health problems such as dementia.
- For severe depression, psychological treatment (CBT) should be used in combination with antidepressant medication.

The full amended guideline can be downloaded at www.guidance.nice.org.uk/CG23/guidance/pdf
Antidepressants are the major contributor to the costs associated with mental health problems in the community with an annual cost of around £44 million per year in Scotland.

**Non-pharmacological treatment of depression**

Medication is not necessarily the best option for treating cases of mild depression. Studies of mild depression frequently fail to demonstrate that antidepressants have a significant effect, largely as a result of high placebo response rates. Patients tend to express a preference for non-drug therapies; particularly favouring practical support and problem-solving approaches.

Research evidence supports the use of time-limited psychological interventions to address mild to moderate mental health problems in primary care and mechanisms to link people to non-medical sources of support. Unfortunately the availability of non-drug therapies is patchy in many areas, as a result of their cost and the level of support required.

However, the Scottish Executive, through its Centre for Change and Innovation (CCI), has funded a three year ‘Doing Well by People with Depression’ initiative which aims to improve wellbeing for people with depression and improve access to evidence-based interventions. During 2003–06 local development projects have been looking at approaches to improve access to a range of community based services and support including self-help and psychological interventions, the assessment of depressive symptoms and associated problems, and the development of pathways through services and supports. A national team will evaluate the work that has been done and its impact on the management of mild to moderate depression in primary care.

Further information is available on the CCI website [www.cci.scot.nhs.uk](http://www.cci.scot.nhs.uk)

NHS QIS will ultimately incorporate this work into an evidence-based practice guide on depression for primary care, together with proposals on how the approach can be rolled out across Scotland.

Two examples of non-drug approaches are guided self-help and computerised cognitive behavioural therapy (CCBT).

**Guided self-help**

This constitutes more than simply giving patients literature to read, but represents a form of cognitive or behavioural psychology where individuals are taught how to respond differently to feelings or emotions that they might feel in a given circumstance. As healthcare professionals are only needed to introduce the concept and to review the outcome, it could help make psychological therapies more widely available. The major limitation of this approach is the ability of an individual to progress through a self-help work book. Motivation is important to success.

**Computerised cognitive behavioural therapy (CCBT)**

As well as using guided self-help, attempts have been made to increase the availability of psychological therapies by means of information technology. Studies have found that patients accept computer-based treatments, with recovery rates being similar to those seen with face-to-face therapies. Such approaches engage patients in a structured programme of care which replicates the care offered by a therapist in standard CBT. Once more, CCBT requires little direct staff input apart from initial introduction of the programme and evaluation of clinical outcomes.
You can read the NICE evaluation of CCBT at [http://guidance.nice.org.uk/TA97](http://guidance.nice.org.uk/TA97)

To try out CCBT for yourself, visit the MoodGYM at [moodgym.anu.edu.au](http://moodgym.anu.edu.au)

**Electroconvulsive therapy**

Electroconvulsive therapy (ECT) has been used as a treatment for depression since the 1930s. Many healthcare professionals consider it a safe and effective treatment for severe depression. This is particularly true in cases that have failed to respond to other interventions. Many patient groups consider ECT to be an out-dated and potentially harmful treatment.

ECT is now referred to as ‘modified’ ECT because of the use of anaesthesia and muscle relaxants to reduce the risk to patients undergoing the procedure. During treatment, an electrical current is passed briefly through the brain via electrodes. It is not the current itself that provides the benefit but the seizure that accompanies it. Some of the cognitive side-effects, such as memory loss, can be reduced by the use of unilateral ECT, where the electrodes are placed on one side of the head, usually the non-dominant side. However, bilateral ECT is thought to be more effective.

A course of ECT will usually involve six to 12 sessions, given once or twice weekly in either the inpatient or outpatient setting. Apart from memory loss, the other main side-effect of ECT is a transient headache lasting for a few hours after the session. As long-term benefits or risks have not been established, maintenance ECT is no longer recommended.

In May 2003, NICE issued guidance on the use of electroconvulsive therapy. In summary, the guidance recommends that ECT is used only to achieve rapid and short-term improvement of severe symptoms after other treatment options have failed and/or when the condition is considered to be potentially life-threatening, in individuals with:

- severe depressive illness
- catatonia
- a prolonged or severe manic episode.

The decision to use ECT should be made jointly by the individual and the clinician(s) responsible for treatment, on the basis of an informed discussion. Valid consent should be obtained in all cases where the individual has the ability to grant or refuse consent. Consent should be obtained without pressure or coercion, and the individual should be reminded of their right to withdraw consent at any point.

You can read the NICE guidance on ECT at [www.nice.org.uk/pdf/59ectfullguidance.pdf](http://www.nice.org.uk/pdf/59ectfullguidance.pdf)

**Pharmacological treatments for depression**

There is a wide range of antidepressant agents currently available in the UK. They are classified according to their mechanism of action e.g. selective serotonin reuptake inhibitors (SSRIs), or their chemical structure, e.g. tricyclic antidepressants (TCAs). Recently introduced antidepressants are sometimes referred to as ‘third generation’ antidepressants. They have a mechanism of action that is broader than the SSRIs and are better tolerated than most of the TCAs. Examples include venlafaxine, duloxetine, mirtazapine and reboxetine. Some of the third generation agents are marketed as if they have unique mechanisms of action. This is not necessarily true; many TCAs have a mechanism of action similar to those of the third generation agents, e.g. lofepramine is predominantly a noradrenaline reuptake inhibitor (like reboxetine),
imipramine has roughly equal affinity for noradrenaline and serotonin (similar to venlafaxine or duloxetine), and clomipramine is predominantly a serotonin reuptake inhibitor (like the SSRIs).

**Tricyclic antidepressants**
These are amongst the oldest antidepressants currently available, so there is a wide range of experience in their use. They are believed to work as monoamine reuptake inhibitors with different agents having varied specificity for either noradrenaline or serotonin. Their use is now limited by a range of associated problems.

**Poor tolerability**
Patients will frequently stop taking TCAs as they cannot tolerate the side-effects. These include: sedation (can be beneficial at first but might impede long-term concordance); hypotension (postural hypotension is particularly a problem in elderly patients or those prescribed concurrent antihypertensives), anticholinergic side-effects (especially dry mouth, blurred vision, constipation and confusion).

**Toxicity in overdose**
TCAs (with the exception of lofepramine) are considerably more toxic in overdose than SSRIs. The reasons for this are two-fold: their anticholinergic effects result in significant tachycardia and they possess quinidine-like effects which can result in cardiac conductance abnormalities and possibly fatal arrhythmias. It should be remembered that TCAs may cause cardiotoxicity at normal treatment doses as well.

**Use of low doses**
Studies have found that less than 15% of patients prescribed a TCA, excluding lofepramine, will receive an effective dose (more than 125 mg/day). The same study found 99.9% of SSRIs to be prescribed at an effective dose.

However this figure may be misleading as some evidence suggests that there is no difference, in terms of clinical outcome, between low dose and high dose TCAs. Current recommendations are that patients started on low doses of TCAs, who have a clear clinical response, should be maintained on that dose with close monitoring. The problem remains that some patients may be started on low doses of TCA, fail to be monitored properly, and remain on a dose that is ineffective for them. This is not necessarily a problem of drug therapy but highlights a poor level of monitoring.

**Selective serotonin reuptake inhibitors (SSRIs)**
There are currently six SSRIs available in the UK. Fluoxetine was not the first, but is the most widely prescribed. SSRIs work by blocking the post-synaptic reuptake of serotonin. Although this mechanism of action is selective for serotonin they are not serotonin-specific; some SSRIs also block, to a lesser extent, the reuptake of noradrenaline and dopamine.

There is little clinical difference between the SSRIs, especially in terms of efficacy. Product licences include indications for the treatment of depression plus a range of anxiety disorders, which vary between SSRIs. On the whole they are well tolerated with an efficacy that is comparable to other antidepressant groups. SSRIs are particularly favoured for those patients with a clear suicidal intent, due to their lower risk in overdose, however there has been evidence of the risk of suicide ideation in those who take SSRIs, e.g. Seroxat.
Side-effects
On the whole, the SSRIs are well tolerated, but there are a number of well-characterised side-effects: gastrointestinal effects (including nausea and vomiting, constipation, diarrhoea, dyspepsia), headaches (due to central effects of serotonin), sexual dysfunction (although not exclusively associated with SSRIs it may be more prevalent) and occasionally movement disorders.

The use of SSRIs has been associated with an increased risk of gastric bleeding. This is probably due to the antiplatelet effect of serotonin. The bleeding risk appears to be greatest in the elderly, and in those taking non-steroidal anti-inflammatory drugs (NSAIDs).

Although SSRIs are indicated for a range of anxiety disorders they can initially increase levels of anxiety, but this is usually transient. This can be managed by starting at a low dose (10 mg fluoxetine or citalopram, or 50 mg sertraline), or by using a short two-week course of a benzodiazepine.

Third generation antidepressants
This is a disparate group of antidepressants, which includes venlafaxine, mirtazapine, reboxetine and duloxetine. In common with all other antidepressants, they work by increasing the availability of monoamines, either noradrenaline or serotonin or both. This is achieved by blocking pre-synaptic reuptake of the neurotransmitter or in the case of mirtazapine, by an indirect mechanism.

Venlafaxine
Venlafaxine blocks the pre-synaptic reuptake of both serotonin and noradrenaline, although it has a greater effect on serotonin reuptake, especially at lower doses. It has a lower incidence of sedation and anticholinergic side-effects, compared with TCAs, but it does cause a considerable amount of nausea. There is also the risk of dose-related hypertension which can become significant when venlafaxine doses are titrated upwards for additional therapeutic response. This can cause additional problems for patients as venlafaxine is less well tolerated at higher doses.

The Medicines and Healthcare Products Regulatory Agency (MHRA) is now advising that only specialist mental health practitioners, should initiate venlafaxine therapy in those severely depressed or hospitalised who require doses of 300mg daily or above. Venlafaxine is not recommended and should be used with caution in those patients with existing heart disease or uncontrolled hypertension. Regular blood pressure monitoring throughout therapy is recommended. Venlafaxine may be more dangerous in overdose than the other SSRIs.

Mirtazapine
Mirtazapine is described as being a noradrenergic and specific serotoninergic antidepressant (NASSA). It has a low incidence of central serotonin side-effects, such as nausea and headache and sedation may occur at lower doses, which may be a reason to choose mirtazapine for some patients. At higher doses, the arousing effect from increased noradrenergic activity counteracts the sedative effect from central histamine inhibition. A problem with mirtazapine is its association with weight gain; this tends to be more than with other antidepressants but less than with atypical antipsychotics. Mirtazapine is structurally similar to the antidepressant mianserin, which has caused some concern as mianserin is associated, albeit rarely, with neutropenia. If patients taking mirtazapine develop an unexpected sore throat, their neutrophil count should be measured to rule out neutropenia.
Reboxetine
Reboxetine is a specific noradrenaline reuptake inhibitor (NARI) and does not have side-effects normally associated with interaction with other neurotransmitters. However, increasing noradrenaline activity in the brain is associated with an increased level of arousal/alertness, which is unopposed by any central sedative effect seen with other antidepressants. Therefore reboxetine is associated with insomnia, which limits its acceptability to patients. In addition its short half-life means that it is only licensed for twice daily dosing.

Exercise 6
The following side-effects can all be attributed to antidepressants. For each, decide which (there may be more than one) of the antidepressants listed are most commonly associated with the side-effect.

**Antidepressants: amitriptyline, fluoxetine, lofepramine, venlafaxine, mirtazapine**

<table>
<thead>
<tr>
<th>Side-effect</th>
<th>Antidepressant(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drowsiness</td>
<td></td>
</tr>
<tr>
<td>Postural hypotension</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Weight gain</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Sweating</td>
<td></td>
</tr>
<tr>
<td>Muscle tremor</td>
<td></td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*

Delayed onset of action
Although side-effects of antidepressants are usually seen at once, therapeutic effect is not apparent for several weeks. In some patients this may take up to four to six weeks, therefore a six-week trial is needed, particularly in the elderly, before claiming that therapy has not been successful. A patient is not always the best judge of improvement in mood. The gradual response to antidepressant therapy makes it almost impossible to detect changes day-by-day. The best course of action is to advise patients at the start of therapy that they may have to wait a few weeks before experiencing any benefit.
Choosing an antidepressant

Mild depression
Lack of therapeutic evidence for antidepressants in mild depression leads to a poor risk to benefit ratio. NICE guidance recommends consideration be given to non-pharmacological intervention such as practical help and support, guided self-help, regular exercise or watchful waiting (where the individual is reassessed after two weeks to see if there has been any change in mental state).

Antidepressant medication should only be considered for those individuals whose depression persists, despite other interventions, or where the depression is associated with psychosocial and medical problems.

If a patient with a history of moderate or severe depression presents with mild depression, antidepressant drug therapy can be considered as a first-line option.

Moderate or severe depression
In moderate to severe depression, antidepressant drugs should be offered to patients as first-line treatment options, before any psychological interventions. As antidepressants are generally of equal efficacy, the choice of which to use depends more on patient factors, e.g. previous drug treatment, side-effect preferences, risk of suicide, consequences of impaired functioning or the presence of co-morbid medical conditions, pregnancy or breastfeeding.

Frequently an SSRI will be the first-choice antidepressant. If substantial anxiety is present, or if this develops in the early stages of treatment, then an alternative antidepressant may be needed, or a short (two week course) of a benzodiazepine might be necessary. Diazepam 5 mg may be a suitable choice as the long half-life allows daily dosing.

Discussion of prescribing issues in pregnancy and lactation is available in SIGN Guideline 60 Postnatal Depression and Puerperal Psychosis (June 2002). It is recommended that up-to-date advice for individual women who are (or planning to be) pregnant or breastfeeding should be sought from a specialist medicines information pharmacist.

Relapse prevention
Depression is frequently a long-term illness with recurring episodes. Currently it is recommended that patients take antidepressants for at least six months (twelve months for older people) after the resolution of all depressive symptoms. However, it is thought that some patients may benefit from longer treatment with antidepressants. One study found that patients treated for one year after all symptoms resolved, approximately halved their risk of relapse.

To reflect this, it is now recommended that six months (twelve months for older people) after symptoms have resolved, prescribers and patients should review the need for continued treatment. Factors such as presence of residual symptoms, numbers of previous episodes or continued psychosocial difficulties indicate potential benefit from continued antidepressant therapy. Continued therapy may need to be reviewed again after two years. The antidepressant dose should not be reduced during this continued therapy phase.
Discontinuation symptoms
Antidepressants are not addictive. They do not cause tolerance or a craving for bigger doses. However, concerns have been raised about withdrawal reactions, especially if high doses are stopped abruptly. Discontinuation symptoms have been reported for most antidepressants but they are more likely if:

- the drug has a short half-life e.g. paroxetine, venlafaxine
- antidepressants are taken for longer than eight weeks
- anxiety symptoms were exacerbated at the start of therapy
- discontinuation symptoms have been experienced before, either on stopping treatment or missing doses during treatment.

Often the symptoms experienced are vague and non-specific, but they can include ‘flu-like symptoms, excessive sweating, myalgia, shock-like sensations, dizziness, irritability or crying spells. Occasionally, movement disorders, mania and problems with concentration or memory have been reported.

Discontinuation symptoms can be minimised by withdrawing the antidepressant gradually over a four-week period, particularly the shorter acting agents. Alternate day dosing as a means of tapering is inappropriate for drugs with a particularly short half-life, e.g. paroxetine. Fluoxetine has a half life of several weeks and tapering is often unnecessary at doses of 20 mg daily.

Case study 2b

Penny
Penny Gunn is a 26-year-old insurance claims assessor. Over the last few weeks her colleagues have noticed a change in her appearance. She used to be immaculately turned out but now looks distinctly unkempt. Her boss has noticed a deterioration in her work. When he approaches her about this, she says that she just feels so tired and run down at the moment. No matter what time she goes to bed in the evening, she never seems to get more than a couple of hours sleep. During the discussion Penny becomes quite tearful and apologetic. She says she is really trying hard but cannot get things together at the moment.

1. Would you recommend an antidepressant be prescribed at this stage?

2. What additional information might be useful?
Penny tells you that she had a ‘breakdown’ about five years ago, for which her GP gave her some tablets. She said she only took them for a few weeks because her mother had once been prescribed some tablets, which she had ended up taking for the rest of her life. Penny describes herself as normally a confident person.

3. Which antidepressant would be most suitable for Penny and why?

4. What information would you give Penny about her medication?

Turn to the end of the chapter for suggested answers

You should also look on the NES Pharmacy website www.nes.scot.nhs.uk/pharmacy for the Core Pack Pharmaceutical Care of People with Depression as well as the additional supporting material under resources on the NES website above.

4.6 Counselling points on depression

All patients suffering from depression would benefit from the following points being reinforced in a positive manner:

- Depression is an illness, just like diabetes, asthma or heart disease.
- Taking medication for depression is not a sign of weakness, but is an important part of the treatment of depression.
- All antidepressants take around four weeks to have an effect on depression.
- Side-effects are common, but feelings of anxiety, restlessness or suicidal ideas (on initiation, after dose increase or a change of drug) require prompt medical attention.
- Antidepressant drug therapy should be continued for at least six months after all symptoms have resolved.
- Some patients, particularly those with a history of recurrent episodes, may benefit from longer continued therapy.
- Antidepressants are not addictive; they do not cause tolerance or cravings.
Antidepressants can cause a withdrawal reaction if stopped abruptly, so any decision to cease therapy needs to be made in conjunction with the prescriber.

Summary
Depression is more than just ‘feeling blue’. For many sufferers it is a debilitating condition associated with significant functional impairment and profound personal distress.

Treatment options include a variety of psychological and problem-solving therapies as well as drug therapy and in severe cases ECT.

Antidepressant drug therapy should be selected on the basis of severity of the illness and safety and tolerability of the agent. SSRIs are the preferred antidepressants for the drug treatment of moderate to severe depression.

Learning Outcomes
On completion of this chapter you should be able to:
1. Identify the major symptoms associated with depression in adults
2. Apply or advise on the NICE guideline on treatment of depression in adults
3. Apply or advise on the SIGN guideline on the treatment of postnatal depression and puerperal psychosis
4. Take account of the non-pharmacological management of depression in adults in the context of your practice
5. Advise on the mode of action and side-effects of the antidepressants.

Further reading


References


Suggested answers

Exercise 6 (page 83)

<table>
<thead>
<tr>
<th>Side-effect</th>
<th>Antidepressant(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drowsiness</td>
<td>Amitriptyline, lofepramine, mirtazapine</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>Amitriptyline, lofepramine (minimal)</td>
</tr>
<tr>
<td>Constipation</td>
<td>Amitriptyline, venlafaxine</td>
</tr>
<tr>
<td>Nausea</td>
<td>Venlafaxine, fluoxetine</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td>Headache</td>
<td>Venlafaxine, fluoxetine</td>
</tr>
<tr>
<td>Sweating</td>
<td>Amitriptyline, venlafaxine</td>
</tr>
<tr>
<td>Muscle tremor</td>
<td>Fluoxetine</td>
</tr>
</tbody>
</table>

Case study 2a – Penny (page 75)
- Anhedonia (demonstrated by poor self-care and deteriorating work)
- Lack of energy
- Sleep disturbance
- Low self-esteem
- Guilt
- Poor concentration

This could possibly constitute a moderate depressive episode.

Case study 2b – Penny (page 85-86)
1. At this stage it is hard to distinguish between mild or moderate depression. There are possibly enough symptoms present to indicate moderate depression, although it is difficult to establish if all of the symptoms represent a big enough change from pre-morbid functioning.

2. Additional information that might aid diagnosis would include: past psychiatric history, previous treatment with medication and information about pre-morbid personality.

3. An SSRI would probably be the most suitable first-line antidepressant in this case. Fluoxetine, paroxetine or citalopram would be good choices as they are all available as generic medicines.

4. Penny would need the following information:
- reassurance about the effectiveness of antidepressants
- warning that they take about four weeks to have an effect
- emphasis of the importance of taking them regularly
- explanation of the need to keep taking them, even after she feels better.
Chapter 5  Bipolar affective disorder
Objectives

This chapter will enable you to:

- describe the key symptoms of bipolar affective disorder
- discuss the treatment for the different phases of bipolar affective disorder
- describe the treatment of bipolar affective disorder in pregnancy
- list key side-effects and interactions for the different treatments
- explain the need for monitoring with long-term treatment
- discuss SIGN guideline 82. Bipolar Affective Disorder
Chapter 5
Bipolar affective disorder

5.1 Introduction

Bipolar affective disorder (BAD) or ‘manic-depression’, is a disorder characterised by extremes of emotion, ranging from euphoria to despair.

As leading causes of disability adjusted life years (DALY) in men and women aged 15-44 (see Section 1.1: Background), schizophrenia is ranked eighth and BAD ninth, accounting for 2.6% and 2.5% of the global burden of disease respectively.

If the burden of premature death and disabling disease associated with bipolar disorder is virtually the same as it is for schizophrenia, why does BAD remain poorly understood and under-diagnosed? Even the Royal College of Psychiatrists ‘Changing Minds’ campaign doesn’t include bipolar disorder.

Kraeplin was the first person to differentiate between manic psychosis and schizophrenia; however many sufferers are diagnosed with bipolar disorder without ever having a psychotic episode.

Although the initial presentation of bipolar disorder may be one or more major depressive episodes, a diagnosis of BAD can only be made when a patient has had a manic or hypomanic episode – often referred to by patients as a ‘high’.

Mania is a ‘high’ severe enough to disrupt normal functioning; psychotic features such as delusions and hallucinations may or may not be present. If the sufferer retains full functional capability during a ‘high’ it is termed hypomania.

Sometimes patients present symptoms sufficient to satisfy the diagnostic criteria for mania and a major depressive episode (either simultaneously or rapidly alternating between them), a condition known as mixed state. Mixed symptomatology of varying degrees is common.

Isolated mania is rare and the term unipolar mania is no longer used. The term ‘single manic episode’ applies to a first episode of mania with no previous history of major depression, but it is usually only a matter of time before a patient experiences a depressive ‘low’. Recurrence is necessary for a diagnosis of BAD. So, an abnormal behavioural episode may be designated a bipolar disorder after consideration of the frequency and type of abnormal mood.

An important difference between the ICD-10 and DSM-IV classification of BAD is the DSM-IV subdivision of the illness into bipolar I and bipolar II. Bipolar I is diagnosed if the patient has ever experienced a manic or mixed episode and bipolar II is diagnosed if the patient has only experienced hypomania.

Individual episodes are characterised by the mood state, i.e. manic, hypomanic, mixed or depressed and additional descriptors such as ‘with psychosis’ or ‘without psychosis’ are used to further clarify and reflect the severity of the episode.
5.2 Epidemiology

The lifetime risk for bipolar disorder is 1.3–1.6%. Bipolar II is more common than bipolar I. The prevalence of bipolar I disorder is the same in men and women, but bipolar II is more common in women.

The lifetime risk of suicide in bipolar illness is 10–20% and approximately a third of sufferers admit to at least one suicide attempt.

Onset peaks between the ages of 15 and 24, but diagnosis is often some five to ten years later.

5.3 Symptoms of bipolar affective disorder

For symptoms of depression refer to Section 4.3.

The (non-psychotic) symptoms of mania and hypomania are essentially the same but vary in severity and the extent to which they interfere with normal social or occupational functioning. For diagnostic purposes symptoms must be present for at least a week (unless severe enough to require hospitalisation). Abnormal mood is the core symptom and three other symptoms are required for diagnosis (four if mood is only irritable).

Mood
Elevated, expansive or even euphoric but may be irritable. The hypomanic patient may typically appear as the life and soul of the party. Manic patients may seem abnormally happy or overly optimistic but may also become irritable with people around them who don’t share their optimism or frustrated that others can’t keep up with their racing thoughts, ideas or energy level.

Inflated self-esteem
This may vary from feeling exceptionally good about oneself, right through to grandiose delusions of superhuman powers.

Decreased need for sleep
Experiences range from getting by on a few hours sleep a night to going without sleep for days on end. Lack of sleep may intensify the severity of an episode and for some sufferers disruption of the sleep/wake cycle (e.g. jet-lag) can precipitate an episode.

More talkative than usual or pressured speech
There is often an uncontrollable need to keep talking which can range from frequently interrupting conversations, through not letting anyone else get a word in edgewise, to talking incessantly even though no-one else is around or listening. Pressured speech is characteristically copious, rapid, often difficult to understand and frequently loud and emphatic.

Flight of ideas or subjective feeling that thoughts are racing
Ideas flow rapidly and often go off at a tangent. During hypomania this may lead to increased creativity and capacity for lateral thinking, but as the severity of mania intensifies thoughts and ideas come thicker and faster and are usually much more disjointed. The outward manifestation of this is often through pressured speech as the sufferer tries to communicate their thoughts and ideas.
Distractibility
This is defined as an increase in goal-directed activity or psychomotor agitation. In milder states it may manifest as multi-tasking with several projects on the go or increased energy levels. In more severe states the sufferer appears almost inexhaustible, constantly on the go mentally and/or physically.

Excessive involvement in pleasurable activity that has a high potential for painful consequences
Libido is commonly increased during hypomania and mania and can lead to sexual overactivity, promiscuity and inappropriate sexual advances. Unrestrained spending is another common feature of hypomania and mania and in severe episodes is often accompanied by delusions of great wealth.

During hypomanic/manic episodes the sufferer may dress flamboyantly or inappropriately for the occasion, with brightly coloured hair and too much make-up! The amount of care taken with appearance and self-care tends to decline as the severity of the episode intensifies.

Hypomania is often difficult to recognise as the sufferer may appear confident, upbeat, eloquent, energetic, bubbling with ideas and able to restrain themselves appropriately in social or workplace situations. As hypomania intensifies into mania, self-control is lost and symptoms become much more full on. Disinhibition and reckless behaviour can destroy relationships, finances and employment prospects, leaving many lives in pieces long after the mania has subsided. For many, the mood turns ‘black’ and they experience increasing anger, frustration and hostility, often accompanied by delusions of persecution. In mixed state the mood may be low but the flow of ideas, speech and energy levels consistent with mania – a particularly lethal combination.

5.4 Course of bipolar affective disorder

For most sufferers bipolar disorder is a recurrent condition. Recurrence is indicated by either a shift in the polarity of the episode or an interval between episodes of at least two months without symptoms.

A shift in polarity is defined as a clinical course in which a major depressive episode evolves into a manic episode or a mixed episode and vice versa. More than 90% of individuals who have a single manic episode will have further episodes.

Roughly 60–70% of manic episodes occur immediately before or after a major depressive episode. Manic episodes often precede or follow the depressive episodes in a characteristic pattern for a particular person.

The natural course of the illness is highly variable; 10–15% of patients will have more than ten episodes during their lifetime. The interval between episodes tends to get shorter as the person gets older.

Although the majority of individuals with bipolar disorder return to a fully functional level between episodes, 20–30% continue to display mood lability and interpersonal or occupational difficulties.

10–15% of sufferers experience four or more episodes a year; a condition known as rapid cycling. Rapid cycling is associated with a poorer prognosis.
5.5 Aetiology of bipolar affective disorder

**Psychological factors**

As with schizophrenia, BAD is a complex disorder that is almost certainly dependent on a number of factors including an inherited predisposition, environmental stressors and learned behaviours. Major life events may precede the onset of BAD, but stress appears to have a relatively limited role in precipitating episodes. However, individuals can sometimes identify triggers for recurrence and learning to recognise these is an important aspect of long-term management.

**Genetic factors**

There is a great deal of evidence that genes play a major role in susceptibility to BAD. BAD has been found to run in families and relatives of an affected individual have an increased risk of developing the disorder; lifetime risk is five to 10 times higher if a first-degree relative has BAD. This is not proof that genes transmit the disorder; it could be taken as evidence that family members are more likely to share similar life experiences that lead to the onset of BAD. However, twin studies show that risk is 60 times higher if an identical twin is affected. Furthermore, adoption studies show that biological relatives of people with BAD have a greater risk of developing BAD than adoptive relatives. The genetic link seems strong, but the fact that there are pairs of identical twins who are discordant for manic depression shows that there are environmental factors that are also important in developing the illness.

Family members of a patient with BAD also appear to have a higher incidence of other mental illnesses including unipolar depression and schizo-affective disorder which suggests BAD is part of a broader spectrum of disorders. The heterogeneity of BAD makes it a particularly difficult condition to study.

**Neurobiology**

There is little understanding of the neurobiology of bipolar illness. Many neurotransmitters have been studied including dopamine, serotonin, gamma amino butyric acid (GABA) and glutamate. Evidence for a neurobiological basis for BAD is supported by the fact that stimulants and antidepressants can precipitate a manic episode and that psychotropic drugs that affect many aspects of neurotransmission are effective in the management of different elements of BAD.

The monoamine theory suggests that depression is caused by a functional deficit of serotonin and the efficacy of antipsychotics would suggest that mania is a hyperdopaminergic state. The mode of action of lithium is still not fully understood. However, lithium modifies the production and turnover of certain neurotransmitters, particularly serotonin, and it may block dopamine receptors. The most likely mode of action for the anticonvulsants as antimanic agents is potentiation of the inhibitory action of gamma amino butyric acid (GABA).
5.6 Treatment of bipolar affective disorder

There is increasing evidence to support a variety of drugs in the management of bipolar affective disorder; however many are often used outside the terms of their licence. If a pharmaceutical company wants an indication of bipolar disorder in their Summary of Product Characteristics (SmPC), they need to perform a range of studies covering the different features of the disease. Due to the length of time this takes and the complexity of the necessary studies, companies often perform trials on different aspects of BAD and gradually build the licensed indications, e.g. short-term trials in the treatment of acute mania, then prevention of recurrence and finally adjunctive treatment before an all-inclusive licence is possible.

SIGN guideline 82 Bipolar Affective Disorder was published in July 2005 and covers adults aged 18 years and over. This guideline can be read at www.sign.ac.uk/pdf/sign82.pdf


The management of bipolar disorder depends on the phase of the illness being treated:

- acute manic, hypomanic or mixed episode
- acute depressive episode
- mood stabilisation to prevent recurrence.

**Acute manic or mixed episode**

Patients with mania require short-term treatment with medication in an appropriate clinical setting. The aim of treatment is to reduce the severity and duration of the acute episode. Drugs used to treat the manic stage are frequently continued to prevent or delay another relapse. Studies of atypical antipsychotics (olanzapine, quetiapine and risperidone) suggest that combination of an atypical antipsychotic with a mood stabiliser (lithium or valproate) is the best approach. Carbamazepine and lamotrigine have also been used for mania. However consideration may have to be given to the licensed indication for these drugs before they are prescribed.

For acute manic or mixed episodes the main treatment strategies include the following:

**Discontinuation of agents known to precipitate mania**
Antidepressants and stimulants such as illicit drugs, caffeine and some OTC medicines such as cold remedies, codeine and ginseng are known to precipitate mania and should therefore be discontinued.

**Introduction of therapies to treat the manic stage**
These agents include antipsychotics, valproate, lithium and electroconvulsive therapy (ECT).

**Antipsychotics**
Antipsychotics have been shown to be effective. The atypical antipsychotics are used more frequently than the older typical drugs because of increasing evidence that they are effective antimanic agents and because they are less likely to induce EPS than typical antipsychotics. (Refer to Section 3.8 for relative risk of side-effects for atypicals.)
Valproate
Valproate is the generic term used to describe the different formulations valproate semisodium and sodium valproate, both of which are metabolised to the chemically active valproic acid. Valproate semisodium (also known as divalproex) is licensed for the treatment of mania and has shown to be effective in severe mania. Sodium valproate is not licensed in this indication, but is frequently prescribed for mania.

Lithium
Lithium may be used to treat acute mania but takes longer to work than the atypicals or valproate (SIGN guideline 82). The therapeutic levels of lithium for the treatment of acute mania are generally much higher than those required for prevention of recurrence and risk of toxicity is increased, particularly in dehydrated or exhausted patients. Lithium levels above 1.0 mmol/l should always be queried. Other treatments for acute mania are often preferred on the grounds of lower risk of toxicity.

Hypnotics and sedatives
Benzodiazepine and other hypnotics are used to aid sleep. Diazepam, lorazepam and clonazepam are used short-term to control agitation. Benzodiazepines are frequently used in combination with antipsychotics, solely for their sedative properties, to reduce the need for high doses of antipsychotics. Hypnotics and sedatives should always be discontinued (by tapering the dose) as soon as symptoms improve.

Combination therapy
Combinations are often used in acute manic episodes where patients are already on long-term treatment or when patients fail to respond to monotherapy. Evidence shows that antipsychotics such as risperidone, haloperidol, olanzapine or quetiapine, combined with lithium or valproate in acute mania, may be superior to monotherapy.

Electroconvulsive therapy
NICE guidance states that electroconvulsive therapy (ECT) may be used for individuals with severe mania. It may be considered for manic patients who are severely ill and/or whose mania is treatment-resistant, who express a preference for ECT and patients with a severe mania during pregnancy.

Acute depressive episode
Antidepressants are effective in treating depression in bipolar patients but must be used cautiously as they can precipitate a manic or hypomanic episode. Antipsychotics are indicated if psychotic symptoms are present and ECT may be used in severe depression. Psychological treatments such as interpersonal therapy and cognitive behavioural therapy may also be helpful.

Antidepressants
Antidepressants may be prescribed but to minimise the risk of precipitating a manic episode, they are often used in conjunction with a mood stabiliser (both NICE and SIGN recommend co-prescription of a mood stabiliser). However some studies investigating this issue found that adding a mood stabiliser did little to prevent antidepressant-induced mania. SSRIs are less likely to precipitate mania than tricyclics and are the antidepressants of choice. Although antidepressants
should normally be discontinued by tapering, rapid discontinuation may be more appropriate if a patient develops hypomania or mania.

Antipsychotics
Antipsychotics may be used in the treatment of psychotic depression and there is some evidence for the treatment of bipolar depressive episodes with atypical antipsychotics alone or in combination with antidepressants. However atypical antipsychotics are not currently licensed for the treatment of bipolar depression.

Prevention of recurrence
Long-term therapy is aimed at preventing recurrence of mania or depression. The long-term treatments currently used – lithium, valproate, olanzapine and carbamazepine – are generally more effective in preventing recurrence of mania than depression and the term ‘mood stabiliser’ is something of a misnomer. However studies have shown that lamotrigine, but not lithium, prevented relapse of bipolar depression; lamotrigine is not licensed in the UK for this indication. Despite greater efficacy in preventing manic recurrence, long-term treatment is associated with a reduced risk of suicide in bipolar patients. Therefore continuation of acute treatment is recommended, although at present there is no consensus on the length of treatment. The British Association of Psychopharmacology (BAP) guidelines state that the risk of relapse remains high following discontinuation of therapy, and if there is good clinical control of the illness then long-term therapy should continue. If there is an agreement between the patient and doctor to discontinue medication, then the doses should be reduced gradually. This is particularly true of lithium as there is a high risk of relapse.

Lithium
Lithium has the most evidence for reducing suicide risk in bipolar patients. It prevents relapse of mania but it is less effective in preventing depressive relapse. Prescribers should use the highest dose that produces minimal side-effects and aim for plasma levels of 0.4–0.8 mmol/l. Reference sources differ on the target range but it is generally considered that levels above 1.0 mmol/l should be avoided. Patients should be warned of the risk of early relapse if lithium is withdrawn abruptly, and doses should be slowly tapered down over at least six weeks. A history of poor compliance is a contraindication to lithium use because of the risk of recurrence on discontinuation. Although lithium still has the strongest evidence base for long-term efficacy and has traditionally been the long-term treatment of choice, its adverse effects, monitoring requirements and the risk of early relapse of mania associated with sudden discontinuation mean that other long-term treatments are being used more frequently.

Valproate
No valproate preparation is licensed for long-term therapy, although valproate probably does prevent manic and depressive relapses and may even be as effective as lithium in the prevention of relapse. However, a Cochrane review concluded that the increase in prescribing of valproate is not based on reliable evidence of efficacy. SIGN states insufficient evidence to recommend valproate for maintenance. It should not be prescribed routinely for women of child-bearing potential because of the risks of teratogenicity. If there is no effective alternative, adequate contraception should be used, and the woman fully informed of the risks of taking valproate in pregnancy.
Antipsychotics
At present only one atypical antipsychotic (olanzapine) is licensed for long-term treatment. Its use is restricted to patients who have responded well in a manic episode and there is more evidence that olanzapine prevents manic rather than depressive relapses. There is increasing evidence that other atypicals, such as risperidone and quietaipine, are effective long-term treatments, but they are not currently licensed for prevention of recurrence.

Carbamazepine
Carbamazepine is less effective than lithium, but is sometimes used as mono-therapy if lithium is ineffective, especially in patients who do not show the classical pattern of episodic euphoric mania. Evidence is limited and carbamazepine is only licensed for the prophylaxis of manic-depressive psychosis in patients unresponsive to lithium.

Lamotrigine
Lamotrigine is not effective in the prevention of manic or hypomanic relapse but limited evidence suggests that it is effective in preventing recurrence of depression and should be considered where depression is the major burden of the illness. Although lamotrigine is not licensed for this indication there is very little evidence for any other agent and it is being used off-licence more frequently.

Antidepressants
Antidepressants are sometimes continued long-term after treatment of a depressive episode to prevent relapse, but this practice carries a high risk of precipitating hypomania or mania and there is little evidence that addition of a mood stabiliser reduces the risk.

Psychotherapy
Cognitive behaviour therapy (CBT) has shown to be successful in bipolar disorder. The key components include knowledge or ‘psycho-education’, self-monitoring, self-regulation (action plans and modification of behaviours) and increased concordance with medication.

When combined with pharmacological treatment, psycho-education helps improve concordance. Psychotherapy teaches patients to recognise symptoms of recurrence and enables them to seek early treatment thus reducing the incidence and/or severity of recurrent episodes. Patients may be prescribed a short course of hypnotics or an agent to treat mania if lack of sleep or early signs of mania occur. It is essential to address the seriousness of the illness, any reluctance to give up the experience of hypomania or mania, the risk of relapse and the benefits of therapeutic engagement.

There are many tools to aid psycho-education and useful contacts include Bipolar Fellowship Scotland www.bipolarscotland.org.uk the National Electronic Library for Mental Health www.nelh.nhs.uk, the Manic Depression Fellowship www.mdf.org.uk, and the Depression and Bipolar Support Alliance www.dbsalliance.org
Case study 3

Julia
Julia is a 28-year-old lady with a diagnosis of bipolar affective disorder. Julia is prescribed Epilim Chrono 1500 mg at night. She enters the pharmacy and asks to speak to you. She wants to ask your advice on pregnancy, and she has heard that taking folic acid 400μg is recommended.

How appropriate is 400μg of folic acid if Julia is on Epilim?

Check the National Teratology Information Service at www.nyrdtc.nhs.uk/services/teratology/teratology.html or telephone 0191 232 1525.

Attempt to complete the exercise before reading on.

5.7 Adverse effects of medications used in bipolar disorder

Teratogenicity

In the UK the spontaneous malformation rate at birth in the general population is approximately 2–3%, increasing to approximately 5% by 45 years of age. Lithium, valproate and carbamazepine are all associated with an increased risk, generally thought to be around 10%. Lithium is specifically associated with Ebstein’s cardiac disorder; risk in the general population is 1 in 20,000 and on lithium it is 1 in 1,000. Most of the data for valproate and carbamazepine comes from use in epilepsy, which may itself increase the risk of malformations. High doses and multiple agents have also contributed to increased risk in epilepsy studies. Valproate and carbamazepine are associated with neural tube defects (1–2% with valproate and 1% with carbamazepine, which is 50–100 times the spontaneous rate) and folic acid at a dose of 5 mg daily is recommended to reduce this risk. Valproate is also associated with ‘valproate syndrome’ and carbamazepine has been associated with a ‘carbamazepine syndrome’.

Teratogenic risk is highest in the first trimester (organogenesis occurs from day 17–60 after conception); therefore lithium, valproate and carbamazepine are best avoided in the first trimester. However the risk of relapse, with consequent harm to the mother and foetus, is also important. If valproate or carbamazepine are indicated, they should be prescribed at the lowest possible dose, using slow release preparations to avoid high peak levels, along with folic acid. If lithium is prescribed the lowest dose possible should be used, but prescribers need to be aware
that the volume of distribution changes during pregnancy and serum lithium levels should be monitored more frequently.

Most evidence indicates that the older antipsychotics and antidepressants do not increase the risk of malformations. The main problems concern neonatal toxicity, particularly withdrawal in the infant after delivery. Limited evidence suggests that atypical antipsychotics do not increase the risk of malformations but there is insufficient evidence to recommend their use and gestational diabetes may be a problem with the atypicals. There is most experience with chlorpromazine, trifluoperazine and olanzapine for psychosis in pregnancy.

Common ADRs and monitoring requirements

See Table 5, page 104

**Lithium**

*Renal effects*

When first initiated, lithium can cause thirst and polyuria (increased urination), by direct suppression of the anti-diuretic hormone, thereby causing diabetes insipidus. This is generally reversible in the short-term but may be irreversible in the long-term (more than 15 years). High serum concentrations of lithium, including episodes of acute lithium toxicity, may precipitate or accelerate these changes. Renal function should be monitored at least every 12 months in stable patients or whenever the clinical status changes.

*Thyroid effects*

Long-term treatment with lithium is frequently associated with disturbances of thyroid function, including goitre and hypothyroidism. These can be controlled by administration of doses of 50–200 μg levothyroxine daily. Thyroid function should be monitored at least every 12 months in stable patients, or whenever the clinical status changes.

There are other common side-effects of lithium e.g. tremor.

**Haematological effects – valproate and carbamazepine**

Valproate can cause inhibition of platelet aggregation leading to prolongation of bleeding time and thrombocytopenia. This is normally associated with doses above the maximum and is usually reversible. Spontaneous bruising or bleeding is an indication for withdrawal of medication pending investigations.

Patients receiving carbamazepine have a 1 in 20,000 risk of developing agranulocytosis and aplastic anaemia. Approximately one in ten patients develop leucopenia during the first two months on therapy but this is usually transient and benign. Carbamazepine should be discontinued if the patient develops leucopenia which is severe, progressive and accompanied by clinical manifestations or any evidence of significant bone marrow depression.

Other valproate side-effects which are common are weight gain, nausea and alopecia.
Dermatological effects – lamotrigine
Patients receiving lamotrigine have an approximately 1 in 1000 risk of developing potentially life-threatening skin rashes, including Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell’s Syndrome), which usually occur in the first eight weeks of therapy. Rapid dose escalation and concomitant use of valproate increase the risk.

Exercise 7
What are the signs of toxicity with:
lithium

valproate

carbamazepine

lamotrigine

Turn to the end of the chapter for suggested answers
### Table 5 Monitoring required for long-term treatment

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Routine monitoring</th>
<th>Dosage regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lithium</strong></td>
<td>Electrolytes</td>
<td>Serum lithium (0.4–0.8mmol/l, may be lower in elderly) every 3 – 6 months. Serum</td>
<td>Initial dose 400 mg at night (lower in elderly). Maintenance dose 800–1200 mg</td>
</tr>
<tr>
<td></td>
<td>including blood urea, serum creatinine and calcium, T3, T4 and TSH, full blood count (FBC), ECG</td>
<td>creatinine, T3, T4 and TSH, FBC and electrolytes, including calcium; watch for toxicity signs, warn patients about changes in diet or dehydration.</td>
<td>(lower in the elderly and impaired renal function). Doses may be titrated to blood levels and can therefore be outside this range.</td>
</tr>
<tr>
<td><strong>Valproate</strong></td>
<td>Electrolytes</td>
<td>Serum valproate (50-100mg/l), LFTs, FBC, watch for toxicity signs, warn patient about bruising, abdominal swelling and jaundice.</td>
<td>Initial dose 500 mg once a day (Epilim) or 250 mg three times a day (Depakote). Maintenance dose 1000mg to 2500mg.</td>
</tr>
<tr>
<td></td>
<td>including blood urea and serum creatinine, LFTs, FBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Carbamazepine</strong></td>
<td>FBC, Electrolytes, LFTs</td>
<td>Serum carbamazepine (8–12mg/l), FBC, LFTs, electrolytes, watch for toxicity signs, warn patient about sore throat, fever and infections.</td>
<td>Initial dose 400 mg at night increased every two weeks. Maintenance dose 600–1000 mg/day.</td>
</tr>
<tr>
<td><strong>Lamotrigine</strong></td>
<td></td>
<td>Warn patient about rash.</td>
<td>Initial dose 25 mg daily, increase every two weeks by 25 mg. If added to valproate: 25 mg every other day, increase every two weeks.</td>
</tr>
</tbody>
</table>

### Exercise 8

What are the requirements for monitoring lithium therapy under the General Medical Services (GMS) Contract Quality and Outcomes Framework and the standards required for payment?  

*Turn to the end of the chapter for suggested answers*
Lithium has a narrow therapeutic window and patients should be monitored closely. Lithium is a salt, so both dehydration and altered electrolyte balance affect lithium levels. Many drugs interact with lithium, primarily by affecting renal excretion, e.g. NSAIDs and ACE inhibitors. Other interactions include reports of neurotoxicity when lithium is used in combination with antipsychotics, carbamazepine and SSRIs. However, these combinations are generally considered useful.

Carbamazepine is metabolised by and induces (auto-induction) cytochrome P450 3A4 and doses need to be increased every two weeks. Carbamazepine interacts with many drugs that are also metabolised by this enzyme.

Valproate is also metabolised by cytochrome P450 3A3/4 and is an inhibitor of cytochrome P450 2C9/19. Approximately 20% of Asians and 3–5% of Caucasians are poor cytochrome P450 2C9/19 metabolisers. In poor metabolisers, doses may need to be lower than in the general population.

Lamotrigine metabolism is enhanced by enzyme-inducing anticonvulsants. However sodium valproate competes with lamotrigine for hepatic drug-metabolising enzymes and nearly doubles its elimination half-life.

### Case study 4

James

James is a 35-year-old man with a diagnosis of bipolar I disorder. He comes into your pharmacy with a prescription for lithium (Priadel 800 mg nocte). On dispensing this, your computer flags up an interaction between lithium and antipsychotics (he takes risperidone 6 mg nocte).

**How clinically significant is this interaction?**

James also asks whether he can take ibuprofen, which he occasionally uses for a long-term ankle inflammation and for headaches.

**What is your advice?**

*Turn to the end of the chapter for suggested answers*
Exercise 9

Listen to an interview with Dr Kay Redfield Jameson, (professor of psychiatry at Johns Hopkins Hospital, Baltimore, USA and herself a sufferer of bipolar disorder) in which she discusses many aspects of the illness from a personal and professional point of view, including symptoms, treatment, suicide and concordance.

The interview is 20 minutes long but worth it! www.npr.org/ramfiles/fa/20010105.fa.01.ram

Alternatively her books, An Unquiet Mind and Night Falls Fast, give insight and information on bipolar disorder and suicidality respectively.

Summary

Bipolar affective disorder is a common mental illness, occurring with similar frequency to schizophrenia and accounting for a near identical proportion of the global burden of disease. Like schizophrenia the course and severity of the illness varies greatly between sufferers.

The neurobiological basis for bipolar affective disorder is poorly understood compared to schizophrenia and depression. Treatment options vary according to the phase of the illness being treated and include drugs with widely differing modes of action, many of which are used outside the terms of their product licence.

Learning Outcomes

On completion of this chapter you should be able to:

1. Identify and describe the key symptoms of bipolar affective disorder.
2. Discuss the treatment for the different phases of bipolar affective disorder.
3. Be aware of the treatment of bipolar affective disorder in pregnancy and refer as appropriate.
4. List and advise on key side-effects and interactions for the different treatments.
5. Explain the need for monitoring with long-term treatment.
6. Apply or advise on SIGN guideline 82. Bipolar Affective Disorder.

Further reading

www.nmhct.nhs.uk/pharmacy

Geddes J. Bipolar Disorder in Clinical Evidence.
www.clinicalevidence.com/ceweb/conditions/meh/1014/1014.jsp

www.bap.org.uk/consensus/FinalBipolarGuidelines.pdf
References


25 The National Teratology Information Centre, The Regional Drug and Therapeutic Centre, Wolfson Unit, Claremont Place, Newcastle-upon-Tyne, NE2 4HH.


Suggested answers

Exercise 7 (page 103)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Marked tremor, unsteadiness, uncoordination, nausea and vomiting.</td>
</tr>
<tr>
<td>Valproate</td>
<td>Nausea, vomiting, confusion and stupor.</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Ataxia, dizziness, blurred vision, headache, nausea and seeing double.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Involuntary or rapid eye movements, unsteadiness, impaired consciousness and coma.</td>
</tr>
</tbody>
</table>

Exercise 8 (page 104)

<table>
<thead>
<tr>
<th>MH 4</th>
<th>The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the preceding 15 months.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40–90%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MH 5</th>
<th>The percentage of patients on lithium therapy with a record of lithium levels in the therapeutic range within the previous 6 months.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>40–90%</td>
</tr>
</tbody>
</table>

Case study 3 – Julia (page 101)

400 mcg of folic acid is the recommended dose for women with no risk factors who want to become pregnant; however valproate has been associated with an increased risk of foetal malformations. Although pregnancy itself has not been shown to increase the risk of relapse of bipolar disorder, studies have shown there is a high risk of relapse if medication is discontinued. Julia should discuss this subject further with her doctor or psychiatrist to work out the best way forward, taking into account the risks (of the medication and also of becoming unwell) and benefits.

This conversation should take place as early as possible, as the first trimester is the most critical time for foetal malformations. If there is no alternative to Julia taking valproate, folic acid supplementation (5mg daily) is recommended prior to pregnancy – as soon as contraception is discontinued – and throughout the first trimester, to minimise the potential teratogenic risk. The lowest possible dose of valproate, in divided doses and slow-release form, should be used.
Case study 4 – James (page 105)

There is a rare risk of neurotoxicity and extrapyramidal symptoms with this combination; nevertheless this combination is generally considered as a useful one. The main risk appears to be if high doses of both drugs are used and signs of toxicity are ignored. Counsel James on signs and symptoms of lithium toxicity and advise him to contact his doctor if he experiences any of these symptoms.

Ibuprofen can increase levels of lithium to above those recommended. Many other medicines also interact with lithium and patients should be encouraged always to ask the advice of their doctor or pharmacist before taking any non-prescription medicine. Signs such as marked tremor, unsteadiness, uncoordination and vomiting and diarrhoea could indicate that the levels have become too high and the patient should contact their GP as soon as possible to take a blood sample to check the level. Paracetamol is thought to be safe and may be a good treatment for James’s headaches. For his inflamed ankle NSAIDs can be prescribed by the doctor, but are best taken regularly (to avoid irregular lithium levels) and only for short-term use. The lithium dose may need to be adjusted accordingly and close monitoring is essential.
Chapter 6 Anxiety disorders
Objectives

This chapter will enable you to:

- describe the symptoms of anxiety
- discuss the various neurotransmitters and physiological mechanisms involved in anxiety
- describe the clinical features of the major anxiety disorders
- list the main pharmacological and non-pharmacological treatments used in the treatment of anxiety
Chapter 6
Anxiety disorders

6.1 Introduction

Anxiety is a natural, usually self-limiting emotion. However in some people, anxiety can be subjectively intolerable and therefore disabling. It is then considered to be pathological, requiring treatment to enable the sufferer to resume a normal lifestyle.

In its pathological form, anxiety can present with a wide spectrum of symptoms, both physical (somatic) and psychological. Physical and psychological symptoms can reinforce each other, further exacerbating anxiety levels. Diagnosis is difficult; the sufferer may undergo a wide range of investigations to exclude an organic cause for their symptoms. Tackling both types of symptoms can be therapeutic.

Throughout this section, anxiety disorders will be considered under the following six headings:

- generalised anxiety disorder (GAD)
- phobic disorders
- panic disorder
- obsessive compulsive disorder (OCD)
- mixed anxiety and depression
- post-traumatic stress disorder (PTSD).

6.2 Prevalence of anxiety disorders

The prevalence of anxiety disorders in the UK adult population is shown in Table 6.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percentage of the population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td>Generalised anxiety disorder</td>
<td>5%</td>
</tr>
<tr>
<td>Phobic disorders</td>
<td>2%</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>1%</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>2%</td>
</tr>
<tr>
<td>Mixed anxiety and depression</td>
<td>10%</td>
</tr>
</tbody>
</table>

Data: OPCS 1995 household survey
6.3 Symptoms

Anxiety is a normal but unpleasant emotional state, varying in degree from mild unease to intense dread with impending doom. It is characterised by feelings of apprehension, uncertainty and fear and is associated with physiological, autonomic, biochemical, endocrine and behavioural changes.

When a person is suffering from clinical or pathological anxiety they may exhibit either physical or psychological symptoms, or a mixture of both and there is often no apparent reason for their distress. The symptoms of anxiety may easily be misdiagnosed as a physical complaint or they may mask a serious underlying psychiatric disorder.

### Exercise 9

The main symptoms associated with anxiety are listed in a table under four headings: psychological, somatic, respiratory and musculoskeletal. In the space provided, indicate what other diagnoses may be considered for those symptoms.

<table>
<thead>
<tr>
<th>Psychological symptoms of anxiety</th>
<th>Other possible diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor concentration</td>
<td>Sensitivity to noise</td>
</tr>
<tr>
<td>Bad dreams/night terrors</td>
<td>Repetitive worrying thoughts</td>
</tr>
<tr>
<td>Anticipation</td>
<td>Disturbed sleep</td>
</tr>
<tr>
<td>Difficulty in getting off to sleep</td>
<td>Fear</td>
</tr>
<tr>
<td>Restlessness</td>
<td>Irritability</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical/somatic symptoms of anxiety</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Throbbing in the neck</td>
<td>Palpitations</td>
</tr>
<tr>
<td>Nausea</td>
<td>Sweating</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>Chills</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>Trembling</td>
</tr>
<tr>
<td>Discomfort/pain over the heart</td>
<td>Awareness of missed beats</td>
</tr>
<tr>
<td>Butterflies in the stomach</td>
<td>Loose motions/diarrhoea</td>
</tr>
<tr>
<td>Excessive wind</td>
<td>Failure of erection</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>Amenorrhoea</td>
</tr>
<tr>
<td>Frequency/urgency of micturition</td>
<td>Loss of libido</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory symptoms of anxiety</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty with inhaling</td>
<td>Breathlessness</td>
</tr>
<tr>
<td>Parasthesia due to overbreathing</td>
<td>Tightness over the chest</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Fainting</td>
<td>Tingling in the hands and feet</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Musculoskeletal symptoms of anxiety</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Back ache</td>
<td>Neck ache</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*
6.4 The neurobiological basis of fear and anxiety

There appear to be two interlinked brain systems involved in fear and anxiety.

These are:
- the ‘defence system’ – controls responses to present dangers
- the ‘behavioural inhibition system’ – stops a person going into danger.

The defence system originates in the amygdala of the limbic system. The amygdala receives stimuli related to the threat of danger. The cortex and hippocampus assist the amygdala in interpreting these stimuli if necessary. The amygdala then alerts the hypothalamus (endocrine and autonomic responses) and the central grey matter of the brainstem (periaqueductal grey (PAG): emergency motor and autonomic responses, fear-related analgesia) and any other brain centres that are required for effective coping.

The defence system responds to both learned and unlearned threats and participates in the learning mechanism (conditioned responses). Through the PAG, it can initiate either ‘fear, fight or flight’ responses or, alternatively, ‘fear and freeze’ behaviour as appropriate. Electrical stimulation of the PAG causes patients to report the most extreme fear imaginable, with a conviction of impending death and an overwhelming desire to flee. On this and other evidence, the PAG is thought to be the likely seat of panic.

The behavioural inhibition system is thought to be based in the hippocampus and septum of the limbic system but has access to many other brain areas. It is the system responsible for avoidance behaviour.

As may be expected from the complexity of the brain’s anxiety systems, many different neurotransmitters are involved:
- noradrenaline (NA)
- serotonin (SHT)
- gamma aminobutyric acid (GABA)
- cholecystokinin (CCK)
- dopamine (DA)
- neuropeptide Y
- corticotrophin releasing factor (CRF).

Noradrenaline (NA)
Anxiety has been associated with abnormal noradrenergic activity especially in the locus coeruleus, which has projections into the defence and behavioural inhibition systems. Drugs which increase locus coeruleus firing, increasing the release of noradrenaline, such as yohimbine, carbon dioxide and caffeine, provoke anxiety in man, whilst the alpha-2-agonist clonidine, which reduces locus coeruleus activity, is modestly anxiolytic. It may be that susceptibility to anxiety disorders is mediated through a genetically determined, impaired presynaptic noradrenergic regulatory system.
Serotonin (5-HT)
The nature of the involvement of serotonin in anxiety is controversial. It modulates the activity of both the defence system and the behavioural inhibition system. Older theories worked on the assumption that serotonin systems are purely anxiogenic (anxiety-provoking). However none of the subtype-selective 5-HT receptor antagonists developed has yet proved to have clinically useful anxiolytic activity. The more recent ‘Graeff-Deakin hypothesis’ suggests that serotonin is predominantly anxiogenic in the limbic system and forebrain, while being anxiolytic in the PAG. Even this is likely to be an oversimplification as the pharmacological effects of anxiolytics, such as buspirone and the SSRIIs are immediate, while their clinical anxiolytic actions are delayed.

Gamma aminobutyric acid (GABA)
Gamma aminobutyric acid is a major inhibitory transmitter in the brain. GABAergic neurones are widespread throughout the CNS including all the areas involved in the control of fear/anxiety and arousal. It appears to be able to suppress both the defence system and the behavioural inhibition system. The amygdala is particularly sensitive to the GABA-potentiating effects of benzodiazepines. The PAG seems to be less sensitive and this may explain why higher doses of benzodiazepines are needed to treat panic states. Malfunction of the GABA response to stress could contribute to anxiety states in humans.

Cholecystokinin (CCK)
Cholecystokinin is particularly concentrated in those areas implicated in anxiety such as the cerebral cortex, hippocampus, hypothalamus and the PAG. It is also particularly associated with some dopamine and GABA-containing neurones. Intravenous injection of a CCK agonist has been shown to induce panic in healthy volunteers as well as in patients with panic disorder, whilst long-term treatment with imipramine reduced this effect. CCK release is modulated by several other transmitter systems including dopamine and serotonin. CCK antagonists are under investigation as possible therapeutic agents, particularly for the treatment of panic disorder.

Dopamine (DA)
Other than modulating the effect of other transmitter systems the role of dopamine in the aetiology of anxiety disorders remains unclear.

Neuropeptide Y
Neuropeptide Y has anxiolytic properties, as evidenced in animal studies. It is thought that CRF and neuropeptide Y may have opposite effects in the regulation and integration of fear mechanisms.

Corticotrophin Releasing Factor (CRF)
Corticotrophin releasing factor is widely distributed in the brain with the highest concentrations found in those areas that control the hypothalamo-pituitary axis (HPA). It is the primary activator of this axis during stress. It is also thought to play an important role in autonomic, neuroendocrine and behavioural responses to stress initiated by the amygdala.

Animal studies have shown it to have potent anxiogenic properties, and it is thought that CRF may be involved in the anxiety-related actions of other neurotransmitters. Cortisol release from the adrenal cortex is the end result of HPA activation. There are two types of cortisol receptor
in the brain and both play a role in stress/anxiety responses, for instance by modulating 5-HT receptor density.

### Exercise 10

**Neurobiological mechanisms of anxiety – true or false?**

Indicate in the space provided whether you think the following statements are true or false.

<table>
<thead>
<tr>
<th>True or false?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The pituitary body is particularly associated with the expression of anxiety.</td>
</tr>
<tr>
<td>2. GABAergic neurones are anxiogenic.</td>
</tr>
<tr>
<td>3. The cortex is the main site of action of many of the anxiolytics currently prescribed.</td>
</tr>
<tr>
<td>4. A person suffering from anxiety symptoms always suffers both somatic and psychological symptoms.</td>
</tr>
<tr>
<td>5. The PAG is the seat of panic.</td>
</tr>
<tr>
<td>6. If the physical symptoms of anxiety are alleviated the psychological symptoms will automatically remit.</td>
</tr>
<tr>
<td>7. Adrenaline is one of the main neurotransmitters associated with anxiety.</td>
</tr>
<tr>
<td>8. GABA CCK and Neuropeptide Y are all inhibitory transmitters.</td>
</tr>
<tr>
<td>9. Serotonin is predominantly anxiogenic in the limbic system and forebrain and anxiolytic in the PAG.</td>
</tr>
<tr>
<td>10. Anxiety is thought to be due to downregulation of 5-HT receptors.</td>
</tr>
<tr>
<td>11. CCK has anxiogenic properties.</td>
</tr>
<tr>
<td>12. Benzodiazepines exert their anxiolytic effect by opening a chloride ion channel which thus desensitises the neurone.</td>
</tr>
<tr>
<td>13. Neuropeptide Y is anxiolytic.</td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*
6.5 Presentation of anxiety disorders

**Generalised anxiety disorder (GAD)**

Generalised anxiety disorder is characterised by persistent, excessive anxiety, apprehension and worry, which must have been present for at least six months. It is a chronic condition with repeated acute-on-chronic episodes. Occasionally it is focused on something which is entirely trivial or non-consequential. Its onset is usually in early adulthood and it runs a chronic course, with a worse prognosis in females who are affected more often than men.

**Phobic disorders**

A phobia is an irrational fear which is out of all proportion to the situation or object at which it is directed. It is beyond voluntary control and although it is recognised by the sufferer as well as those around them as being excessive, it cannot be reasoned away.

A major phobia is agoraphobia, which is now used to describe a fear of any situation from where the subject sees no quick or easy means of escape.

Social phobia is an extreme, persistent fear of social occasions, especially where strangers are likely to be present. The individual fears that they may be the centre of attention and behave in a manner that will be embarrassing or humiliating, for example, blushing or fainting.

A simple, specific or isolated phobia is an extreme, persistent or irrational fear of a specific object or situation such as spiders, snakes, injections, blood, flying, heights, bridges, tunnels etc. Phobias that persist into adult life usually run a chronic course.

**Panic disorder (PD)**

Panic may occur as a component of any of the other anxiety disorders, but panic disorder is characterised by repeated, unpredictable attacks of severe anxiety which occur without warning and are unrelated to any specific situation. Autonomic symptoms predominate, peaking in severity within ten minutes. If a person prefers to go into an anxiety-provoking situation alone he is more likely to be suffering from a phobia than panic disorder.

**Obsessive compulsive disorder (OCD)**

Obsessive compulsive disorder (OCD) is characterised by:

- Time-consuming obsessions and compulsions which interfere with a person’s day-to-day functioning, work and relationships.
- The avoidance of things which trigger the compulsive behaviour.

Obsessions are thoughts, ideas, impulses or images which are unwelcome, persistent and recurrent. The sufferer realises they are absurd or irrational and a product of their mind but they are powerless to control them. Some common obsessions are:
- worrying about contamination with dirt or germs
- being overly concerned about symmetry or the orderly arrangement of things
- worrying about unusual sexual thoughts
- aggressive impulses
- concern about things one knows one should not worry about.

Compulsions are repetitive, purposeful actions, performed in response to an obsession, according to certain rules and designed to neutralise or prevent discomfort. The sufferer knows that his behaviour is unreasonable.

Common compulsions are:

- hand-washing
- cleaning
- counting
- checking
- touching
- rearrangement to achieve symmetry
- measuring
- hoarding
- needing to ask or confess.

If the compulsion is resisted, anxiety levels increase until it is resumed.

**Mixed anxiety and depressive disorder (MAD)**

This diagnosis is applied when symptoms of both anxiety and depression are present, but neither is sufficiently severe to justify a single diagnosis.

**Post-traumatic stress disorder (PTSD)**

The clinical features of this anxiety disorder involve an intense, prolonged and sometimes delayed response to a particular trauma such as a natural disaster, major fire, traffic accident, rape or major assault.

The condition is characterised by emotional numbness and detachment, which is followed by flashbacks, recurring memories and vivid dreams. There is obvious distress on re-exposure leading to avoidance of similar circumstances.

An exceptionally stressful event is essential for this particular diagnosis, but the sufferer may not have been harmed physically themselves nor even been personally threatened. Those involved in other ways, for example bystanders or members of the rescue services, are also at risk. Not all those directly involved may be equally affected, which suggests that a degree of personal vulnerability is required. This may be genetic or acquired later in life.
6.6 Management of anxiety

On 6 December 2004, NICE issued a guideline on the management of anxiety in primary, secondary and community care.

*NICE guideline: CG22 Anxiety: management of generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults in primary, secondary and community care.*

www.nice.org.uk/pdf/CG022NICEguideline.pdf

The guideline on anxiety recognises that whilst medication has an important role to play, there are also many effective alternatives. It recommends that patients should be offered any of the following three types of intervention, taking into account patient preference. In descending order of long-term effectiveness, these interventions are:

- psychological therapy, such as CBT
- medication, such as an SSRI licensed for generalised anxiety disorder
- self-help, such as the use of written materials based on CBT principles

The guideline also recommends:

- Involving individuals in an effective partnership with healthcare professionals, with all decision making being shared, improves outcomes.
- Access to information, including support groups, is a valuable part of any package of care.
- There are positive advantages of services for people with anxiety being based in primary care rather than in a hospital setting.

Therapies for anxiety can be divided into:

- Pharmacological – single and combined treatments
- Non-pharmacological – psychological
- Combinations of pharmacological and non-pharmacological treatments
- Psychosurgery (not covered here).

**Pharmacological treatments for anxiety**

The following have all been used to treat anxiety symptoms:

- barbiturates
- propanediols
- benzodiazepines
- beta-blockers
- azaspirodecanediones
- antipsychotics
- tricyclic antidepressants (TCAs)
- selective serotonin reuptake inhibitors (SSRIs)
- monoamine oxidase inhibitors (MAOIs)
- reversible inhibitors of monoamine oxidase type A (RIMAs)
- sodium valproate
- antihistamines.
The first two groups, although rarely used now, set the scene for the history and progress of anxiety treatment.

**Barbiturates**

The barbiturates, like the benzodiazepines, are GABA-A receptor potentiators. When the chloride ion channel is opened by GABA, a barbiturate molecule enters and ‘props it open’ for a considerable time. This means that barbiturates can cause a massive potentiation of GABAergic effects. Because of their low therapeutic index and high dependence risk, barbiturates are now considered unsuitable for the treatment of anxiety.

**Propanediols**

Although their chemical structure is different from that of the benzodiazepines, propanediols also act on the benzodiazepine receptor. However, they are less effective anxiolytics than the benzodiazepines and are now rarely used. Due to their particularly strong muscle relaxant effect they have occasionally been useful when anxiety is accompanied by severe muscle tension. Meprobamate is a propanediol but it has been shown to have an abuse potential and as a result is now classified as a controlled drug. It is therefore rarely used.

**Benzodiazepines**

Until relatively recently, the commonest approach to a presentation of anxiety was to prescribe a benzodiazepine and historically they have been considered first-line treatment. However, their use has been associated with significant long-term problems and the Committee on Safety of Medicines (CSM) issued the following guidance concerning the use of benzodiazepines.

‘Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling or subjecting the patient to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness. The use of benzodiazepines to treat short-term ‘mild’ anxiety is inappropriate and unsuitable.’

Benzodiazepines have long been known to cause sedation, impair psychomotor function and to release aggression in susceptible individuals. Some people can also become dependent on them and they have the capacity to cause psychological impairment after long-term use. When taken chronically they not only lose much of their therapeutic efficacy but they may also produce a wide range of adverse effects.

Despite this, benzodiazepines remain the most effective remedy for acute, transient anxiety. They potentiate the effects of GABA by binding to a specific site, the benzodiazepine receptor, located on the GABA-A/chloride receptor complex. They act by increasing the affinity of the GABA site, making it easier for GABA to open the chloride channel. As a result, the channel opens more frequently. Unlike barbiturates, benzodiazepines require the continued presence of GABA, which puts a limit on their effects. For this reason they have a much more favourable therapeutic index than the barbiturates.

Benzodiazepines with a high potency and a long half-life are best for the relief of anxiety as they are less likely to cause withdrawal problems. For this reason diazepam, with a half-life of 14 – 17 hours and active metabolites giving a half-life of up to 72 hours, is particularly suitable.

Respiratory insufficiency may occur during treatment with benzodiazepines, especially when respiration is impaired for other reasons, such as in asthma or chronic obstructive airways disease.
**Beta-adrenergic blockers**

These are used primarily to treat the somatic or physical symptoms of anxiety. They control palpitations, tremor, sweating and shortness of breath and are therefore likely to be ineffective in patients in whom the psychological aspects of anxiety predominate.

Side-effects include fatigue, reduced work capacity and sexual dysfunction. Sleep disturbance with nightmares has also been reported particularly with propranolol.

Beta-blockers may be used in combination with more specifically centrally acting anxiolytics to cover the full range of symptoms. Of the beta-blockers, only propranolol and oxprenolol are licensed for the treatment of anxiety. Atenolol is also frequently prescribed. Despite all of this however, the evidence base for the efficacy of beta-blockers in the treatment of anxiety remains weak.

**Azaspirodecanediones**

Buspirone is the only azaspirodecanedione currently available in the UK. It is a partial agonist at the inhibitory 5-HT$_{1A}$ auto-receptors and in this way inhibits 5-HT transmission. This effect however occurs quite rapidly while the clinical anxiolytic effect takes some weeks to develop. It is thought that repeated treatment with buspirone may desensitise these receptors and this together with a modest post-synaptic 5-HT$_{1A}$ agonist effect may lead to an overall increase in 5-HT transmission. This is consistent with the perceived mechanism of action and the delayed clinical effect of both the TCAs and SSRIs.

Buspirone has a short elimination half-life but a slower onset of action than the benzodiazepines, taking at least two weeks to show an effect. It is therefore not suitable for the treatment of acute or transient anxiety states and is not effective in the treatment of panic disorder. Although it is only licensed for short-term use, in order to prevent relapse, treatment may be required for several months after the anxiolytic effect has become apparent. Optimum dosage is suggested to be between 60 mg and 90 mg per day, however the maximum licensed dose is 45 mg daily. Doses of 30 mg or less have been shown to be no better than placebo.

Side-effects including drowsiness, dizziness, headache, nausea, restlessness, nervousness, light-headedness and excitement occur most commonly at the beginning of treatment.

**Antipsychotics**

The mechanism of the anxiolytic action of the antipsychotics is uncertain and may be related to their well-known effect of causing emotional blunting. They will also reduce agitation. Used at about one fifth of their antipsychotic dose, certain members of this group, such as haloperidol, flupentixol, promazine, trifluoperazine and previously thioridazine may be useful anxiolytics with a relatively fast onset of action.

Extrapyramidal side-effects are rare but not unknown at this dose, so the risk of tardive dyskinesia in the long term must always be considered. Drowsiness and lethargy are also possible as is hypotension, especially in the elderly and frail. Many of these antipsychotics have significant anticholinergic profiles which further limits their usefulness in this group of patients particularly those at risk of cognitive decline.

Use of some of the atypical antipsychotics for the treatment of anxiety symptoms on an ‘as required’ basis is a recent phenomenon despite the lack of an evidence base for this. The effect seen is likely to be one of mild sedation as a result of their action at histamine H$_1$ receptors, rather than a specific anxiolytic effect. They are not included in the NICE guidance.
Tricyclic antidepressants (TCAs)
Tricyclic antidepressants appear to be effective in the treatment of certain forms of anxiety, including generalised anxiety disorder and panic disorder, although these are not licensed indications for most of these agents. They have been particularly useful in cases of mixed anxiety/depression but their anxiolytic effect is more likely to be attributable to their sedative effects rather than to significant specific anxiolytic activity. The exception to this is clomipramine which has additional licenses for the treatment of obsessional and phobic states, due to its potency at the serotonergic receptor resulting in an increase in 5-HT transmission within the CNS. Like the antidepressant effect, it takes two to three weeks for the anxiolytic effect to be apparent. Panic attacks may become more frequent during this initial lag-phase.

Side-effects such as dry mouth, blurred vision, constipation and sedation may be a problem at the beginning of treatment while weight gain and sexual dysfunction can cause difficulties later.

Plasma levels of TCAs are increased by phenothiazines, disulfiram, cimetidine and calcium channel blockers. They should not normally be prescribed with MAOIs. Clomipramine is particularly dangerous when combined with certain members of this group such as tranylcypromine.

Selective serotonin reuptake inhibitors (SSRIs)
These compounds specifically inhibit the re-uptake of 5-HT (serotonin) which occurs early in treatment. Like the antidepressant effect, the anxiolytic action takes some weeks to develop fully. For full enhancement of 5-HT transmission it may also be necessary for the 5-HT₁A inhibitory receptors to be desensitised. This is thought to occur only after continued treatment.

Gastrointestinal disturbances and sexual dysfunction are common and weight loss can occur initially with fluoxetine. Transient insomnia, agitation and anxiety have occurred at the beginning of treatment to the extent that some patients have to be encouraged to continue with the medication. Treatment is usually long-term and to be fully effective doses sometimes need to be at the higher end of the dosage scale.

In order to overcome any initial increase in anxiety symptoms and thus to improve compliance the initial dosage should be as low as possible, building up only gradually to the optimum dose according to the patient’s tolerance. This is especially true for patients with panic disorder. In some cases it may be prudent to prescribe a short course of a suitable benzodiazepine to cover the first two or three weeks of treatment when an exacerbation of anxiety may be unacceptable.

In view of the relative lack of troublesome side-effects, safety, lack of abuse potential and dependence, members of this group are particularly suitable for long-term treatment.

Extrapyramidal side-effects have been reported with paroxetine as has a discontinuation syndrome when it has been stopped abruptly. The additional licensed indications of the SSRI antidepressants are summarised in Table 7 overleaf.
**Table 7 Additional licensed indications for the treatment of anxiety disorders with the newer antidepressants**

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Anxiety with depression</th>
<th>GAD</th>
<th>Panic disorder</th>
<th>OCD</th>
<th>Social phobia</th>
<th>PTSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Females only</td>
</tr>
<tr>
<td>Citalopram</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Clinically important interactions have been reported between the SSRIs and warfarin, anticonvulsants and antipsychotics. They may increase the plasma levels of the TCAs and should not be prescribed in conjunction with an MAOI which may only be started two weeks after an SSRI has been discontinued (five weeks for fluoxetine).

**Monoamine oxidase inhibitors (MAOIs)**

Certain members of this group of antidepressants are thought to have additional anxiolytic effects. Some patients with resistant morbid anxiety, particularly if phobic symptoms are also present, may respond when all else has failed.

MAOIs such as phenelzine and tranylcypromine irreversibly inhibit both types of monoamine oxidase leading to serious consequences when foods rich in tyramine such as cheese or Marmite are consumed. Clinically significant interactions involving dangerous hypertensive effects can occur when MAOIs are combined with sympathomimetics, L-dopa and opiate analgesics. Serotonin syndrome may occur if they are taken with an SSRI or clomipramine.

Side-effects include insomnia, dizziness and postural hypotension with weight gain and sexual dysfunction occurring after long-term use. Their side-effect profile, potential interactions and essential dietary precautions limit the usefulness of this group.

Reference should be made to the current British National Formulary (BNF) in relation to the appropriate ‘wash out’ periods required before and after treatment with an MAOI.

**Reversible inhibitors of monoamine oxidase type A (RIMAs)**

Moclobemide is the only RIMA currently available in the UK. They are reversible inhibitors of monoamine oxidase type A only. This means there is no significant interaction with moderate amounts of tyramine-containing foods.

Moclobemide has definite safety advantages over conventional MAOIs, but its anxiolytic effect is not proven. It is not licensed for the treatment of anxiety.

Side-effects include insomnia, headache and nausea. The pressor effects of sympathomimetics may be enhanced by moclobemide and it should not be used with antidepressants that potentiate the effects of 5-HT.
Sodium valproate
Although not licensed for the treatment of anxiety, sodium valproate has recently been reported to be effective in certain of the anxiety disorders. This might be expected from its ability to potentiate GABA.

Sodium valproate has been used in generalised anxiety disorder and has been shown in a small case series to be useful in panic disorder.

Antihistamines
Antihistamines have been considered by some to be appropriate alternatives to thioridazine, particularly promethazine and trimeprazine. However, they are not licensed for anxiety and any benefits seen may be a reflection of their sedative properties, rather than a true anxiolytic effect. Alternatively, hydroxyzine may be considered since it is an antihistamine with an additional licence for the treatment of short-term anxiety.

Combined pharmacological treatments
Combination therapy is often better than any single agent alone. For instance panic disorder is sometimes effectively treated with an SSRI and a benzodiazepine together for the first three to four weeks. Once the antidepressant is working then the benzodiazepine can be tailed off over one or two weeks without complication. Similarly, beta-blockers and benzodiazepines can usefully be used together to address the whole range of symptoms, with the benzodiazepine being gradually withdrawn once the somatic symptoms, are under control. Other useful combinations may be MAOIs and benzodiazepines for social phobia and panic disorder and an SSRI with either buspirone or a benzodiazepine for GAD and resistant panic disorder.

www.bap.org.uk/consensus/anxiety_disorders.html

Non-pharmacological strategies in the treatment of anxiety disorders
Specialised psychological treatment may not be readily available in primary care and elsewhere there may be long waiting lists. Often brief counselling and structured problem-solving techniques are effective and these may be available from the GP. Anxiety management techniques and relaxation tapes may also be of use. These are more generally available.

It would appear that for the majority of anxiety disorders a combination of drug and non-drug strategies, when available, is the ideal approach.

The symptoms of anxiety can occur in three body systems:

- physical (mainly due to stimulation of the autonomic nervous system)
- behavioural (e.g. avoidance behaviours or a constant need for reassurance)
- cognitive (unpleasant thoughts, themselves anxiety provoking).

These three systems constantly interact. Cognition worsens the physical symptoms which in turn contribute to behavioural changes, which then affect cognition and so on.
The following psychological tools are amongst those available for the treatment of the various anxiety states:

- simple psychotherapy
- relaxation training
- behavioural therapy
- cognitive therapy
- cognitive behavioural therapy.

**Simple psychotherapy**
The nature and prognosis of the disorder as well as the origin of the symptoms are carefully explained to the patient. Simple support is usually sufficient to help the patient overcome his symptoms with only a minimal amount of medication if they have been triggered by a temporary problem or a curable physical illness.

**Relaxation training**
A form of relaxation training is useful for many anxious patients. It aims to train an individual to reduce their anxiety-provoking response to stress. Relaxation therapy may also be of benefit. Various techniques may be employed including hypnosis, massage, yoga and transcendental meditation.

**Behavioural therapy**
Behavioural therapy is used to treat patients with specific phobias which are accompanied by marked avoidance of a feared situation. ‘Desensitisation’ or ‘graded exposure’ is a graduated approach in which only minimal anxiety is allowed to develop, by teaching the patient to confront the feared situation under controlled conditions using relaxation therapy to diminish their anxiety.

In contrast ‘flooding’ allows marked anxiety to develop through encounters with extreme phobic situations from the beginning of treatment. The sufferer is exposed to the feared situation or object directly until the anxiety response is overcome. This approach is quicker than desensitisation therapy, but its suitability for a particular individual will depend upon their age, physical condition and motivation.

**Cognitive restructuring/cognitive therapy**
These techniques are aimed at altering the way a person perceives himself and the outside world as well as the way he thinks. They involve training the individual to identify thoughts or beliefs that have previously been associated with anxiety and to change these into more positive and helpful thought patterns.

**Cognitive behavioural therapy (CBT)**
This is a strategy which combines elements of both behavioural and cognitive therapy. Rational analysis of symptoms, talking through difficult occasions, encouragement to make positive self-statements, facing up to, rather than avoiding problems, are all methods used to demonstrate the self-limiting nature of attacks.

Computerised CBT (CCBT) is now available and is an attractive proposition in primary care since it is cost-effective and does not require a skilled professional. In February 2006, NICE issued
guidance (Technology Appraisal Guidance Number 97) on the use of CCBT, which was a review from their earlier guidance from 2002. The re-appraisal of the use of CCBT for depression and anxiety recommends two CCBT packages: ‘Beating the Blues’ for the management of mild and moderate depression and ‘Fearfighter’ for the management of panic and phobia.

**Combined pharmacological and psychological treatments**

Combinations of pharmacological and psychological treatments may have advantages or disadvantages for the patient. Combined pharmacological and psychological treatments have been shown to be of benefit in the treatment of OCD, panic disorder, agoraphobia and GAD.

On the other hand, medication may reduce the symptoms to a point where the patient stops the psychological treatment because he believes it is not necessary or an anxiolytic may impair learning, memory and concentration to the point where psychological treatments lose their effectiveness.

A summary of treatment choices is presented in Table 8.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Possible medication</th>
<th>Psychological therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute stress</td>
<td>Benzodiazepines – short course</td>
<td></td>
</tr>
<tr>
<td>GAD</td>
<td>Buspirone, TCAs /SSRIs, Beta-blockers, Benzodiazepines, Venlafaxine SR</td>
<td>Psychotherapy, CBT, Relaxation, Anxiety management</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>TCAs/SSRIs, Benzodiazepines and SSRIs, MAOIs? Valproate? Inositol?</td>
<td>CBT</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>Benzodiazepines – short course</td>
<td>Behavioural therapy, Group therapy, CBT</td>
</tr>
<tr>
<td>Social phobia</td>
<td>MAOIs/RIMAs, MAOIs and benzodiazepines</td>
<td>Behavioural therapy</td>
</tr>
<tr>
<td>Specific phobias</td>
<td>Medication is not effective</td>
<td>Behavioural therapy</td>
</tr>
<tr>
<td>PTSD</td>
<td>TCAs/SSRIs</td>
<td>Psychotherapy, Counselling</td>
</tr>
<tr>
<td>OCD</td>
<td>TCAs/SSRIs</td>
<td>CBT</td>
</tr>
<tr>
<td>Performance anxiety</td>
<td>Beta-blockers</td>
<td></td>
</tr>
</tbody>
</table>
## Exercise 11

<table>
<thead>
<tr>
<th>True or false?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A person who suffers from social phobia will always sit at the back of a crowded room if they can.</td>
</tr>
<tr>
<td>2. The optimum dose of an SSRI in the treatment of panic disorder is usually half the optimum antidepressant dose.</td>
</tr>
<tr>
<td>3. Chronic treatment with buspirone can lead to tolerance.</td>
</tr>
<tr>
<td>4. GAD occurs typically for the first time in middle age.</td>
</tr>
<tr>
<td>5. Isobel tends to panic when her daughter is late home from school. Therefore she must suffer from panic disorder.</td>
</tr>
<tr>
<td>6. Psychological strategies in the management of phobias tend to work better than medication.</td>
</tr>
<tr>
<td>7. There is a genetic component to the aetiology of panic disorder.</td>
</tr>
<tr>
<td>8. For an accurate diagnosis of GAD DSM-IV requires the symptoms to have been present for three months.</td>
</tr>
<tr>
<td>9. Phobias respond well to medication.</td>
</tr>
<tr>
<td>10. Monamine oxidase inhibitors may be effective in the treatment of panic disorder.</td>
</tr>
<tr>
<td>11. Antipsychotics may be useful in the treatment of GAD.</td>
</tr>
<tr>
<td>12. Agoraphobia is a fear of farmers.</td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*
Case study 5

Maggie
Maggie sits in the doctor’s surgery wringing her hands and crossing and uncrossing her legs. She is complaining of upper epigastric pain which persists despite her trying every antacid on the chemist’s shelves. She has had several endoscopies, none of which revealed any abnormality. She has also mentioned lower back pain and numerous headaches which do not seem to respond to the common analgesics.

She is a frequent visitor to the doctor who can never find anything wrong with her. She says she is worried about the future, but cannot explain why exactly. Every time she thinks about it her heart races and she breaks out in a cold sweat. Sometimes she thinks she is going to have a heart attack. The doctor tells her she should go out more and find a hobby to occupy her time. She replies that she never feels well enough. He reassures her that nothing is wrong, but knows full well that she will be back to see him very soon. She has been like this for the last two years ever since her son got married.

What diagnosis might you suggest for Maggie?

What supports this suggestion?

What would you suggest the doctor might prescribe for Maggie? Give your reasons.

Is there any other help that might be available?

Turn to the end of the chapter for suggested answers
Summary

Anxiety is a normal response to danger but pathological anxiety can lead to profound personal distress and grossly impaired functioning. Anxiety presents in many ways, from the chronic, pervasive, exaggerated response to everyday stressors characterised by generalised anxiety disorder, to the acute, intense, irrational fear associated with phobias. Cognitive symptoms are often accompanied by physical symptoms and frequently lead to adaptive behaviours which further reinforces the individual’s state of anxiety.

Psychological therapies are more effective than pharmacological treatments in the long-term management of anxiety states, but drug therapy remains a valuable treatment modality, alone or in combination with non-drug interventions, for many individuals.

Learning Outcomes

On completion of this section you should be able to:
1. Identify the symptoms of anxiety.
2. Discuss the various neurotransmitters and physiological mechanisms involved in anxiety.
3. Identify and appreciate the clinical features of the major anxiety disorders.
4. Make use of the main pharmacological and non-pharmacological therapies used in the treatment of anxiety as appropriate to your practice.

Further reading


<table>
<thead>
<tr>
<th>Psychological symptoms of anxiety</th>
<th>Other possible diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor concentration</td>
<td>Sensitivity to noise</td>
</tr>
<tr>
<td>Bad dreams/night terrors</td>
<td>Repetitive worrying thoughts</td>
</tr>
<tr>
<td>Anticipation</td>
<td>Disturbed sleep</td>
</tr>
<tr>
<td>Difficulty in getting off to sleep</td>
<td>Fear</td>
</tr>
<tr>
<td>Restlessness</td>
<td>Irritability</td>
</tr>
<tr>
<td></td>
<td>Depression, Dementia, Schizophrenia, Drug/alcohol abuse or withdrawal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical/somatic symptoms of anxiety</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Throbbing in the neck</td>
<td>Palpitations</td>
</tr>
<tr>
<td>Nausea</td>
<td>Sweating</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>Chills</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>Trembling</td>
</tr>
<tr>
<td>Discomfort/pain over the heart</td>
<td>Awareness of missed beats</td>
</tr>
<tr>
<td>Butterflies in the stomach</td>
<td>Loose motions/diarrhoea</td>
</tr>
<tr>
<td>Excessive wind</td>
<td>Failure of erection</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>Amenorrhoea</td>
</tr>
<tr>
<td>Frequency/urgency of micturition</td>
<td>Loss of libido</td>
</tr>
<tr>
<td></td>
<td>Cardiac problem, Hiatus hernia, Menopausal problems, UTI, Gastric ulcer, Thyrotoxicosis, Phaeochromocytoma, Hypoglycaemia, Excessive caffeine intake</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory symptoms of anxiety</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty with inhaling</td>
<td>Breathlessness</td>
</tr>
<tr>
<td>Parasthesia due to overbreathing</td>
<td>Tightness over the chest</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Faintness</td>
<td>Tingling in the hands and feet</td>
</tr>
<tr>
<td></td>
<td>Asthma, Chronic obstructive pulmonary disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Musculoskeletal symptoms of anxiety</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Back ache</td>
<td>Neck ache</td>
</tr>
<tr>
<td>Headache</td>
<td>Back problems</td>
</tr>
<tr>
<td></td>
<td>Neuralgia</td>
</tr>
<tr>
<td>Exercise 10 (page 117)</td>
<td>True or false?</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>1. The pituitary body is particularly associated with the expression of anxiety.</td>
<td>False</td>
</tr>
<tr>
<td>2. GABAergic neurones are anxiogenic.</td>
<td>False</td>
</tr>
<tr>
<td>3. The cortex is the main site of action of many of the anxiolytics currently prescribed.</td>
<td>False</td>
</tr>
<tr>
<td>4. A person suffering from anxiety symptoms always suffers both somatic and psychological symptoms.</td>
<td>False</td>
</tr>
<tr>
<td>5. The PAG is the seat of panic.</td>
<td>True</td>
</tr>
<tr>
<td>6. If the physical symptoms of anxiety are alleviated the psychological symptoms will automatically remit.</td>
<td>False</td>
</tr>
<tr>
<td>7. Adrenaline is one of the main neurotransmitters associated with anxiety.</td>
<td>False</td>
</tr>
<tr>
<td>8. GABA CCK and Neuropeptide Y are all inhibitory transmitters.</td>
<td>False</td>
</tr>
<tr>
<td>9. Serotonin is predominantly anxiogenic in the limbic system and forebrain and anxiolytic in the PAG.</td>
<td>True</td>
</tr>
<tr>
<td>10. Anxiety is thought to be due to downregulation of 5-HT receptors.</td>
<td>False</td>
</tr>
<tr>
<td>11. CCK has anxiogenic properties.</td>
<td>True</td>
</tr>
<tr>
<td>12. Benzodiazepines exert their anxiolytic effect by opening a chloride ion channel which thus desensitises the neurone.</td>
<td>False</td>
</tr>
<tr>
<td>13. Neuropeptide Y is anxiolytic.</td>
<td>True</td>
</tr>
</tbody>
</table>
## Exercise 11 (page 128)

<table>
<thead>
<tr>
<th>Exercise</th>
<th>True or false?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A person who suffers from social phobia will always sit at the back of a crowded room if they can.</td>
<td>True</td>
</tr>
<tr>
<td>2. The optimum dose of an SSRI in the treatment of panic disorder is usually half the optimum antidepressant dose.</td>
<td>False</td>
</tr>
<tr>
<td>3. Chronic treatment with buspirone can lead to tolerance.</td>
<td>False</td>
</tr>
<tr>
<td>4. GAD occurs typically for the first time in middle age.</td>
<td>False</td>
</tr>
<tr>
<td>5. Isobel tends to panic when her daughter is late home from school. Therefore she must suffer from panic disorder.</td>
<td>False</td>
</tr>
<tr>
<td>6. Psychological strategies in the management of phobias tend to work better than medication.</td>
<td>True</td>
</tr>
<tr>
<td>7. There is a genetic component to the aetiology of panic disorder.</td>
<td>True</td>
</tr>
<tr>
<td>8. For an accurate diagnosis of GAD DSM-IV requires the symptoms to have been present for three months.</td>
<td>False</td>
</tr>
<tr>
<td>9. Phobias respond well to medication.</td>
<td>False</td>
</tr>
<tr>
<td>10. Monamine oxidase inhibitors may be effective in the treatment of panic disorder.</td>
<td>True</td>
</tr>
<tr>
<td>11. Antipsychotics may be useful in the treatment of GAD.</td>
<td>True</td>
</tr>
<tr>
<td>12. Agoraphobia is a fear of farmers.</td>
<td>False</td>
</tr>
</tbody>
</table>
Case study 5 – Maggie (page 129)

What diagnosis might you suggest for Maggie?

Generalised anxiety disorder.

What supports this suggestion?

- She appears anxious and apprehensive in her body language.
- She is worried but does not really know why.
- She has several somatic symptoms which do not appear to have a physical cause.
- She has been the same for a long time.
- Her ‘perceived ill health’ is stopping her enjoying life.

What would you suggest the doctor might prescribe for Maggie? Give your reasons.

A chronic treatment for generalised anxiety disorder such as an SSRI, buspirone or possibly venlafaxine. An SSRI might cause an initial exacerbation of some of her symptoms and should be started cautiously – a short course of diazepam may be needed initially. Buspirone may take some time to be effective but would not exacerbate her symptoms – this delay would probably not matter in view of the chronicity of her condition. At an effective dose it would be more expensive than an SSRI.

Is there any other help that might be available?

A therapist or CPN might be available to offer anxiety management or relaxation training.
Chapter 7  Sleep disorders
Objectives

This chapter will enable you to:

● describe a normal sleep pattern
● relate examples of the factors which can affect sleep patterns
● describe the non-pharmacological treatment strategies for insomnia
● advise on appropriate pharmacological treatment of insomnia
● discuss the NICE guidance on the use of the ‘Z’ hypnotics
● discuss the presentation and management of some other sleep disorders
Sleep is a vital biological process that is necessary to restore both body and mind. It is usually taken for granted, unless it is disturbed. Sleep disorders, although not dangerous in themselves, have a profound effect on quality of life, relationships, employment and personal safety.

Wakefulness and sleep are controlled by specific nuclei embedded in the mid-brain and hind-brain. Sleep patterns are generally linked to environmental changes – primarily the day–night cycle. Neurotransmitters such as serotonin (5-HT), noradrenaline, acetylcholine and gamma-aminobutyric acid are all thought to be implicated in the sleep–wake cycle.

Sleep is encouraged by the absence of provoking stimuli. These sensory stimuli stimulate the Reticular Activating System (RAS), especially if they are intense, varying or meaningful. Activation of the RAS opposes sleep processes.

Studies have identified a pattern consisting of five different stages of sleep which can be divided into two distinct physiological states known as rapid eye movement (REM) and non-rapid eye movement (non-REM) sleep.

**REM sleep**

Is characterised by rapid sweeping of the eyes under the eyelids. During this phase blood circulation to the brain is increased, dreaming is common and the brain shows a high level of activity. A person in REM sleep is in the deepest stage of sleep and difficult to wake. REM sleep is thought to be associated with the restoration of memory, the repair of brain tissue and the laying down of memories.

**Non-REM**

Sleep can be divided into four stages characterised by a gradual slowing of electrical activity within the brain, progressive relaxation of the muscles and slower more regular breathing:

**Stage 1**  
Starts with yawning and the eyes beginning to feel heavy, represents the transition from wakefulness to sleep

**Stage 2**  
Represents the first real stage of deep sleep
**Stages 3 and 4**
Initially occur about an hour after falling asleep and are collectively known as ‘slow wave sleep’ or ‘deep sleep’.

**A normal sleep pattern**
Cycling between REM and non-REM sleep continues during a normal night in periods of approximately ninety minutes. This pattern is referred to as ‘sleep architecture’. Progressively shorter and shorter cycles of non-REM sleep are interspersed with lengthening periods of REM sleep, which ensures that both body and mind are rested and refreshed on waking. During sleep deprivation, non-REM sleep outweighs REM sleep. This disturbs the sleep architecture, leaving the sufferer feeling tired and unrefreshed on waking.

**What is a good night’s sleep?**
There is considerable individual variation in the normal sleep pattern. What seems to be important is not the actual time spent sleeping but the balance between non-REM and REM sleep; that is the quality of sleep or sleep architecture.

The need for sleep is at least in part influenced by daytime activity, the need for growth and basal metabolic rate. People whose metabolic rate is naturally high during the day have more non-REM slow wave sleep and sleep longer than people whose metabolic rates are lower. Infants have the most slow wave sleep and the amount declines with age, paralleling the decline in cerebral and body metabolism that accompanies old age. For instance, sleep time at night is reduced to about six hours in a 70-year-old with daytime napping reducing it even further. Old people also have much less slow wave sleep and more awakenings after they have gone to sleep.

Although sleeplessness is common, it is by no means trivial. Difficulty in sleeping can be extremely distressing to the individual, as can the consequences of a lack of sleep. Sometimes merely the fear of not being able to get to sleep is enough to prevent the onset of sleep.

Sleeplessness can manifest itself in a variety of ways:
- difficulty in falling asleep – problems with sleep latency
- waking during the night several times
- prolonged periods of wakefulness during the night
- early morning waking
- waking in the morning not feeling refreshed.

About one third of all adults will report one or more of the above sleep problems and, in addition to those who suffer from the above temporary bouts of sleeplessness, there are those people who suffer from chronic or prolonged insomnia lasting many months or years. This can be severe and disabling.
7.2 Insomnia

Insomnia is characterised by difficulty initiating or maintaining sleep. It can be caused by a wide range of factors. See Table 9 below for some examples of the causes of insomnia.

Table 9 Causes of insomnia

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>Ageing, pregnancy, medical disorders – pain, incontinence or the fear of incontinence, a UTI, coughing/wheezing, pruritus, nocturnal angina, orthopnoea from CHF, menstrual cycle</td>
</tr>
<tr>
<td>Psychiatric illness</td>
<td>Depression, anxiety, hypomania, panic, dementia, PTSD</td>
</tr>
<tr>
<td>Dietary factors</td>
<td>Caffeine, alcohol, chocolate</td>
</tr>
<tr>
<td>Social/psychological</td>
<td>Bereavement, work stress, financial worries, relationship difficulties</td>
</tr>
<tr>
<td>Environmental</td>
<td>Noise, cold, heat, a snoring partner, a restless partner, small children, staying up late or coming home late, allergies (to mattress etc)</td>
</tr>
<tr>
<td>Sleep/wake cycle disturbance</td>
<td>Shift work, jet lag</td>
</tr>
<tr>
<td>Drugs – direct effect</td>
<td>CNS stimulants</td>
</tr>
<tr>
<td>Drugs – chronic use</td>
<td>Cardiovascular drugs, beta-blockers, some antidepressants</td>
</tr>
<tr>
<td>Drugs – withdrawal</td>
<td>Opioids, benzodiazepines</td>
</tr>
</tbody>
</table>

Insomnia is rarely a diagnosis in its own right – it is usually a symptom of some other condition. There are two aids to assist in establishing a diagnosis and identifying possible aetiological factors when presented with an individual complaining of problems sleeping. The first is to take a detailed sleep history. Areas of enquiry include the following:

- nature of the specific sleep problem
- onset, duration and cause of symptoms
- 24-hour sleep-wake cycle
- daily routine, dietary habits, lifestyle
- drug use, prescribed and illicit
- psychiatric/medical history
- family history of sleep disorder
- psychological profile
- life events
- current social situation.

It is also important at this stage to try to elicit any signs or symptoms of anxiety or depression and to assess the patient for any physical disorder that may be causing them night-time discomfort.
A sleep history such as this will reveal most of the cardinal signs and symptoms of the common sleep disorders. Information from a partner or carer may also be of use here. A small minority of patients may require polysomnography or other special laboratory investigation for an accurate diagnosis. It is also often helpful to send the patient away with a sleep diary in which they record details of their routine.

Insomnia may be classified according to duration into:

**Transient**  
*Lasting only a few days.*  
This is usually situational and may be the result of jet-lag, short-term hospitalisation or minor stress. It is usually self-limiting, not requiring treatment. It may also be a case of rebound insomnia caused by withdrawal from hypnotic or anxiolytic drugs, particularly the benzodiazepines.

**Short term**  
*Lasting one to four weeks.*  
This may be caused by such things as shift work, illness or bereavement. It usually ceases when the cause is removed. If there is an underlying physical or psychiatric problem then this should be treated accordingly.

**Chronic or long term**  
*Lasting for more than a month.*  
This can be caused by any of the factors identified in Table 7, but more often results from long-standing poor sleeping habits (poor sleep hygiene). In a minority of insomniacs this may have started in infancy. In such individuals there may be a ‘conditioned insomnia’ where their whole routine of going to bed and trying to sleep has become associated with a low expectation of success.

**Is lack of sleep harmful?**

Many people worry because they fear lack of sleep will do them mental or physical harm. Reassurance can be valuable here. Insomnia is very unpleasant and it can lead to a lack of alertness the next day but it is not harmful in itself. The sufferer should be aware that they are at extra risk in performing tasks that require concentration, just as if they had taken a sedative but apart from that, insomnia does no actual harm.

**Insomnia and depression**

There is a complicated relationship between depression and sleep. Insomnia is a feature of depression and untreated insomnia may lead to depression. Medicines that are known to cause depression often directly cause insomnia. It is not always easy to distinguish between drug-induced insomnia and persistent insomnia that occurs as part of an underlying condition. This controversy is compounded by the fact that in the past depression has been treated by sleep deprivation.

Typical sleep problems associated with depression include:

- difficulty in falling asleep
- early REM onset
increased REM sleep duration
intermittent wakefulness during the night
reduced slow-wave sleep
reversal of the slow-wave distribution in the first and second sleep cycle
early morning wakening
not feeling refreshed after sleep.

Some antidepressants, but not the SSRIs, have an immediate effect on sleep, in most cases resulting in REM sleep suppression and in some cases causing drowsiness and daytime sedation.

Insomnia in elderly people

Sleep patterns change with age, with sleep becoming more fragmented and of a shorter duration. Although REM sleep is preserved, the elderly tend to sleep more lightly. A healthy person of 70 is likely to need about two or three hours less sleep than a young adult. In some cases, it may be that elderly people who complain of insomnia are only experiencing the natural reduction in their need to sleep that comes with age.

There is considerable evidence linking melatonin, produced by the pineal gland, with the sleep wake cycle. Circulating melatonin concentrations decrease in old age and its time of secretion is delayed. Melatonin deficiency thus seems to be a key feature of insomnia in elderly people and replacement therapy may be beneficial.

Other conditions requiring multiple medications are more common in the elderly and both these factors can interfere with sleep patterns.

7.3 Management of insomnia

Many people are reluctant to seek help for insomnia, either because they feel that nothing can be done or because they believe that the only solution is sleeping tablets, to which they may become addicted.

However, there are other, non-drug treatment strategies and these are becoming more and more popular. They include herbal remedies, aromatherapy, relaxation therapy and the promotion of healthy sleeping habits. When all else has failed it is sometimes necessary to consider drug treatment, but only for short-term use. Hypnotics can improve the quality of life if used correctly.

Non-pharmacological strategies for the management of insomnia

Good sleep hygiene advice
When taken seriously, sleep hygiene advice can avoid the necessity for a hypnotic and improve the quality of sleep. Such advice includes:

- Establish a regular routine – go to bed and get up at the same time each day.
- Say ‘no’ to naps – try not to sleep during the day.
- Cut out late cravings – avoid caffeine-containing drinks such as tea, coffee and cola, particularly at bedtime. If necessary, avoid any drink close to bedtime to avoid having to get
up to go to the toilet. Reduce alcohol and nicotine intake just before bed-time and avoid rich foods.

- **Relax before retiring** – a warm bath, soft music or a good book can help to put you in the mood for sleep.

- **Unwind the mind** – put anxieties away and gently let the mind and body unwind before bed. Try writing down unsolved problems and filing them away until the morning. Relaxation exercises or a relaxation tape can help clear an overactive mind.

- **Exercise early** – take plenty of day-time exercise and fresh air, but avoid too much exercise close to bed-time.

- **Comfort comes first** – sleep in a comfortably warm, dark, well-ventilated, quiet room in a comfortable bed. Make sure you have warm feet. A milky drink before bed-time may help.

- **Go to bed to sleep** – do not read or watch television in bed, put the light out straight away.

- **If all else fails** – get up and do something else in another room. Only go back to bed when the urge to sleep has returned.

**Sleep diaries**
Some people find it difficult to develop a good sleep routine. It may be useful for them to keep a sleep diary, making a note of the times of going to bed and waking, periods of wakefulness, evening activities and how they affect sleep patterns plus a note of food and drink consumed during the evening. This information can promote changes to lifestyle to adopt a better routine and improve the quality of sleep.

**Preventing racing thoughts**
Racing thoughts that continually circle the mind are a very common cause of sleeplessness. Assuming another psychiatric disorder has been excluded, these can be dealt with by:

- spending half an hour relaxing before going to bed
- trying to keep eyes open in the dark
- ignoring irrelevant ideas and thoughts
- thinking pleasant thoughts in bed
- emphasising positive achievements
- maintaining a positive attitude to being able to get to sleep
- visualising a pleasant scene.

**Herbal remedies**
A variety of herbal remedies is available without prescription from pharmacies, health stores and supermarkets, which claim to help relaxation and promote sleep. These often contain valerian, gentian, passiflora, humulus and hops either alone or in combination. Others recommend sleeping on herb-filled pillows.
Aromatherapy
Aromatherapy, using lavender oil, introduced into a room via an odour diffuser, has been reported as being successful in replacing drug treatment for insomnia in a small psychogeriatric unit. Many people use lavender oil on their pillows at night but this is not advisable for people with epilepsy.

Melatonin
Melatonin replacement therapy may prove beneficial in alleviating sleep disorders in the elderly. It may also have a specific effect in restoring the sleep patterns of those suffering from ADHD and has been shown to be effective in minimising jet lag.

Pharmacological treatment of insomnia
Drug treatment is not always needed or desirable, but if insomnia is severe and disabling, a hypnotic should be prescribed at the lowest possible dose, ideally to be taken intermittently and for no longer than seven nights. The reason for this is that many hypnotic agents are particularly prone to produce tolerance and dependence. All hypnotics are licensed for short-term use only and none should be taken for longer than two to four weeks, including the tapering-off period.

An important property of a hypnotic is that the person taking it should awake refreshed with no ‘hangover’ the following day. Therefore agents with a short elimination half-life are usually preferred. However, some people complain that whilst these agents induce sleep rapidly, their effect is only short-lived resulting in wakefulness in the early hours. Rather than doubling the dose at bedtime, it can be more effective to reserve part of the dose to be taken on waking in the early hours.

The most important principle is to avoid hypnotic therapy if at all possible. Even short-term use can, on occasions, result in long-term harm. For instance, there is evidence that the use of benzodiazepine hypnotics following bereavement may actually prolong the adaptive response by their effects on memory, thus increasing the risk of the individual developing an abnormal or even pathological grief reaction.

Withdrawal symptoms, in particular rebound insomnia, may occur when a hypnotic is abruptly discontinued, but its reintroduction should be resisted. Prolonged use of any hypnotic may lead to both psychological and physiological dependence.

The following all have sedative/hypnotic properties, either as a result of histamine H1 blockade or the potentiation of GABA – but not all are recommended for use in the treatment of insomnia:

- barbiturates
- clomethiazole
- chloral derivatives
- phenothiazines
- benzodiazepines
- cyclopyrrolones
- imidazopyridines
- pyrazolopyrimidines
- tricyclic antidepressants
- antihistamines.
Barbiturates
Before the introduction of the benzodiazepines, barbiturates were frequently prescribed as hypnotics. Nowadays they are rarely used for this purpose because they carry such a high risk of dependence, daytime sedation and withdrawal phenomena.

Clomethiazole
Clomethiazole potentiates the effect of GABA. Like the barbiturates it is dangerous in overdose especially in combination with alcohol. Tolerance may develop and it can cause dependence. It is no longer considered suitable for routine use in the elderly, but may on occasions be of use in the short term for addressing extreme agitation or aggression in this particular client group.

Chloral derivatives
Chloral derivatives, like the barbiturates, work by potentiating the effects of GABA. Chloral derivatives may cause dependence as well as confusion, skin rashes, gastric irritation, marked respiratory depression and hypotension and are dangerous in overdose.

Phenothiazines
These are histamine H₁ antagonists, which accounts for their sedative effects. Promazine and low-dose chlorpromazine are sometimes used as night sedatives, especially when there is an underlying anxiety or associated agitation, particularly in the elderly. They may be an appropriate choice when smaller doses are already being prescribed during the day for anxiety or agitation.

Benzodiazepines
Whilst all of the benzodiazepines have the capacity to induce sleep at a certain dosage, nitrazepam, temazepam and lormetazepam are the most popular. Benzodiazepines disturb sleep architecture: sleep-time is increased overall but the amount of slow wave and REM sleep is reduced. Light sleep is prolonged which mainly accounts for the increased sleeping time.

The shorter-acting ones, temazepam and lormetazepam should be tried first before the longer-acting nitrazepam, flunitrazepam and flurazepam which have the capacity to cause daytime confusion and drowsiness due to their long-elimination half-lives and accumulation of active metabolites. Daytime performance and memory can therefore be affected and tolerance to the hypnotic effect may develop.

Abrupt discontinuation may lead to rebound insomnia and withdrawal symptoms. Although generally safe in overdose, pronounced respiratory depression can occur when benzodiazepines are taken in combination with alcohol.

Cyclopyrrolones
Zopiclone is the only cyclopyrrolone marketed for insomnia. Benzodiazepine receptors have been subdivided into BZ₁, BZ₂ and BZ₃ subtypes (also known as omega 1, 2 and 3). Which one is present on a GABA-A/chloride complex depends on which sub-units are present. The GABA-A/chloride complex consists of 5 protein sub-units surrounding the central channel. These sub-units are a ‘mix and match’ of five from 13 or more different types available. The benzodiazepines bind non-selectively to all three. Zopiclone binds preferentially to only two of the three benzodiazepine receptor subtypes. This may account for its predominantly hypnotic rather than anxiolytic effect.
The elimination half-life of zopiclone, as well as its active metabolite is 3.5 to six hours. It therefore has a low incidence of residual daytime problems. It has been reported as providing sleep of six to eight hours’ duration. A dose of 7.5 mg delays the onset of the first period of REM sleep but does not consistently affect the overall duration of REM sleep. It does not therefore appear to disturb sleep architecture.

Imidazopyridines 
The only imidazopyridine currently on the market is zolpidem. It is structurally unrelated to all other hypnotics. It binds preferentially to only one of the benzodiazepine receptor subtypes which probably accounts for its predominantly hypnotic effect. It has been shown to be as effective a hypnotic as flunitrazepam, flurazepam and oxazepam.

Psychomotor or cognitive function the morning after a night-time dose of zolpidem is not impaired compared to placebo. It is rapidly absorbed, being effective within 30 minutes and it is effective for up to six hours with the elimination half-life being about two hours. It is metabolised by the liver but there are no active metabolites.

In the elderly and those patients with impaired liver function plasma concentrations are increased. REM sleep is not affected by the normal adult dose of 10 mg. Overall sleep duration is increased and this is accounted for by an increase in non-REM sleep.

Pyrazolopyrimidines 
Zaleplon is a novel pyrazolopyrimidine sedative recently marketed as a hypnotic. It binds selectively as an agonist at the omega 1-benzodiazepine receptor subtype, like zolpidem. It has the most rapid elimination rate of any hypnotic in clinical use and no active metabolites.

Clinical studies have shown that zaleplon is a safe and effective hypnotic, with a minimum effective dose for non-elderly patients of 10 mg. No serious adverse events were reported by volunteers treated with up to 60 mg as a single dose, only mild headache and dose-related extensions of the drug’s pharmacological activity.

Zaleplon is licensed for the treatment of sleep initiation problems at the beginning of the night, but its extremely short duration of action may allow a second dose later, without risk of residual drowsiness the following morning. This would be an advantage for patients who have sleep maintenance problems or difficulties resuming sleep after being awakened in the middle of the night.

Hypnopompic hallucinations and disinhibition syndromes 
All short-acting compounds which act at the benzodiazepine receptor can give rise to hypnopompic hallucinations – persistence of the imagery of a dream into the waking state. These sensory disturbances can happen to anyone on waking unexpectedly, but are more common after a dose of a short acting hypnotic. Triazolam, the short-acting benzodiazepine withdrawn from the market a few years ago, was best known for this, but it can also occur with zopiclone and zolpidem. Disinhibition syndromes have also occurred with the use of ultra short-acting hypnotics and this was the reason for the withdrawal of triazolam.
Tricyclic antidepressants
These should not be used for their sedative effects alone, which are due mainly to their histamine H₁ antagonism, but only when there is evidence of an underlying mood disorder. Their side-effects and toxicity outweigh any potential benefit when used purely as sedatives.

Antihistamines
There is little data to support the use of antihistamines as hypnotics but there may be a place for them in certain selected cases especially where insomnia is exacerbated by a skin irritation in the elderly or small children. Most produce residual sedation due to their long half-lives and they can be toxic in overdosage.

Withdrawal of hypnotics
Following abrupt discontinuation of hypnotics, relapse of insomnia to pre-treatment levels or worsening of insomnia (rebound) may occur. The severity of this depends on the type of drug taken as a hypnotic, the dose and the length of treatment. Withdrawal reactions to zopiclone and zolpidem after treatment for up to four weeks have only occasionally been reported and occur significantly less often than with the benzodiazepines. To date, rebound effects have not been reported with zaleplon but there is not yet much long-term data on the newer compounds.

Both zolpidem and zopiclone are potentially useful for withdrawing patients from long-term benzodiazepine dependency especially when tapering the dose of the benzodiazepine has failed.

Dependence
It must be remembered that prolonged use of any hypnotic may lead to both psychological and physical dependence. Studies of up to four weeks of zopiclone and zolpidem use have not demonstrated evidence of dependence or withdrawal problems. However, it appears that they can cause dependence with long-term use. As with all hypnotics, the risk increases in those patients at risk as a result of previous drug misuse and dependent personalities.

The use of hypnotics in the elderly
It may be entirely natural for a person to wake during the night, get up, potter about and then go back to bed when they are ready. Such behaviour needs correcting only if it is troublesome or dangerous to the individual concerned. The need for hypnotics may be reduced or avoided if the elderly person is more active during the day and avoids day-time naps. Attention to good sleep hygiene is therefore important.

In 1988 a British survey showed that over a million elderly people took a prescribed hypnotic every single night. Elderly people should not take the older hypnotics on a long-term basis because of the risks of residual daytime sedation and consequent falls. Impaired renal function prolongs the effects of these drugs, further increasing the risks. Long-term use of these older drugs is still prevalent in residential care. Consideration should be given to substituting these hypnotics with the newer shorter acting ones.

Great care should be taken when withdrawing an older hypnotic after long-term administration in an elderly person; for instance, fitting may occur if withdrawal is carried out too abruptly.
Hypnotics and driving
There are not many on-road driving studies examining the residual effects of hypnotics. Current knowledge is largely limited to neuropsychological studies, which have mostly been single dose studies. These indicate that the risk is greater for the older, longer half-life compounds. However, a short half-life does not necessarily confer less risk and zopiclone, in particular, stands out as increasing the risk of a road traffic accident, the risk appearing to be greater early in the course of treatment.

Exercise 12
Consider the following vignettes and answer the questions attached giving brief reasons for your answers. Some suggested answers may be found at the end of this chapter.

a. Betty has severe arthritis and has recently had a hip replacement. She is in constant pain and is unable to sleep at night because she can’t get comfortable.

Would a sleeping tablet help Betty?

b. Tracey is 34 years old. She has four small children under five and her husband has just left her. She is worried that she will not be able to pay the bills. She goes to her doctor complaining of daytime tiredness due to the fact that she is not sleeping at night.

What, if anything, should the GP prescribe?

c. Cyril is 70 and retired. He has recently given up his allotment as it was too much for him. He has started getting up in the night to make a pot of tea and read a book for a while before going back to bed. This disturbs his wife who says that he must go to their doctor to get a sleeping tablet.

Is Cyril’s wife correct?

Turn to the end of the chapter for suggested answers
NICE guidance on the management of short-term insomnia with zaleplon, zolpidem and zopiclone

This Technology Appraisal Guidance Number 77 was published in April 2004. 

The main points may be summarised as follows:

- When hypnotics are considered appropriate for the management of severe insomnia that is interfering with normal daily life, they should be prescribed for short periods of time only, strictly in accordance with their licensed indications.

- There is no compelling evidence to distinguish between the ‘Z’ hypnotics and the shorter-acting benzodiazepines. Thus the agent with the lowest purchase price should be prescribed, taking into account the daily dose and price per dose.

- Switching from one of the ‘Z’ hypnotics to another should only occur if a person experiences adverse effects directly related to the hypnotic; then a compound with a higher acquisition cost may be used.

- A patient who has not responded to one of the ‘Z’ drugs should not be switched to any of the others.

This guidance is intended to lead to a reduction in overall prescribing of hypnotics, as well as a significant cost saving. In 2002, a total of 3.9 million prescriptions for the ‘Z’ hypnotics were written with a net ingredient cost of £15.9 million.

7.4 The presentation and management of other sleep disorders

Other sleep disorders, listed in Table 10, whilst not as common as insomnia, are still widespread in the general population and may have serious medical and legal implications.

<table>
<thead>
<tr>
<th>Table 10 Other sleep disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom</strong></td>
</tr>
<tr>
<td>Too much sleep – sleeping in the day-time as well as the night</td>
</tr>
<tr>
<td>Sleeping at the wrong time – day instead of night</td>
</tr>
<tr>
<td>Unusual happenings in the night – may not subjectively disrupt sleep</td>
</tr>
</tbody>
</table>
Narcolepsy

Narcolepsy is a rare condition with a prevalence of about 0.05%. There is often a delay in making a diagnosis, with the result that patients may develop problems at school or at work as well as home before it is recognised that they have this disorder. A lack of public awareness means that sufferers are often labelled by their peers, employers, teachers or parents as lazy.

The main features of narcolepsy are:

- Short, irresistible episodes of sleep during the day – often at strange times, such as while eating or holding a conversation.
- Catalepsy – sudden episodes of muscle weakness – such that a person may fall and hurt themselves – triggered by emotion such as laughter or the anticipation of laughter or fear. It may be mistaken for epilepsy.
- Sleep paralysis – the inability to move while falling asleep or waking up.
- Hypnagogic and hypnopompic hallucinations – intense auditory or visual experiences which are difficult to distinguish from reality and which occur at the beginning or end of sleeping respectively.
- Disturbances of sleep during the night characterised by tossing and turning, leg jerks, nightmares and frequent waking.

The peak onset of disabling symptoms is between the ages of 15 and 25 although some studies report about half of patients presenting after the age of 40. Referral to a neurologist is sometimes necessary to confirm the diagnosis. Treatment involves the use of strong central nervous stimulants.

Amphetamine and related compounds

Agents, such as dexamphetamine and methylphenidate (not licensed in the UK for narcolepsy) have been used for narcolepsy for many years. They delay sleep and increase alertness but can cause agitation and paranoid psychosis. Depression and fatigue often follow a period of stimulation and there is a high rate of tolerance, especially when high doses are used. Amphetamine abuse as a result of its euphoric effect is not uncommon.

Modafinil

Modafinil is not a general central nervous system stimulant but it does promote alertness and wakefulness. Unlike the amphetamines it does not increase motor activity nor does it have any significant effect on sympathetic activity. It does not cause euphoria or any other mood change and is not hallucinogenic. There is little potential for dependency and so far tolerance has not been reported. It is effective in about 75% of patients and has a longer duration of action than amphetamines.

TCAs and SSRIs are treatments for catalepsy with the TCAs, particularly clomipramine, being more effective but responsible for more troublesome side-effects. Their anti-cataleptic effect is apparent within the first few days of treatment and thus may be mediated in a different way from their antidepressant effects. Dreams and nightmares usually partially respond to these treatments and benzodiazepines may help night-time insomnia.
Sleep apnoea syndrome

This condition is particularly prevalent in middle-aged men with thick necks and is strongly associated with loud snoring. Normally the airway narrows during sleep but in patients with this condition it completely collapses. Treatment is often carried out at a specialist sleep-disorder breathing centre and involves continuous positive airway pressure via a mask worn during the night.

Sleep–wake cycle disorders

The period that we sleep is usually determined by our internal clock, triggered by light cues of day and night. Many other factors determine our tendency to fall asleep including social and environmental factors and the length of time since the last sleep period. It is when these factors do not coincide with the body’s innate circadian sleep-wake rhythm that these disorders occur. They are characterised by the desire to sleep during the day and the inability to sleep at night.

Jet lag

A rigid adherence to regular routines for eating and exercise should be effective as should the implementation of simple sleep hygiene measures and the use of appropriately timed light – two hours of bright light (daylight is best) in the morning and none in the evening.

Shift work

It is often difficult to return to a normal pattern of sleep and wakefulness after a period of shift work. However, regular shift changes, rotating shifts clockwise and dividing sleep so that there is a long main sleep period and then a short nap before work can all help. Modafinil is now licensed for excessive sleepiness associated with ‘moderate to severe chronic shift work sleep disorder’.

Disorders in which environmental cues may be reduced

These include schizophrenia, learning disabilities and visual impairment. Sufferers of these conditions may have difficulty sleeping at night. This has been managed in the past by a methodical, systematic shift of sleeping time over a long period. More recently the use of bright morning light has proved to be a more successful aid in resetting the body clock, accompanied by a conscious reinforcement of environmental and social cues for waking and sleeping.

Melatonin has been used to re-set the circadian rhythm in these disorders usually at a dose of 2.5–10 mg at the appropriate phase of the cycle – at night to bring on sleep and in the morning to delay it. The use of melatonin as a hypnotic has been less successful.

Night terrors and sleep walking

These often co-exist and arise from slow-wave sleep. The patient is usually unaware of these events, appearing to be asleep and uncommunicative throughout. Injury may occur to himself or to others. These terrors are thought to be due to a welling up of anxiety from deep centres in the brain which is normally inhibited by cortical mechanisms. Treatment with benzodiazepines or paroxetine may be successful.

Nocturnal panic attacks can be distinguished from night terrors by the fact that the patient awakes fully from light sleep before the symptoms have reached a peak and is fully aware of the attack.
Nightmares
These arise out of REM sleep and are reported by the patient as structured, often stereotyped dreams which are very distressing. Usually the patient wakes up and remembers the dream in vivid detail. Psychological treatment or drug treatment with agents that suppress REM sleep, such as the MAOIs, may be appropriate.

Sleep paralysis
This also arises from REM sleep and is a state of being fully conscious and aware without being able to move. It only lasts for a few seconds and is usually aborted by auditory or somatosensory stimuli. It may be due to an incomplete arousal from REM sleep so that consciousness is restored but the atonia remains. It is extremely frightening, so reassurance is important.

REM behaviour disorder
This is a lack of paralysis during REM sleep so that dreams may be acted out, often resulting in injury to the individual or others. It can occur as a result of drug or alcohol withdrawal but it may be chronic and associated with a neurological disorder. Treatment with clonazepam has been successful.

Periodic limb movements in sleep
Many people experience jerking or kicking movements of the limbs, usually the legs, during sleep, which tend to increase with age. In some people they become excessive and distressing and may occur more than 25 times an hour. They can then be associated with arousals from sleep in which case referral to a specialist sleep centre is indicated.

Summary
Sleep of adequate quality and duration is essential to mental and physical wellbeing. Inadequate sleep can lead to considerable personal distress and impaired mental and physical functioning. Non-drug treatments are the preferred intervention for the management of insomnia and there are many strategies available to help restore satisfactory sleep patterns. Hypnotics should normally be reserved for the treatment of severe and disabling insomnia.

Learning Outcomes
On completion of this chapter you should be able to:
1. Describe a normal sleep pattern.
2. Use examples of the factors which can affect sleep patterns in the context of your practice.
3. Advise on non-pharmacological treatment strategies for insomnia.
4. Advise on appropriate pharmacological treatment of insomnia.
5. Apply the NICE guidance on the use of the ‘Z’ hypnotics.
6. Assess the presentation and management of some other sleep disorders and advise or refer as appropriate.
Further reading
Novak M, Shapiro CM. Drug induced sleep disorder. *Drug safety* 1997 Feb. 16 (2) 133-149.

Suggested answers

Exercise 12 (page 147)

a. In the first instance Betty’s pain relief should be considered. If it is inadequate, then suitable adjustment may obviate the need for a sleeping tablet.

b. If Tracey is not showing any symptoms indicative of depression and support and counselling are not enough, then a short course of a short-acting hypnotic such as zolpidem or zopiclone – no more than two weeks – may allow her to face her current situation and think clearly unhindered by sleeplessness.

c. Cyril is showing some of the natural changes in sleep pattern with age – an explanation of this to his wife is necessary here. Medication is not required. Separate bedrooms may be the answer!
Chapter 8  Dementias
Objectives

This chapter will enable you to:

- describe the key differences between the three most common dementias
- discuss the roles of cholinesterase inhibitors and N-methyl-D-aspartate (NMDA) receptor antagonists in various stages of dementia
- identify side-effects of medication and options for their management
- differentiate between the need for non-pharmacological and pharmacological treatments for associated behavioural and psychological symptoms in dementia (BPSD)
- identify possible ways to improve pharmaceutical care for people with dementia
8.1 Introduction

The dementias are arguably some of the most insidious and cruel of all diseases, with a seemingly relentless progression from mild memory impairment through to behavioural and personality changes, to a complete inability for the individual to complete any activities of daily living or to communicate effectively within their surrounding environment.

Dementia has been described as a syndrome where there is progressive impairment in two or more areas of cognitive function (these include memory, language, visuospatial and perceptual ability, thinking and problem-solving or personality) with the result that work, social function and relationships are affected. This impairment occurs in the absence of delirium (acute confusional state) or other psychiatric disorders such as depression or schizophrenia. Dementia is generally irreversible except for a small number of so-called ‘pseudo-dementias’ (about 1% of all dementias), which are remediable and will be discussed briefly later.

8.2 Epidemiology

The prevalence of dementia varies according to epidemiological studies, the age of the subjects sampled, the method of determining the presence, severity and type of cognitive impairment and the regions or countries being studied. However, dementias are primarily a disease of the elderly, with the prevalence doubling every five years over the age of 65 years. Between the ages of 65 and 69 years the prevalence is 2% but this rises to 20% in the 85–89 year-old age group. The incidence is estimated at one new case per 100 population per year, with the prevalence being higher in men until the age of 74 years, but higher in women thereafter. In 2001, the National Institute for Clinical Excellence approximated the number of people with dementia in England and Wales as 700,000 and of these 400,000 would have Alzheimer’s disease (AD).

8.3 Symptoms

The presence of a dementia may be indicated by any of the following symptoms that cannot be explained by another cause.

- Memory loss, especially for recent events; in severe dementia, long-term memory is also impaired (e.g. not recognising family members).
- Difficulties with learning and retaining new information; this may be demonstrated by the person misplacing objects (e.g. car keys or spectacles) or being more repetitive.
- Having trouble with complex tasks such as cooking, driving or dealing with finances.
• Reduced ability to reason and problem solve.
• Impairment of spatial and visuospatial awareness (e.g. bumping into objects, getting lost in a familiar place).
• Language problems are demonstrated by an inability to find the right word or to follow conversations.
• Behavioural changes such as seeming to be more irritable, more passive or withdrawn or more suspicious (see section 8.8).

The clinical features of dementia are many and varied, with the clinical picture being determined by the patient’s pre-morbid personality. Individuals with good social skills can maintain a social façade despite gross intellectual impairment. For example, they may claim that their watch is broken when they are asked the time, and then they may ask what the time is so that they can fix their watch. Individuals that are in social isolation or have visual or hearing impairment are less likely to be able to compensate so well. Generally, the disorder develops gradually and is often only noticed (by relatives or carers) after a change in social circumstance or physical illness. Clinical features change over the time-course of the disorder, and are often subdivided into early, mid and late symptomatology (see Table 11).

Table 11 The changing clinical features of dementia

<table>
<thead>
<tr>
<th></th>
<th>Early</th>
<th>Mid-stage</th>
<th>Late-stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious</td>
<td></td>
<td>Emotions and responses to events blunted</td>
<td>Often unresponsive</td>
</tr>
<tr>
<td>Irritable</td>
<td></td>
<td>Sudden mood changes occur, often with explosive angry outbursts with no cause</td>
<td></td>
</tr>
<tr>
<td>Depressed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thinking</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slowed and impoverished content</td>
<td></td>
<td>Syntactical errors (getting words within a sentence in the wrong order)</td>
<td>Grossly fragmented and incoherent</td>
</tr>
<tr>
<td>Concrete thinking and decreased flexibility and preservation</td>
<td></td>
<td>Nominal dysphasia (impaired content, order and/or understanding of speech)</td>
<td>Speech often meaningless, unintelligible or the patient is mute</td>
</tr>
<tr>
<td>Impaired judgement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>False ideas, especially persecutory, gain ground easily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speech – searching for words</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 11 (continued) The changing clinical features of dementia

<table>
<thead>
<tr>
<th>Early</th>
<th>Mid-stage</th>
<th>Late-stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Behaviour</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disorganised, distractible, restless and inappropriate</td>
<td>Self-neglect</td>
<td>Disorientated</td>
</tr>
<tr>
<td>Loss of interest and initiative</td>
<td>Neglect of social conventions</td>
<td>Incoherent</td>
</tr>
<tr>
<td>Personality changes – neurotic traits exaggerated</td>
<td>Behaviour often aimless, with stereotypes and mannerisms occurring</td>
<td>Double incontinence</td>
</tr>
<tr>
<td>Hallucinations or delusions common</td>
<td>Wandering</td>
<td></td>
</tr>
<tr>
<td>Antisocial behaviours, including sexual disinhibition and shoplifting</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired memory</td>
<td>Impaired attention</td>
<td>Disorientation in time, place and person</td>
</tr>
<tr>
<td>Difficulty in new learning</td>
<td>Impaired concentration</td>
<td></td>
</tr>
<tr>
<td>Memory loss for recent events rather than remote</td>
<td>Disorientation in time</td>
<td></td>
</tr>
<tr>
<td>Excuses or confabulation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 8.4 Diagnosing dementia

The most important part of the diagnostic procedure is taking an accurate and detailed history, paying particular attention to intellectual functioning and neurological symptoms. The mode of onset and the progression of symptoms should be detailed. Psychological tests, such as a mini-mental state examination (MMSE) and assessments for depression should be performed as part of the differential diagnosis process. These can then be used to monitor progression of the disease or associated depressive states as appropriate.

Dementia presenting in individuals of 65 years or less, has no predominant cause, whereas dementia presenting in individuals older than 65 years generally has a degenerative or vascular cause. However, before a diagnosis is made of a progressive dementia, all remediable causes of dementia should be excluded.

Recent clinical practice research has suggested that as little as 1% of all dementia syndromes may be remediable, but to establish a ‘probable’ diagnosis of a dementia all other causes need to be excluded. Remediable causes of dementia include:

- depressive pseudo-dementia
- hypothyroidism
normal pressure hydrocephalus, other space-occupying lesions in the brain
vitamin deficiency for example; thiamine, B12, folate, or iron deficiencies and elevated plasma and total homocysteine levels
acute confusional state (delirium).

Exercise 13
Suggest five possible causes of an acute confusional state:
1.
2.
3.
4.
5.

Turn to the end of the chapter for suggested answers

Any remediable causes should be identified and treated as early as possible in the presentation of the illness. An assessment of the degree of disability and the individual’s social circumstance should be made, and the necessary service support implemented. It is important to improve the functional ability of the individual as much as possible and relieve any distressing symptoms.

Some of the benefits of early diagnosis are:
- Excludes reversible conditions.
- Helps the patient and their family to plan for future care.
- Allows for personal affairs (e.g. updating wills, deciding on power-of-attorney for future needs) to be put in order while the patient still has insight.
- Allows the patient to take part in discussions about their future care while they still may have insight into their condition.
- Allows the early access by the patient and their family of support groups (Alzheimer’s Disease Association) for further information and planning purposes.
- Helps to determine the prevalence of the disease.
- Allows future research treatments that may slow or halt the progression of the disease to be more effectively targeted to the right stage of the disease.
- Allows for the appropriate medical treatment to be started at the most beneficial time.
8.5 Classification of the dementias\textsuperscript{1–5}

Alzheimer’s disease (AD) accounts for about 60\% of all cases of dementia. Dementia with Lewy Bodies (DLB) accounts for about 20\% and vascular dementia (VaD) accounts for 10\%. The remaining 10\% are generally subdivided into two further classifications:

- Frontotemporal dementias (which include Pick’s disease, frontal lobe dementia with or without motor neurone disease and the primary aphasias).
- Subcortical dementia syndromes (that is those involving the basal ganglia, midbrain and brainstem such as Huntington’s chorea; Parkinson’s disease (PD) and/or possibly Parkinson’s disease dementia (PDD); hypoparathyroidism; multiple sclerosis; AIDS dementia complex and normal pressure hydrocephalus).

There are many other diverse causes including multiple sclerosis, Creutzfeldt-Jakob disease, HIV infection or progressive supranuclear palsy.

There is however considerable overlap of disease states with dementias of mixed aetiology (that is a combination of AD and VaD, or DLB and PDD) being relatively common. For example it is estimated that perhaps only 37\% of people have pure AD, that 60\% are of mixed aetiology and the remaining 3\% comprise all other dementia syndromes. All diagnoses are ‘probable’ as confirmation is only possible at post mortem.

A useful table of comparisons to aid a diagnosis has been collated to help differentiate between depression, delirium and dementia (Table 12).

<table>
<thead>
<tr>
<th></th>
<th>Depression</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Sudden</td>
<td>Sudden</td>
<td>Insidious</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Generally rapid progression</td>
<td>Fluctuating: lucid intervals during day, worse at night</td>
<td>Usually stable (except VaD – stepwise deterioration, and DLB – fluctuations in consciousness and cognitive function during any day)</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Weeks or months</td>
<td>Hours to weeks</td>
<td>Months or years</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>Impaired</td>
<td>Impaired, distractability</td>
<td>Relatively unaffected</td>
</tr>
<tr>
<td><strong>Alertness</strong></td>
<td>Usually normal</td>
<td>Abnormally high or low</td>
<td>Usually normal</td>
</tr>
<tr>
<td><strong>Orientation</strong></td>
<td>Usually impaired for time and place</td>
<td>Usually impaired</td>
<td>Impaired in later stages</td>
</tr>
<tr>
<td><strong>Memory</strong></td>
<td>Person aware of memory loss</td>
<td>Usually impaired</td>
<td>Normal in early stages</td>
</tr>
<tr>
<td><strong>Thinking</strong></td>
<td>Slowed</td>
<td>Disorganised, occasionally delusional</td>
<td>Impoverished</td>
</tr>
</tbody>
</table>
Table 12 (continued) Differential diagnosis of depression, delirium and dementia

<table>
<thead>
<tr>
<th></th>
<th>Depression</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Speech</strong></td>
<td>Poverty, reduced rate</td>
<td>Incoherent, rambling</td>
<td>Difficulty in finding words</td>
</tr>
<tr>
<td><strong>Perception</strong></td>
<td>Hallucinations rare – usually auditory</td>
<td>Illusions and hallucinations – usually visual</td>
<td>Hallucinations absent in earlier stages, common later</td>
</tr>
<tr>
<td><strong>Sleep–wake cycle</strong></td>
<td>Disrupted, early morning wakening</td>
<td>Usually disrupted</td>
<td>Usually normal</td>
</tr>
</tbody>
</table>


### Alzheimer’s disease (AD)

Progressive mental deterioration in old age has been recognised and described throughout history. However, it was not until the early part of the 20th century that a collection of brain cell abnormalities were specifically identified by Dr Alois Alzheimer, a German physician, in 1906. He lectured about a woman who had died after years of experiencing severe memory problems, confusion and difficulty understanding questions. Upon her death, he performed an autopsy on her brain and described dense deposits outside and around the nerve cells (amyloid plaques). Inside the nerve cells he noted the presence of twisted bands of fibres (neurofibrillary tangles). The observation of the plaques and tangles at autopsy is still required to obtain a definitive diagnosis of Alzheimer’s disease. The formation of amyloid plaques and neurofibrillary tangles (NFTs) are thought to contribute to the degradation of the neurons in the brain and the subsequent symptoms of Alzheimer’s disease (Figure 6). In Alzheimer’s disease, there is an overall shrinkage of brain tissue (Figure 7).

**Figure 6** Neurofibrillary tangles and amyloid plaques
**Amyloid** is a general term for a family of protein fragments found in the brain. Amyloid is thought to play a key role in the pathology of Alzheimer’s disease. In a healthy brain, these protein fragments would be broken down and eliminated. In Alzheimer’s disease, the fragments accumulate to form hard, insoluble fragments.

**Neurofibrillary tangles** primarily consist of tau protein, which forms part of a structure called a microtubule. The microtubule helps transport nutrients and other important substances from one part of the nerve cell to another. In Alzheimer’s disease the tau protein is abnormal and the microtubule structures collapse.

In the early stages of Alzheimer’s disease, short-term memory begins to decline when the cells in the hippocampus degenerate. The ability to perform routine tasks also declines. As AD spreads through the cerebral cortex, judgment declines, emotional outbursts may occur and language is impaired. Progression of the disease leads to the death of more nerve cells and subsequent behaviour changes, such as wandering and agitation. The ability to recognise faces and to communicate is completely lost in the final stages. Patients lose bowel and bladder control and eventually need constant care. This stage of complete dependency may last for years before the patient dies. The average length of time from diagnosis to death is four to eight years, although it can take 20 years or more for the disease to run its course (see Table 13).

The cholinergic system is critical to normal memory and other cognitive functions. In AD there is selective loss of cells in the basal forebrain. These cells produce acetylcholine (ACh) and project diffusely into the hippocampus, basal nucleus of Meynert and the entorhinal cortex. The depletion of neurons in this area correlates with memory and cognitive decline in AD.

When the first mild symptoms of AD occur, there is already a significant deficit in ACh. Levels eventually reduce by 40–90% in moderate to severe AD. Other affected neurotransmitter systems are: noradrenaline; dopamine; serotonin; glutamate and gamma aminobutyric acid (GABA).

**Figure 7** Cross-sections of a normal brain and a brain affected by Alzheimer’s disease

The *sulci* (grooves or furrows in the brain) are noticeably widened and there is shrinkage of the *gyri* (the folds of the brain’s outer layer). In addition, the *ventricles* are noticeably enlarged.
A useful reference which explains many of the changes occurring in people with Alzheimer’s disease in lay language and which also has some helpful illustrative diagrams is *Alzheimer’s Disease: Unravelling the Mystery* published by the National Institute of Aging, National Institutes of Health in 2002. This may be downloaded via [www.nia.nih.gov/Alzheimer’s/Publications/UnravelingTheMystery](http://www.nia.nih.gov/Alzheimer’s/Publications/UnravelingTheMystery).

The majority of AD is idiopathic but risk factors for developing AD so far identified include:

- increasing age
- a family history – familial Alzheimer’s disease (FAD) of late onset is associated with the ApoE ε4 allele on chromosome 19
- Down’s syndrome
- early onset AD is associated with gene mutations on chromosomes 1, 14 and 21.

Research has highlighted that the following factors may also be implicated. These are:

- head injury – amyloid is deposited in the brain within 24 hours of injury
- gender – females have greater incidence than men
- education – a high level of education is a protective factor in FAD
- ongoing intellectual activity – the ‘use it or lose it’ hypothesis suggests continued learning is protective
- environmental toxin as a neurotoxin rather than a causative factor e.g. excessive alcohol intake, pesticides, aluminium levels in water or diet.

It is likely that AD occurs as the result of complex interplay between genetic predisposition and personal and environmental influences.

**Table 13 Progression and staging of Alzheimer’s disease**

<table>
<thead>
<tr>
<th>Progression</th>
<th>Clinical Presentation</th>
<th>Associated physical problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early stages 1–3 years</td>
<td>Recent memory impairment, forgetting names, losing direction when out and about, depression, impaired activities of daily living, language difficulties</td>
<td>Visuospatial problems (e.g. walking into things)</td>
</tr>
<tr>
<td>Mid-stages 2–10 years</td>
<td>Amnesia, aphasia, inability to calculate solutions, inability to problem-solve, personality change, behavioural changes e.g. wandering, psychiatric changes e.g. delusions; inability to bathe, eat, toilet or dress without assistance</td>
<td>Falls, accidents involving cooking or other activities, impaired motor skills, may forget to eat and therefore have nutritional problems, may be unable to use the toilet correctly and develop chafing due to poor hygiene and soiling</td>
</tr>
<tr>
<td>Late stages 8–12 years</td>
<td>Short and long-term memory loss, mutism or nonsensical speech, posture becomes rigid and in flexion, double incontinence, complete dependence on others, seizures</td>
<td>Inability to communicate their needs, e.g. hunger, toileting, inability to swallow or chew food, decreased immune response, susceptibility to infections increased, double incontinence, bedridden patients are at risk of pressure sores developing, pneumonia</td>
</tr>
</tbody>
</table>
Dementia with Lewy bodies (DLB)

Lewy body dementia is a progressive, fluctuating dementia associated with primarily visual hallucinations, periods of confusion and other psychotic symptoms. It is also associated with early gait disturbances, extrapyramidal features such as rigidity, bradykinesia, tremor and fixed posture (signs of parkinsonism). Sufferers demonstrate an extreme sensitivity to the extrapyramidal side-effects of antipsychotic medication. This may be explained by deficits in nigrostriatal dopamine neurones. Treatment with antipsychotics is best avoided where DLB is suspected.

Lewy body dementia is characterised by the histological feature of the presence of Lewy bodies (an intracellular inclusion of a round hyaline mass) in the cerebral cortex and substantia nigra. Senile plaques may also be present, but NFTs are absent. Lewy bodies are also found in the post-mortem brains of patients with Parkinson’s Disease, Pick’s disease and Huntington’s chorea. However, in non-demented Parkinson’s Disease patients, Lewy bodies are predominantly found in the subcortical regions and the loss of choline acetyltransferase (CAT) in the cortex is modest. In Parkinson’s Disease patients with dementia (PDD), Lewy bodies are present in the cortex and there is pronounced loss of CAT.

Vascular dementia (VaD)

Vascular dementia (VaD) generally presents with sudden onset and the dementia follows a step-wise progression, with periods of stability followed by periods of rapid decline. Generally there is a history of hypertension, stroke or transient ischaemic attack (TIA). There are focal neurological signs (which describe the physical or psychological symptoms directly related to the area of brain damage) which are absent in AD, and often emotional lability and depression. Common associated clinical features are early memory problems, apraxia, agnosia, dysarthria and dizziness. Generally insight is more preserved than in AD, but this often leads to increasing distress for the patient, as they are more aware of the prognosis of the disease.

In late stage VaD, there is a shuffling gait, which can be distinguished from Parkinson’s disease by its broad base and preserved arm swing. Fitting and continued episodes of cerebral ischaemia are also late features of VaD.

Risk factors for VaD include: family history; male gender; hypertension; history of stroke or TIA; diabetes mellitus; smoking or atrial fibrillation (AF).

The National Service Framework for Coronary Heart Disease education programme aims to improve the control of hypertension, AF and diabetes in primary care. An improvement in these areas may result in a decrease in the proportion of vascular dementia observed. Preventative therapy may include aspirin and the introduction of a statin. Evidence indicates that treatment with a statin may lower the risk of developing vascular dementia in patients 50 years or older, independent of the presence or absence of untreated hyperlipidaemia.

Features that distinguish VaD and DLB from AD are illustrated in Table 14.
Table 14  Distinguishing features of VaD and DLB compared to AD

<table>
<thead>
<tr>
<th>Vascular dementia</th>
<th>Dementia with Lewy bodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional lability and depression</td>
<td>Fluctuating course</td>
</tr>
<tr>
<td>Sudden onset with stepwise progression</td>
<td>Early gait disturbance and parkinsonism</td>
</tr>
<tr>
<td>In early stages patient has insight</td>
<td>Extreme sensitivity to antipsychotic agents</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td>Less severely impaired recent memory</td>
</tr>
<tr>
<td>Focal neurological signs such as gait disturbance, exaggeration of deep tendon reflexes or weakness of an extremity</td>
<td>Associated with hallucinations, periods of confusion and psychotic symptoms</td>
</tr>
<tr>
<td>Late features include: shuffling gait with a wide base, seizures and continued episodes of cerebral ischaemia</td>
<td></td>
</tr>
<tr>
<td>CT indicating ischaemia and multiple infarction</td>
<td></td>
</tr>
</tbody>
</table>

8.6 Assessment tools in dementia

Assessment scales and tools can be used to chart the clinical course of the disease and allow for comparisons between different population groups and different studies. They generally classify the stage of AD into categories of mild/early AD, moderate or mid-AD or severe/end stage AD, by the severity of the clinical features presented. There are also assessment tools to assess cognitive function; activities of daily living; behaviour, global function, quality of life and caregiver burden. For an interactive overview see Family Practice Notebook at [www.fpnotebook.com/NEU18.htm](http://www.fpnotebook.com/NEU18.htm) (accessed 10 May 2005)

NICE guidance classifies the stages of AD according to an individual’s score on the Folstein Mini Mental State Examination (MMSE), which is an assessment of cognitive function and scored out of 30 (indicative of normal function).

Current research guidance on the efficacy of pharmacological treatments in people with dementia, places emphasis and importance on the use of assessment tools to monitor disease progress; especially the following:

- Clinicians’ Interview-Based Impression of Change (CIBIC), which is a measure of global outcome.
- Progressive Deterioration Scale (PDS); which is a measure of functional/quality of life.
- Behavioural Psychological Scale for Dementia (BPSD); which measures the incidence and severity of behavioural changes.
- Neuropsychiatric Inventory (NPI) which also measures the presence of neuropsychiatric symptoms.
NICE questions the value of these instruments (except for the MMSE in mild to moderate disease) to measure the real-life functional changes that may be meaningful to patients and their carers; for example being able to dress themselves, feed themselves or occupy themselves with a book or other activity.

8.7 Management of cognitive features of dementia

The treatment of any neurodegenerative disorder has two principal aims:

- the arrest or delay progression of the disease by increasing the functioning of deficient neurotransmitter pathways
- the management of any associated behaviour problems.

This therapeutic strategy should be underpinned by the following principles:

- maintaining a safe and structured environment for the patient
- maximising the remaining functional abilities
- ensuring that nutritional needs and any appropriate medical care for concomitant physical pathology are met
- maintaining the dignity of the patient
- at the end stages of the disorder, adhering to accepted principles of palliative care.

Pharmacological treatment of cognitive symptoms of dementia

There are two classes of pharmacological agents licensed for the treatment of the symptoms of AD: the cholinesterase inhibitors (donepezil, rivastigmine and galantamine) and the NMDA receptor antagonists (memantine).

Neurotransmitters and Alzheimer’s disease

Acetylcholine (ACh) is an important neurotransmitter in the brain and spinal cord. Central cholinergic neurons are of two types, local circuit cells and projection cells.

Local circuit cells have relatively short axons, so that the whole neuron is contained within a single brain region. Cholinergic nerves in the basal ganglia of the extrapyramidal system are examples of local circuit cells. Anti-Parkinsonian, atropine-like drugs, that block muscarinic receptors, act here.

Projection cells generally have longer axons and connect two or more different brain regions. The most important cholinergic projection cells lie in the basal nuclei of the forebrain and send axons to almost all areas of the cerebral cortex. Cholinergic terminals are therefore widespread in the cortex.

Activation of excitatory presynaptic nicotinic ACh receptors enhances ACh release. It has been suggested that the presence of these receptors could account for the (disputed) claims of reduced incidence of Alzheimer’s disease in smokers.

Memantine is a non-competitive antagonist at the phencyclidine binding site within the ion channels of the Glu-NMDA receptor. At low doses it is thought to prevent the harmful excesses of excitotoxicity.
Cholinesterase Inhibitors (ChEIs) and Alzheimer’s Disease

In November 2006, NICE reviewed an earlier TA to produce the Technology Appraisal Guidance Number 111, covering donepezil, galantamine, rivastigmine and memantine (NMDA receptor treatment antagonist) for the treatment of AD.

The new NICE guidance differs from earlier recommendations in that donepezil, galantamine and rivastigmine are recommended as options only in the management of patients with moderate Alzheimer’s disease (MMSE score of between 10 and 20 points). When the MMSE score falls below 10 points, patients should not normally be prescribed any of these three drugs. As with the 2001 NICE guidance, memantine is not normally recommended as a treatment option for people with Alzheimer’s disease. The Final Appraisal Determination was issued in May 2006. The updated guidance is now available via the NICE website; under the section of www.nice.org.uk/appraisals

NICE also produced a clinical guideline (CG42) for Dementia in November 2006. http://guidance.nice.org.uk/CG42/niceguidance/pdf/English

SIGN also produced a guideline for Scotland in February 2006 for the ‘Management of patients with dementia’. www.sign.ac.uk/pdf/qrg86.pdf

These agents however are licensed for the symptomatic treatment of mild to moderate AD and exert their pharmacological activity by inhibiting the enzyme acetylcholinesterase (AChE) to increase the availability of acetylcholine (ACh) at sites of neurotransmission. Galantamine also enhances the action of ACh on nicotinic receptors. Although these agents belong to the same group they all produce their pharmacological effect in a slightly different way, so if a response to one agent is not seen, then it is justifiable to try another (See Table 15).
<table>
<thead>
<tr>
<th>Table 15 Differences in ChEIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>AChEI</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
</tr>
<tr>
<td><strong>Time to serum max</strong></td>
</tr>
<tr>
<td><strong>Effect of food on absorption</strong></td>
</tr>
<tr>
<td><strong>Serum t1/2</strong></td>
</tr>
<tr>
<td><strong>Protein binding</strong></td>
</tr>
<tr>
<td><strong>Metabolism and excretion</strong></td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
</tr>
</tbody>
</table>

**Cautions with ChEIs**

ChEIs should be prescribed with caution in the following patients: those with ‘sick sinus syndrome’ or other supraventricular conduction abnormalities; patients with concomitant asthma, obstructive pulmonary disease or those with, or at risk from, peptic ulcer disease. Rivastigmine should be prescribed with caution in patients with renal impairment or mild to moderate hepatic impairment. All ChEIs cause gastrointestinal effects such as diarrhoea, muscle cramps, fatigue, nausea, vomiting, insomnia and dizziness. These are generally mild and transient, and often disappear within a few days of continued treatment. However in some patients these effects may be severe and result in significant weight loss. To reduce these effects, the medication can be taken after food and dose titrations should be over four-week periods (but remember that this may prolong the time to reach the maximum therapeutic dose), and an anti-emetic may be prescribed. If there is no history of PD or DLB, then long-acting metoclopramide may be given during the dose titration period. The alternative is domperidone at 10–20 mg three or four times daily.

Selection of any medication for a person with dementia should include an analysis of its propensity to cause anticholinergic effects. Any of the following agents is likely to produce anticholinergic effects which will interfere with memory and may exacerbate or cause confusion: hyoscine, oxybutynin, procyclidine, antipsychotics (including chlorpromazine, thioridazine, flupentixol, fluphenazine, zuclopenthixol, clozapine, olanzapine), tricyclic antidepressants, furosemide, digoxin and cimetidine.
The controversy of treatment with ChEIs
Treatment with the licensed ChEIs remains a controversial issue, although much of this controversy is centred on cost. The evidence to date, although compelling in some areas, is yet to fully prove a long-term benefit in the treatment of AD. Some patients show no benefit, others improve with time and others continue to decline.

The recently published AD2000 study, found that donepezil was no different from placebo in the primary endpoints of institutionalisation or disease progression. However, the endpoints of the trial had been designed to show a difference in a recruitment population of 3000 patients and only 565 patients entered the study.

Interestingly, the authors of AD2000 commented that when they followed up patients who had withdrawn from the study they had significantly worse cognitive and functional decline than those who continued on active treatment.

Withdrawal/switching dilemmas with ChEIs
If a patient seems to have no improvement in objective scores but also no deterioration, it could be argued that the neurodegenerative process is being held at steady state. Therefore the agent should be continued. If the patient fails to tolerate the maximum effective dose of a particular agent it seems appropriate to try an alternative rather than withdrawing treatment altogether.

Some specialist centres have initiated a policy that when a patient’s disease shows sign of deterioration using objective and subjective measures then the agent should be withdrawn. However, they stress the importance of careful follow-up of the patient over the next three months and if the deterioration is increased, to restart the agent. Memantine may be of greater benefit at this stage in a patient’s treatment as it is licensed for use in patients with moderately severe to severe Alzheimer’s disease.

There is increasing evidence to support the observation that some patients may respond to a change in ChEI after an initial trial with a first agent where no response was demonstrated.

Local monitoring procedures for ChEIs
Although NICE recommended a barrage of treatment assessments for patients on ChEIs, many centres also use indicators that are important to the caregiver and/or the patient. Things such as being able to make a cup of tea; being able to enjoy an interactive game or completing a simple jigsaw; being able to take part in conversation; being able to wash, dress or eat for themselves. Monitoring is often a trade-off between best practice and what is realistically achievable within the framework of NHS budget and human resource.

Other pharmacological effects of ChEIs
Recent research has suggested that ChEIs are beneficial in reducing behavioural and psychological symptoms of dementia (BPSD) as shown in Table 16. Therapeutic efficacy in VaD, DLB, dementia associated with Down’s syndrome and PDD have also been demonstrated. These are all unlicensed indications, but as dementias are a syndrome, the use of ChEIs in other dementias is understandable.
Table 16  Efficacy of ChEIs in reducing behavioural and psychological symptoms of dementia

<table>
<thead>
<tr>
<th>Behaviour</th>
<th>Donepezil</th>
<th>Rivastigmine</th>
<th>Galantamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation/aggression</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Irritability</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Anxiety</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Abnormal movements</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Apathy</td>
<td>–</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Depression</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Delusions</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>+</td>
<td>not examined</td>
<td>+</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Euphoria</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sleep</td>
<td>not examined</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Appetite</td>
<td>not examined</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>

**Key**

+ statistically significant improvement
– no significant effect

NMDA receptor antagonists

Memantine is the first NMDA-receptor antagonist to be licensed in the United Kingdom for the treatment of moderately severe to severe AD. NMDA is involved in the regulation of glutamatergic transmission. An excess of glutamate causes overstimulation of NMDA receptors, which allows free-flow of calcium into the cell. Sustained levels of excess glutamate lead to a chronic overexposure of calcium, which in turn leads to cell degeneration and ultimately cell death. Memantine binds to the NMDA receptors to block the glutamate-gated receptor channels. It allows the physiological activation of the receptors (which are involved in memory formation), but it blocks the pathological activation (which is involved in cell degeneration).

Dosing starts at 5 mg once daily, increasing to a maximum of 10 mg twice daily, but is reduced in moderate renal impairment. Concomitant prescribing of other NMDA antagonists should be avoided, for example amantadine, ketamine and dextromethorphan. The main side-effects are hallucinations, confusion, dizziness, headache and tiredness.

Memantine may cause significant improvements in cognitive function, behavioural disturbance and global outcome. There is guidance on the use of memantine in dementias covered by SIGN (February 2006) at [www.sign.ac.uk/guidelines/published/index.html](http://www.sign.ac.uk/guidelines/published/index.html) and NICE (November 2006) [http://guidance.nice.org.uk/CG42](http://guidance.nice.org.uk/CG42) and [http://guidance.nice.org.uk/TAIII/guidance/pdf/English](http://guidance.nice.org.uk/TAIII/guidance/pdf/English)

Future pharmacological strategies in dementia

These include intra-cerebral administration of nerve growth factor or brain stem cells; the development of 5-HT_{1A} antagonists and anti-amyloid vaccines.
8.8 Management of non-cognitive symptoms\textsuperscript{20–26}

**Behavioural and psychological problems**

Frank psychiatric changes can include: hallucinations, persecutory delusions, depression and personality changes. Other features of AD such as irritability, nocturnal wakening, aggressive behaviour, resistive behaviour and restlessness also present major challenges for carers and physicians alike. It is important to identify any underlying treatable cause.

Consider the following:

- Is the patient in pain?
- Is there underlying depression?
- Is there a superimposed delirium?
- Is the patient dehydrated?
- Is there an underlying acute confusional state?
- Is the patient’s communication hampered by visual, hearing or speech difficulties?
- Has the patient recently moved from another care environment?
- Is a patient more distressed in certain situations?

It is important to remember that AD is a progressive disorder and that the clinical features that were a problem at one stage of the illness will not necessarily be the clinical feature presenting at a later stage. Therefore the need for continued review and judicious use of any medication is strongly advised. The advice from the Scottish Intercollegiate Guidelines Network (SIGN) (see note below) and the National Service Framework for Older People is to observe the behaviour for at least one month to determine causes, changes and what stops it, before starting any pharmacological treatment.

Often it is the behavioural changes that upset family and carers most. Continually being asked the same question or re-orientating people can be very tiresome. It is important for family and carers to know that their loved one cannot help their behaviour and sometimes the repeated questions are because they feel unsafe. The Alzheimer’s Society provides a useful support for family members. It provides not only advice on how to handle these situations but will also organise respite care (even for a few hours a day) so that the family can continue to have a semblance of a life of their own. The Alzheimer’s Society has branches in most locations but further details can be found at www.alzheimers.org.uk

In Scotland, Alzheimer Scotland provides some useful educational leaflets written in easily readable language. www.alzscot.org

**Note**

SIGN Guideline No. 86 ‘Management of Patients with Dementia’ (February 2006) represents a revision of the previous SIGN Guideline No. 22. Pharmacological interventions, including ChEIs are assessed only on the basis of their clinical effectiveness. SIGN Guideline No. 86 additionally endorses the use of ChEIs for the management of associated symptoms in people with Alzheimer’s disease in addition to its use for treatment of cognitive decline in these people. In addition, SIGN endorses the use of galantamine in treating cognitive decline in people with mixed dementias and the use of rivastigmine to treat cognitive decline and in the management of associated symptoms in people with dementia with Lewy bodies. The guidance is available via www.sign.ac.uk
Psychotic symptoms
Patients with AD often have associated psychotic symptoms such as persecutory delusions and hallucinations. Historically these symptoms were often treated with typical antipsychotics such as thioridazine, haloperidol, promazine or chlorpromazine and more recently with the atypicals, risperidone or olanzapine. However, risperidone and olanzapine were reported by the Committee on Safety of Medicines as being associated with an increased risk of mortality due to cerebrovascular events. If an antipsychotic agent is indicated, it should be started at a low dose, titrated slowly, reviewed regularly and withdrawn as soon as possible.

If psychosis is present, it should be treated, but the use of antipsychotics often extends to control of antisocial or disruptive behaviours. Almost a decade ago, research demonstrated a statistically significant association between the rate of cognitive decline and the prescribing of antipsychotics. Under the OBRA guidelines in the USA such treatment without the patient’s consent is illegal. Typical antipsychotics are particularly unsuitable in the elderly because of their higher risk of EPS, anticholinergic side-effects and tendency to cause postural hypotension (increasing the risk of falling). Patients with Lewy body dementia are extremely sensitive to the extrapyramidal side-effects of typical antipsychotics.

Information on current recommended pharmacological treatments in Scotland can be obtained in the guidance produced by the Royal College of Psychiatrists and SIGN Guideline No. 86 (Feb 2006). www.rcpsych.ac.uk

Agitation
In 1998, the Expert Consensus Guidelines for the Treatment of Agitation in Older Persons with Dementia were published. These can be accessed via www.psychguides.com. They give guidance on two treatment strategies – environmental intervention and the use of medication.

The guidelines describe mild agitation as being behaviour which is somewhat disruptive but non-aggressive such as moaning, pacing, crying or arguing. They describe severe agitation as behaviour that is aggressive or endangers the patient or others, e.g. screaming, kicking, throwing objects, scratching others or self-injury.

Their first recommendation is that the family and/or caregiver(s) are educated about dementia and agitation and are encouraged to join a support group.

The environmental intervention is divided into the subgroups of:

- Physical and psychological structuring, e.g. provide routine, the use of night-lights at night and bright lights during the day (reinforcement of sleep-wake cycle) and familiar articles such as family pictures.
- Behavioural interventions – providing reassurance, reducing isolation and providing stimulating activities.

The most important aim is to identify the trigger for any problem behaviour. For example, television programmes may trigger aggression especially if the patient has difficulty separating reality from fantasy.
Depression
This is generally only a problem in the early stages of AD as insight into feelings and awareness are generally lost by the later stages. An agent with the least anticholinergic and extrapyramidal side-effects is the drug of choice. Sertraline or citalopram can be used, but these agents can exacerbate anxiety in the short-term and are also mood-alerting, so should be given in the morning. Trazodone administered at night is an option if agitation and restlessness are a problem.

Incontinence
As social awareness declines and the patient no longer remembers they actually need to go to the toilet, or they cannot find the toilet, alternative measures are needed. Taking the patient to the toilet at regular intervals during the day helps establish a toilet regimen. If the patient is doubly incontinent, the use of a ‘constipating and laxative’ regimen is often employed. The patient is kept deliberately constipated using codeine or loperamide and then given a stimulant laxative or enema once or twice weekly to produce a controlled bowel action. Toilet-training involves less medication and less distress and discomfort for the patient.

Seizures
Often end-stage AD is associated with the development of seizures. These should be controlled with the appropriate agent for the patient. Treatment options include sodium valproate and phenytoin. Treatment should be monitored for efficacy and any possible side-effects or any change in cognition should be explained to the carer or family.

Sexual disinhibition or sexual aggression
Sexual disinhibition, not uncommon in dementia or other neurodegenerative disorders, is often manifested as inappropriate nudity, public masturbation, stripping or direct advances. The patient may simply not realise they are not alone in their own bedroom. Behavioural management and distraction strategies work well. Medroxyprogesterone and cyproterone acetate, have been used in male patients for the management of more aggressive sexual behaviour. An effect is generally seen in 10 to 14 days as testosterone levels are reduced. The continued need for this medication should be reviewed at regular intervals.

Sleep disorders
Dementia is often associated with a disturbance of the sleep-wake cycle. Even short-acting benzodiazepines and ‘Z’ hypnotics are not indicated as they result in a classic ‘hangover’ effect the next morning and can also cause confusion, impair memory and increase the risk of falls. Small doses of clomethiazole (which increases the inhibitory effects of GABA) can be used for brief periods to control nocturnal wakening, but it is highly addictive. Psychosocial methods such as minimising daytime napping, lowering lights, decreasing external stimuli (noise from televisions and nursing stations), warm milky drinks or a hot bath before bed may also help.

Wandering
Wandering is often aimless and without direction, but unchecked the patient can sometimes disappear. Treatment with typical antipsychotics is potentially dangerous in ‘wanderers’ with dementia as they frequently cause confusion and postural hypotension, which increases the risk of falls in a mobile patient. It is generally safer to ensure the environment is free from obstruction and allow patients to pace.
8.9 Older people and their medicines

The physiological changes of the ageing process result in altered pharmacokinetics and pharmacodynamics in the elderly, increasing their risk of adverse drug reactions and iatrogenic disease. The elderly often suffer from chronic disease and the resulting polypharmacy increases the risk of drug interactions. Medication should be reviewed frequently; at least once every six months.

Concordance is a significant problem in people with dementia because of the inherent memory problems. The challenge is to develop an individualised system that helps the person and their carer or family to manage their medication effectively. NICE guidance insists that the person needs to have ‘a carer or care worker’ who can ensure compliance with treatment with a ChEI. This may determine whether a once daily ChEI is prescribed.

The pharmacist needs to consider the patient’s ability to read the label, understand the directions and access their medication, e.g. blister pack, bottle or compliance aid. A simplified repeat ordering system with the full quantity supplied each time ensures all medicines can be ordered simultaneously, minimising scope for confusion.

It is often important to know who else is involved in the patient’s care in case you need to discuss a change in treatment or functional status. Education of the carer and family is also very important.

Exercise 14

List five areas in which you may be able to provide help or advice when providing medicines for people with dementia.

1. 
2. 
3. 
4. 
5. 

Turn to the end of the chapter for suggested answers
8.10 Communicating with patients

The most important thing to remember when talking to patients with dementia, is that they are still able to communicate and may enjoy the opportunity to do so. However it is advisable to get corroborative or supporting information from relatives or caregiver(s) when necessary, e.g. when taking a medication history. Patients may make things up, rather than upset you, if they think that they should be able to remember an answer to a question but cannot.

The fundamental principle of communication with patients with dementia is to try and capitalise on preserved memory systems:

- speak clearly and audibly
- slow your speech rate
- simplify your vocabulary
- simplify your sentences
- use direct language wherever possible
- limit the number of participants in the conversation
- vary the pitch and tone of your voice
- use a pleasant, accepting tone
- talk about the here and now, not the abstract
- ensure that what you say is understood
- ask closed (‘yes’ or ‘no’) questions
- summarise if the patient forgets
- avoid teasing and sarcasm.

Summary

The dementias are a heterogeneous group of neurodegenerative disorders that result in progressive mental decline.

Non-drug therapies are important in enabling patients and their carers to cope with cognitive decline and challenging behaviours.

The objectives of drug intervention in the management of dementias are to arrest or reduce the rate of disease progression and to manage associated behavioural and psychological symptoms.

The nature and severity of symptoms often changes over the course of the disease and therapy should be reviewed at regular intervals.
Learning Outcomes

On completion of this chapter you should be able to:

1. Identify and describe the key differences between the three most common dementias.
2. Consider the impact of the roles of cholinesterase inhibitors and N-methyl-D-aspartate (NMDA) receptor antagonists in various stages of dementia.
3. Identify side-effects of medication and options for their management.
4. Differentiate in your practice between the need for non-pharmacological and pharmacological treatments for associated behavioural and psychological symptoms in dementia (BPSD).
5. Identify and contribute to the possible ways to improve pharmaceutical care for people with dementia.

Further reading


bmj.bmjjournals.com/cgi/content/full/329/7457/75

Overshott R, Burns A. Clinical Assessment in Dementia. Psychiatry 2004;3(12):13-17

Working group for the Faculty of the Psychiatry of Old Age Royal College of Psychiatry, Royal College of General Practitioners, British Geriatric Society and Alzheimer’s Society following CSM restriction on risperidone and olanzapine. Guidance for the management of behavioural and psychological symptoms in dementia and the treatment of psychosis in people with history of stroke/TIA. March 2004 www.rcpsych.ac.uk/college/faculty/oap/professional/guidance_summary.htm
References


28 Working group for the Faculty of the Psychiatry of Old Age Royal College of Psychiatry, Royal College of General Practitioners, British Geriatric Society and Alzheimer’s Society, following CSM restriction on risperidone and olanzapine. *Guidance for the management of behavioural and psychological symptoms in dementia and the treatment of psychosis in people with history of stroke/ TIA.* London: March 200426.

Suggested answers

Exercise 13 (page 158)
Substance withdrawal or substance intoxication
Endocrine disturbances especially hypo- or hyperparathyroidism; Cushing’s syndrome, hypo- or hyperthyroidism, Addison’s disease
Electrolyte disturbances especially low blood glucose, hyponatraemia or hypercalcaemia
Organ dysfunction for example, hepatic encephalopathy, renal failure, hypoxia or heart failure
Systemic infection, commonly urinary or respiratory tract infections
Other systemic causes such as metastatic cancer, lymphoma or porphyria

Exercise 14 (page 173)
Medicines management:
● side-effects and how to manage them
● symptomatic treatment not curative
● dose titration
● withdrawal issues
● compliance issues
● carer role in monitoring medication
● other chronic conditions
● behavioural problems
● other problems

Education:
● on the disease
● support services
● local memory clinics

Advice
● local and national support groups
● advocacy
● living wills
● social service issues
Chapter 9  Multiple pathology, multiple problems
Objectives

This chapter will enable you to:

- recognise the impact physical illness and non-psychotropic drug therapies have on psychotropic drug selection and vice versa
- discuss ‘polypharmacy’ in mental health
- identify common drug interactions involving psychotropic medication and have an understanding of their mechanism
- discuss changing and stopping psychotropic medication
Chapter 9
Multiple pathology, multiple problems

9.1 Introduction

It is rare for patients to present as a textbook case with a single diagnosis and one medication. Although physical illness predisposes to some mental illnesses, e.g. depression associated with chronic pain or a major stressful event such as heart attack or stroke, it is a golden rule of mental illness that it can affect anyone, including hypertensives, asthmatics, diabetics, epileptics, etc. It is therefore essential to consider physical health as well as mental health when selecting psychotropic medication. Whatever the medication, the more prescribed, the greater the potential for drug interactions and iatrogenic disease.

There are higher levels of physical morbidity and mortality in patients with severe mental illness compared to the general population.

9.2 Psychotropic medication and physical illness

Psychotropic drugs can adversely affect some physical illnesses therefore medication choice needs to be made very carefully, considering the risks and benefits of prescribing (and not prescribing). Close monitoring of the physical illness, psychiatric illness and/or medication may be required. Furthermore some psychotropic medication can cause or mimic the signs/symptoms of a physical condition, e.g. antipsychotics and Parkinson’s disease.

Exercise 15

Consider the list of physical conditions below and indicate what issues they may present in relation to psychotropic drugs. The first one is completed for you.

<table>
<thead>
<tr>
<th>Physical condition</th>
<th>Issues raised with respect to psychotropic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>Antidepressants and antipsychotics can lower the seizure threshold</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines increase the seizure threshold</td>
</tr>
<tr>
<td></td>
<td>Many anticonvulsants interact with a wide range of psychotropic drugs</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td></td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td></td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*
The presentation of some physical conditions can be very similar to the symptoms of mental illness.

Exercise 16
Mrs Jones is recently retired and comes into the pharmacy wanting to buy a ‘health tonic’. She says she’s been feeling tired recently, lacking in energy and motivation and is having problems concentrating and remembering things.

Which of the symptoms detailed above are also associated with the following illnesses?

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symptom(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td></td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*

It is also important to remember that some medications used to treat physical illnesses have been associated with causing psychiatric symptoms.

Exercise 17
Which psychiatric disorders can the following drugs precipitate or worsen?

<table>
<thead>
<tr>
<th>Medication</th>
<th>Psychiatric disorders precipitated or worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td></td>
</tr>
<tr>
<td>Diclofenac</td>
<td></td>
</tr>
<tr>
<td>Methyldopa</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td></td>
</tr>
</tbody>
</table>

*Turn to the end of the chapter for suggested answers*
9.3 Dual diagnosis

There is no agreed definition of the term dual diagnosis, which refers to two concurrent disorders. However, with respect to psychiatric co-morbidity, it is generally understood to be a combination of mental illness and substance misuse. It is recognised that psychiatric co-morbidity covers a broad spectrum of mental health and substance misuse problems.

There are four categories of dual diagnosis:

1. A primary diagnosis of a major mental illness with a subsequent (secondary diagnosis) of substance misuse which adversely affects mental health.
2. A primary diagnosis of drug dependence with psychiatric complications leading to mental illness.
3. A concurrent substance misuse and psychiatric disorder.
4. An underlying traumatic experience resulting in both substance misuse and mood disorders, e.g. post-traumatic stress disorder.

Identification of the primary diagnosis may be problematic. This is because of the mimicking effect of signs and symptoms of mental illness by signs of intoxication and withdrawal of substance use that can lead to misdiagnosis. It is necessary to assess symptoms and syndromes carefully to identify a genuine disorder, as characterised by a DSM IV or ICD 10.

The nature of the relationships between mental disorders and substance misuse use are complex for the following reasons:

- Substance use (even one dose) and withdrawal from substances may lead to psychiatric syndromes or symptoms.
- Intoxication and dependence may produce psychological symptoms.
- Substance use may exacerbate or alter the course of a pre-existing mental disorder.
- Primary mental disorder may precipitate substance use disorder which in itself may lead to psychiatric syndromes.

Psychiatric co-morbidity (dual diagnosis) is not a new issue but it is only relatively recently that it has been recognised by practitioners and policy makers. As a complex area of health and social care, it requires further research in the UK, since the evidence base to date is primarily based on studies in the USA.

A study carried out in Australia, found that among 53 psychiatric hospital inpatients with a diagnosis of substance misuse and schizophrenia, 40% misused mainly alcohol, 40% misused cannabis, 8% amphetamines and 20% misused more than one substance. Of these 80% reported substance use for the relief of anxiety and dysphoria. A US study found that 47% of schizophrenic patients, and 61% bipolar patients, had a substance-related disorder. In the UK it is estimated that one third of patients in mental health services have a substance misuse problem, and around 50% of patients in drug and alcohol services have a mental health problem (most commonly depression or personality disorder).
Introduction to pharmaceutical care in mental health


Other commonly implicated substances include GHB, (crack) cocaine, anabolic steroids, opiates (e.g. heroin, morphine, dihydrocodeine), LSD, ecstasy, magic mushrooms, poppers (alkyl nitrites), solvents, benzodiazepines, ketamine, caffeine and nicotine.

Table 17 Psychiatric effects when particular substances are misused

<table>
<thead>
<tr>
<th>Substance misused</th>
<th>Psychiatric condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Anxiety, Depression, Alcohol hallucinoses, Withdrawal leading to shakes (DTs)</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Paranoia/Delusions leading to psychosis, Low mood leading to depression, Anxiety</td>
</tr>
<tr>
<td>Cocaine when taken with alcohol, a centrally active metabolite cocaethylene is formed which has a longer t1/2, and is more potent than cocaine</td>
<td>Formication (cocaine bugs), Paranoia leading to psychosis, Depression</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Low mood leading to depression, Amphetamine psychosis</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>Mid-week crash/comedown, Altered mental state resembling psychosis</td>
</tr>
<tr>
<td>Heroin</td>
<td>Low mood/depression, Anxiety disorders</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Anxiolytic, Sleep aid. Can be taken with opiates to intensify effect. Also common with stimulant users to aid sleep</td>
</tr>
</tbody>
</table>

Psychiatric disorders and common misused substances:

- **Bipolar Affective Disorder** Increasing prevalence with alcohol and cocaine misuse.
- **Schizophrenia** Increasing prevalence with cannabis and alcohol misuse.
- **Post Traumatic Stress Disorder (PTSD)** Increasing prevalence with alcohol and opiate misuse.
- **Affective disorders** (including anxiety) Increasing with use of alcohol and opiates.
- **Personality Disorders** Increasing with use of alcohol and benzodiazepines.

Pharmacists are likely to encounter people with dual diagnosis requiring pharmacy services for both their mental illness and substance misuse. They may require the following services:

- advice and support
- needle exchange service
- signposting towards appropriate services
● dispensing and information provision:
  – substitute medication, e.g. methadone, buprenorphine (Subutex)
  – detoxification medication, e.g. lofexidine, chlordiazepoxide
  – substance aversion medication, e.g. disulfiram, naltrexone
  – medication for their mental illness
  – compliance support/monitoring
  – medication for substance misuse-associated complications, e.g. hepatitis, infections at injection sites.

In addition, pharmacists can provide a professional link between services, as it is often the case that one service looks after the mental illness and another, the substance misuse.

Pharmacists should be aware that individuals with mental health problems and a co-occurring substance misuse problem are likely to present with problems often associated with the substance misusing fraternity which include: criminality, financial worries (debt) chaotic lifestyles, homelessness, physical ill health and general poor hygiene. These factors may contribute to non-compliance of a recommended treatment regime or relapse.


9.4 Polypharmacy

Polypharmacy is an ill-defined term, generally referring to the use of more than one medication to treat a certain condition, but can also be defined as using more than one type of drug from the same class. This is generally considered to be poor prescribing practice, particularly when both medicines belong to the same class of medication. However, the use of more than one medication from different classes is often accepted practice within psychiatric treatment protocols.

For example the use of a typical and an atypical antipsychotic would generally be considered poor practice – NICE guidance on atypical antipsychotics for schizophrenia states that:

‘atypical and typical antipsychotic drugs should not be prescribed concurrently, except for short periods to cover changeover of medication’.

However the long-term combination use of an antipsychotic and a mood stabiliser may be appropriate for treating bipolar disorder if the patient fails to respond to monotherapy and continues to experience sub-threshold symptoms or relapses – British Association of Psychopharmacology (BAP) Guidelines.1
Exercise 18

List some of the potential benefits and problems of polypharmacy

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There are a variety of reasons why polypharmacy may occur in the treatment of mental illness, they include those listed below.

- **Prophylaxis against an undesirable effect, e.g. someone with a diagnosis of bipolar disorder (manic depression) requiring antidepressant medication may be on a mood stabiliser to protect against the antidepressant provoking a manic/hypomanic episode (refer to Section 5.6 for further information). The combination is thought to provide a unique effect only achieved by using more than one drug (not usually supported by a strong evidence base but there is good evidence to support the combination of an antipsychotic and mood stabiliser in mania refer to Section 5.6 for further information.**

- **Treatment of the psychotropic drugs’ side-effects, e.g. EPS with the older typical antipsychotics (and some atypicals) being treated with an antimuscarinic agent such as procyclidine or akathisia in the early stages of treatment with an SSRI being treated with a benzodiazepine (maximum two weeks).**

- **Medication not being regularly reviewed, e.g. continuation of an antimuscarinic agent to treat EPS without reviewing the need for it.**

- **Augmentation of treatment in treatment resistance, e.g. addition of lithium to an antidepressant or sulpiride to clozapine. Such practices are only appropriate under specialist supervision.**

- **Changing from one drug to another (see later section for more information) – sometimes the person appears to be much better during the cross-titration and both medications are continued intentionally. However, at other times this may be an oversight!**

- **Where distressing symptoms are unlikely to respond to medication immediately, e.g. for severe anxiety and/or insomnia in depression – a short course of an anxiolytic/ hypnotic may be helpful for the first one to two weeks of antidepressant treatment.**

- **In the experience of the patient, or sometimes the prescriber, a particular combination has proved/is being successful (albeit that this may be due to a ‘placebo’ response).**

- **In the hope of producing an earlier onset of action, e.g. pindolol with antidepressants – (refer to Section 4.4 for further information).**
To avoid exceeding the BNF maximum dose of one medication, a second medication is added – this is not a safer or better option: it is difficult to know which is producing the response and there is a greater potential for interactions. Furthermore this approach doesn’t work: when two or more antipsychotics are combined, the doses should be added together and calculated as a percentage of the BNF maximum, so the maximum is still exceeded.

To treat relapse in a patient prescribed a depot antipsychotic an oral antipsychotic is often added for several months until symptoms resolve or a higher dose of depot becomes effective.

Exercise 19
Suggest possible rationales for the following prescriptions:

Patient 1
36-year-old male
Lithium Carbonate MR (Priadel) 800 mg ON
Semisodium valproate 500 mg BD
Patient 2
28-year-old female
Risperidone long-acting injection 25 mg IM every two weeks
Risperidone tablets 2 mg BD
Procyclidine 5 mg BD
Patient 3
45-year-old male
Paroxetine 20 mg OD
Diazepam 2 mg TDS

Turn to the end of the chapter for suggested answers
9.5 Drug Interactions

Many psychotropic/psychotropic and psychotropic/non-psychotropic combinations involve an interaction. Most are predictable, some are of limited clinical relevance and many can be managed safely. However a few are potentially very dangerous and should be avoided. It is important to be aware of what may happen when drugs are combined and advise accordingly.

Interactions between drugs are either pharmacodynamic (the effects of one medication are changed by the presence of another at its site of action) or pharmacokinetic (one medication interferes with the absorption, distribution, metabolism and elimination of another medication).

**Pharmacodynamic interactions**

Below are some examples:

<table>
<thead>
<tr>
<th>Additive effect on</th>
<th>By drugs such as</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postural hypotension</td>
<td>Tricyclic antidepressants, benzodiazepines, antipsychotics, antihypertensive medication</td>
</tr>
<tr>
<td>CNS depression</td>
<td>Tricyclic antidepressants, benzodiazepines, antipsychotics, older antihistamines, alcohol</td>
</tr>
<tr>
<td>Anticholinergic effects</td>
<td>Tricyclic antidepressants, antimuscarinics, antipsychotics, hyocine hydrobromide</td>
</tr>
<tr>
<td>Risk of serotonin syndrome*</td>
<td>Antidepressants in high dose or in combination with other antidepressants, tramadol or lithium</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opposing effect on</th>
<th>By drugs such as</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>Caffeine</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Typical (and some atypical) antipsychotics versus anti-parkinsonian medication</td>
</tr>
</tbody>
</table>

*Serotonin syndrome is due to an excess of serotonin in the synapse causing hyper-stimulation and presents with the following symptoms: restlessness, agitation, fever, diaphoresis (excessive sweating), diarrhoea, tremor, shivering, hyper-reflexia, poor coordination, myoclonus, confusion, convulsions. It can be fatal.

**Pharmacokinetic interactions**

The majority of pharmacokinetic interactions associated with psychotropic medication are related to metabolism. The liver breaks down many psychotropic medications, through the cytochrome P450 enzyme system. This enzyme system has many subtypes, e.g. 2D6, 1A2, and medications are metabolised by different subtypes. Essentially medications that inhibit a particular enzyme subtype are likely to increase the level of that enzyme’s substrate and vice versa if the enzyme is induced. However, to complicate the issue, most medications can affect and are substrates for more than one enzyme subtype.
Below are some commonly encountered pharmacokinetic interactions:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect on enzyme</th>
<th>Examples of effect on other medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Induces CYP3A4/4</td>
<td>Reduces the level of diazepam, quetiapine, risperidone, valproate, zopiclone</td>
</tr>
<tr>
<td>Triazole antifungals, macrolide antibiotics</td>
<td>Inhibits CYP3A4/4</td>
<td>Increases the level of diazepam, carbamazepine, quetiapine, risperidone, valproate, zopiclone</td>
</tr>
<tr>
<td>Fluvoxamine, cimetidine, erythromycin, omeprazole</td>
<td>Inhibits CYP1A2</td>
<td>Increases the level of clozapine, diazepam, theophylline, some TCAs</td>
</tr>
<tr>
<td>SSRIs (fluoxetine, paroxetine, sertraline)</td>
<td>Inhibits CYP2D6</td>
<td>Increases the level of some TCAs, venlafaxine</td>
</tr>
</tbody>
</table>

**Exercise 20**

For each of the following prescriptions, comment on the possible drug interactions and on what action you would take.

1. Mrs White presents with a prescription for:  
carbamazepine 200 mg BD, increase to 400 mg BD after one week.  
You note from her PMR that she normally takes risperidone 2 mg BD.

2. Mr Brown comes to the pharmacy with a prescription for:  
chlorpromazine 200 mg BD, procyclidine 5 mg BD.  
He says he’s had both medications before ‘for ages’.

201
3. Mr Green presents with a prescription for: phenelzine 15 mg OD. Last week you dispensed a prescription for fluoxetine 20 mg OM (30).

4. Mrs Orange brings in her regular prescription for: Lithium carbonate (priadel) 400 mg ON together with a new script for Diclofenac 50 mg TDS prn.

9.6 Stopping medication

There will be times when it is necessary to stop a psychotropic medication. Sometimes it is necessary to stop the medication abruptly; for example due to a severe physical illness or a severe adverse drug reaction. Ideally however, the dose of psychotropic medication should be gradually reduced to avoid discontinuation symptoms and prevent relapse. This is normally possible if the reason for stopping medication is non-urgent, e.g. due to lack of effect (despite adequate dose being taken for an adequate duration) or annoying but not serious side-effects that persist beyond two weeks and/or are unacceptable to the individual.

Problems associated with stopping

Some drugs such as benzodiazepines and some hypnotics are addictive, and if used regularly for over four weeks do need to be withdrawn very gradually; for example by reducing the dose by approximately one-eighth every two weeks. If stopped abruptly, the person may suffer with symptoms such as agitation, anxiety, insomnia, panic attacks, tremor, dry mouth, headache, palpitations, loss of appetite/weight, sweating, tinnitus, perceptual disturbances and seizures.
Other drugs, although not addictive, do need to be withdrawn gradually to prevent withdrawal problems. The extent and symptoms of withdrawal depends on the medication, duration of treatment and dose.

**Antidepressants**

It is now recognised that all antidepressants have the potential to cause discontinuation symptoms, particularly if they have been taken continuously for eight or more weeks, although some antidepressants e.g. paroxetine and venlafaxine, seem particularly troublesome on discontinuation. Where possible, antidepressants should be withdrawn gradually (over a four week period or longer if required) to prevent this occurring, although this is probably not necessary with a normal dose (20 mg/day) of fluoxetine due to its very long half-life.

Discontinuation effects may be similar to the original depressive symptoms, but can also include flu-like symptoms (myalgia, chills, headache), insomnia, excessive dreaming, ‘shock like’ sensations, dizziness and irritability. These effects usually occur within five days of stopping the antidepressant and do not usually last more than one to two weeks, resolving if the antidepressant is reinstated.

**Drugs with anticholinergic (antimuscarinic) activity (e.g. procyclidine, and some antipsychotics and antidepressants)**

The sudden withdrawal of such medications can result in cholinergic rebound which presents as nausea, vomiting, diarrhoea, headache and restlessness.

**Other medications**

If some medications are withdrawn abruptly this can precipitate an acute episode of mental illness. For example, if lithium is abruptly stopped this is highly likely to provoke an affective episode of mania or depression. Lithium should be reduced over at least four weeks to minimise the likelihood of this occurring. Abrupt cessation of most antipsychotics, particularly clozapine, can result in rebound psychosis.

### 9.7 Changing medication

There are different ways of changing from one medication to another. The choice of strategy is usually influenced by factors such as;

- the medications involved
- the reason for the medication change
- the patient’s location (for example, an inpatient can be more closely monitored but is probably more acutely unwell)
- the patient’s preference/past experience of medication change
- the risk/consequences of relapse.
### Exercise 21

Listed below are four different ways of changing medication. **List one advantage and one disadvantage of each strategy.**

Start the new medication, in addition to the original medication. When the new medication is at a therapeutic dose remove the original medication.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
</table>

Stop the original medication one day, start the new medication the next day.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
</table>

Cross titrate, i.e. gradually reduce the dose of the original medication (to zero), as the dose of the new medication is gradually increased.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
</table>

Allow a washout period between medications, i.e. a period without medication.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
</table>

*Turn to the end of the chapter for suggested answers*
Exercise 22

Mrs Taylor was started on amitriptyline 25 mg at night, and advised to increase the dose by 25 mg every night until she reached a dose of 150 mg. Her GP phones you to tell you that Mrs Taylor is not willing to take the amitriptyline anymore and therefore he would like to change her to fluoxetine 20 mg in the morning.

a. What questions would you ask the GP?

b. What advice would you give?

c. What monitoring might you advise?

Turn to the end of the chapter for suggested answers

Summary

Severe mental illness often presents with complex symptomatology that may require a combination of psychotropic agents. Mental illness secondary to substance misuse is also common as is the misuse of substances to self-medicate primary mental illnesses. Psychotropic polypharmacy is a frequently encountered problem.

The symptoms of mental illness often fluctuate over time and the emphasis of treatment may change accordingly from management of an acute episode to prevention of relapse or cessation of treatment.

Physical and mental illness often co-exist giving rise to enormous potential for drug interactions and requiring careful consideration of the treatment of each condition with respect to the other.
Learning Outcomes

On completion of this chapter you should be able to:

1. Recognise the impact physical illness and non-psychotropic drug therapies have on psychotropic drug selection and vice versa.
2. Assess the impact of ‘polypharmacy’ in mental health in the context of your practice.
3. Identify common drug interactions involving psychotropic medication and have an understanding of their mechanism.
4. Discuss and consult with people about changing and stopping psychotropic medication.

Further reading


Reference

   www.bap.org.uk/consensus/FinalBipolarGuidelines.pdf

Suggested answers

Exercise 15 (page 181)

<table>
<thead>
<tr>
<th>Physical condition</th>
<th>Issues raised with respect to psychotropic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>Antidepressants and antipsychotics can lower the seizure threshold. Benzodiazepines increase the seizure threshold. Many anticonvulsants interact with a wide range of psychotropic drugs.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Antipsychotics, especially some of the atypical antipsychotics, increase the risk of developing diabetes and exacerbate existing diabetes. Antidepressants can also affect glycaemic control.</td>
</tr>
</tbody>
</table>
| Cardiovascular disease | Psychotropic drugs can affect the cardiovascular system in various ways such as:
  ● changing the heart rate
  ● altering the blood pressure (e.g. causing postural hypotension)
  ● prolonging the QTc interval (predisposes to potentially fatal Torsades de Pointes)
  ● causing arrhythmias and conduction disturbances |
| Parkinson’s disease | Antipsychotics, especially the older ones, cause extrapyramidal side-effects, also referred to as pseudo-Parkinsonism. Some antidepressants have been associated with causing movement problems too, e.g. paroxetine. |
## Exercise 16 (page 182)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symptom(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Tired, lacking in energy and motivation, problems concentrating, memory problems.</td>
</tr>
<tr>
<td>Dementia</td>
<td>Problems concentrating (distractable), memory problems.</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Lack of energy, problems concentrating, memory problems.</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Lack of energy, tired.</td>
</tr>
</tbody>
</table>

## Exercise 17 (page 182)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Psychiatric disorders precipitated or worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Agitation, hypomania, psychosis (delusions, hallucinations, paranoia), depression, anxiety, insomnia, aggression.</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Nervousness, depression, insomnia, anxiety, psychotic reaction.</td>
</tr>
<tr>
<td>Methyldopa</td>
<td>Psychosis, depression.</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Euphoria, psychological dependence, depression, insomnia, psychosis, ‘aggravation of schizophrenia’.</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Confusion, depression, hallucinations.</td>
</tr>
</tbody>
</table>

## Exercise 18 (page 186)

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased therapeutic benefit</td>
<td>Increased risk of drug interactions.</td>
</tr>
<tr>
<td>May be more acceptable to the patient, e.g.</td>
<td>More complex medication regimens are more difficult to comply with.</td>
</tr>
<tr>
<td>if they’ve done well on a combination before.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased risk of side-effects.</td>
</tr>
<tr>
<td></td>
<td>More expensive both in terms of drug costs and prescription charges.</td>
</tr>
</tbody>
</table>

## Exercise 19 (page 187-189)

**Patient 1 – 36-year-old male**

Lithium Carbonate MR (Priadel) 800 mg ON
Semisodium valproate 500 mg BD
- Change from mood stabiliser to another, i.e. cross titration
- Addition of second drug due to lack of efficacy with monotherapy
- Lack of communication between primary and secondary care resulting in unintentional combination therapy
Patient 2 – 28-year-old female
Risperidone long-acting injection 25 mg IM every two weeks
Risperidone tablets 2 mg BD, Procyclidine 5 mg BD
- Depot antipsychotic preparations take several months to reach steady state and during this time oral medication is often continued. (Note: Risperidone long-acting injection only releases the majority of the dose into the body three weeks after it is administered.)
- Risperidone can cause EPSE. These are usually dose-related, occurring more commonly at doses above 4–6 mg/day. Procyclidine may therefore be needed, however as the advantage of risperidone, i.e. lack of EPS, is not being realised, it may be better to consider alternative treatment.
- Medication may not have been reviewed; procyclidine may have been prescribed when she was on typical antipsychotic medication and its use has not been reviewed since she started on an atypical antipsychotic.
- If it is more than three weeks since she began to receive the resperidone long-acting injection, the oral risperidone should ideally be stopped, or at least be under regular review. If the combination has continued for longer than four weeks (SmPC minimum time between dose increments; in practice probably leave for longer before increasing the depot dose), perhaps the dose of the injection needs increasing to 37.5 mg every two weeks.

Patient 3 – 45-year-old male
Paroxetine 20 mg OD, Diazepam 2 mg TDS
- He may be suffering the severe anxiety and/or depression. Although the anxiety may resolve as the antidepressant takes effect this may take around two weeks. The diazepam treats this in the interim.
- Paroxetine could be causing anxiety. Diazepam is not a long-term solution in this situation and perhaps the choice of antidepressant needs to be reviewed.
- His anxiety/depression is usually well controlled on the paroxetine however he is currently under a lot of stress and is experiencing breakthrough symptoms of anxiety.
- He has been prescribed diazepam for a non-psychiatric indication.
Exercise 20 (page 191-192)

1. **Mrs White presents with a prescription for carbamazepine 200 mg BD increase to 400 mg BD after one week. You note from her PMR that she normally takes risperidone 2 mg BD.**

**Interactions**
- Carbamazepine is a potent enzyme inducer and can halve the serum level of risperidone potentially rendering it ineffective and risking the relapse of psychosis.
- Risperidone may lower the seizure threshold and may be the reason why carbamazepine is prescribed, although this is unlikely – see action required to check indication for carbamazepine.

**Actions required**
- Identify the indication for the carbamazepine.
- Contact the prescriber regarding the risperidone/carbamazepine interaction and advise that the dose of risperidone may need to be increased. Could an alternative mood stabiliser/anticonvulsant that does not interact be prescribed?
- Counsel Mrs White accordingly.

2. **Mr Brown comes to the pharmacy with a prescription for chlorpromazine 200 mg BD, procyclidine 5 mg BD. He says he’s had both medications before ‘for ages’.**

**Interaction**
- Increased risk of anti-muscarinic side-effects eg constipation.

**Actions required**
- Would be reasonable to dispense.
- Enquire whether Mr Brown is happy with/suffering any side-effects with his medication.
- If appropriate, provide printed information, refer him to reliable internet resources, for example the patient information section of the NICE schizophrenia guideline.
- Consider asking prescriber to review the ongoing need for the procyclidine (may no longer be required, also possibly increases the risk of developing tardive dyskinesia).

3. **Mr Green presents with a prescription for: phenelzine 15 mg OD. Last week you dispensed a prescription for fluoxetine 20 mg OM (30).**

**Interaction**
- Fluoxetine and phenelzine interact with potentially life-threatening consequences. A washout period is essential and in the case of fluoxetine this is at least five, ideally six weeks.

**Actions required**
- Do not dispense the prescription.
- Ask Mr Green when he last took a dose of fluoxetine.
- Contact the prescriber to advise of the need for a five to six week washout period between the drugs, or to consider another antidepressant.
4. Mrs Orange brings in her regular prescription for Lithium carbonate (priadel) 400 mg ON together with a new script for Diclofenac 50 mg TDS pm.

Interaction
- Diclofenac can increase lithium levels by about a quarter, probably due to inhibition of renal prostaglandin causing reduced renal blood flow. Depending on MRs Orange’s current lithium level, this could result in lithium toxicity.

Actions required
- Contact the prescriber, check that he is aware of the interaction and will be monitoring the lithium levels closely (as per initiation of lithium); consider reducing lithium dosage unless pre-NSAID levels allow for potential increase without toxicity.
- Consider suggesting an alternative analgesic, e.g. paracetamol, sulindac, aspirin or a topical preparation.
- If oral diclofenac is considered essential, suggest the dose is taken regularly rather than when required – more consistent and manageable effect on lithium level.
- Counsel Mrs Orange regarding the interaction, check that she knows what the early signs of lithium toxicity are (tremor, nausea, diarrhoea).
Exercise 21 (page 194)

Start the new medication, in addition to the original medication. When the new medication is at a therapeutic dose remove the original medication.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensures condition is treated throughout</td>
<td>Risk of interactions/toxicity</td>
</tr>
<tr>
<td></td>
<td>Need to ensure the process is completed, i.e. first medication is stopped</td>
</tr>
</tbody>
</table>

Stop the original medication one day, start the new medication the next day.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less complicated for the patient and prescriber to manage</td>
<td>Risk of withdrawal problems</td>
</tr>
<tr>
<td></td>
<td>Risk of interactions</td>
</tr>
<tr>
<td></td>
<td>Some medications need gradual titration of dose</td>
</tr>
</tbody>
</table>

Cross-titrate, i.e. gradually reduce the dose of the original medication (to zero), as the dose of the new medication is gradually increased.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimises likelihood of withdrawal problems</td>
<td>Complicated for the patient to follow</td>
</tr>
<tr>
<td>Allows gradual introduction of new medication, minimises side-effects</td>
<td>Risk of interactions</td>
</tr>
</tbody>
</table>

Allow a washout period between medications, i.e. a period without medication.

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoids risk of drug interactions</td>
<td>Leaves illness untreated for prolonged period of time (washout periods usually one to two weeks, depending on medication, five weeks for fluoxetine)</td>
</tr>
<tr>
<td>May be more straightforward to manage</td>
<td>This may not be acceptable to the patient but could point out that a few days washout is unlikely to affect symptoms</td>
</tr>
</tbody>
</table>
Exercise 22 (page 195)

a. What questions would you ask the GP?

- Is Mrs Taylor’s refusal to continue with the amitriptyline due to side-effects? A slower titration rate would probably reduce the incidence of side-effects; (however, an SSRI is a better choice anyway).
- What other medication is she taking currently?
- How did she get on with any antidepressants taken previously?
- What dose has she got to? NICE suggests that not everyone needs to reach a dose of 150mg to achieve efficacy.
- How long ago did she start the amitriptyline?

b. What advice would you give?

- Reduce the dose of amitriptyline to around 50mg/day and start fluoxetine. Reduce/stop the amitriptyline over the next week.

Note
This advice would depend upon how long Mrs Taylor had taken the amitriptyline for and what dose she had reached. A long duration of high dose of amitriptyline would require a more cautious reduction in amitriptyline dose.

c. What monitoring might you advise?

- mental state – if Mrs Taylor did not achieve a therapeutic dose of amitriptyline, her depression has been without treatment for some time.
- side-effects: e.g. nausea, headache, agitation, insomnia.
- any other adverse drug reactions, e.g. serotonin syndrome, rash.
Chapter 10

The role of the pharmacist in managing mental health
Objectives

This chapter will enable you to:

- consider the issues that affect concordance in mental health patients
- identify some information resources that are available to you that could be of use with your patients and assess their place in your practice
- monitor for side-effects and drug interactions
- assist patients in an advocacy role to ensure that they receive the most appropriate drug therapy
- identify five of your patients with mental health problems who are most at risk from poor pharmaceutical care
- discuss the attitudes, needs and perspectives of users and carers to the medicines prescribed for mental health problems
Chapter 10

The role of the pharmacist in managing mental health

10.1 Introduction

Working with patients with mental health problems presents pharmacists with both opportunities and challenges. Pharmacists have opportunities to use their training and develop their skills; but often have to examine their own pre-conceptions of mental health and mental illness.

Previous sections have concentrated on supporting a knowledge base in relation to the concept of mental illness, specific mental illnesses and effective therapeutic interventions. This section is designed to show how pharmacists can build on this core knowledge and skill to become more effective members of the mental health workforce.

10.2 Setting the scene

Mental health has been one of the key clinical priorities for NHS Scotland since 1995. The vision of how services for all people with mental health problems and their informal carers should be structured comes from the essential features in the Framework for Mental Health Services in Scotland (1997). The Framework is a ‘living’ document and remains relevant to the latest thinking and policy advances by additions when and where necessary of new sections or expanded entries to the text. For example: additional service profile on services for women with postnatal depression (March 1999), guidance on services for those with an eating disorder (October 2001), additional service profile on Perinatal Mental Illness and Postnatal Depression Hospital Admission and Support Services (March 2004) and services profile for co-ordinated services for those with dementia and their carers (November 2004).

Our National Health: a plan for action, a plan for change (Scottish Executive, 2001) endorsed the principles of the Framework as providing a joint planning template for health, social work, housing agencies and voluntary sector partners for the provision of a modern comprehensive range of services and support from hospital to domiciliary care.

Model schemes for pharmaceutical care provided an opportunity for community pharmacists to support people with mental health problems in the community.

Partnership for Care. Scotland’s Health White Paper (Scottish Executive, 2003) further promotes joint working between health service, local authorities, the voluntary sector and communities. Modernisation of NHS Scotland by systematic redesign, and integration is envisaged to form a single system, working to improve the patient’s pathway of care and to promote better use of shared resources.

The SEHD Delivering for Mental Health which was published in December 2006 in response to one of the key recommendations from Delivering for Health, to develop a national Mental Health Delivery Plan by the end of December 2006. The principles should accelerate improvements in
mental health services and that where possible these services should be delivered as locally as possible, provide systematic support for people with long-term conditions, reduce the health inequality gap and actively manage admissions and discharges to and from hospital. Pharmacists have a key role to play in working with other healthcare professionals, social work colleagues, carers and patients in delivering this agenda.


The strategic work programme of NHS Quality Improvement Scotland (NHSQIS) for 2005–08 outlines their plans to improve the quality of mental health services in Scotland, to deliver better outcomes for all those receiving mental health services. The current challenges include the new Mental Health Act, establishment of Community Health Partnerships and new ways of working with other agents including the Care Commission, NHS Education for Scotland, Mental Welfare Commission, Social Work Inspection Agencies as well as the Mental Health and Well Being Support Group. The strategic work programme can be viewed at www.nhshealthquality.org/nhsqis/files/Final%20Strategy.pdf

Refer to Chapter 1 (Section 1.7) for the following:

- SIGN Guidelines
- NHS QIS Standards
- NICE technology appraisals
- NICE guidelines

Many of these documents are weighty and you are not expected to access and read them all! However you should be aware of how the key elements are being implemented in your locality and how your practice could make a positive contribution. More broadly, the policies outlined in Communities and Neighbourhoods are also relevant to tackling the social exclusion and discrimination experienced by people with mental health problems.

The National Institute for Mental Health in England is working to improve the way mental health services are provided. Part of their work is to ensure that people working in mental health share the same values. The document The Ten Essential Shared Capabilities: A Framework for the Whole of the Mental Health Workforce was developed as a starting point for this. The document can be accessed at www.nimhe.org.uk/downloads/78582-DoH-10%20Essentials.pdf

Although this document has been developed for practice in England it provides an opportunity to reflect on your practice. Similar values are also seen within the Millan principles relating to the Mental Health (Care and Treatment) (Scotland) Act. (See Chapter 1.)

The Ten Essential Shared Capabilities for Mental Health Practice

**Working in partnership**
Developing and maintaining constructive working relationships with service users, carers, families, colleagues, lay people and wider community networks. Working positively with any tensions created by conflicts of interest or aspiration that may arise between the partners in care.

**Respecting diversity**
Working in partnership with service users, carers, families and colleagues to provide care and interventions that not only make a positive difference but also do so in ways that respect and value diversity including age, race, culture, disability, gender, spirituality and sexuality.
Practising ethically
Recognising the rights and aspirations of service users and their families, acknowledging power differentials and minimising them whenever possible. Providing treatment and care that is accountable to service users and carers within the boundaries prescribed by national (professional), legal and local codes of ethical practice.

Challenging inequality
Addressing the causes and consequences of stigma, discrimination, social inequality and exclusion on service users, carers and mental health services. Creating, developing or maintaining valued social roles for people in the communities they come from.

Promoting recovery
Working in partnership to provide care and treatment that enables service users and carers to tackle mental health problems with hope and optimism and to work towards a valued lifestyle within and beyond the limits of any mental health problem.

Identifying people’s needs and strengths
Working in partnership to gather information to agree health and social care needs in the context of the preferred lifestyle and aspirations of service users their families, carers and friends.

Providing service user-centred care
Negotiating achievable and meaningful goals; primarily from the perspective of service users and their families. Influencing and seeking the means to achieve these goals and clarifying the responsibilities of the people who will provide any help that is needed, including systematically evaluating outcomes and achievements.

Making a difference
Facilitating access to and delivering the best quality, evidence-based, values based health and social care interventions to meet the needs and aspirations of service users and their families and carers.

Promoting safety and positive risk-taking
Empowering the person to decide the level of risk they are prepared to take with their health and safety. This includes working with the tension between promoting safety and positive risk taking, including assessing and dealing with possible risks for service users, carers, family members, and the wider public.

Personal development and learning
Keeping up-to-date with changes in practice and participating in life-long learning, personal and professional development for one’s self and colleagues through supervision, appraisal and reflective practice.

Throughout this section consider how your response to each exercise fulfils at least one of the shared capabilities and identify any personal learning needs necessary to enable you to expand your capabilities in your CPD portfolio.
Pharmaceutical Care in Mental Health

The role of the pharmacist for mental health patients can be wide and varied depending on the sector of care that the pharmacist works in, their interest in getting more involved in caring for mental health patients and their expert knowledge and skills. The community pharmacist is a frontline healthcare professional who is likely to see their mental health patients or carers on a regular basis. Some of the initiatives that they may wish to get involved in are listed below:

- Involvement in any local Community Health Partnership (CHP) initiatives for mental health patients.
- Collaborate with other professionals, local authorities, carers and patients in relation to mental health services in the local area.
- Provide information in their pharmacy on self-help groups/ websites/ support groups etc. They should also consider the availability of information in other languages depending on their local patient group.
- Be mindful that individuals with mental health problems often have poorer physical health than individuals without mental health problems. The reasons for this are many, but side effects from psychotropic medication are known to play a significant part.
- Carry out a needs assessment for patients e.g. there is a national Needs Assessment Tool developed for Depression available from the NES website resources section www.nes.scot.nhs.uk/pharmacy/resources. As a result of the needs assessment the pharmacist may then deliver pharmaceutical care in some of the following areas depending on the patient’s needs:
  - Ensure the prescribed drug is on the local formulary.
  - Can the prescribed regime be reviewed with regards to dose/frequency/duration? Could other non-pharmacological treatments be recommended?
  - Are there any contra-indications to the prescribed treatment regime that the GP should be made aware of?
  - Advise and counsel the patient of any side-effects they may experience e.g. dry mouth with the tricyclic antidepressants can be alleviated by sucking sugar-free sweets or chewing sugar-free chewing gum, and then need for attention to dental care.
  - Advise the patient on any drug interactions with other medicines (prescribed or OTC) e.g. St Johns Wort has various clinically significant interreactions.
  - If antidepressants are being changed, is the ‘switching’ process being carried out in a safe and appropriate manner?
  - Advise the patient on how other issues can impact on their mental health and the treatment of it e.g. substance misuse.
Exercise 23

Consider how you would respond to a patient or carer presenting with a new prescription and request for information about each of the following:

Ramipril for hypertension

Simvastatin for secondary prevention in diabetes

Citalopram for depression

Lithium after a recent manic episode

Olanzapine for residual psychotic symptoms previously treated with haloperidol

There are no right or wrong answers to the exercise, but you may have considered it appropriate to discuss what the medicine is for, when and how to take the medicine, what the expected benefits of treatment are, any possible side-effects and how to deal with them, any special considerations, e.g. interactions and cautions. If you felt more confident discussing hypertension and diabetes than depression and psychosis, you are not alone. However, it may be an indication that you need to re-examine your knowledge of psychotropic medication, your understanding of mental illness or your attitude to mental health – or even all three.
Case study 6

John
John is a young man who has been using your pharmacy for some years. He has been prescribed lithium 800 mg SR nocte for the last 14 months since his previous admission to hospital. He was discharged from an inpatient mental health unit two months ago following an acute manic relapse. John presents his repeat prescription for dispensing. It does not include lithium.

What are the possible explanations and how would you respond?

Turn to the end of the chapter for suggested answers

10.3 Information needs of patients and their carers

Pharmacists may have preconceived ideas about the information patients need about their medication. It is important to invite questions and tailor replies to the needs of the patient and their carers.

Information leaflets are a common and relatively easy means of providing information in response to questions by patients, but vary widely in their suitability for individuals. When considering which ones best suit which patients, the issues to consider are:

- the range of questions covered
- the depth of detail in answering a particular question
- the language used – text that…
  - uses short words (not longer than three syllables)
  - uses short sentences (less than 15–20 words per sentence) and
  - avoids jargon
- is usually easiest to read.
Case study 7

A man appears in your pharmacy with a prescription for risperidone. His address is not local and he appears anxious to talk to you. He explains that he doesn’t have schizophrenia or any other kind of psychotic disorder and doesn’t understand why he has been given risperidone. He is also unhappy about taking a drug that labels him as ‘mad’ and which will make him fat.

How will you deal with this situation and what care issues can you identify?

Turn to the end of the chapter for suggested answers

Practice point

Extend your consideration of jargon to the language that you use with your patients. How could you communicate with patients more effectively? Make notes in your CPD portfolio to help you do this.

Some people want very superficial information; others want lots of detail. Some people want answers to very specific questions; others want general information. Try and build up a range of information to cater to varying needs. Ask your local acute, mental health or primary care division what information they provide. Other sources of patient information include:

- **Well Informed** leaflets cover the typical issues dealt with on a manufacturer’s patient information leaflet, but avoid the legal requirements. They are usually written to answer questions about specific drugs. [www.northmersey.nhs.uk/Informed/WIMEDCONTENTS.HTM](http://www.northmersey.nhs.uk/Informed/WIMEDCONTENTS.HTM)

- United Kingdom Psychiatric Pharmacy Group (UKPPG) patient advice leaflets available on a CD ROM offer answers to fewer questions but in much more depth. Many users and carers appreciate the table of side-effects and how to treat them. The leaflets are generally about groups of drugs. [www.ukppg.org.uk/ukppg-pals.html](http://www.ukppg.org.uk/ukppg-pals.html)
Norfolk and Waveney Mental Health Partnership NHS Trust pharmacy department website – detailed and wide ranging but still generally deal with groups of drugs. www.nmchte.nhs.uk/pharmacy/drug_idx.htm

Manufacturer’s PILs are available from the Electronic Medicines Compendium. www.medicines.org.uk

Patient groups (for example, Rethink, Mind, Alzheimer’s Society, Manic Depression Fellowship).

Royal College of Psychiatrists – excellent generic information resources on the illnesses and their treatments. www.rcpsych.ac.uk/mentalhealthinformation.aspx

The National Electronic Library for Mental Health – evidence based treatment summaries for healthcare professionals currently only available for antidepressants. Less detailed information leaflets on antidepressants, antipsychotics, benzodiazepines, mood stabilisers and anticholinergic medication are also available. www.nelmh.org/home_therapeutic_approaches.asp?c=20

Leaflets may be required in languages other than English or in large print. There are a also a wide variety of other formats available – videos and DVDs from www.videosforpatients.co.uk in their What you really need to know about series and helplines for example, MIND Infoline, Breathing Space, NHS24 and UKPPG. Further information is available in Appendix 3 and in the resource pack developed by NES and SPMH for ‘Depression’. www.nes.scot.nhs.uk/pharmacy/resources/depression_resource/depression_resource.html

**Practice point**

Search out new patient information resources. The Internet is a good place to start as long as you are confident about judging the content of unaccredited websites. Make notes in your CPD portfolio to help you do this.

### 10.4 Patients at special risk

People at particular risk of mental illness are those who have undergone a major life event in the last six months; e.g. bereavement, divorce or redundancy. Others at risk include people living alone, people with co-morbidity, substance misusers and those who have a blood relative with mental health problems.

**Practice point**

Do you have patients who you are concerned about and want to keep an eye on? Do you record observations and incidents that concern you? Make a note in your CPD portfolio to remind you to consider it soon.
10.5 Concordance with medication

Concordance is a complex issue at the best of times but the same fundamental principles apply to concordance in mental healthcare that apply in the management of physical conditions. Professionals involved in patient care, the patient and, if appropriate, their carer should reach agreement on an appropriate treatment plan. Without concordance, non-adherence to treatment is often justified. Once an agreement has been reached on the treatment strategy, the carer and members of the community mental health team (CMHT) should ensure that patients adhere to their therapy. Non-adherence with therapy in mental illness is no more common than in any other illness but may have serious consequences beyond the immediate health of the patient, e.g. broken relationships, financial difficulties, family breakdown.

Exercise 24

List some of the influences that contribute to non-adherence and consider how these might vary in the context of different illnesses and indeed different stages of a mental illness.

What support can you offer your patients who have compliance problems?

Turn to the end of the chapter for suggested answers
Case study 8

A regular customer informs you that her elderly mother is depressed and has come to live with her for a while until she starts to feel better. She tells you that her mother is refusing to take her antidepressants because ‘they don’t work’. She has been thinking of opening the capsule and sprinkling the contents into a fruit yogurt. She wants to know if the medication will still work if she does this.

What is your response and what are the care issues in this situation?

Turn to the end of the chapter for suggested answers
10.6 Stopping the medication

One of the most common questions asked of pharmacists is ‘When can I stop taking my medicines? I don’t want to get hooked on these.’ This is often a more complicated question than it first appears. On the one hand, pharmacists are keen to ensure that patients don’t take medication for longer than necessary. On the other hand, they know that stopping medication is one of the primary causes of relapse.

Pharmacists should also be aware of discontinuation syndrome which can arise if antidepressant therapy is abruptly stopped. They should be aware of what the symptoms are and offer reassurance to patients.

Case study 9

Sara
Sara, a school teacher, became depressed following a series of assaults at school. This coincided with a period of difficulties with her teenage daughter and her husband (who was having an affair). She recently returned to work after a three-month break and is finding the environment very stressful. For the last four months she has taken paroxetine 30 mg daily, which she feels has helped her greatly. Unfortunately she feels nauseous from time to time and her daughter keeps calling her a ‘junkie’, saying that she should not be taking drugs. She asks ‘Should I stop taking the medicines? I feel fine now.’

Which of the following course(s) of action would you follow?

a. Support her in her desire to stop taking the medicines.
b. Advise her to reduce the medicines very slowly. She should discuss with her GP a reduction of 10 mg now and see how it goes in a month.
c. Not want to get involved or give an opinion and refer her to her GP.
d. Tell her that it is usual for treatment to continue for six months to a year, and if she stops taking the antidepressant now the likelihood is that she will relapse.
e. Tell her that any decision to stop the medication should be following a discussion with the prescriber.
f. Tell her that there are other effective treatments that may not cause so much nausea.
g. Tell her that it may be possible to reduce the dose to 20 mg daily and achieve the same results with fewer side-effects.
h. Refer her to the NICE patient guide for managing depression. www.nice.org.uk/pdf/CG023publicinfo.pdf

Turn to the end of the chapter for suggested answers
10.7 Prodromes for mental illness

Many patients have minor symptoms in the days or weeks preceding an acute episode or are aware of factors that often precipitate an episode. Often a pattern is established and such ‘prodromes’ are particularly important for patients with frequent relapses, when relapses are severe or episodes are difficult to treat. Patients and their carers and family can be taught to recognise the early signs of a relapse and get professional advice quickly. Rapid interventions may prevent relapse or reduce the duration or severity of the episode. Some patients are particularly good at using prodromes to manage their mental health problems and self-management techniques are being taught by the mental health charities.

For more information see www.rethink.org/recovery/self-management

Case study 10

Edward
Edward is a 68-year-old man who takes lithium (Priadel) 600 mg SR tablets at night for bipolar affective disorder. He is normally well and effectively maintained on this dose but recently complained about having problems swallowing his tablets. You told him that a liquid was available and suggested that he should ask his GP to prescribe it.

Several months later Edward comes into the pharmacy with his prescription for Priadel liquid 5 ml at night. He says he’s never felt better and you find it difficult to get a word in edgeways in the conversation.

What questions would you ask and what would you do?

Turn to the end of the chapter for suggested answers
10.8 An advocacy role for pharmacists

There are a number of organisations, run by former mental health service users, which provide assistance to patients and their carers. One of the most common requests of the various helplines operated by these organisations is for advice and assistance about medicines. The people operating the helplines feel unable to answer many of the questions as they do not have the right access to professional advice.

This was one of the core reasons why the UK Psychiatric Pharmacy Group telephone helpline was established. The helpline is run by pharmacists from the Maudsley Hospital in South London and is financially supported by the National Institute for Mental Health in England [www.nimhe.org](http://www.nimhe.org). The fact that there is such a demand for medication information from a helpline suggests that the assistance available locally does not fully meet the needs.

No doubt you are confronted with issues on a regular basis. Do you feel that it is your responsibility to speak on the patient’s behalf, or do you prefer to represent the prescriber and the medical perspective? Consider the following situation.

**Case study 11**

Danny

Danny suffered from schizophrenia, the main features of which were that he developed paranoid delusions of a persecutory nature, which resulted in his behaviour becoming unacceptable. During his 15-year illness, many aspects of his pharmaceutical care were less than optimal:

- he was prescribed flupentixol decanoate depot injection which caused him to gain a considerable amount of weight.
- he remained on the medicine for many years without a review.
- he was prescribed medication to assist weight loss which was contraindicated and on which he became dependent (taking up to 200 tablets per month).
- he stopped accepting the antipsychotic and became ill.

**How could intervention by a community pharmacist have assisted Danny?**
There are no right or wrong answers, but this case raises the following issues:

- When you have concerns about a patient’s drug treatment, how effectively can you influence the action of the prescriber?
- Do you have many patients who remain on long-term treatments without review?
- Do you know who else to contact who may be able to influence the action and behaviour of the patient?
- How explicitly do you counsel your patients about side-effects?
- How does Danny’s case fit the recommendations of the NICE technology appraisal for newer (atypical) antipsychotics?

Practice point

If you found you were ‘out of your depth’, what additional resources do you need to be able to offer more help? Make notes in your action planner to help you.

10.9 The specialist mental health pharmacist

Specialist mental health pharmacists have been appointed in most areas of Scotland and are usually based within secondary care. Specialist mental health pharmacists have a complementary and supporting role to non-specialist pharmacists (community and hospital) in the management of patients with mental health conditions. Community pharmacists should find out who the local specialist mental health pharmacist(s) is/are in their local areas in order that they can support you in developing your services to mental health patients in your practice.

Scottish Pharmacy in Mental Health (SPMH) is a group open to membership from pharmacy staff (hospital, primary care, academia, community pharmacists and pharmacy technicians) interested in pharmaceutical care within mental health. SPMH aims to encourage, develop and promote the delivery of quality pharmaceutical care within mental health. Several clinical meetings and a seminar are organised each year and a newsletter is circulated to members at least twice a year. Membership is free – details are available at the website www.spmh.org.uk

The United Kingdom Psychiatric Pharmacy Group (UKPPG) is a UK-wide special interest group for all pharmacists and pharmacy support staff who work in mental health. Membership of the group offers a number of opportunities – the bulletin and newsletter keep members up-to-date with topical issues; training courses and an international annual psychiatric pharmacy conference are available; an e-discussion group can be used to pose your queries and get support from colleagues around the world. The website address is www.ukppg.org.uk

In parallel, the United Kingdom Mental Health Pharmacy Technicians Network (UKMHPTN) is working to represent and fulfil the needs of pharmacy technicians working in mental health. Its website address is www.pastonsites.co.uk/ukppg/technicians.html
A few years ago, it was felt that a mechanism of accreditation was required for specialist mental health pharmacists, for a number of reasons. Principally, the new clinical governance agenda that the government was proposing was a challenge that the UKPPG could not realistically deliver. The College of Mental Health Pharmacists (CMHP) was developed and now works to encourage the recognition and accreditation of specialist mental health pharmacists in the UK. Accreditation is by submission of a portfolio of evidence in conjunction with an oral viva voce exam. Pharmacists are accredited against a wide range of core competencies including pharmacology, clinical practice and management issues.

Further information is available on the website www.ukppg.org.uk/cmhp.html

10.10 What do users think?

It is government policy to encourage healthcare providers to invite users of services to give their opinion of those services. Mental health services should involve both current and past service users in designing the future service. In preparing this section, a local mental health charity was invited to provide a digest of users’ views of community pharmacy services. Many users were complimentary of the services offered and held the local community pharmacist in high regard. They also, however, suggested some areas where changes in attitude or practice may help.

People reported that:
- They are often treated in an ‘off hand’ manner.
- The counter staff cause embarrassment by asking or allowing other customers to hear the details of their medication.
- Even though the pharmacist knows from the prescribed medicine that the patient has mental health problems, they can still behave in an ‘off hand’ and inappropriate manner.
- Patients have to ask for information about the side-effects of medication, which may indicate that information about side-effects is not always provided.

Other suggestions included:
- Even if details of the medication have been explained on numerous occasions, pharmacists should offer this information.
- People wanted to be able to discuss other prescribed alternatives to their medication with the pharmacist.
- A poster could invite people to discuss side-effects and alternatives to prescribed medication with the pharmacist, to take the onus for this initiative off the service user.
- People wanted an independent opinion on their medication, as little information is given by their doctors or nurses.
- People wanted an explanation if a ‘different’ medication is given, e.g. when given a branded instead of a generic drug or vice versa, as this change can cause confusion and concern.
- Information leaflets about prescribed medicines could be added to the medication bag.
There is often a perception among service users that a request to a nurse or doctor for information is interpreted as the patient being ‘unwell’ or intending to stop taking medication. Pharmacists would be an appropriate alternative as they have no ‘power’ to change the medication or dose.

It was felt that pharmacists need to promote themselves more proactively in this role – stressing their independence, confidentiality and accredited competence.

Changing to a generic presentation without warning causes confusion – ‘I know I take a white round tablet in the morning but there is no white round one there!’ *

People want a supportive attitude from pharmacy staff – some pharmacists showed a lack of knowledge, sympathy or understanding of their patients’ conditions; others have a negative attitude when their clients are unwell.*

**Sources include:**
‘Service users’ experiences of medication.’ *Pendulum*, Autumn 2003: 9


*Comments from the Manic Depression Fellowship – personal communication.

**Practice point**
Does this feedback from service users prompt you to take action? Identify three areas of your practice that you wish to improve on. Make notes in your RPSGB CPD records at [www.uptodate.org.uk](http://www.uptodate.org.uk)

**Exercise 25 - answer here**

**Community Pharmacy Contract in Scotland**

The New Community Pharmacy Contract in Scotland has been introduced to modernise NHS community pharmacy services by developing a new system of remuneration for community pharmacists, which provides incentives to improve and deliver quality care health services focussing on the provision of pharmaceutical care rather than the supply function.

The outline framework of the New Contract consists of two main elements:

- **Essential Pharmaceutical Care Services** – centrally negotiated (terms of service and remuneration) consisting of the:
  - Public Health Service
  - Minor Ailment Service
  - Chronic Medication Service
  - Acute Medication Service.

- **Additional Services** – these will be locally negotiated with a national framework and benchmark tariff available to support the process.
Within the Essential Services, the Public Health Service and the Minor Ailment Service were introduced in 2006, with the plan to introduce the other parts in 2007/08.

Additional Services will be subject to local NHS Board negotiation, for example – the supply and supervision of methadone and needle exchange services which may be important as substance misuse can accompany mental health problems. In addition, smoking cessation services may be important since there is a high incidence of cardiovascular and respiratory problems amongst people with enduring mental illnesses. Details on additional local services will be available from your local NHS Board.

Public Health Service (PHS)

Pharmacies will be paid a fixed fee for delivering public health messages to communities as part of the Scottish Executive’s drive to use community pharmacies as ‘healthy living walk in centres’. This service provides an opportunity for community pharmacists to provide education and advice on smoking cessation, substance misuse and lifestyle behaviours.

‘Those who suffer from mental illness have greater risk of, and higher rates of, heart disease, diabetes, respiratory disease and infections. They also have higher rates of smoking, alcohol consumption and drug misuse. They die younger and have a poorer quality of life’.


Practice Point

Consider how the Public Health Service could help to improve the health and wellbeing of people with mental illness.

Minor Ailment Service (MAS)

The service allows patients who are exempt from NHS prescription charges to receive advice and/or treatment for any presenting common clinical conditions from a community pharmacy, free of charge.

The advantages of MAS include:

- enhanced services to patients
- greater use of pharmacists’ skills
- enhancement of the pharmacist’s local primary care role and better integration with other members of the local primary health care team
- better access to NHS services for patients as no appointment is necessary to see a pharmacist.

Conditions covered by the service include: athlete’s foot, bites and stings, back pain, diarrhoea, cough, fever, hay fever, headache/earache, head lice, mouth ulcers, soft tissue injury, sore throat, sprain/strain, vaginal thrush, nasal congestion, constipation, and indigestion/heartburn/stomach upset.

Patients with mental health problems often present with minor ailments particularly due to the side-effects of medication, e.g. constipation, blurred vision, headaches or perhaps due to poor self care e.g. athlete’s foot.
Chronic Medication Service (CMS)
This service will allow pharmacists to manage a patient’s medication for up to 12 months as part of a shared care arrangement with the patient and his or her GP. A patient’s medicines will be dispensed, monitored and reviewed. Patients involved in the service will need to register with the pharmacy.

Within Scotland the ‘Pharmaceutical Care Model Schemes’ (PCMS) were the forerunners of the new contract and will form the clinical and practice components of the CMS. Patients with mental health problems benefited from these schemes for example by – improved concordance with medication, reduction in the impact of side-effects, minimisation of the risk of drug interactions, and reduced opportunity for overdose.

Medication regimes used to treat mental health problems and any concurrent physical illness may be complex. Compliance is further compromised by inadequate understanding and knowledge of medication, unpleasant side-effects and illness-related factors such as poor motivation, lack of insight and impaired memory. In addition, patients with enduring mental illnesses have a high incidence of cardiovascular and respiratory problems. There is also a high incidence of diabetes in people with schizophrenia and those treated with antipsychotics, particularly olanzapine and clozapine. As a result, patients with mental health problems may be included in your delivery of the Chronic Medication Service.

Practice Point
Half of people with long-term conditions fail to take their medicines properly.
Consider how the CMS could benefit someone with an enduring mental illness.

Summary
Managing mental health problems can be both demanding and rewarding. Often the most challenging aspect is addressing personal lack of understanding and pre-conceptions about mental illness.

Some pharmacists may aspire to become specialists in this area, while others will be content to fulfil a supporting role. Whatever your aspirations, your personal contribution will be greatly enhanced by an ability to engage effectively with people suffering from mental disorders and their carers.

Further reading
1 Scottish Association for Mental Health. ‘All you need to know?’ 2004 (A survey of mental health service users’ views on psychotropic medication) www.samh.org.uk
2 NSF (now Rethink), MIND, MDF (now the Bipolar Organisation). ‘A Question of Choice’ 2000 (A survey of people’s views on medicine and other interventions for mental health illness. www.rethink.org/how_we_can_help/publications/a_question_of.html
Learning Outcomes

On completion of this chapter you should be able to:

1. Consider the issues that affect concordance in mental health patients and take account of these in your consultation with patients.
2. Identify suitable information resources, assess their place in your practice and make available for use with your patients.
3. Adapt procedures to monitor for side-effects and drug interactions.
4. Assist patients in an advocacy role to ensure that they receive the most appropriate drug therapy.
5. Identify five of your patients with mental health problems who are most at risk from poor pharmaceutical care.
6. Consider the attitudes, needs and perspectives of users and carers. Inform and involve them as appropriate with the medicines prescribed for mental health problems.

Suggested answers

Case study 6 – John (page 210)

Discontinuation of lithium may be intentional. Is there any evidence of alternative treatment, e.g. valproate? The simplest solution would be to ask John why there is no lithium on his prescription. Many patients have difficulty coming to terms with their illness and may lack insight when ill and find it easy to deny the illness when well.

Some may simply enjoy the experience of hypomania (although full blown mania is often far from pleasant) and resent medical interference. If it is apparent from the information John provides that he has decided not to take lithium anymore he is at high risk of manic relapse. He may be aware of the fact and choose to accept the risk but it would be helpful to know what his reasons for discontinuing treatment are. Often patients are reluctant to discuss their concerns about medication with people immediately involved in their care for fear that it will be interpreted as a sign they are becoming ill again.

Pharmacists are in the advantageous position of being experts on medicines but having no power to impose treatment on patients and this can make it easier for patients to discuss their beliefs and concerns about treatment. Whatever the outcome of your discussions, it would be appropriate to contact John’s GP and/or community mental health team and alert them to the fact that he is no longer taking lithium so that they can make appropriate provision for follow-up.
Case studies with Pharmaceutical Care Issues

Case study 7 (page 211)

<table>
<thead>
<tr>
<th>Pharmaceutical Care Issue</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient needs correct factual information</td>
<td>Find out what the risperidone is being used for hold. Ask the patient why they went to the doctor. What information (if any) has he been given? Is he consulting the internet? Which website(s) is he consulting? Can you recommend a particular site that might be more helpful? What are his symptoms? (It is possible that the risperidone is being used off license for another indication? If so, how will you describe ‘off license’ use to this individual?)</td>
</tr>
<tr>
<td>Patient is aware of stigma associated with medication and illness</td>
<td>Discuss and reassure the patient about stigma. Refer to ‘SeeMe’ etc. if required for further support</td>
</tr>
</tbody>
</table>

Exercise 24 (page 213)

Reasons for non-adherence

- Lack of insight (psychotic illnesses in particular).
- Lack of motivation (depression – apathy, mania – enjoys the highs, substance misuse – enjoys the effects of continued misuse).
- Distrust (delusional beliefs about medication).
- Denial of illness.
- Poor previous experience with medication (eg manic switching on antidepressant therapy).
- Family, personal or cultural prejudices about the illness.
- Forgets (poor cognition – dementia, schizophrenia).
- Runs out of medication (poor personal organisation or social isolation, eg dementia, schizophrenia, depression).
- Fear of dependence or addiction.
- Side effects of medication (actual or anticipated).
- Medication regime inconvenient or too complicated.
- Poor doctor patient relationship.
- Lack of information about the illness or the treatment.
- Ill-informed or incorrect information.
**Exercise 24 (continued)**

**Support a pharmacist could offer:**
- Determine the reasons for non-adherence, i.e., accidental or deliberate.
- Identify the factors contributing to non-adherence.
- Address the need for more information about drug therapy and possible alternatives, either personally or via external sources, e.g., UKPPG National Medication Helpline number (Telephone: 020 7919 2999 available 11am–5pm weekdays).
- Counsel patients on the benefits of treatment and the risks associated with defaulting from treatment.
- Refer to GP, CMHT member, care coordinator.
- Consider compliance aids, alternative formulations, simplified regimes, etc.
- Provide details of local and national support services and self-help organisations, e.g., NHS24, Bipolar Fellowship Scotland, Depression Alliance, National Schizophrenia Fellowship (Scotland).

**Case Study 8 (page 214)**

<table>
<thead>
<tr>
<th>Pharmaceutical Care Issue</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covert administration of medication</td>
<td>What is a pharmacist's professional and ethical obligation in such a situation? Consult RPSGB legal department for advice Or Mental Welfare Commission for Scotland See website <a href="http://www.mwcscot.org.uk/goowpratice/guidancedocuments">www.mwcscot.org.uk/goowpratice/guidancedocuments</a></td>
</tr>
<tr>
<td>Patient and her daughter need accurate information about the condition and its treatment, what will you tell them?</td>
<td>Ascertained why patient thinks ‘medication won’t work’ You might have to explain that the antidepressant effect can take time</td>
</tr>
<tr>
<td>Prescribing in the elderly What issues are specific to the elderly that need to be addressed?</td>
<td>Polypharmacy (might have physical co-morbidity) Administration of medication (may need a compliance aid) Increased susceptibility to side effects</td>
</tr>
</tbody>
</table>
Case study 9 – Sara (page 215)
Answers d, e, f, g and h apply, but if she is insistent, warn her of the problems associated with abrupt discontinuation.

Case study 10 – Edward (page 216)
From Edward’s presentation, there is a concern that he may be developing hypomania – rapid speech, expansive mood. This may progress to mania.

600 mg lithium carbonate daily does not equate to lithium citrate 5 ml daily. Non-modified release preparations of lithium must be given twice daily; lithium carbonate 200 mg (5.4 mmol Li⁺) is equivalent to lithium citrate 509 mg. Total daily dose was 16.2 mmol Li⁺, equivalent to 7.5 ml (8.1 mmol) lithium citrate twice daily. This is a mistake which can be made by psychiatrists, GPs, nurses and pharmacists, which puts the patient’s mental health status at real risk.

Ask Edward if he is taking his medication and how long he has been feeling like this?

Actions to be taken
1. Contact whoever arranged the swap from tablets to liquid – the GP, psychiatrist or CMHT key-worker. Has he had a 12-hour lithium blood test recently? The results will show that the serum lithium concentration has dropped from 0.75 – 0.23 mmol.
2. Liaise with the GP and change the prescription to Priadel liquid 7.5 ml bd. Repeat the standard 12-hour lithium level in about 5 – 7 days time.
3. Dependent on Edward’s mental health state, alert the CMHT or his key-worker so that close monitoring can be instituted and/or a short course of an appropriate anti-manic medication can be prescribed.
Glossary

The following glossary of terms is taken from the National Service Framework for Mental Health, the National Electronic Library for Mental Health and similar sources for Scottish mental health definitions.

Acute dystonia
Involuntary contraction of the skeletal muscles of the face, neck and trunk that occur as a side-effect of antipsychotic medication.

Affective or mood disorders
These reflect a disturbance in mood, resulting generally in either depression or elation, which is often chronic or recurrent in nature. There are usually also associated alterations in activity, sleep and appetite. Affective disorders vary greatly in severity and include bipolar mood disorder or manic depressive illness. They may also be often associated with symptoms of anxiety.

Akathisia
A subjective feeling of motor restlessness felt mostly in the legs that occurs as a side-effect of antipsychotic medication.

Akinesia
An extrapyramidal side-effect of antipsychotic medication characterised by apathy and a decrease in spontaneous movement.

Anticholinergic effects
Includes dry mouth, blurred vision, constipation, urinary retention, hypotension.

Antipsychotic drugs
Drugs used to treat psychosis, including schizophrenia and mania. They also have tranquillising effects, reducing agitation.

Anxiety
A mood state in which feelings of fear predominate and where the fear is out of proportion to any threat. Frequently associated with physical symptoms which include fast pulse rate, palpitations, sweating, shaking, ‘pins and needles’. Anxiety disorders can include simple phobias, fear of a specific object or situation, generalised anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder or post-traumatic stress disorder.

Approved Social Worker (ASWs) (England)
see MHO for Scotland
Approved social workers are social workers specifically approved and appointed under Section 114 of the Mental Health Act 1983 by a local social services authority ‘for the purpose of discharging the functions conferred upon them by this Act’. Among these, one of the most important is to carry out assessments under the Act and to function as the applicant in cases where compulsory admission is deemed necessary. Before being appointed, social workers must undertake post qualifying training approved by the Central Council for Education and Training in Social Work (CCETSW).

Assertive outreach (assertive community treatment, intensive case management)
An active form of treatment delivery: the service can be taken to the service users rather than expecting them to attend for treatment. Care and support may be offered in the service user’s home or some other community setting, at times suited to the service user rather than focused on service providers’ convenience. Workers would be likely to be involved in direct delivery of practical support, care co-ordination and advocacy as well as more traditional therapeutic input. Closer, more trusting relationships may be developed with the aim of maintaining service users in contact with the service and complying with effective treatments.
Atypical antipsychotic drugs
Newer and more expensive antipsychotic drugs which have a different range of side-effects from the standard antipsychotics, and generally have a lower incidence of extrapyramidal side-effects.

Care co-ordinator (or key worker)
A worker (team member) with responsibility for co-ordinating CPA reviews for mental health service users with complex needs and for communicating with others involved in the service user’s care. Care co-ordinators usually have the most contact with the service user.

Care management
A system of organising care to vulnerable adults by local authority social services departments. It involves assessing needs, care planning, the organisation of care packages within available resources, monitoring and review and close involvement with service users and carers. For mental health service users it should be integrated with the Care Programme Approach.

Care Programme Approach (CPA)
The CPA provides a framework for care co-ordination for service users under specialist mental health services. The main elements are a care co-ordinator, a written care plan, and at higher levels, regular reviews by the multi-disciplinary health team and integration with the social services care management system. Updated and simplified guidelines, with two levels of CPA, standard and enhanced, were published by the Department of Health in association with the National Service Framework. (Also used within NHS Scotland).

Carers
Relatives or friends who voluntarily look after individuals who are sick, disabled, vulnerable or frail.

Clinical governance
A framework through which NHS organisations are accountable for continuously improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will improve.

Cognitive behaviour therapy
A form of psychological treatment based on learning theory principles used mostly in depression but increasingly shown to be a useful component of treatment in schizophrenia.

Commission for Health Improvement (CHI)
A national body responsible for overseeing and supporting the implementation of clinical governance and the quality of clinical services.

Community mental health nurse/community psychiatric nurse (CPN)
Mental health nurse with specific expertise in working with patients in the community, in functioning in a multidisciplinary team and in working across the inpatient/community interface.

Co-morbidity
The simultaneous presence of two or more disorders, often refers to combinations of severe mental illness, substance misuse, learning difficulties and personality disorder. The term dual diagnosis or complex needs may also be used.

Compliance therapy
The frequent finding of poor compliance with prescribed treatments in individuals with severe mental ill health has led to the development of a cognitive-educational treatment package. The aim is to improve a patient’s understanding of their illness and to identify and tackle reasons for lack of adherence to suggested treatments.
**Crisis Resolution/Home Treatment Team**
Specialist multidisciplinary team providing support and treatment at the patient’s home as an alternative to hospital admission or to support early discharge from hospital.

**Depression**
A negative mood state which involves a feeling of sadness. Depression can range from mild to severe, with the treatment depending on the severity. Depression can frequently coexist with and complicate other physical illnesses. The most frequent disorder found in the National Morbidity Survey was a mixed anxiety-depression.

**Disengagement**
Loss of contact with services by the service user.

**Dual diagnosis**
Dual diagnosis and complex needs are used to describe people with a combination of drug and alcohol misuse and mental illness, a combination of medical needs, including diagnosis, treatment and rehabilitation; and social needs, including housing, social care and independent living. Some of those in this group may also have a history of offending and involvement in the criminal justice system. They are all amongst the most socially excluded.

**Eating disorders**
These disorders include anorexia nervosa and bulimia nervosa. They are disorders that tend to have an early onset in childhood or adolescence and are less frequently seen in males. Anorexia nervosa involves a distortion of body image in which the person believes they are much fatter than they actually are. They very carefully restrict their intake of calories, exercise to excess, are markedly underweight and may be very secretive. Bulimia nervosa involves episodic binges of over-eating, and self-induced vomiting and laxative abuse in some cases. They may maintain a more normal body weight but can have severe physical complications.

**Extrapyramidal side-effects**
Includes acute dystonia, akathisia, Parkinsonism, akinesia, and tardive dyskinesia.

**First-level advice from NHS 24**
First-level advice to provide comprehensive information about services and treatments that are available locally. If necessary, NHS 24 aims to ensure callers are directed to the right service, providing referral on to specialist helplines or mental health services.

**Gender dysphoria** *(gender identity disorder)*
A conviction that one is ‘trapped’ in a body of the wrong gender. Tends to have been present from childhood. The individual wishes to live in the opposite gender role from their biological one and often pursues the goal of achieving surgical gender reassignment.

**Home treatment**
Treatment may be offered in a patient’s home rather than in clinical settings, either by a separate team or by a community mental health team. Frequent home visits by various members of the multidisciplinary team can lead to an avoidance of some hospital admissions and provide support to informal carers. Such services should be available at weekends and in evenings as well as during office hours.

**Independent sector**
Voluntary, charitable and private care providers of services to people with mental health problems.

**Mental disorder**
Mental disorder is defined in the 1983 Mental Health Act and Mental Health Scotland (1984) Act as ‘mental illness, arrested or incomplete development of mind, psychopathic disorder and any other disorder or disability of mind’. The Act does not define mental illness, which is a matter for clinical judgement.
Mental health
An individual’s ability to manage and cope with the stresses and challenges of life.

Mental Health Officers (MHOs) Scotland
Are specialist qualified social workers, with at least two years experience and an additional MHO qualification. They provide a statutory, specialist, social work service 24 hours a day. They are employed by the local council and NOT the NHS. They act as a safeguard to ensure that medical, and nursing staff consider alternatives that may be available, before, admitting a person to hospital under a statutory order.

Mental health organisations
Health and social care commissioners and providers of specialist mental healthcare, including independent sector providers.

Mental health services
Specialist provision of mental health and social care provision integrated across organisational boundaries.

Mental illness
Range of diagnosable mental disorders that excludes learning disability and personality disorder.

National Institute of Clinical Excellence (NICE) (England)
Established in April 1999, the Institute is responsible for promoting clinical excellence and cost-effectiveness, producing and issuing clinical guidelines.

Neuroleptic malignant syndrome
This rare and potentially fatal side-effect of antipsychotic medication is characterised by altered consciousness, high temperature, and muscular rigidity.

Parkinsonism
Tremor, muscular rigidity, or absence of movement that occurs as a side-effect of antipsychotic medication.

Personality disorder
This covers a variety of clinically significant conditions and behaviour patterns, which tend to be persistent and to arise in childhood or adolescence. They are not secondary to other mental disorders but may coexist with them. The disorder will generally involve problematic relationships and may be associated with personal distress. A very small subgroup of those with personality disorder may be antisocial and dangerous.

Psychological therapies
Talking therapies, including psychotherapy, counselling, family therapy, and cognitive behaviour therapy.

Psychotropic drugs
Medication used in the treatment of mental disorder.

Regional Secure Units (RSU) known as Medium Secure Units in Scotland
Medium secure units are for individuals who are thought to pose special risks, particularly of violence to others. (See Security – medium).

Schizophrenia
Schizophrenia is a severe psychotic mental illness in which there may be distorted perceptions and thinking, as well as inappropriate or blunted mood. Individuals with this disorder may hold beliefs that seem impossible to others.
Security

Low
Some local hospitals have wards with locked doors and above average staff ratios. Also known as intensive care or high dependency units.

Medium
Medium units, including Regional Secure Units (see above) which care for patients whose behaviour is too difficult or dangerous for local hospitals but who do not require the higher levels of security available in special hospitals.

High
Provided by the three special hospitals in England – Ashworth, Broadmoor, and Rampton and one in Scotland (State Hospital, Carstairs). Their patients are often very dangerous and violent and require intensive care, supervision and observation within the most secure surroundings.

Service user(s)
People who need health and social care for their mental health problems. They may be individuals who live in their own homes, are staying in care, or are being cared for in hospital.

Social care
Personal care for vulnerable people, including individuals with special needs which stem from their age or physical or mental disability, and children who need care and protection. Examples of social care services are residential care homes, home helps and home care services. Local authorities have statutory responsibilities for providing social care.

Substance misuse
Includes illicit drug use, such as heroin and other opiates, amphetamines, ecstasy, cocaine and crack cocaine, hallucinogens, cannabis, and prescribed drugs such as benzodiazepines, as well as substances such as alcohol. Substance misuse can cause psychological, physical, social and legal problems.

Supervised discharge
Under the 1995 Mental Health (Patients in the Community) Act consultant psychiatrists may apply for powers of supervision of patients following discharge from hospital. A supervisor, typically a community psychiatric nurse acting as care co-ordinator, has the power to ‘take and convey’ the patient to a place of treatment, but not to treat them.

Tardive dyskinesia
Potentially irreversible involuntary movements of the mouth, lips, and tongue, and possibly involving limb and trunk movements, which occur as a side-effect of antipsychotic medication.

Glossary
Appendix 1

Mental healthcare through the ages

2,000 BC
Mesopotamian priest-physicians dealt with mental disturbance which was attributed to demonic possession, whilst ‘lay’ physicians dealt solely with physical injury. This was the first known division between mental and physical symptoms.

c460 BC
Hippocrates wrote 76 treatises which are still considered to be the foundations of modern medicine and psychiatry. He described melancholia, postpartum psychosis, mania, phobias and paranoia and believed that thoughts and feelings occur in the brain, rather than the heart.

c400 BC
Plato proposed a view of the soul (psyche) as a charioteer driving two horses, one noble, the other driven by base desires. The charioteer struggles to balance their conflicting impulses.

c110 BC
Cicero designed an interview format used throughout the Roman empire containing the following items:

- **Nomen**: clan/tribe, region, connections
- **Natura**: sex, nationality, family status, age, physique
- **Victus**: education, association, habits/lifestyle
- **Fortuna**: rich/poor, free/slave, social class
- **Habitus**: appearance
- **Affectio**: passions, emotions, temperament
- **Studium**: interests
- **Consilium**: motivation
- **Factum**: working history
- **Casus**: significant life events
- **Orationes**: form and content of discourse

which remained in use for 1600 years until the dissolution of the monasteries.

25 BC–50 AD
The influence of enlightened views of the Roman doctors began to decline, and Cornelius Celsus recommended starvation, fetters and flogging and anything ‘which thoroughly agitates the spirit’. He reinstated the idea that some illnesses were caused by the anger of the gods, and his words were used in the Middle Ages to justify the burning of witches.

50–130 AD
Aretaeus established the fact that manic and depressive states occur in the same individual and that lucid intervals exist between manic and depressive episodes. He also understood that not everyone with mental illness is destined to suffer intellectual deterioration, a fact not adequately emphasised until the 20th century.

130 AD
Soranus of Ephesus stressed the importance of convalescence and aftercare. He also suggested that mania should be treated with the alkaline waters of the town that contained high levels of lithium – a treatment rediscovered by John Cade in the 1940s.
Rhazes was a chief physician at a Baghdad hospital where there was a psychiatric ward. Because the Arabs had no fear of demons, patients were kindly treated and appear to have made use of forms of behaviour therapy.

12th century
Medieval laymen had more enlightened attitudes toward mental health problems than did professionals; poetry and other literature present very realistic views of the subject. In the early days of the Bethlehem hospital (Bedlam), patients were treated with concern and issued with arm badges to wear so that they could be returned to hospital if their symptoms recurred. Vagrants sometimes counterfeited the badges so that they could be taken for former patients of Bedlam!

14th century
People with mental health problems were considered witches and again became victims of persecution.

15th century
Two Dominican monks wrote Malleus Maleficorum (The Witches’ Hammer), a gruesome and pornographic book which became the witch-hunter’s bible. A lot of the information was about deviant behaviour, much of it overtly sexual. This was at least partly due to the belief that insanity was caused by possession by the devil, and a devil possessed a witch by copulating with her. As the ultimate salvation of the immortal soul was more important than the comforts of the possessed body, physical punishments such as drowning and burning were used to make the body an intolerable refuge for the devil. Dissemination of the book was greatly facilitated by the development of printing and it ran into 10 editions.

16th century
Demonology and witch-hunts continued while others had more enlightened beliefs. Juan Luis Vives (b. 1492) put forward a concept of treatment for mental distress which we would do well to bear in mind today:

‘Since there is nothing in the world more excellent than man, nor in man than his mind, particular attention should be given to the welfare of the mind; and it should be considered a highest service if we either restore the minds of others to sanity or keep them sane and rational….

One ought to feel great compassion for so great a disaster to the health of the human mind, and it is of utmost importance that the treatment be such that insanity be not nourished and increased, as may result from mocking, exciting or irritating madmen…’

Weyer (b. 1515) had a profound influence on the treatment of mental distress, emphasising that illnesses attributed to witches came from natural causes. He also considered the effects of drug-induced hallucinations, and provided clinical descriptions of auditory hallucinations and persecution mania.

17th century
There was a belief that if mad people behaved like animals, they should be treated like animals. Thomas Willis, a neuroanatomist and doctor, advocated intimidation via threats and beatings. In contrast to this Robert Burton proposed a therapeutic programme of exercise, music, drugs and diet and stressed
the importance of discussing problems with a close friend (or a doctor).

In the 17th century people with mental health problems were often cared for privately. This system of private treatment began with Helkiah Crooke, physician to James I and Bethlem Hospital who took patients into his own home for treatment. From boarding a single lunatic it was a short step to providing accommodation for numbers of patients, and thus setting up a private madhouse. Thomas Allen, a physician at Bethlem Hospital also ran a private asylum.

18th century
New asylums were built to house people with mental health problems separately from houses of correction and poor houses. The New Bethlem appeared so magnificent it was thought ‘everyone might become half mad in order to lodge there’. However palatial it looked, it was built on a land-fill site and deteriorated rapidly! Whilst mental hospitals in London were reasonably managed, the provincial institutions were often very poor.

In 1774 it became essential to produce a medical certificate confirming insanity before non-pauper lunatics could be confined, but the rights of paupers were totally disregarded. For the wealthy there was still the option of being a private patient of a doctor or clergyman.

William Battie (1703–1776) was a pioneer in the care of mental patients who helped raise the ‘mad business’ to a respectable medical speciality. He believed that institutionalising patients in asylums was, in itself, therapeutic. His name gave rise to the term ‘batty’.

Novel therapies of the 18th century included water immersion therapy, non-injurious torture (!), a special spinning stool to rearrange the contents of the brain and a form of ECT for which the rich paid sixpence and the poor were ‘electrified gratis’.

19th century
At the beginning of the century there was public outcry about conditions in asylums and a select committee report describes appalling conditions of inadequate clothing, cramped and crowded accommodation filthy with excrement on straw, with patients chained to the walls, and in one case, a surgeon who was known to be drunk and insane. Despite this a lot of doctors were proud to work in the new asylums and there was a new endeavour to study insanity which culminated in Emil Kraepelin’s (1856–1927) systematic classification of mental disease which forms the basis of modern systems.

Alfred Meyer (1866–1950) believed in, seeing the patient in his own world. His wife became what was later called a social worker, visiting Meyer’s patients to learn more about their home backgrounds. Rather than seeing disturbance as the result of brain pathology he saw it as a reaction or maladjustment involving the total person. He helped to change the hospital’s approach from custody to active therapy, and stressed the importance of unhurried conversations with patients.

In the second half of the 19th century, Darwin’s Origin of Species (1859) led to a pessimistic feeling that insanity, instead of being concerned with the will and moral management was a hereditary incapacity, leading to reduced concern for the unfortunate, and a feeling that the mad ought to be locked up. The 1845 Lunacy Act was about running good hospitals; the 1890 Lunacy Act was about locking people up.

At the end of the 19th century advances in general medical knowledge led to a search for organic causes of mental distress. Instead of doctors in asylums going out and playing cricket with patients, they began to spend their time on research in the hope of finding the causes of the conditions they were treating.
20th century

The search for organic causes and treatments for mental health problems continued, spurred on by the successful identification and treatment of conditions such as phenylketonuria and thyroid conditions. The observation of changes in emotional state in people treated for other conditions, e.g. the antidepressant effect of iproniazid for tuberculosis, began the continuing search for biochemical treatments for every kind of mental state.

Sedatives such as morphine, hyoscyamus and chloral were widely used. Patients with mania were treated with apomorphine and hyoscine to induce vomiting in order to wear them out and thus calm them. Bromide was fashionable for a while and lead to the development of deep sleep treatment, whereby patients would sleep for prolonged periods and awaken apparently free of psychotic symptoms. When bromide was deemed too toxic it was replaced by barbiturates until deep sleep therapy was finally discredited in the 1960s.

Other physical treatments used in the 20th century include insulin coma therapy and camphor injections to induce fits in the 1930s.

Psychosurgery was used in the mid-20th century with an enthusiasm verging on abandon, and an appalling level of technical crudeness. However a refined version is still practised on a small number of patients. The Mental Treatment Act 1930 introduced the category of voluntary patients and the notion of rehabilitation.

During the 1950s the tradition of caring for mentally ill people within large institutions came under intense criticism from both inside and outside the system. There was a growing realisation that the structure and organisation of mental hospitals was essentially pathogenic.

In 1961 Enoch Powell made his ‘water tower’ speech at a meeting of the National Association for Mental Health, announcing the proposed closure of the large psychiatric institutions with the development of care in the community.
Appendix 2

Psychological treatments of mental illness

The 18th century saw the beginning of modern psychology as a separate discipline. The word psychology was used in the first half of the century to mean the philosophical analysis and interpretation of mental phenomena. In the latter half of the 19th century its reference shifted from the philosophical to the scientific study of mental phenomena.

Wilhelm Wundt (1832–1920) is commonly regarded as the founder of scientific psychology. Although other people began experimental psychology earlier, Wundt had the first laboratory for teaching and research in the subject.

Alexander Bain (1818–1903) was not an experimenter but wrote two very influential books, *The Senses and the Intellect* (1855) and *The Emotions and the Will* (1859). At the same time there were considerable influences from the growing understanding of the physiology of the nervous system.

One development of the late 18th century that had a significant influence on the development of psychological practice was Mesmerism. Mesmer began by using magnets in the belief that they exercised some influence on the human body. He later abandoned this notion, but induced a number of phenomena, which are now recognised as suggestion and hypnosis. An active school of hypnosis developed in Paris under the leadership of Charcot who established a notable neurological clinic at La Salpetriere.

In the closing years of the 19th century several medical psychologists were developing psychogenic theories of the neuroses. Outstanding among them were Pierre Janet (1859–1949) and Sigmund Freud (1856–1939) who was a pupil and protégé of Charcot.

Janet’s view was that the neurotic lacked sufficient mental energy to hold his psyche together in a state of integration; as a result parts of it functioned in disassociation from the rest. Freud’s view by contrast was that there were diverse mental energies in conflict with one another.

Freud’s ideas are the basis for psychoanalytic theory. Although this began as a contribution to psychopathology, it quickly expanded into a more general theory. The interpretation of dreams, the explanation of slips of the tongue and of the pen, and the account of the psychic origins of art, religion and society began with Freud and have become part of everyday currency. Literature and literary criticism, art, morality and religion have all felt this influence.

In the 20th century, there have been two major developments in psychology: Gestalt theory (a holistic approach), and behaviourism (a stimulus-response theory). These two approaches begin to merge in the techniques of cognitive behavioural therapy, which is increasingly practised at the present time.

In the 1st World War the treatment of shell shock with talking therapies by psychiatrists such as William Rivers led eventually to treatment for what is now called post-traumatic stress disorder, with debriefing for victims of traumatic incidents such as hostages, and eventually to the regular provision of counselling for survivors of traumatic incidents. The approach to traumatic stress in the 2nd World War was a spur to the evolution of group therapy by people such as Wilfred Bion and Foulkes.

The second half of the 20th century has seen the development of ‘anti-psychiatry’, whose main proponents were Ronald Laing and Thomas Szasz. Laing and his followers
set up the Philadelphia Association, and also Kingsley Hall, an experimental therapeutic community whose most famous patient was Mary Barnes who was encouraged to regress into babyhood as a means of achieving her recovery from psychosis.

Ronald David Lang was born in the Govanhill district of Glasgow and went on to study medicine at Glasgow University. He worked in psychiatry at Gartnavel Royal Hospital from 1953 to 1956.

Szasz has described mental illness as a metaphorical illness because ‘the mind (whatever that is) is not an organ or part of the body. Hence it cannot be diseased in the same sense as the body can’. He takes the view that any psychiatric diagnosis is a licence for coercion and the exercise of psychiatric power. ‘If mental illness is not a disease why then treatment or indeed admission?’ He also accepts that the corollary of this is that if patients have rights, they also have responsibilities, and should, for example accept responsibility for all their actions whatever their state of mind when they committed them. He has concluded that the only help that can be given to patients is through psychotherapy.

Psychotherapeutic treatment has declined in the latter part of this century, partly because of a case brought in 1979 against a private psychiatric clinic in the USA by a physician with psychotic depression. The patient sued successfully on the grounds that he should have been treated with proven effective medication rather than spending seven months undergoing in-depth psychoanalysis, and the case left a strong impression that treating psychiatric illness with psychoanalysis constituted malpractice.

New perceptions of mental illness are beginning to develop, informed partly by people like Szasz and Laing, and partly by the growing perception of a need for sensitivity in dealing with people from other cultures whose mental distress may be expressed as a spiritual crisis in a way that has become almost unknown in Western culture.

At the end of the 20th century, rather than adopting either ‘the medical model’ or ‘the social model’ of mental illness, people working in the field of mental ill health are beginning to recognise that mental distress has many different causes, and many different disciplines and approaches have a part to play in treatment. Distress may be explained in terms of responses to circumstances, of brain chemistry, of genetics, and all are increasingly seen not to be mutually exclusive but to interact and play a part in mental health: life events almost certainly change brain chemistry for good as well as for ill, and many different treatments may be successful in different circumstances.

One of the most widely practised psychological therapies is cognitive behavioural therapy (CBT). Although there are many variants of CBT, these are unified by the proposition that psychological problems arise as a direct consequence of faulty patterns of thinking and behaviour. Patients tend to misinterpret situations or symptoms in ways that undermine their coping. Their abnormal behavioural patterns exacerbate and consolidate these problems. The critical factor lies in how patients assess specific situations or problems, as summarised by Epictetus, a first century Greek philosopher: ‘Men are disturbed not by things, but the views they take of them.’

The link between psychological problems and faulty patterns of thinking and behavior can be illustrated by Beck’s original model of depression. He proposed that negative
thinking in depression has its origins in attitudes and assumptions arising from experiences early in life. Such assumptions can be positive and motivating, but they can also be too extreme, held too rigidly, and be highly resistant to revision. Once a person is depressed a set of cognitive distortions known as the cognitive triad (negative view of oneself, current experience, and the future) exert a general influence over the person’s day-to-day functioning, and negative automatic thoughts become increasingly pervasive. Other biases in information-processing also act to consolidate the depression.

Although CBT was originally developed as a treatment for depression, it has wide-ranging applications in the management of residual psychotic symptoms, panic disorders, social phobias, etc. In CBT, the therapist and patient work together to identify specific patterns of thinking and behaviour that underpin the patient’s difficulties. Treatment continues between sessions with homework assignments both to monitor and challenge specific thinking patterns and to implement behavioural change. CBT is increasingly available in the form of self-help books and interactive computer programmes.
Appendix 3

Support agencies, self-help groups and useful websites

These contact details are correct as at September 2007.

Alcohol Concern
Alcohol Concern
64 Leman Street
London E1 8EU
Telephone: 020 7264 0510
Fax: 020 7488 9213
Email: contact@alcoholconcern.org.uk
Website: www.alcoholconcern.org.uk

Alcohol Concern is the national agency on alcohol misuse. It works to reduce the levels of alcohol misuse and to develop the range and quality of helping services available to problem drinkers and their families.

Alzheimer’s Disease International
ADI is an umbrella group of Alzheimer associations throughout the world. Each of its members is the national Alzheimer association in their country who support people with dementia and their families.

Website: www.alz.co.uk

Alzheimer Europe
Alzheimer Europe is a non-governmental organisation aimed at raising awareness of all forms of dementia through coordination and cooperation between Alzheimer and related disorders organisations in Europe, as well as organising support to the people with the disease and their carers.

Website: www.alzheimer-europe.org

Alzheimer Scotland
Alzheimer Scotland helps people with dementia, their carers and families.
Alzheimer Scotland provides information, runs practical services, and campaigns.
Membership includes carers, relatives, people with dementia, professionals, groups and organisations.

Alzheimer Scotland
22 Drumsheugh Gardens
Edinburgh EH3 7RN
Telephone: 0131 243 1453
Website: www.alzscot.org
Dementia helpline: 0808 808 3000

Association for Post Natal illness (APNI)
APNI offers support to mothers suffering from post-natal illness. Leaflets in Bengali, Gujarati, Hindi, Punjabi, and Urdu are also available.

APNI
145 Dawes Road
Fulham
London SW6 7EB
Helpline: 020 7386 0868
Website: www.apni.org

Bipolar Fellowship Scotland
Bipolar Fellowship Scotland aims to provide information, support and advice for people affected by bipolar disorder, and all who care.

Bipolar Fellowship Scotland
Studio 1016, Mile End Mill
Abbeymill Business Centre
Seedhill Road
Paisley PA1 1TJ
Telephone: 0141 560 2050
Website: www.bipolarscotland.org.uk
Breathing Space
Breathing Space is a free and confidential service for any individual who is experiencing low mood or depression, or who is unusually worried and in need of someone to talk to. Breathing Space specifically, but not exclusively, targets young men who are experiencing difficulty in their lives and aims to provide help ‘at an early stage to prevent problems escalating.

Website:  www.breathingspacescotland.co.uk

Breathing Space
Clyde Contact Centre
Beardmore Street
Clydebank  G81 4HX
Telephone:  0141 435 3901
Helpline:  0800 83 85 87  6pm to 2am

British Association for Counselling and Psychotherapy (BACP)
BACP House
15 St John’s Business Park
Lutterworth
Leicestershire LE17 4HB
Helpline:  0870 443 5252
Website:  www.bacp.co.uk

Centre for Counselling and Diagnosis in Dementia
National Hospital for Neurology and Neurosurgery
Queen Square
London  WC1N 3BG
Website:  www.dementia.ion.ucl.ac.uk
The official website of the Dementia Research Centre.

The Children’s Trust
The Children’s Trust is a national charity working with children who have multiple disabilities and complex health needs. Based in Surrey but its services (including respite facilities, hospice facilities, rehabilitation, education for parents) are offered to children from across the UK.

Children’s Trust
Tadworth Court
Tadworth
Surrey  KT20 5RU
Telephone:  01737 365000
Fax:  01737 365001
Email:  enquiries@thechildrenstrust.org.uk
Website:  www.thechildrenstrust.org.uk

Chinese Mental Health Association–Wah Sum Helpline
Wah Sum Helpline is a confidential; service which offers information, advice, service referral, signposting and emotional support to Chinese people suffering from mental distress and their carers.

Helpline:  0845 1228660
Monday to Friday, 10am – 8pm

The Chinese Mental Health Association (CMHA)
CMHA provides support within the Chinese community in the UK and has translated several MIND booklets into Chinese – these are available from:

CMHA
2nd Floor, Zenith House
155 Curtain Road
London  EC2A 3QY
Telephone:  020 7613 1008
Monday to Friday, 9.30am – 5.30pm
Website:  www.cmha.org.uk
Choose Life
The Choose Life website is an information and education resource as part of the national strategy and action plan to prevent suicide in Scotland. Provides a list of helplines for people who are feeling suicidal to contact.
Website:  www.chooselife.net

CJD Surveillance Unit
The incidence of Creutzfeldt-Jakob disease (CJD) is monitored in the UK by the CJD surveillance unit based at the Western General Hospital in Edinburgh, Scotland. Also refers onto other organisations concerned with CJD.
Website:  www.cjd.ed.ac.uk

Cruse Bereavement Care
Cruse Bereavement Care provides counselling and support to promote the well-being of bereaved people and to enable them to understand their grief and cope with their loss. It offers information, advice, education and training services.
Cruse
Riverview House
Friarton Road
Perth PH2 8DF
Telephone: 01738 444 178
Website:  www.crusescotland.org.uk

Cruse Bereavement Care’s Youth Involvement Project – road for you (rd4u)
A website designed for young people to offer support after the death of someone close.
Website:  www.rd4u.org.uk
Freefone 0808 808 1677 Monday to Friday
helpline:  9.30am – 5.00pm

Cry-sis Support Group
Cry-sis offers support to families with excessively crying, sleepless and demanding babies. It runs a national network of self-help telephone contacts and provides information and advice.
BM Crysis
London WC1N 3XX
Helpline: 08451 228 669 9am to 10pm
Website:  www.cry-sis.org.uk

Defeat Depression
Defeat Depression provides accessible information, education, support and better understanding of the most common mental health problems for carers, families and those affected.
Website:  www.depression.org.uk

Dementia.com
Dementia.com provides information for caregivers and healthcare professionals. Subscribers can customise the site, receive newsletters and benefit from the Medline mail service, providing access to over 3 million online articles.
Website:  www.dementia.com

Depression Alliance
Depression Alliance
212 Spitfire Studios
63–71 Collier Street
London N1 9BE
Telephone: 0845 123 2320
Website:  www.depressionalliance.org
Depression Alliance is the leading UK charity for people with depression and offers information. Support and understanding for people who suffer with depression and for their relatives who want to help.
Depression Alliance Scotland
Depression Alliance Scotland provides information and support both for anyone affected by depression and their friends and family.
3 Grosvenor Gardens
Edinburgh EH12 5JU
Telephone: 0131 467 3050
Website: www.depressionalliancescotland.org
or www.dascot.org
The website offers a link to a free online course ‘Living Life to the Full’. This is a life skills course which utilises a cognitive behavioural therapy approach and was developed by The Glasgow Institute for Psychosocial Interventions in association with Depression Alliance Scotland
Website: www.livinglifetothefull.com

Destigmatize
Destigmatize provides information on mental health problems, particularly anxiety, in a variety of Asian languages including Urdu, Punjabi, and Hindi. Aims to destigmatise mental health in the ethnic minorities.
Destigmatize
National Phobics Society
Zion Community Resource Centre
339 Stretford Road
Hulme
Manchester M15 4ZY
Telephone: 0870 122 2325
Website: www.destigmatize.org.uk

Drugscope
Drugscope is the UK’s leading independent centre of expertise on drugs. Its aim is to inform policy development and reduce drug-related risk.
Drugscope
40 Bermondsey Street
London SE1 3UD
Telephone: 020 7940 7500
Website: www.drugscope.org.uk

ECT Anonymous
ECT Anonymous publishes information on the damaging effects of ECT.
ECT Anonymous
14 Western Avenue
Riddlesden
Keighley BD20 5DJ
Telephone: 01535 661493
Self-help group enquiries to:
Una Parker
8 Wenthill Close
Ackworth
Pontefract WF7 7LP
Telephone: 01977 704659
Website: www.ontheside.org/ukfed/ectanon.htm
Education and Resources for Improving Childhood Continence (ERIC)
ERIC
34 Old School House
Britannia Road
Kingswood
Bristol BS15 8DB
Telephone: 0117 960 0401
Helpline: 0845 370 8008 (10am – 4pm Monday to Friday).
Language live is available to callers who do not have English as a first language.
Website: www.eric.org.uk

ENABLE Scotland
ENABLE Scotland campaigns for a better life for children and adults with learning disabilities and, by providing services, supports them and their families to participate, work and live in their local communities.
ENABLE
6th Floor, 7 Buchanan Street
Glasgow G1 3HL
Telephone: 0141 226 4541
Website: www.enable.org.uk

Families Anonymous
To help families and friends of people with drug dependency problems. Runs self-help groups.
Families Anonymous
Doddington and Rollo Community Association
Charlotte Despard Avenue
Battersea
London SW11 5HD
Helpline: 0845 1200 660
to locate local groups or for further information
Website: www.famanon.org.uk

Foundation for People with Learning Disabilities
Here you will find the latest news and events on learning disability issues, as well as information on topics such as advocacy, accommodation and employment and further links. In addition there is information on the GOLD programme (Growing old with learning disabilities).
Website: www.learningdisabilities.org.uk

The Genetic Interest Group (GIG)
A national alliance of organisations people affected by genetic disorders/diseases. Its primary goal is to promote awareness and understanding of genetic disorders so that high quality services for people affected by genetic conditions are developed and made available to all who need them.
Website: www.gig.org.uk

Gingerbread
Gingerbread provides information about support for lone parents.
Gingerbread
1307 Argyle Street
Glasgow G3 8TL
Telephone: 0141 576 5085/7976
Website: www.gingerbread.org.uk

HeadsUpScotland
HeadsUpScotland is a national project aiming at improve the mental health of all children and young people by ‘promotion, prevention and care’.
HeadsUpScotland
Scottish Development Centre for Mental Health
172 Leith Walk
Edinburgh EH6 5EA
Telephone: 0131 555 8430
Website: www.headsupscotland.co.uk
Hearing Voices Network
To offer information, support and understanding to people who hear voices and those who support them.
Hearing Voices Network
79 Lever Street
Manchester M1 1FL
Telephone: 0845 122 8641
Email: info@hearing-voices.org
Website: www.hearing-voices.org

Hearing Voices Network Dundee
Aims to create acceptance that hearing voices is a valid experience with many explanations, and erasing the stigma for voice hearers.

126–220 Hilltown
Dundee DD3 7AU
Telephone: 01382 223023
Website: www.hearingvoicesnetwork.co.uk

Highland Users Group (HUG)
HUG is a network of mental health service users which aims, by campaigning, to improve the rights, services and treatments of people with mental health problems.

Highland Community Care Forum
Highland House
20 Longman Road
Inverness IV1 1RY
Telephone: 01463 718817
Website: www.hug.uk.net

Holiday Care Service
To provide a free information and advice service to anyone who has difficulty finding a suitable holiday on account of age or disability. Also advises single parents, people living alone and people under severe financial pressure and runs a holiday helpers scheme. This recruits and introduces holiday carers/companions to people seeking holiday help.

Holiday Care Service
7th floor, Sunley House
Bedford Park
Croydon CR0 2AP
Telephone: 0845 124 9971 Information
Telephone: 0845 124 9974 Access advice
Website: www.holidaycare.org.uk

In Touch
In Touch provides information on all aspects of mental handicap and to run a contact service for parents of children with rare disorders.

In Touch
10 Norman Road
Sale
Cheshire M33 3DF
Telephone: 0161 905 2440
Fax: 0161 718 5787
Website: www.inclusive.co.uk/support/intouch.shtml
Invalids at Home
Invalids at Home
Bamford Cottage
South Hill Avenue
Harrow
Middlesex HA1 3PA
Telephone: 020 8864 3818
To provide financial help to substantially handicapped or chronically ill people living at home, who are in need. Grants can be made for almost any expense not statutorily covered.

The LivingWorks Program
The LivingWorks Program provides training for ‘suicide first aid’, aiming to provide caregivers with intervention strategies to prevent suicides.
Website: www.livingworks.net

Mental Health Act (Care and Treatment) (Scotland) Act 2003
Training on the Act for frontline health and social care professionals can be accessed online from NHS Education for Scotland.
Website: www.nes.scot.nhs.uk/mha

Mental Health Foundation
The Mental Health Foundation provides information about mental health issues, and aims to help people survive, recover from and prevent mental health problems.
Mental Health Foundation
Scotland Office
5th Floor, Merchants House
30 George Square
Glasgow G2 1EG
Telephone: 0141 572 0246
Website: www.mentalhealth.org.uk

Mental Welfare Commission for Scotland (MWCScotland)
The MWC Scotland is the statutory body with responsibility for protecting the welfare of people with mental disorder (including learning disabilities) in Scotland.
Telephone: 0131 222 6111
Website: www.mwcscot.org.uk

Mouth and Foot Painting Artists
To encourage physically and mentally handicapped children to take part in painting, music and drama. Gives financial help.
Mouth and Foot Painting Artists
9 Inverness Place
London W2 3JG
Telephone: 020 7229 4491
Website: www.mfpa.co.uk

Mildmay Hospital UK
Mildmay Hospital specialises in the care of people at all stages of HIV infection – from initial diagnosis through to final phase, including rehabilitation for people with cognitive deficits caused by the HIV virus.
Website: www.mildmay.org.uk
MIND
(National Association for Mental Health)
Telephone helpline and useful publications including factsheets on mental health problems and ‘Making sense’ booklets e.g. lithium, antidepressants, antipsychotics.
MIND
15–19 Broadway
London E15 4BQ
Telephone: 020 8519 2122
MindinfoLine: 0845 766 0163
Monday to Friday, 9.15am – 5.15pm
(Language Line available for translation and interpreting service with access to over 100 languages. Three-way conferencing facilitates communication through trained interpreters. Deaf or speech impaired enquirers can be assisted on the same number – prefixing with 18001 if using BT Textdirect)
Website: www.mind.org.uk

MINDOUT
An active campaign aiming to stop stigma and discrimination surrounding mental health. Useful downloads including employers’ pages providing resources for staff management to use in the workplace.
Website: mindout.clarity.uk.net

Moodjuice
Moodjuice Forth Valley is an internet site offering information and advice to those suffering troublesome thoughts, feelings and actions. Self-help guides e.g. depression, anxiety, stress, panic and sleep problems, can be printed off from the site.
Website: www.moodjuice.scot.nhs.uk

Multikulti Language Choice
Aims to support citizenship through culturally appropriate and accurately translated information – debt, employment, health, housing, immigration, and welfare benefits.
Understanding Depression, Postnatal Depression, and How to Improve Your Mental Wellbeing available in Albanian, Bengali, Chinese, English, Farsi, French, Gujarati, Portuguese, Somali, Spanish, Turkish and Urdu.
Website: www.multikulti.org.uk

Multiple Sclerosis Society
The Society funds MS research, runs holiday homes and respite care, provides grants, education, information, publications and training on MS, and a freephone specialist telephone support service.
Website: www.mssociety.org.uk
Helpline: 0808 800 8000

Multiple Sclerosis Society Scotland
The MS Society Scotland is part of the MS Society and has a network of 36 branches in Scotland.
MS Society Scotland
National Office
Ratho Park
88 Glasgow Road
Ratho Station
Newbridge EH28 8PP
Telephone: 0131 335 4050
Website: www.mssocietyscotland.org.uk

National Statistics
Website: www.statistics.gov.uk
National Programme to Improve the Mental Health and Well Being of the Scottish Population
The programme flows from the Scottish Executive’s commitments to social justice and health improvement with respect to mental health.
Website:  www.show.scot.nhs.uk/sehd/mentalwellbeing

National Institute for Mental Health in England (NIMHE)
NIMHE aims to improve the quality of life of people of all ages who experience mental distress and is responsible for supporting the implementation of positive change in mental health and mental health services in England.
NIMHE
Room 8E 46
Quarry House
Quarry Hill
Leeds LS2 7UE
Telephone: 0113 254 5127
Website:  nimhe.csip.org.uk/home

National Phobics Society
The National Phobics Society provides advice and counselling to combat phobias, depression and obsessional neurosis. Also produces newsletter and access to online support.
National Phobics Society
Zion CRC
339 Stretford Road
Hulme M15 4ZY
Telephone: 0870 122 2325
Website:  www.phobics-society.org.uk

National Schizophrenia Fellowship (Scotland)
The National Schizophrenia Fellowship (Scotland) works to improve the wellbeing and quality of life of those affected by schizophrenia and other mental illness, including families and carers.
National Schizophrenia Fellowship (Scotland)
130 East Claremont Street
Edinburgh EH7 4LB
Telephone: 0131 557 8969
Website:  www.nsfscot.org.uk

National Self-Harm Network (NSHN)
NSHN provides support to people that self-harm and the people it affects.
NSHN
PO Box 7264
Nottingham NG1 6WJ
Email: info@nshn.co.uk
Website:  www.nshn.co.uk

NCH Careline
To provide a confidential telephone counselling service for children, young people, and adults under stress.
NCH Careline
Cardinal Heenan Centre
326 High Road
Ilford
Essex IG1 1QP
Telephone: 020 8514 5444  Administration
Telephone: 0845 122 8622  Counselling
Website:  www.ukselfhelp.info/careline

NHS24
NHS24 provides confidential health advice and information for people in Scotland.
Telephone: 0845 24 24 24
Website:  www.nhs24.com
**Overeaters Anonymous**
Overeaters Anonymous offers practical help to people with eating disorders
Overeaters Anonymous
PO Box 19
Stretford
Manchester M32 9EB
Website: www.oagb.org.uk

**Parkinson’s Disease Society**
Some people with Parkinson’s develop dementia. The Society offers information advice, and support for people with Parkinson’s and their families
Website: www.parkinsons.org.uk

**Penumbra**
Penumbra provides a wide range of person-centred support services for adults and young people across Scotland with mental health problems including Korsakoff’s syndrome.
Penumbra
Norton Park
57 Albion Road
Edinburgh EH7 5OY
Website: www.penumbra.org.uk
Telephone: 0131 475 2380

**Pick’s Disease Support Group**
For carers of frontotemporal dementia:
Pick’s Disease, Frontal Lobe Degeneration, Dementia with Lewy Bodies, Corticobasal Degeneration and Alcohol Related Dementia.
Website: www.pdsq.org.uk
Also gives Scottish contact details

**Princess Royal Trust for Carers**
Provides information, advice and support to carers.
Website: www.carers.org

**Progressive Supranuclear Palsy (PSP-Europe) Association**
Provides information and support to sufferers of this progressive neuro-degenerative disease, their carers and their families across Europe and internationally, and promote awareness of the disease, particularly in the UK.
The PSP Association
PSP House
167 Watling Street West
Towcester
Northants NN12 6BX
Telephone: 01327 322410
Website: www.pspeur.org
Helpline: 01939 270889 Counselling

**QUIT**
QUIT aims to help people stop smoking by various methods. Smokers Quitline offers advice, moral support and referral to nearest smoking cessation services. Also runs information resource service for healthcare professionals and workplace courses.
QUIT
Ground Floor
211 Old Street
London EC1V 9NR
Telephone: 020 7251 1551
Fax: 020 7251 1661
Email: info@quit.org.uk
Smoker’s Quitline: 0800 002200
Website: www.quit.org.uk

**Rape Crisis Scotland**
Rape Crisis Scotland provides support and information for women and girls who have experienced any form of sexual violence at any time in their lives.
Website: www.rapecrisisscotland.org.uk
Relate Scotland
Relate Scotland (formerly Couple Counselling Scotland) provides confidential counselling for couples (people in marriage or other intimate relationships) in Scotland.

Relate Scotland
18 York Place
Edinburgh EH1 3EP
Telephone: 0845 119 6088
Website: www.relatescotland.org.uk

The Richmond Fellowship Scotland
The Richmond Fellowship operates 140 services across Scotland supporting people to live as independently as possible within their own homes and communities.

The Richmond Fellowship Scotland
3 Buchanan Gate
Buchanan Gate Business Park
Cumbernauld Road
Stepps
North Lanarkshire G33 6FB
Telephone: 0845 013 6300
Website: www.trfs.org.uk

Samaritans
Samaritans offer a confidential 24 hour service for people in distress or despair.

See website or local telephone directory for nearest branch.

Chris
PO Box 90 90
Stirling FK8 2SA
National Helpline: 08457 90 90 90
Email: jo@samaritans.org
Website: www.samaritans.org.uk

SANE
Operates a national out-of-hours help-line (SANELINE) giving practical information, crisis care and emotional support to anybody affected by mental health problems (including carers).

SANELINE: 0457 67 8000 1pm – 11pm

SANE
1st Floor, Cityside House
40 Adler Street
London E1 1EE
Telephone: 020 7375 1002
Website: www.sane.org.uk

Schizophrenia Association of GB (SAGB)
SAGB provides advice for sufferers and promotes research.

SAGB
Bryn Hyfryd
The Crescent
Bangor
Gwynedd LL57 2AG
Telephone: 01248 354048
Website: www.sagb.co.uk

Scottish Association for Mental Health (SAMH)
SAMH provides services for people across Scotland who experience mental health problems, homelessness, addictions and other forms of social exclusion.

SAMH
Cumbernae House
15 Carlton Court
Glasgow G5 9JP
Telephone: 0141 568 7000
Website: www.samh.org.uk
Scottish Huntington’s Association
The association provides information, advice, support and publications for families affected by Huntington’s disease in Scotland.
Website: www.hdscotland.org

Scottish Huntington’s Association Youth Project
Provides advice and information on an individual and group basis to children and young people living in a family with Huntington’s Disease.
Website: www.hdscotland.org/youth

Scottish Pharmacy in Mental Health (SPMH)
Membership of SPMH is available (free) to technicians and pharmacists working in mental health in hospital, community, primary care and academia. SPMH aims to develop best practice in pharmaceutical care within mental health by providing education and training through meetings and a newsletter.
Website: www.spmh.co.uk

Scottish Recovery Network
The Scottish Recovery Network aims to engage communities across Scotland in debate on how best to promote and support recovery from long-term mental health problems.
Scottish Recovery Network
Baltic Chambers
320 – 321
50 Wellington Street
Glasgow G2 6HJ
Telephone: 0141 240 7790
Website: www.scottishrecovery.net

Seasonal Affective Disorder Association (SADA)
SADA informs the public and healthcare professionals about SAD and supports and advises sufferers of the illness.
PO Box 989
Steyning
West Sussex BN44 3HG
Telephone: 01903 814942
Website: www.sada.org.uk

See Me
The See Me campaign challenges stigma and discrimination around mental ill-health in Scotland.
See Me
9–13 Maritime Street
Edinburgh EH6 6SB
Telephone: 0131 624 8945
Website: www.seemescotland.org

TACADE (The Advisory Council on Alcohol and Drug Education)
TACADE supports professionals (particularly teachers) in social, Health and citizenship education (including drugs, alcohol, tobacco and sexual health) for children and young people.
TACADE
Old Exchange Building
St Ann’s Passage
Manchester M2 6AD
Telephone: 0161 836 6850
Email: ho@tacade.co.uk
Website: www.tacade.com
**Turning Point Scotland**

Turning Point Scotland provides customised community care packages for people who have been socially excluded as a result of mental health, learning disability, homelessness or drug or alcohol misuse.

Turning Point Scotland
54 Govan Road
Glasgow G51 1JL
Telephone: 0141 427 8200
Website: www.turningpointscotland.com

**United Kingdom Advocacy Network (UKAN)**

The UK Advocacy Network (UKAN) was founded in 1990 to be a national resource, linking mental health user groups of all types. The common aim is the use of advocacy in many forms to empower people who use specialist services.

UK Advocacy Network
Volserve House
14–18 West Bar Green
Sheffield S1 2DA
Telephone: 0114 272 8171
Email: office@u-kan.co.uk
Website: www.u-kan.co.uk

**United Kingdom Psychiatric Pharmacy Group (UKPPG)**

The UKPPG exists to ensure best treatment with medicines for people with mental health needs and their carers. This is being achieved by developing educational facilities and accreditation for pharmacists, providing support through local and national resources and providing a network of support for mental health pharmacists.

Email: contact@ukppg.org.uk
Website: www.ukppg.org.uk

**Victim Support Scotland**

Victim Support Scotland helps people affected by crime – victims, witnesses and others – by providing emotional support, practical help and essential information.

Victim Support Scotland
15–23 Hardwell Close
Edinburgh EH8 9RX
Telephone: 0131 668 4486
Website: www.victimsupportsco.demon.co.uk

**WellScotland**

Information on the Scottish Executive’s National Programme for Improving Mental Health and Well-being in Scotland launched in October 2001 and the initiatives to change knowledge, attitudes and behaviour towards mental health.

Website: www.wellscotland.info/index.html

**Women’s Royal Voluntary Service Scotland (WRVS Scotland)**

WRVS provide a wide range of services to support people in need who might otherwise feel lonely and isolated, whether at home, in hospital, or in times of crisis.

WRVS Scotland
6 Hill Street
Edinburgh EH2 3JZ
Telephone: 0131 225 9835
Website: www.wrvs.org.uk
Introduction to pharmaceutical care in mental health
Multiple choice questionnaire and answer sheet
Congratulations

You have now made it to the end of the pack.

However, we require one more task of you – to complete the attached self-assessment questionnaire. This allows you to test your understanding of the package and to receive feedback on the answers.

Tick each answer as true or false.

Detach the answer sheet on the last page along the perforation and copy your choices onto this sheet. We would also really appreciate any of your comments about all aspects of the pack. Your comments allow us to improve future distance learning packages. Once completed with your name and address details, return it to:

**NHS Education for Scotland (Pharmacy)**
3rd floor, 2 Central Quay
89 Hydepark Street
Glasgow G3 8BW

Alternatively, you may wish to complete the multiple choice questions online at the NES Pharmacy website at www.nes.scot.nhs.uk/pharmacy/MCQtesting/

You will receive an instant score if you choose this method!

If you are not resident in Scotland, you should return your completed multiple choice questionnaire to the appropriate centre for pharmaceutical postgraduate education.

Please note there is no negative marking, so do attempt all the questions by ticking the appropriate true/false box.
Multiple choice questionnaire

- Please answer the following questions by ticking the appropriate box.
- Transfer your answers on to the enclosed answer sheet at the back and return it in the envelope provided for marking.
- You will then receive a record of completion showing the number of study hours this represents.

Background

1. In relation to the statistics for mental health in the UK, which of the following statements are correct:

a) One in five people will be affected by a mental disorder at some time during their lives.

b) One in four families is likely to have at least one member with a mental disorder.

c) Unipolar depression accounts for 10% of years of life lived with disability (YLD) for all diseases and injuries.

d) Alzheimer’s disease is one of the top 20 causes of disability for men and women of all ages.

2. Mental Health services have developed over the years with many new support systems and organisations being set up. Which of the following statements are true:


b) The ‘Choose Life’ strategy launched in 2002 is a 10-year plan aimed at reducing suicide in Scotland by 20%.

c) ‘Breathing Space’ is a free and confidential phone line which is aimed specifically, but not exclusively, at young men between 16 – 40 years who are a vulnerable at-risk suicide group.

d) ‘See me’ was launched in 2004 to raise awareness that people can and do recover from long-term and serious mental health problems.
Introduction to pharmaceutical care in mental health

Neurochemistry and neuroanatomy

3. Psychopharmacology is complex and sometimes contentious. A basic understanding of the structure and function of neurons and synapses is essential to understand the mechanism of action of psychotropic drugs:

a) The action potential is self propagating and does not diminish as it travels along the neuron.  
   true ☐  false ☐

b) The effect of the neurotransmitter serotonin (SHT) is inactivated by enzymatic breakdown outside the cell.  
   true ☐  false ☐

c) There are six small molecule transmitters involved in one way or another, in the synaptic mechanisms of most psychoactive drugs.  
   true ☐  false ☐

d) Receptors are the key to specificity in the nervous system and allow the development of selective drug development.  
   true ☐  false ☐

Schizophrenia

4. Schizophrenia is a condition, which comes under the umbrella term of psychotic disorders.

a) The incidence of schizophrenia is equal in both sexes (but onset is earlier in males).  
   true ☐  false ☐

b) There are increased rates of schizophrenia found in affluent areas of large cities.  
   true ☐  false ☐

c) People with schizophrenia usually only have positive symptoms present when they are first diagnosed.  
   true ☐  false ☐

d) A genetic predisposition to schizophrenia exists with a 12% prevalence rate if one parent is schizophrenic.  
   true ☐  false ☐

5. The management of schizophrenia involves a comprehensive package of care aimed at addressing all of the person’s clinical, emotional and social needs:

a) Chlorpromazine was the first drug used to treat the symptoms of schizophrenia.  
   true ☐  false ☐

b) The ‘atypical’ antipsychotics have more risk of side-effects such as extrapyramidal symptoms than the traditional antipsychotics.  
   true ☐  false ☐

c) Clozapine is effective in treatment-resistant schizophrenia.  
   true ☐  false ☐

d) Hyperprolactinaemia only occurs with typical antipsychotics.  
   true ☐  false ☐
Depression

6. Depression is the third most common reason for consultation in general practice. In relation to this condition, which of the following statements are correct:
   a) It is now common practice to define depression as mild, moderate or severe which is related to the number and duration of symptoms.  
      true □  false □
   b) Overall the causes of depression are probably multifactorial.  
      true □  false □
   c) There is no genetic link to an individual developing a depressive illness.  
      true □  false □
   d) Depression and its treatment are linked to the serotonergic and noradrenergic pathways in the brain.  
      true □  false □

7. Psychological therapies are receiving increasing prominence as options for the treatment of depression, but the use of antidepressant medication remains important. Which of the following are true:
   a) The recovery rates with computerised cognitive behavioural therapy (CCBT) are less than those seen with face-to-face therapies.  
      true □  false □
   b) Electroconvulsive therapy (ECT) should only be used for severe non-responsive depressive illness, when the condition could be considered as potentially life-threatening.  
      true □  false □
   c) Tricyclic antidepressants are less commonly used now due to their side-effects and increased risk of suicide.  
      true □  false □
   d) The third generation antidepressants such as venlafaxine are more effective than traditional antidepressants.  
      true □  false □

8. In relation to depression which of the following statements are correct:
   a) Tricyclic antidepressants are highly toxic in overdose.  
      true □  false □
   b) Weight gain can be a sign of depression.  
      true □  false □
   c) Antidepressant drug therapy can be stopped as soon as the symptoms have resolved.  
      true □  false □
   d) All selective serotonin reuptake inhibitors can be stopped abruptly.  
      true □  false □
Bipolar disease

9. Bipolar affective disorder (BAD), or ‘manic-depression’ is a disorder characterised by extremes of emotion, ranging from euphoria to despair.

a) The lifetime risk of suicide in bipolar illness is 30%.  
   \[ \text{true} \square \text{false} \square \]

b) During a manic episode, bipolar patients may require little or no sleep.  
   \[ \text{true} \square \text{false} \square \]

c) 5% of sufferers experience four or more episodes a year which is known as rapid cycling, associated with a poorer prognosis.  
   \[ \text{true} \square \text{false} \square \]

d) Genes play a major role in susceptibility to BAD.  
   \[ \text{true} \square \text{false} \square \]

10. There is increasing evidence to support a variety of drugs in the management of bipolar affective disorder. Which of the following are correct:

a) Lithium can be used to treat acute mania but takes longer to work than the atypicals.  
   \[ \text{true} \square \text{false} \square \]

b) Lithium levels of greater than 1.0mmol/l are required for a therapeutic effect.  
   \[ \text{true} \square \text{false} \square \]

c) Carbamazepine is only licensed for the prophylaxis of manic-depressive psychosis in patients unresponsive to lithium.  
   \[ \text{true} \square \text{false} \square \]

d) Cognitive behaviour therapy (CBT) has been shown to be useful in bipolar disorder.  
   \[ \text{true} \square \text{false} \square \]

Anxiety

11. In its pathological form, anxiety can present with a wide spectrum of symptoms, both physical (somatic) and psychological.

a) Due to the complexity of the brains anxiety systems, there are a variety of neurotransmitters involved.  
   \[ \text{true} \square \text{false} \square \]

b) Repetitive, purposeful handwashing is a form of obsessive-compulsive disorder (OCD).  
   \[ \text{true} \square \text{false} \square \]

c) Post-traumatic stress disorder (PTSD) involves an intense, prolonged and sometimes delayed response to a traumatic event.  
   \[ \text{true} \square \text{false} \square \]

d) Agoraphobia is the fear of enclosed spaces.  
   \[ \text{true} \square \text{false} \square \]

12. There are various options available for the management of anxiety disorders:

a) CBT has only short-term effectiveness.  
   \[ \text{true} \square \text{false} \square \]

b) Barbiturates are one of the mainstay treatments for anxiety.  
   \[ \text{true} \square \text{false} \square \]

c) Beta-blockers are mainly useful for the physical symptoms of anxiety.  
   \[ \text{true} \square \text{false} \square \]

d) Antidepressants are often used in the treatment of anxiety disorders.  
   \[ \text{true} \square \text{false} \square \]
13. Sleep is a vital biological process that is necessary to restore both body and mind. In relation to this which of the following statements are correct:

a) Non-REM sleep is characterised by rapid sweeping of the eyes under the eyelids.  
   □ true  □ false

b) REM sleep is the deepest stage of sleep.  
   □ true  □ false

c) Insomnia can involve both difficulty initiating or maintaining sleep.  
   □ true  □ false

d) The older you are the more likely your sleep pattern will be more fragmented and of shorter duration.  
   □ true  □ false

14. Non-drug treatment strategies and where necessary drug treatment can be used to manage insomnia. As a result:

a) A variety of herbal remedies are available which claim to help relaxation and promote sleep.  
   □ true  □ false

b) The use of lavender oil on a pillow at night is not recommended for people with epilepsy.  
   □ true  □ false

c) All hypnotics are licensed for short-term use only.  
   □ true  □ false

d) Zopiclone has an elimination half-life of 3.5 to 6 hours hence it has a low incidence of residual daytime problems.  
   □ true  □ false

15. In the management of anxiety which of the following statements are correct:

a) Psychological plus pharmacological therapies are useful in combination.  
   □ true  □ false

b) Barbiturates still have a role to play.  
   □ true  □ false

c) Panic disorders can be treated initially with an SSRI and a benzodiazepine.  
   □ true  □ false

d) Of the beta-blockers, only propranolol and oxprenolol are licensed for the treatment of anxiety.  
   □ true  □ false
**Dementia**

16. In dementia where there is a progressive impairment in two or more areas of cognitive function.

a) It is primarily a disease of the elderly, with prevalence increasing every 5 years over the age of 65 years.  
   - [ ] true  
   - [ ] false

b) Long-term memory loss is more affected than memory of recent events.  
   - [ ] true  
   - [ ] false

c) When dementia presents in individuals under the age of 65 years it is usually of vascular origin.  
   - [ ] true  
   - [ ] false

d) Alzheimer’s disease is likely to result from an interplay of genetic predisposition along with personal and environmental influences.  
   - [ ] true  
   - [ ] false

17. In the pharmacological management of dementias:

a) Donepezil, rivastigmine and galantamine are cholinesterase inhibitors (ChEIs).  
   - [ ] true  
   - [ ] false

b) If there is no response to one of the ChEIs it is not worth trying any of the others.  
   - [ ] true  
   - [ ] false

c) All of the ChEIs can cause gastrointestinal side-effects.  
   - [ ] true  
   - [ ] false

d) Memantine is an NMDA-receptor antagonist licensed for early Alzheimer’s Disease.  
   - [ ] true  
   - [ ] false
**Miscellaneous**

18. There are higher levels of physical morbidity and mortality in patients with severe mental illness compared to the general population. As a result:

a) Psychiatric co-morbidity often relates to a broad spectrum of mental health and substance misuse problems.  
   **true**  **false**

b) Most pharmacokinetic drug interactions related to the use of psychotropic medication are related to metabolism.  
   **true**  **false**

c) Clozapine therapy should be stopped if the patient develops neutropenia.  
   **true**  **false**

d) When changing psychiatric medications a ‘washout period’ is **always** required.  
   **true**  **false**

19. Working with patients with mental health problems presents pharmacists with both opportunities and challenges. Which of the following statements are correct:

a) The Framework for Mental Health Services in Scotland outlines the vision of how services for all people with mental health problems should be structured.  
   **true**  **false**

b) People with long-term mental health problems are more likely to develop other problems such as diabetes, obesity, coronary heart disease and stroke, compared to the general population.  
   **true**  **false**

c) Pharmacists have a role in advising patients on concordance and stopping medication.  
   **true**  **false**

d) The Scottish Pharmacy in Mental Health (SPMH) group is open to membership from all pharmacy staff interested in mental health.  
   **true**  **false**

20. In relation to mental health:

a) Approximately 30% of patients treated with typical antipsychotics develop parkinsonian side-effects which usually occurs early in treatment.  
   **true**  **false**

b) There is little clinical difference between the available SSRIs.  
   **true**  **false**

c) Flattened mood is classified as a negative symptom.  
   **true**  **false**

d) Alzheimer’s disease (AD) accounts for about 60% of all cases of dementia.  
   **true**  **false**
Introduction to Pharmaceutical Care in Mental Health

1 a  2 a  3 a  4 a  
   b  b  b  
   c  c  c  
   d  d  d  

5 a  6 a  7 a  8 a  
   b  b  b  
   c  c  c  
   d  d  d  

9 a  10 a  11 a  12 a  
   b  b  b  
   c  c  c  
   d  d  d  

13 a  14 a  15 a  16 a  
   b  b  b  
   c  c  c  
   d  d  d  

17 a  18 a  19 a  20 a  
   b  b  b  
   c  c  c  
   d  d  d  

Your details

Name

Address

Postcode

RPSGB registration number

Post to
NHS Education for Scotland (Pharmacy)
3rd floor, 2 Central Quay
89 Hydepark Street
Glasgow  G3 8BW

Telephone: 0141 223 1600
Fax: 0141 223 1651
Email: pharmacy@nes.scot.nhs.uk
Website: www.nes.scot.nhs.uk/pharmacy

Comments
If no CD is here, please call 0141 223 1600.

Introduction to Pharmaceutical Care in Mental Health

NHS Education for Scotland (Pharmacy)
3rd Floor, 2 Central Quay
89 Hydepark Street
Glasgow
G3 8BW
Telephone 0141 223 1600
Fax 0141 223 1651
E-mail pharmacy@nes.scot.nhs.uk
Website www.nes.scot.nhs.uk/pharmacy