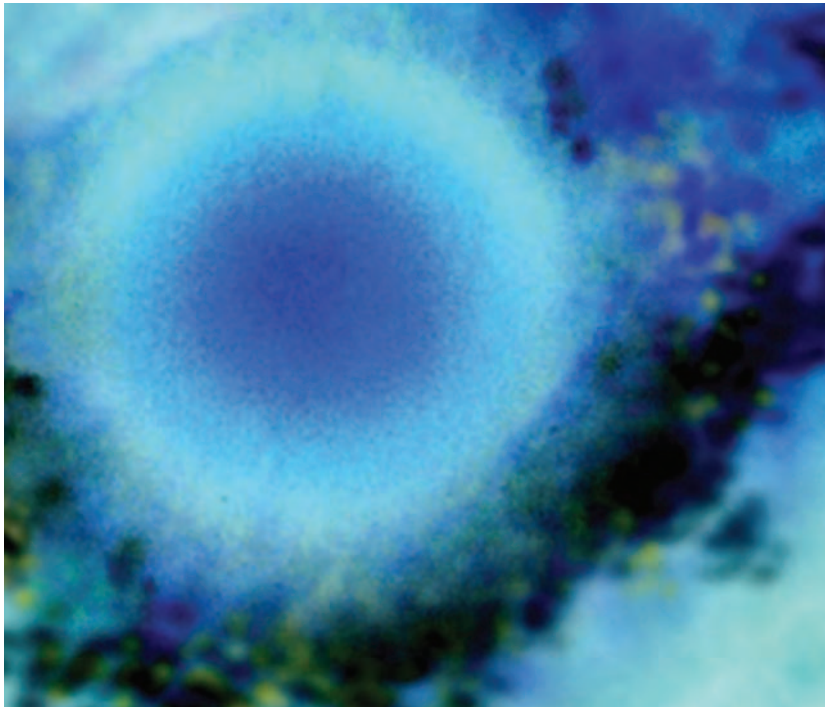


Fast Facts



# Fast Facts: Parkinson's Disease

**K Ray Chaudhuri, Christopher G Clough and  
Kapil D Sethi**  
Third edition



HEALTH PRESS



# Fast Facts: Parkinson's Disease

Third edition



**K Ray Chaudhuri MD FRCP DSc**

Professor of Neurology and Movement Disorders,  
and Consultant Neurologist  
National Parkinson Foundation Centre of Excellence  
King's College Hospital and  
University Hospital of Lewisham, London, UK



**Christopher G Clough MD FRCP**

Medical Director  
King's College Hospital  
London, UK



**Kapil D Sethi MD FRCP**

Professor of Neurology and  
Director, Movement Disorders Program  
Georgia Health Sciences University  
Augusta, Georgia, USA

**Declaration of Independence**

This book is as balanced and as practical as we can make it.  
Ideas for improvement are always welcome: [feedback@fastfacts.com](mailto:feedback@fastfacts.com)



Fast Facts: Parkinson's Disease  
First published 2003; second edition 2007  
Third edition May 2011

Text © 2011 K Ray Chaudhuri, Christopher G Clough, Kapil D Sethi  
© 2011 in this edition Health Press Limited  
Health Press Limited, Elizabeth House, Queen Street, Abingdon,  
Oxford OX14 3LN, UK  
Tel: +44 (0)1235 523233  
Fax: +44 (0)1235 523238

Book orders can be placed by telephone or via the website.

For regional distributors or to order via the website, please go to:

[www.fastfacts.com](http://www.fastfacts.com)

For telephone orders, please call +44 (0)1752 202301 (UK, Europe and Asia–  
Pacific), 1 800 247 6553 (USA, toll free) or +1 419 281 1802 (Americas).

Fast Facts is a trademark of Health Press Limited.

All rights reserved. No part of this publication may be reproduced, stored in  
a retrieval system, or transmitted in any form or by any means, electronic,  
mechanical, photocopying, recording or otherwise, without the express permission  
of the publisher.

The rights of K Ray Chaudhuri, Christopher G Clough, and Kapil D Sethi to be  
identified as the authors of this work have been asserted in accordance with the  
Copyright, Designs & Patents Act 1988 Sections 77 and 78.

The publisher and the authors have made every effort to ensure the accuracy of this  
book, but cannot accept responsibility for any errors or omissions.

For all drugs, please consult the product labeling approved in your country for  
prescribing information.

Registered names, trademarks, etc. used in this book, even when not marked as  
such, are not to be considered unprotected by law.

A CIP record for this title is available from the British Library.

ISBN 978-1-905832-88-0

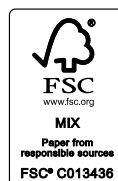
Chaudhuri KR (K Ray)  
Fast Facts: Parkinson's Disease/  
K Ray Chaudhuri, Christopher G Clough, Kapil D Sethi

Medical illustrations by Dee McLean, London, UK.

Typesetting and page layout by Zed, Oxford, UK.

Printed by Latimer Trend & Company Limited, Plymouth, UK.

Text printed with vegetable inks on biodegradable and recyclable  
paper manufactured using elemental chlorine free (ECF) wood  
pulp from well-managed forests.



|  |     |
|--|-----|
| Glossary                                   | 5   |
| Introduction                               | 7   |
| Epidemiology, pathophysiology and genetics | 9   |
| Diagnosis                                  | 30  |
| Drug treatment                             | 48  |
| Neurosurgery                               | 82  |
| Other therapies and support                | 96  |
| Long-term complications                    | 104 |
| Other parkinsonian syndromes               | 118 |
| Developments                               | 133 |
| Useful resources                           | 140 |
| Index                                      | 142 |

## Glossary

**Ballism:** exaggerated involuntary movements leading to wild throwing gestures of the limbs (ballistic movements)

**Bradykinesia (akinesia):** slowness (absence) of movement

**Chorea:** involuntary, fast bodily movements, usually affecting the distal limbs

**Cogwheel rigidity:** a ratchet-like resistance or intermittent relaxation of tension under passive flexion, in the presence of tremor

**COMT:** catechol-*O*-methyl transferase; enzyme that metabolizes levodopa and dopamine by 3-*O*-methylation

**DaTSCAN:** a diagnostic radiopharmaceutical, comprising radioiodine-labeled ioflupane (<sup>123</sup>I) in an ethanolic solution, which is administered intravenously; the chemical binds with dopamine transporters in specific areas of the brain and shows up on single-photon emission tomography

**Diphasic dyskinesia:** abnormal movements that come on with the onset of levodopa response and recur as levodopa wears off

**DLB:** dementia with Lewy bodies; a progressive dementia, with hallucinations and fluctuating levels of attention

**Doll's eye movement:** the patient is asked to fixate straight ahead, and full eye movements are then demonstrated by moving the head (by flexion, extension and rotation)

**Dyskinesia:** abnormal involuntary movements caused by drug treatment for Parkinson's disease

**Festination/festinating gait:** characteristic gait of Parkinson's disease with small hurrying steps, often accompanied by difficulty in gait initiation and sudden 'freezing' (stops and falls)

**Fluorodopa:** isotope-labeled neurotransmitter administered for positron emission tomography

**Lead-pipe rigidity:** constant resistance to passive flexion, in the absence of tremor

**Lewy bodies:** intracytoplasmic neuronal inclusions found in the substantia nigra; pathological hallmark of Parkinson's disease

**MPTP:** 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; by-product of pethidine synthesis produced illicitly and causing parkinsonism in drug addicts; now used to create animal models

**MSA:** multiple system atrophy; neurodegenerative disorder characterized by symptoms causing slowness of movement, abnormal drop in blood pressure and bowel and bladder problems

**'On/off' syndrome:** sudden fluctuation from an 'on' state (dyskinesia and reversal of parkinsonism) to an 'off' state (parkinsonism), secondary to levodopa treatment

**Parkinsonism:** the syndrome comprising rest-tremor, rigidity and bradykinesia

**Peak-dose dyskinesia:** abnormal movements that come on in the middle of levodopa response (usually related to the highest serum level of levodopa)

**PET scan:** brain image taken by positron emission tomography using radioactively labeled neurotransmitters or ligands

**PSP:** progressive supranuclear palsy; a rare neurodegenerative disorder that impairs movement and balance, with characteristic abnormalities of eye movements

**Serotonin (5-hydroxytryptamine, 5-HT):** neurotransmitter important in maintaining equable mood

**SPECT scan:** single-photon emission computed tomography used for DaTSCAN analysis (a radiopharmaceutical used for the differential diagnosis of parkinsonian syndromes and essential tremor; *see* DaTSCAN above)

**Sphincter electromyography:** needle electrode test of the anal sphincter to detect loss of electrical activity in multiple system atrophy

**Stereotactic surgery:** brain surgery performed through a small hole in the skull (burr or stereotaxy hole) using instruments attached to a stereotactic frame screwed to the skull

**Striatum:** basal ganglia nuclei comprising the caudate nucleus and putamen

**Substantia nigra:** black substance in the midbrain containing pigmented dopaminergic neurons

**Thalamus:** main sensorimotor nucleus, adjacent to the third ventricle

**Wilson's disease:** early-onset dystonic condition caused by abnormal copper metabolism

## Introduction

Parkinson's disease, first described by James Parkinson in 1817 in *An Essay on the Shaking Palsy*, is one of the most important disabling illnesses of later life. It is estimated to affect 1% of 70-year-olds, but is also seen in younger people, with 10% of cases occurring before the age of 50.

The disease has become the pathfinder for other neurodegenerative disorders, since discovery of dopamine deficiency within the basal ganglia led to the development of the first effective treatment for a progressive neurodegenerative condition. Dopamine-replacement therapy substantially reduces the symptoms of Parkinson's disease in most patients, improving their quality of life and initially appearing to decrease mortality.

Since earlier editions of this book there have been many advances in the diagnosis and management of Parkinson's disease and in the care available for individuals with the condition. New genes have been described, and new methods to aid diagnosis such as transcranial ultrasound have been developed. Non-motor symptoms of Parkinson's disease – the long-neglected Cinderella of Parkinson's management – have emerged as the key determinant of quality of life and challenge to treatment. Developments in therapy such as human-fetal-cell transplantation or gene therapy continue to be assessed. Meanwhile, the therapeutic armamentarium continues to expand, with the licensing of rasagiline, rotigotine (the first dopamine agonist transdermal patch) and once-daily formulations of ropinirole and pramipexole, improved injection devices for apomorphine, and an intrajejunal infusion of levodopa.

Guidelines highlighting the important role of multidisciplinary care have been published, while the focus of research has shifted from a bias towards motor symptoms to non-motor symptoms, with the publication of specific tools to assess and flag these important problems.

Although it is difficult to measure the specific economic cost of Parkinson's disease, studies suggest that the illness adversely affects the

health-related quality of life of patients and imposes a significant economic burden on society comparable with that of other chronic conditions such as congestive heart failure, diabetes and stroke. Non-motor symptoms such as visual hallucinations, dementia and falls cause hospitalization and institutionalization, and have a major impact on the cost of the illness. Depression, sleep dysfunction, fatigue and anxiety have been identified as some of the key symptoms of the illness. These are tied to progression of underlying disease, and an important advance has been the employment of novel trial designs to study interventions that slow disease progression. Encouraging but inconclusive results have emerged using the monoamine oxidase B (MAOB) inhibitor rasagiline in a delayed-start design.

The annual direct cost of managing patients with Parkinson's disease at home is estimated at £4189; the cost rises to £19 338 for full-time institutionalization. Furthermore, the total direct cost of Parkinson's disease in patients in 'good health' is three times lower than for those in 'poor health'. These figures do not take into account hidden indirect costs such as loss of income from premature retirement, for both the patient and carer.

Given the burdens that Parkinson's disease can impose, we hope that this book will provide doctors, nurses and therapists with the latest information in order to improve as much as possible the lives of patients with Parkinson's disease and related disorders. We believe the book is the best of its kind because it looks at the 'holistic' care of patients with Parkinson's. Most books focus on drug therapy, genetic research or treatment for motor symptoms. Yet an overwhelming body of evidence and patient testimony underlines the importance of non-motor symptoms, the need for multidisciplinary care and the use of tools that empower patients. In *Fast Facts: Parkinson's Disease*, we address all of these aspects in an effort to provide a truly useful and unique resource.

## **Epidemiology**

Parkinson's disease is one of the most common neurodegenerative diseases, but estimating its incidence and prevalence is problematic as there is no 'in-life' marker for idiopathic Parkinson's disease; the diagnosis can only be made with certainty if Lewy bodies (intracytoplasmic aggregations of misfolded protein in the brain) are found in the substantia nigra and other brain regions after death (see pages 11–13). Case ascertainment in community studies is difficult, and often other parkinsonian syndromes may be included.

**Incidence and prevalence.** 'Incidence' is the number of new cases in a specified time frame, and is not modified by factors affecting survival. Estimates of the annual incidence of Parkinson's disease are in the range of 4–20 per 100 000 individuals. The variability is accounted for by differences in the populations studied and by inclusion or exclusion of other clinical entities, such as essential tremor.

'Prevalence' is the total number of cases in a given population at one time. A widely accepted approximate figure for the prevalence of Parkinson's disease is 200 per 100 000 individuals. In the USA, it is estimated that between 750 000 and 1.5 million people have the disease. In the UK, there are approximately 120 000–130 000 diagnosed cases, but many more affected individuals may remain undiagnosed.

**Age, sex and ethnicity.** Both the incidence and prevalence of Parkinson's disease increase with age, and the prevalence may be as high as 1 in 50 for patients over the age of 80 years. Men are 1.5 times more likely than women to develop the condition. Hospital-based studies and some community studies (e.g. the Copiah County study) have suggested that Parkinson's disease is less common in the black population. However, Parkinson's disease has been found in all the ethnic populations studied.

**Mortality.** In 1967, Hoehn and Yahr published the first mortality study of Parkinson's disease in the pre-levodopa era. They found that up to 61% of patients were severely disabled or dead after 5–9 years of follow-up, which increased to more than 80% in those followed up for more than 10 years. Overall in this early study, mortality was three times that expected in the general population. Of more than 20 reports on Parkinson's disease and mortality, 11 reported mortality increases of 1.5–2-fold, while the others reported increases greater than 2-fold.

Several researchers have suggested that disability and mortality in Parkinson's disease show a sex difference, with significantly greater mortality in women. However, there are other studies suggesting a poorer prognosis in men. Berger reported relative risks of death of 3.1 for men with Parkinson's and 1.8 for women with the disease, although these figures are much higher than those reported in other studies. A study by Japanese investigators suggested a mean age at death of 71.9 years in men and 74.2 years for women. In Japan, female patients appear to lose approximately 7 years of longevity compared with men once Parkinson's disease is diagnosed.

Although some would say that the life expectancy of patients with Parkinson's disease appears to have been prolonged, their lifespan is still probably less than that of the general population, as indicated in the Japanese study. The cause is complex. Improved survival is thought to be a result of the introduction of effective symptomatic therapy such as levodopa, while decreased or delayed mortality from comorbidity may partly account for the decreased mortality in younger people. Studies have suggested that relative survival for people with Parkinson's disease diagnosed before the age of 60 is similar to that for the general population, but for those who are older at diagnosis relative survival is less than expected.

In general, before the use of levodopa the relative risk of death with Parkinson's disease was about 3.0. The 15-year follow-up study of the Sydney cohort by Hely and colleagues, published in 2005, indicated that modern treatment had reduced this risk to 1.86. However, reassessment of this cohort by the same researchers at 20 years reported a revised risk similar to the pre-levodopa era of 3.1. So the

## 2 Diagnosis

When, in 1817, James Parkinson first described the features of paralysis agitans in 6 patients, he did not refer to the typical cogwheel rigidity, and mistook bradykinesia for paralysis. Nevertheless, his description of the tremor, posture (Figure 2.1) and clinical course of the disease has hardly been improved. Most cases of Parkinson's disease are easily recognizable at an early stage, but many are missed if tremor is absent; gradual slowing in performance may be instead attributed to aging or aches and pains, and loss of function may be ascribed to other causes.



**Figure 2.1** Paralysis agitans, as first described by James Parkinson, depicting the characteristic fixed posture. Neurologist Sir William Richard Gowers drew this illustration in 1886 as part of his documentation of Parkinson's disease in *A Manual of Diseases of the Nervous System*.

Parkinsonism is a clinical syndrome (Table 2.1) and may have a number of causes. When the condition appears to be idiopathic, and, in particular, responds to levodopa therapy, it is referred to as Parkinson's disease.

## Early indicators

Signs may be subtle in the early stages of the disease. In suspected cases it is often helpful to ask patients what tasks they find difficult.

TABLE 2.1

### Diagnosis of parkinsonism

#### Essential features

- Bradykinesia and one (or more) of the following:
  - tremor (resting)
  - rigidity (cogwheel or lead-pipe; see page 35)
  - postural instability

#### Additional features

- Fixed, stooped posture
- Dystonic postures, e.g. striatal hand
- Hypomimia ('masked' face)
- Shuffling, short-step gait (with or without festination)
- Freezing episodes (sometimes known as paradoxical akinesia)
- Seborrhea of the scalp
- Constipation
- Bladder symptoms (sometimes known as pseudoprostatism)
- Bulbar symptoms
  - dysarthria
  - dysphagia
- Pain
- Mental and cognitive disturbance