

and delivering lectures for Abbott, Pfizer, MSD, Janssen-Cilag, Leo, and Basilea and does consultancy for Merck and Novartis; MHB is employed by SIGN; JL was paid to attend one Abbott Advisory Board meeting and to deliver postgraduate education by Leo, has received meeting expenses from Pfizer, and has undertaken trials funded by Janssen-Cilag, Merck, Serono, Schering-Plough, Abbott, and Pfizer; HW has been paid to provide expert testimony to the Psoriatic Arthritis Advisory Panel and to develop and deliver a Wyeth educational presentation, and has received expenses from Abbott to attend one conference; HW's institution will receive payment for participating in a study of the validity of the PEST questionnaire; RR received travel costs and a conference registration fee from Wyeth; ADO was paid to attend one Abbott advisory board meeting, one Schering-Plough advisory board meeting, and to deliver lectures for Wyeth and Abbott, and received expenses to attend one conference from Wyeth and one conference from Janssen-Cilag; ADO's institution has received grants to conduct clinical trials of biologics for Abbott, Wyeth, Schering-Plough, and Janssen-Cilag; no other relationships or activities that could appear to have influenced the submitted work.

Provenance and peer review: Commissioned; not externally peer reviewed.

Patient consent not required (patient anonymised, dead, or hypothetical).

- 1 Rapp SR, Feldman SR, Exum ML, Fleischer AB Jr., Reboussin DM. Psoriasis causes as much disability as other major medical diseases. *J Am Acad Dermatol* 1999;41(3 Pt 1):401-7.
- 2 Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. *JAMA* 2006;296:1735-41.
- 3 Kaye JA, Li L, Jick SS. Incidence of risk factors for myocardial infarction and other vascular diseases in patients with psoriasis. *Br J Dermatol* 2008;159:895-902.
- 4 Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB, Gelfand JM. Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol* 2006;55:829-35.
- 5 Kimball AB, Jacobson C, Weiss S, Vreeland MG, Wu Y. The psychosocial burden of psoriasis. *Am J Clin Dermatol* 2005;6:383-92.
- 6 Reich K, Kruger K, Mossner R, Augustin M. Epidemiology and clinical pattern of psoriatic arthritis in Germany: a prospective interdisciplinary epidemiological study of 1511 patients with plaque-type psoriasis. *Br J Dermatol* 2009;160:1040-7.
- 7 Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of psoriasis and psoriatic arthritis (SIGN guideline 121). 2010. www.sign.ac.uk/guidelines/fulltext/121/index.html.
- 8 Ibrahim G, Buch M, Lawson C, Waxman R, Helliwell PS. Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and development of a new instrument: the psoriasis epidemiology screening tool (PEST) questionnaire. *Clin Exp Rheumatol* 2009;27:469-74.

PRACTICE POINTER

Managing Parkinson's disease during surgery

K A Brennan,¹ R W Genever²

¹Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

²Chesterfield Royal Hospital NHS Foundation Trust, Calow, Chesterfield S44 5BL, UK

Correspondence to: R W Genever
Richard.Genever@chesterfieldroyal.nhs.uk

Cite this as: *BMJ* 2010;341:c5718
doi: 10.1136/bmj.c5718

People with Parkinson's disease undergoing surgery are at increased risk owing to their condition and to potential omission of medication. This article looks at what doctors need to consider in this situation and how specialist assistance can be accessed

Parkinson's disease is a common condition affecting over 100 000 people in the UK.¹ People with Parkinson's disease who undergo surgery have increased mortality and longer hospital stays than people without this condition.² Missing dopaminergic medication during a period of perioperative starvation can result in life threatening complications.^{3 4} This problem can be further compounded if the absorption of drugs is impaired.⁵ Recognising these hazards is the first step in an approach that may reduce the risk of suboptimal medication faced by people with Parkinson's disease, using three principles.

- Advance planning
- Appropriate prescribing
- Advice from specialists.

Methods

We reviewed the available literature using PubMed and Google scholar databases up to May 2010. Further papers were identified from the references of articles found by the initial search. We also searched the Cochrane Library. Much of the evidence was based on case reports so selection of papers according to the grade of evidence was not attempted. A study published in July 2010 that added substantial new evidence was included.

Potential complications of missing medication

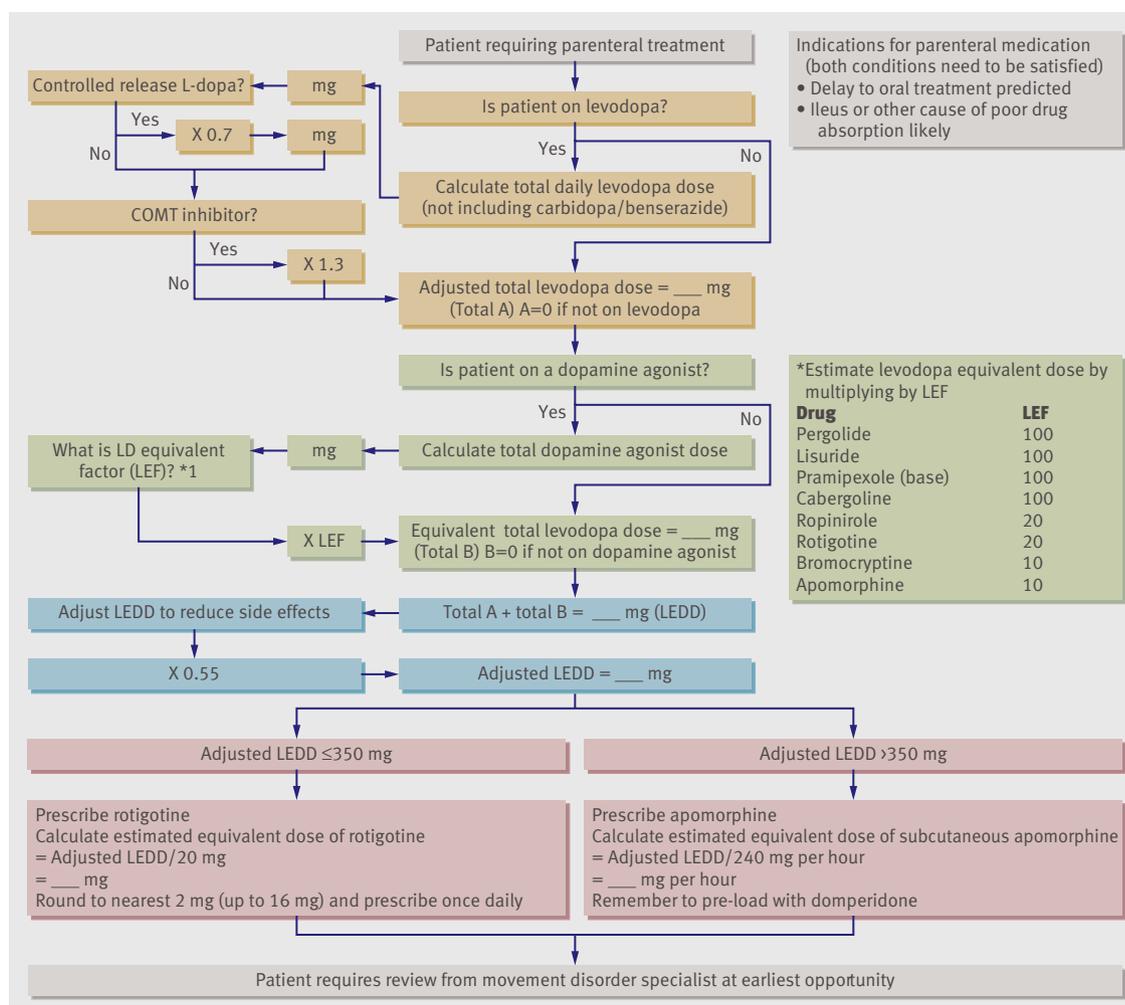
The consequences of missing Parkinson's medication can vary enormously. Some people can tolerate a missed tablet without experiencing any major effects. Others become immobile. However, in some situations, missing dopaminergic medication can precipitate a condition known as neuroleptic malignant like syndrome, associated with fever, confusion, raised concentrations of muscle enzyme, and even death. This syndrome is most common in people with more severe Parkinson's symptoms and those on the largest doses of levodopa.⁶

What particular risks are faced?

Some of the risks relate to Parkinson's disease itself and others to the effects of omitting medication. A retrospective cohort study of 234 people with Parkinson's disease and 40979 controls undergoing major abdominal surgery found a higher incidence of aspiration pneumonia, bacterial infection, and urinary tract infection in the group with Parkinson's.²

Case reports have described other perioperative complications in people with Parkinson's disease, including postoperative respiratory failure and postextubation laryngospasm. Other reports mention exacerbation of Parkinson's symptoms during surgery and a case of severe neuroleptic malignant like syndrome precipitated by perioperative starvation for coronary artery bypass grafting.^{3 4}

Access to the correct medication at the right time remains a problem for people with Parkinson's disease when they are admitted to hospital. This concern has led to a national awareness campaign from the charity Parkinson's UK.⁷ Lack of awareness of the importance of maintaining medication at the time of surgery places patients at increased risk.



Algorithm for estimating parenteral doses of drugs for Parkinson's disease

Reducing the risks

Advance planning

As part of a Parkinson's disease education programme, patients should be encouraged to ask that their movement disorder team is consulted before admission. This will enable those at greatest risk to be identified and their treatment individually tailored. The referral could come from the patient's general practitioner, the surgical outpatient department, or the pre-assessment clinic.

The aim is to establish whether the patient's treatment regimen should be altered for the period around their operation and to consider any additional measures that might be preferable.

Who should give the specialist advice?

Where available, a nurse specialising in Parkinson's disease can play a key part. They may be able to advise directly or discuss the case with the patient's consultant. In areas without specialist nurse support the advice should come directly from the patient's geriatrician or neurologist.

Unplanned surgery and complicated elective surgery

Specialist preoperative advice cannot always be obtained, particularly for urgent surgery. To allow a treat-

ment plan to be enacted at any time, we recommend that hospitals develop a protocol for this situation. We propose a flowchart (figure) to guide a non-specialist until more specific advice can be obtained from the movement disorder team.^{8,9} Clinicians who are unfamiliar with medication for Parkinson's disease may require assistance from a pharmacist.

Anaesthetic and surgical considerations

Pre-operative

All patients having surgery under general or regional anaesthetic require preoperative fasting. However, it is recognised that it is safe to continue clear oral fluids up to 2 h before elective surgery.¹⁰ It is routine practice to continue oral medications until the time of anaesthetic induction. This practice should be encouraged in patients with Parkinson's. Consideration should be given to placing such patients at the start of the operating list, facilitating greater predictability over the time of fasting and surgery, and ensuring optimum early postoperative disease management.

Induction—regional versus general anaesthesia

Several factors affect the choice of anaesthesia. Regional anaesthesia allows monitoring of Parkinson's symp-

toms and should be considered in people who require very frequent dopaminergic medication. In exceptional circumstances oral medication can be administered intraoperatively, although a case of exacerbation of parkinsonism despite using this approach has been reported.³

Some motor symptoms of Parkinson's disease, such as severe dyskinesia, might make a general anaesthetic preferable. The anaesthetist should be aware of the effects of routinely used anaesthetic drugs on parkinsonism. Propofol is commonly used to induce anaesthesia and two case studies have shown that it can exacerbate dyskinesia.¹¹ However, propofol may temporarily suppress tremor associated with Parkinson's disease¹² so it continues to be the first choice of most anaesthetists. Its antiemetic effect may also be beneficial.

The need for intubation should be assessed on an individual basis. Severe Parkinson's disease is associated with excessive salivation that is often due to swallowing dysfunction. If dysphagia is suspected, intubation is the safer choice. In these patients, anticholinergics can increase the viscosity of saliva, further impairing swallowing, and should be used with caution.¹³

Intraoperative

Antiemetics are routinely given intraoperatively. Centrally acting dopamine antagonists such as prochlorperazine and metoclopramide are likely to exacerbate Parkinson's disease. Domperidone is preferable as it has a largely peripheral mode of action and may be given as a suppository. Other appropriate anti-emetics include 5-hydroxytryptamine-3 antagonists such as ondansetron and the antihistamine cyclizine.

Some patients will have a deep brain stimulator in situ and this should be recorded prominently in the medical notes. Electrocautery may damage the intracranial leads hence the manufacturers recommend its avoidance. However, where necessary, bipolar diathermy should be used.¹⁴

Post-operative

An assessment of Parkinson's disease should be made at the earliest opportunity and a judgement made about the patient's ability to absorb enteral medication. A strict nil-by-mouth instruction or active vomiting will mandate an alternative route. The need for parenteral medication is extended in the presence of ileus or delayed gastric emptying. Advice from the Parkinson's disease specialist nurse or consultant should be sought.

Appropriate prescribing

The overall strategy should be to maintain Parkinson's treatment that closely resembles the patient's usual treatment. Several changes can be recommended, depending on the particular drugs in use and the nature of surgery.

Using a different preparation of the same drug treatment

Patients who usually receive levodopa can be given dispersible co-beneldopa via a nasogastric tube during lengthy surgery. A patient with severe Parkinson's disease undergoing liver resection was maintained without appar-

ent exacerbation of his condition using this approach. Previous operations had resulted in marked rigidity and inability to swallow secretions in the same patient.¹⁵

This technique is unsuitable when evidence indicates paralytic ileus. Two cases of worsening parkinsonism have been reported in patients whose recovery was complicated by ileus despite receiving orally disintegrating co-careldopa.⁵

When switching from controlled release levodopa to dispersible co-beneldopa a dose reduction of around 30% is suggested due to lower bioavailability in controlled release form.^{16 17}

Using alternative Parkinson's drugs in the perioperative period

Enteral medication would not be appropriate for a patient in whom post-operative ileus or delayed gastric emptying is expected. The choices for this patient are suboptimal treatment with its associated risks, or a parenteral drug (apomorphine or rotigotine).

Apomorphine is a highly potent dopamine agonist which is delivered subcutaneously. Switching a patient from oral treatment to apomorphine for the duration of surgery would avoid the problems of drug absorption seen with paralytic ileus. Due to its high potency, even patients on large doses of treatment are likely to get effective control of their symptoms from apomorphine. The main disadvantages are emetogenesis (which necessitates concomitant use of domperidone), neuropsychiatric side-effects such as hallucinations, and hypotension.

Rotigotine is a relatively new agent. It is also a dopamine agonist and is delivered transdermally with a patch. In an open label study, 14 patients were switched from their usual treatment to rotigotine the day before they underwent surgery. The switchover was felt by clinicians and patients to be easy and only one patient had a side effect (transient hallucinations and nausea) that was likely to have been caused by their medication.¹⁸ Its advantages are ease of use and tolerability but it may not be sufficiently potent to provide adequate treatment for patients on higher dose treatment regimens.

Switching to apomorphine or rotigotine

A number of articles have proposed levodopa equivalent doses for the various treatments. By using these data and head-to-head studies of rotigotine and ropinirole, it is possible to construct an estimated dose equivalent table for all the currently available drugs (see figure).^{8 9} In this situation our practice is to initially prescribe a lower than equivalent dose to reduce the risk of side effects but early review and adjustment of the dose is recommended.

Advice from a specialist

Even with an agreed advance plan or a written protocol, patients who do not rapidly regain the ability to take their usual Parkinson's medication should be seen by a Parkinson's disease specialist nurse or movement disorder consultant at the earliest opportunity. This allows the treatment plan to be adjusted according to the initial response.

Review of Parkinson's patients by a neurologist following knee replacement has been shown to reduce length of

stay.¹⁹ Further research is required to establish whether this benefit can be transferred to Parkinson's patients undergoing different types of surgery.

Contributors: RG initially developed the concept of the paper and led on the review of Parkinson's disease medication research. KB provided the review of anaesthetic papers. Both authors wrote and edited the article jointly. RG is guarantor.

Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that RG has received sponsorship to attend medical conferences from Boehringer Ingelheim, Glaxo Smith Kline, Teva and Lundbeck, and Orion. RG has received honoraria for speaking at meetings from Glaxo Smith Kline and Orion. RG has received honoraria for sitting on advisory boards from Glaxo Smith Kline and Boehringer Ingelheim. KB has no relationships with any companies that might have an interest in the submitted work in the previous 3 years; and RG and KB have no non-financial interests that may be relevant to the submitted work.

Provenance and peer review: Not commissioned, externally peer reviewed.

- Schrag A, Ben-Schlomo Y, Quinn NP. Cross-sectional prevalence survey of idiopathic Parkinson's disease and parkinsonism in London. *BMJ* 2000;321:21-2.
- Pepper PV, Goldstein MK. Postoperative complications in Parkinson's disease. *JAGS* 1999;47:967-72.
- Reed AP, Han DG. Intraoperative exacerbation of Parkinson's disease. *Anesth Analg* 1992;75:850-3.
- Stoltz M, Thummler D, Schurch M, Renggli J-C, Urwyler A, Pargger H. Fulminant neuroleptic malignant syndrome after perioperative withdrawal of antiParkinsonian medication. *Br J Anaesth* 2004;96:868-71.
- Iyer SS, Morgan JC, Sethi KD. Absorption of orally disintegrating levodopa requires intact small bowel function. *Neurology* 2005;65:1507.
- Ueda M, Hamamoto M, Nagayama H, Otsubo K, Nito C, Miyazaki T, et al. Susceptibility to neuroleptic malignant syndrome in Parkinson's disease. *Neurology* 1999;52:777-81.

- Parkinson's UK. "Get it on time" campaign. www.parkinsons.org.uk/about_us/policy_and_campaigns-1/campaigns/get_it_on_time_campaign.aspx.
- Wenzelburger R, Zhang B-R, Pohle S, Klebe S, Lorenz D, Herzog J, et al. Force overflow and levodopa-induced dyskinesias in Parkinson's disease. *Brain* 2002;125:871-9.
- LeWitt PA, Boroojerdi B, MacMahon D, Patton J, Jankovic J. Overnight switch from oral dopaminergic agonists to transdermal rotigotine patch in subjects with Parkinson disease. *Clin Neuropharmacol* 2007;30:256-65.
- Brady M, Kinn S, Stuart P, Ness V. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev* 2009;7:CD005285.
- Krauss JK, Akeyson EW, Giam P, Jankovic J. Propofol-induced dyskinesias in Parkinson's Disease. *Anesth and Analg* 1996;83:420-2.
- Anderson BJ, Marks PV, Flutter ME. Propofol—contrasting effects in movement disorders. *Br J Neurosurg* 1994;8:387-8.
- Nicholson G, Pereira AC, Hall GM. Parkinson's disease and anaesthesia. *Br J Anaesth* 2002;89:904-16.
- Davies RG. Deep brain stimulators and anaesthesia. *Br J Anaesth* 2005;95:424.
- Furuya R, Hirai A, Andoh T, Kudih I, Okumura F. Successful perioperative management of a patient with parkinson's disease by enteral levodopa administration under propofol anesthesia. *Anesthesiology* 1998;89:261-3.
- Sinemet CR and Half Sinemet CR, Summary of product characteristics. Last updated on the eMC 20/11/2009. <http://emc.medicines.org.uk/medicine/9650/SPC/SinemetCRandHalfSinemetCR>.
- Madopar CR. Summary of product characteristics. 2009. <http://emc.medicines.org.uk/medicine/1707/SPC/MadoparCRCapsules125>.
- Wüllner U, Kassubek J, Odin P, Schwarz M, Naumann M, Häck H-J, et al. Transdermal rotigotine for the perioperative management of Parkinson's disease. *J Neural Transm* 2010;117:855-9.
- Mehta S, Vankleunen JP, Booth RE, Lotke PA, Lonner JH. Total knee arthroplasty in patients with Parkinson's disease: impact of early postoperative neurologic intervention. *Am J Orthop* 2008;37:513-6.

Accepted: 16 September 2010

ANSWERS TO ENDGAMES, p 1001. For long answers go to the Education channel on bmj.com

PICTURE QUIZ

A 35 year old smoker with shortness of breath

- Multiple cysts, ground glass opacities, and fibrotic changes are the main abnormalities seen on these images.
- The differential diagnoses include smoking related interstitial lung diseases (desquamative interstitial pneumonia, respiratory bronchiolitis-interstitial lung disease, pulmonary Langherhans' cell histiocytosis), sporadic lymphangioleiomyomatosis, idiopathic interstitial pneumonias (atypical form of idiopathic pulmonary fibrosis, fibrotic form of non-specific interstitial pneumonia), and chronic hypersensitivity pneumonia.
- Bronchoalveolar lavage and a differential cell count on the fluid obtained (to look for lymphocytosis, pigmented macrophages, and CD-1a cells). A surgical lung biopsy should be performed when the images on high resolution computed tomography are not typical of a specific interstitial lung disease, as in this case. The biopsy showed areas of subpleural fibrosis as well as bronchocentric fibrosis with occasional fibroblastic foci.
- The consensus after the multidisciplinary approach was that the diagnosis was chronic hypersensitivity pneumonia as a result of misuse of cocaine.
- Drug discontinuation is essential. Although the use of steroids is controversial, methylprednisolone and cyclophosphamide were used to treat pulmonary fibrosis.

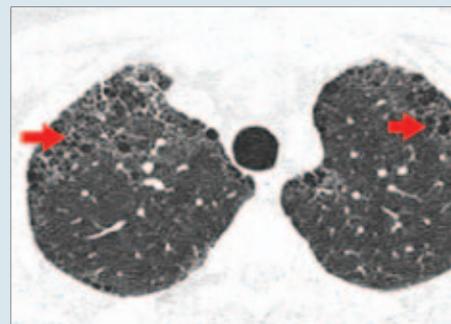


Fig 1 | High resolution computed tomography of the chest showing multiple cysts in the upper lung zones

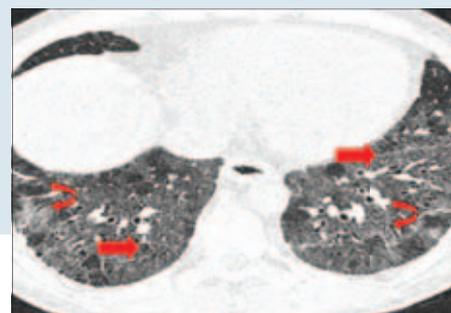


Fig 2 | High resolution computed tomography of the chest showing ground glass opacities and fibrotic changes in the lower lung zones

STATISTICAL QUESTION

The Normal distribution

Answers a, b, c, and d are all true.

ON EXAMINATION QUIZ

A patient with splenomegaly

Answer D is correct.