Decline in cognitive functioning after surgery, particularly in the elderly, has been anecdotally appreciated by the profession and public for many years. It is a well established phenomenon after cardiopulmonary bypass and recent research reveals it to be a surprisingly common outcome after other types of major surgery. Much remains unknown about its aetiology, but the implications for anaesthesia and surgery in an increasingly long-lived population are considerable.

Three clinical conditions are worthy of discussion and need to be distinguished from each other, that is, delirium, dementia, and postoperative cognitive dysfunction (POCD).1

**Delirium**

Delirium is the acute onset of disturbed mental function; it is surprisingly common in elderly hospitalized patients and the time course is often short. Alteration of consciousness may be a feature. Visual hallucinations may occur with fleeting delusional thoughts. Anxiety and distress are common. There is a diurnal variation of symptoms with a variety of behaviours, from aggression to withdrawal (leading to a mistaken diagnosis of depression).

There may be a predisposing cause, such as urinary tract or chest infection, or it may be related to drugs including alcohol or caffeine withdrawal. In particular, drugs with anticholinergic actions are implicated in delirium. Many drugs, including digoxin, thiazide diuretics, and corticosteroids have mild anticholinergic actions that may, when used in combination with other drugs with similar effects, contribute to delirium. Opioids, sedatives and disturbances of calcium, sodium, and glucose homeostasis are also associated factors. Failure of communication may be a consequence of loss of dentures, glasses or hearing aids; this may lead to a mistaken diagnosis.

**Dementia**

Dementia refers to a series of chronic organic brain syndromes associated with irreversible pathology; delirium is frequently mistaken for dementia. Many of the causes of dementia are associated with a failure of cholinergic transmission; therefore, patients are very sensitive to anticholinergic drugs. Anticholinesterases are used in some patients to improve cognitive function. In its most easily recognized form, dementia presents as a global deterioration of cognitive ability in the absence of clouding of consciousness, that is, the patient who responds appropriately when introduced but who clearly is mistaken as to where he or she is when asked a few simple questions during the preoperative visit.

The very nature of hospital admission, particularly for emergency or trauma surgery, means that delirium may occur in the patient with dementia. Indeed, the latter is considered a risk factor for the former. However, it is important that due consideration is given to the potentially reversible part (delirium) of the symptom complex before assuming that the patient’s problems are an inevitable consequence of dementia. In practice, it is important that a confident diagnosis of dementia is made by the community services (e.g. general practitioner, nursing home), rather than in an acute postoperative situation.

The diagnosis and clinical features of the dementias are beyond the scope of this article. Suffice to say that there are a number of diseases in which dementia is a feature. Alzheimer’s disease is one of the most important examples of a progressive chronic condition associated with cognitive decline. Chronic decline also occurs in Parkinson’s disease and widespread cerebrovascular disease.

**Anaesthetic assessment**

It is important to assess the severity of cognitive disturbance. The Mini-Mental State Examination (MMSE) is a test of global cognitive function2 that can be performed at the bedside. It consists of a series of questions on orientation and simple commands to assess comprehension (Table 1). Variations in MMSE allow comparison to be made with time and measure

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**Key points**

Perioperative delirium and longer term cognitive disturbance are common and disabling consequences of anaesthesia and surgery in the elderly.

Evidence is emerging that the risk of postoperative delirium can be predicted by preoperative screening of otherwise asymptomatic patients.

The risk of prolonged postoperative cognitive dysfunction (POCD) is ~10% following major surgery in patients of more than 60 yr of age. Increasing age is a risk factor and the incidence in patients of more than 80 yr of age may be as high as one in three.

Regional anaesthesia reduces the risk of cognitive impairment in the immediate postoperative period but appears to have no effect on the incidence of prolonged POCD.

The risks of cognitive decline should always be considered and discussed when major surgery is contemplated in elderly patients.

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patients had MMSE scores however, the data are striking. More than a quarter of these confusion, and no details of anaesthetic technique are recorded. MMSE examinations. Four patients failed to complete the after hip arthroplasty for several days, undertaking serial performance in a battery of neuropsychological tests that would<br>expected in <3.5% of controls. This dry statistical statement equates to a catastrophic loss of cognitive ability; it is the difference between a person who is capable of living independently and one who is not. POCD can be usefully defined as a long term, possibly permanent, disabling deterioration in cognitive function following surgery. The statement that ‘Granddad was never the same after his operation’ is occasionally heard and may reflect the lay person’s view of POCD. It is difficult to get a reliable estimate of how prevalent and disabling such conditions are. Hence the approach used by the investigators in the International Study of Postoperative Cognitive Dysfunction to define the condition in terms of a statistical abnormality, rather than any particular clinical features.

Research into POCD is fraught with problems. Observed over time, a proportion of the elderly population will suffer cognitive decline in any event, and some studies are hampered by the lack of an appropriate control group. Also, the development of other pathologies within the study period may affect the results. The tests used to detect POCD vary among studies, making comparison difficult. The level of difficulty of the tests themselves is important—too easy and they fail to detect more subtle degrees of impairment, too difficult and they discourage the subject, thus influencing performance in the tests. Furthermore, performance in cognitive testing is sensitive to the environment in which it is carried out, the manner in which it is administered, the mood of the subject at the time, and the number of times it is administered. Allowance must be made for all of these factors when interpreting the data. Recruiting patients to take part in studies of POCD is not easy. Patients who feel they may be vulnerable to cognitive decline may elect not to take part, or withdraw subsequently if they feel that their cognitive performance has worsened. Postoperative depression and coping mechanisms may also play a part; subjective reporting of cognitive decline is more common than that detected by testing.5

Despite these difficulties, some research has been carried out in this area. The largest study of POCD carried out to date, in a cohort of more than 1200 patients of more than 60 yr of age, found an incidence of POCD of ~25% at 1 week and 10% at 3 months postoperatively.6 Further follow up of the affected patients showed that the incidence of cognitive problems eventually fell towards that in matched controls but that ~1% had unresolved POCD up to 2 yr after operation. The older patients within the study showed a higher incidence, approaching one in three in the relatively small group of more than 80 yr of age, and further studies have shown a correspondingly smaller risk in younger patients.7 It is clear that increasing age is in itself a risk factor for developing POCD.

### Possible causes of POCD

#### Emboli

There is much evidence to suggest that multiple cerebral emboli are the cause of cognitive deterioration following cardiopulmonary bypass. Whilst many other types of surgery do not carry such a direct risk of cerebral embolization it seems nevertheless plausible as a causative factor.

#### Perioperative physiological disturbances

Biochemical disturbances, notably hyponatraemia, are a well recognized cause of postoperative delirium. There is no evidence,

### Table 1: Aspects of cognitive function tested by the MiniMental State Examination

<table>
<thead>
<tr>
<th>Orientation in time</th>
<th>Orientation in place</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetition of named objects</td>
<td>Repetition of simple phrase</td>
</tr>
<tr>
<td>Ability to undertake simple arithmetic</td>
<td>Recall of objects named earlier in the interview</td>
</tr>
<tr>
<td>Naming of objects shown by examiner</td>
<td>Execution of simple tasks by written and spoken command</td>
</tr>
<tr>
<td>Writing a simple sentence</td>
<td>Copying a simple design</td>
</tr>
</tbody>
</table>

Progress following illness or surgery. The MMSE is scored out of a total of 30, with points being awarded for correct answers in the various aspects of function tested. An MMSE score of <23 is not diagnostic of dementia but does offer supporting evidence. Lower degrees of impairment of MMSE scores (e.g. 26–29) imply a degree of cognitive deficit which, while not indicative of dementia, may have implications for postoperative management. It is becoming apparent that, even in the absence of dementia, MMSE scores of 28 or less are associated with more than a 2-fold increased risk of developing postoperative delirium compared with scores of 29 or 30. Specific deficits of attention appear to be associated with an even higher level of increased risk.3

Performance of a complete MMSE may be difficult to justify in an asymptomatic preoperative patient. However, it is reasonable to assume that a patient who is unable to recall simple information pertaining to time and place (e.g. date or hospital) will score significantly less than the maximum 30 points. Such information may be of serious clinical significance when it comes to predicting the possibility of postoperative confusion.

The time course of acute cognitive dysfunction, as assessed with serial MMSE measurements following major surgery, has been described. Duggleby and Landers6 assessed 66 patients after hip arthroplasty for several days, undertaking serial MMSE examinations. Four patients failed to complete the study, for reasons that might arguably be attributable to confusion, and no details of anaesthetic technique are recorded. However, the data are striking. More than a quarter of these patients had MMSE scores <26 on the third postoperative day and, even by day 5, MMSE scores in a few patients failed to return to preoperative levels. These patients were relatively young (mean age 64.8, range 50–80).

#### Postoperative cognitive dysfunction

POCD has been defined for research purposes as deterioration in performance in a battery of neuropsychological tests that would be expected in <3.5% of controls. This dry statistical statement equates to a catastrophic loss of cognitive ability; it is the difference between a person who is capable of living independently and one who is not. POCD can be usefully defined as a long term, possibly permanent, disabling deterioration in cognitive function following surgery. The statement that ‘Granddad was never the same after his operation’ is occasionally heard and may reflect
however, that biochemical disturbances cause prolonged POCD. Perhaps more surprisingly, there is no evidence that perioperative hypoxaemia or hypotension, even quite profound or prolonged, is associated with POCD.6

Pre-existing cognitive impairment

Studies of POCD exclude patients who are already cognitively impaired, but it is possible to demonstrate a lower risk of POCD in patients with a higher level of intellectual performance preoperatively. It is likely that the converse is true and a pre-existing dysfunction increases the risk of POCD.

Other factors

Serum concentrations of known markers of brain damage such as neurone specific enolase and S-100 beta protein do not appear to correlate with the development of POCD. Many other factors have been considered as possibly contributing to the risk. They include variations in the handling of anaesthetic and other drugs, changes in the normal adrenal response to surgery in old age, and the possibility of a ‘risk gene’ for POCD in a manner analogous to Alzheimer’s disease. There is currently no good evidence to support any of these theories.

The known predisposing factors for early and late POCD are summarized in Table 2.

Anaesthetic technique and postoperative cognitive impairment

Good perioperative anaesthetic care is regarded as one of the key means of reducing postoperative complications in any group of patients, and it seems reasonable to assume that this also applies to POCD in elderly patients. Therefore, it is surprising and disappointing that fundamental parameters such as oxygenation and blood pressure do not seem to influence the incidence. Nevertheless, there are important considerations for the anaesthetist which can affect postoperative cognitive function.

Premedication

Benzodiazepines may cause disorientation and confusion in the elderly. Surprisingly, however, the use of preoperative benzodiazepines is associated with an apparent 2-fold reduction in prolonged POCD (from 9.9 to 5%). This is thought to be the result of a deterioration in patients who have such medication withdrawn acutely, rather than a direct protective effect of the drug. Certainly patients who are taking drugs to support their cognitive function, including the anticholinesterase drugs such as donepezil, should not have them stopped perioperatively. There are grounds to believe that sudden stopping of anticholinesterases may precipitate cognitive failure that may be difficult to reverse.

Conduct of anaesthesia

There is no strong evidence to support the use of any particular drugs. However, there are significant associations between early POCD, and both increasing duration of anaesthesia and respiratory complications; therefore attention can be directed to the avoidance of these factors where possible.

Recent research has focussed more particularly on the possible benefits of regional over general anaesthesia. Many anaesthetists actively promote the use of regional anaesthetic techniques in the elderly. Lower limb joint replacement, for instance, is commonly performed under regional anaesthesia alone. There may be a number of good medical reasons in a given individual for recommending regional above general anaesthesia alone. There may be in the absence of these, it is often felt that elderly patients recover more quickly and with less cognitive disturbance following regional anaesthesia. Available evidence from patients randomized to receive either regional or general anaesthesia shows that, in the first week after surgery, the incidence of cognitive impairment is indeed reduced where regional techniques were used (12.7% vs 21.2%); however, this difference does not persist at 3 months. Regional anaesthesia does not appear to be superior to general anaesthesia in preventing prolonged POCD.8 The reduced risk of ‘early’ POCD may have important implications for physical recovery, cooperation with postoperative therapy, and length of hospital stay.

Recent evidence suggesting that patients are at risk from POCD as a consequence of admission to hospital supports the concept of day case surgery. Obviously, this can only be undertaken where support services (e.g. competent relatives, practice nurses, social services) are involved and investigations completed before admission.

Future developments

The precise aetiology of POCD remains obscure and the subject of further research. What is known can nevertheless be applied to clinical practice in an effort to reduce the incidence. It is clear that cognitive dysfunction in the immediate postoperative period and that persisting for months or years are two distinct entities. Although early postoperative delirium does not have the implications for long term care attached to prolonged POCD, its presence can impair recovery and prolong hospitalization in a vulnerable group of patients. Recognition of the special challenges of perioperative care in elderly patients have made this an emerging
subspecialty of anaesthesia, within which an awareness of the importance of cognitive outcome is most important.

It appears that a subset of the elderly population stands at the top of a ‘slippery slope’, vulnerable to prolonged or permanent cognitive decline after surgery. It is not currently possible to identify which patients are at particular risk, or which elements of the process of hospitalization, anaesthesia, surgery, and postoperative care may be precipitating the deterioration. At present it is incumbent upon anaesthetists, surgeons, and all involved in the perioperative care of elderly patients to consider the risk of POCD whenever surgery is contemplated and to discuss the issue with patients and their families. For some patients and some procedures, consideration of these risks may ‘move the goalposts’ such that they no longer consider the proposed operation to be in their best interests.

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References


Please see multiple choice questions 30–30.