The August 2005 update for: Delirium in Old Age.

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Introduction

The updates are organised by chapter headings from the book. The first update (October 2002) covered the period from manuscript submission to publication. If you know of work which you think should be included here, or you disagree with what has been included in some way, please email suggestions to alastair.macdonald@iop.kcl.ac.uk.

This update is cumulative- all new evidence from the literature following manuscript submission is included, and is still assigned to the chapter headings from the book. However, under each chapter heading the material is divided into emerging themes and footnotes, the latter mostly in the form of an annotated bibliography. Note that

- When new material relates to more than one chapter, it may be repeated in different chapter sections.
- No material specific to the topic of delirium at the end of life is included in this update; there is now a book on this topic: Delirium - Acute Confusional States in Palliative Medicine Caraceni and Grassi, OUP http://www.oup.co.uk/isbn/0-19-263199-3
- case reports of new putative precipitating causes of delirium, especially medications, are not now included unless the evidence is overwhelming or alternatively tickles my fancy

There will be no further updates after August 2005.

Chapter 1: The concept of delirium: Historical antecedents and present meanings.

This topic has been recently reviewed by Francis, (2004) in a journal issue devoted to delirium.

Emerging themes

The need to embrace complexity

In a thoughtful commentary on a systematic review of delirium prevention and treatment interventions- one which comes to no firmer conclusions than its predecessor (Weber, Coverdale, & Kunik, (2004), Rockwood and Bhat have called for an end to univariate thinking in relation to the complexities of delirium causation and management (2004). They argue that we need to think more about the phenomenology (e.g distinguishing visuospatial from other forms of attention), shift emphasis away from primary causes of delirium within the brain, acquire more scepticism about Occam's razor, and what they call decerebrate evidence-based medicine. They conclude with a call for "scholarly enquiry in the face of complexity". Rockwood provides an example of this in a review of the relationship between frailty and delirium (2004). The former concept attracts much suspicion from psychiatrists, and in this analysis which is heavily dependent on self-reported variables, the influence of dementia is not really considered.

The relevance of taxonomy: distinguishing delirium and dementia

Cole and colleagues in Montreal have examined the phenomenology of delirium in relation to dementia ((2002). Subjects screen-positive (incident or prevalent) for any cognitive impairment were administered the Confusion Assessment Method (Inouye, van Dyck, Alessi *et al*, (1990) and supplementary information gathered to make a DSM-IIIR diagnosis of delirium. Dementia was "diagnosed" by categorisation using the IQCODE (Jorm, (1994). Over half their sample had both diagnoses. They found some differences in symptoms between delirious patients with and without dementia, but there was generally much overlap. They conclude that the criteria of DSM-IIIR delirium discriminate reasonably well between delirium and non-delirium, irrespective of "diagnosis" of pre-existing dementia. Lundstrom and colleagues followed up 78 patients who were not obviously demented but with a femoral neck fracture for 5 years (2003). They found that both pre- and post-operative delirium were highly correlated with the emergence of dementia. They reassert the increasingly accepted possibility that delirium after such an event is a marker for previously unrecognised dementia, as well as the possibility discussed in the textbook that delirium accelerates the onset of dementia.

The relevance of taxonomy: official classifications of delirium

Cole and colleagues have compared the application of DSM-IIIR and DSM-IV criteria for delirium to the same population (Cole, Dendukuri, McCusker *et al*, (2003) and found the latter more inclusive. This has been confirmed by Laurila et al (2004a) who compared the application of DSM-III, DSM-III-R, DSM-IV and ICD-10 criteria in 230 patients with and without dementia. DSM-IV identified the highest rates- almost double that by the earlier DSM versions in people without dementia The ICD-10 criteria appear very minimalist indeed. It must be remembered, however, that ICD-10 specifies a maximum duration for dementia which no DSM version does. These differences make comparisons between studies over time difficult. Laurila and colleagues have gone on to present data on the outcomes for patients with delirium diagnosed using the different criteria are available (Laurila, Pitkala, Strandberg *et al*, (2003). At baseline there were differences in the presence of pre-existing dementia, and whether or not living in permanent

institutional care in a total sample of 425 patients. However, there were no differences in outcome between patients identified as delirious by the different criteria but they concluded that the DSM-IV has identified new subjects who would not previously have been identified as delirious but who shared the same dismal prognosis.

The relevance of subsyndromal delirium

Cole et al have examined the impact of delirium symptoms in 181 patients that did not meet DSM-IV delirium criteria - "sub-syndromal delirium: SSD" (Levkoff, Liptzin, Cleary *et al*, (1996) at medical admission, of whom 164 had at least one follow-up assessment (Cole, McCusker, Dendukuri *et al*, (2003). In terms of demographics and outcomes patients with SSD were intermediate between patients meeting DSM-IV criteria for delirium and those with no symptoms of delirium at all, and the authors confirm Levkoff's view that the category "delirium" represents the tip of a dimensional iceberg. Marcantonio and colleagues have also suggested that patients with some symptoms of delirium after hip fracture but who fall short of current diagnostic criteria may have similarly poor outcomes to those with definite but mild delirium (2002) . Bourdel-Marchasson et al. have found that subsyndromal delirium, especially incident, is as important as full delirium as a predictor of institutionalisation in 427 patients admitted to a Bordeaux geriatric department. Other factor include nutritional impairment, female sex, falls or stroke (but not known pre-admission cognitive impairment) (2004). It is perhaps a pity that this concept was not referred to in a study of the prodromes of delirium in hip fracture in which certain behaviours were found to be predictive of full delirium, rising in frequency before the frank state emerged (Duppils and Wikblad, (2004b). Such a study deserves replication in a new sample before any clinically useful guidelines can be derived.

However, a note of caution has been sounded by Royall, (2004) in a careful and thought-provoking editorial. He has questioned the nature of subsyndromal states, and has produced evidence for his scepticism in relation to subsyndromal cognitive impairment as a concept (but not about subsyndromal depression). He asks if the presence, in a subsyndromal state, of an outcome intermediate between that of normals and the full-blown state necessarily validates the former. He asks "is shortness of breath equivalent to subsyndromal pneumonia if it presents in the absence of fever?". A provoking questioned for most clinicians, but most of us are then lost in the remainder of his argument, in which he suggests that if the introduction of nonlinear variables into a regression analysis alongside the linear one under question subverts its importance then the case is not made for a subsyndromal state.

The possibility of ungeneralisable results from ethical research

Many delirium and dementia researchers are increasingly anxious about the impact of tightening ethical strictures on the validity of their research. We have shown how applying the most ethically sensitive methods of assessing capacity to consent to a delirium study led to both a catastrophic shortage of recruits to the study, but more importantly introduced bias: patients who could tolerate a tedious test of their understanding of the project were less impaired than those admitted to the project in the usual fashion (Adamis, Martin, Treloar *et al*, (2005). Refusal rates were also highest in the group subjected to the formal capacity assessment. The American Alzheimer's association has published generally helpful consensus guidelines on the ethical framework of research with cognitively impaired adults (2004). Although they require that the capacity of all patients possibly lacking it is formally tested, the rigour of the capacity assessment should be related to the risks presented by the research. Sensibly, for low-risk projects, an informal assessment of capacity is all that is required. This is in keeping with our study showing the baleful effects of an over-zealous capacity assessment. Less helpful, however, is that there is no provision whatsoever for any research on patients with cognitive impairment for whom no proxy can be identified. Also, the

guidelines are predictably vague in relation to fluctuating capacity -- the state particularly affecting delirium research. These two issues (need for a proxy and fluctuating capacity) pose definite difficulties for delirium research in acute medical settings, especially in countries who have not yet formally adopted any sort of legal proxy system for non-financial matters. Until pseudoethical strictures are removed from research with impaired adults there is a real danger that our knowledge about delirium will be confined to a peculiar subset of these states in a peculiar subset of individuals.

Footnotes

ICD-10 has been found wanting in a brief account of an exhaustive search of the literature on delirium in people with learning disabilities by Simpson, (2003). Specifically, he suggests that the criteria should include a statement "compared to the person's usual ability" and that symptoms suggestive of delirium include abnormal rate of transition (slow or rapid) between levels of wakefulness, increased time to respond to prompts, emotional lability and irritability.

Philpott (2002) has claimed precedence over Lipowski in the genesis of the idea of hypoactive delirium.

Charlton & Kavanau (2002) have suggested that the standard definitions of delirium exclude phenomenologically identical states in acute psychiatric disorders, and thus proscribe useful investigation in these disorders. (For example, two cases of delirious mania in older people have recently been reported (Weintraub and Lippmann, (2001)). Charlton & Kavanau also agree with Fleminger, (2002) on the importance of sleep disturbance in the phenomenology, and perhaps genesis of, delirium- this has been observed in an intensive care unit (Shiihara, Nogami, Chigira *et al*, (2001).

Eikelenboom and colleagues have constructed a cogent neuroinflammatory hypothesis to explain both the genesis of delirium and depression in dementia (2002). En passant, they question the distinction between delirium and dementia, reviving spectrum concepts from 19th century German psychiatry. If they are discrete conditions, as is assumed by Cole et al (2002) and Fick et al (2002) in their review of studies with "validated operational definition/measure of dementia and delirium" then all well and good; if they are not, then such work loses value.

An interesting question about the relationship between delirium and depression is raised by Ueki and Ogawa who report 3 cases of patients whose recovery from severe delusional depression was associated with the onset and disappearance of a delirium (2004). In two there was an apparent independent cause (cerebral infarction and asphyxia) but in the other there was not. Does delirium have an effect on depression similar to ECT (Borchardt and Popkin, (1987)? Or does the extra care given when delirium supervenes have psychological benefits? The possibility that the delirium marks a milestone in the evolution of late onset depression to dementia is not applicable in these cases, who were followed up, in one instance for 5 years.

Hobson, (2004) has drawn a parallel between delirium and dreaming, and suggests that some of the neurobiology of sleep might be studied with benefits in delirium research

In a thoughtful review of the nature of delirium subtypes Stagno, Gibson, & Breitbart, (2005) have pointed out that the classic distinction between hypoactive and hypoactive delirium relies on motor activity, and a more telling distinction might be between higher and lower arousal states independent of physical activity. Although the classic distinction has already yielded fruit in discovering differences in outcome, they argue for further elaboration of the subtypes, and clarification of the best way to "cleave nature at its joints".

Chapter 2: The instrumentation of delirium

Caution about "psychometrics" of scales at last emerging

Bhat and Rockwood have cautioned against the assumption that the inter- rater reliability of delirium rating scales can be assumed to be as good as that shown in original published studies of these scales (2005) They point out that delirium research is carried out in a wide range of settings, with a wide range of raters, and make the obvious point that reliability should be re-evaluated when the setting in which the scales used his different from that in which she was developed. However they do not go so far as to say that it should be re-evaluated every time it is used, and it appears that they are confident that inter- rater reliability is not also significantly affected by the raters themselves.

Instruments

Confusion Assessment Method(CAM)

The CAM itself has been validated in emergency rooms (Monette, Galbaud du, Fung *et al*, (2001). It is now available in Portuguese (Fabbri, Moreira, Garrido *et al*, (2001). Gonzalez and colleagues in Barcelona have translated the CAM into Spanish but could not resist changing it in order to "improve its psychometric properties" (2004). These included inter-rater reliability, concurrent validation and convergent validity,. Using small samples, they were able to convince themselves that they had achieved this objective. Their adaptation essentially replaced the CAM with a structured interview and could be regarded as a completely different approach to assessment from the original. The creation of only slightly different versions of the same measure, however, is to be deplored.

Inouye and colleagues (2005) have developed a version of the CAM that can be derived from clinical records. They found that it was less accurate than the clinical assessment, but sufficiently useful to be used in audit and quality improvement programmes when individual patient assessment was not feasible.

A Finnish study of the relationship between the CAM and ICD110/DSM categories has found a lower rate of agreement than previous studies- the best was with DSM-IV Laurila, V, Pitkala *et al*, (2002)

Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)

Ely, Margolin, Francis *et al*, (2001) have validated a modification of the Confusion Assessment Method (CAM) for intensive care units (CAM-ICU). It as been directly compared with its parent by McNicoll, Pisani, Ely *et al*, (2005). The CAM appeared to pick up some subtle cases of delirium there will not identified by the CAM-ICU. However this was particularly true for patients who were still able to talk. It is suggested that, although there was broad agreement between the two versions, the CAM-ICU might be better in patients unable to talk. Bergeron and colleagues have legitimately pointed out that disturbance of consciousness, a feature measured by most DSM-based delirium measures, is not likely to be a particularly helpful sign in intensive care unit delirium (2005). They therefore recommend the use of the CAM-ICU which does not rely upon this sign. Lin

and colleagues (2004) reported on its use in 120 patients who were mechanically ventilated. Many were over the age of 65. Senior psychiatrists provided independent assessment of delirium, and they found a high level of criterion validity. There was a significant relationship between delirium and survival. 22.4% of their sample develop delirium, but these were not broken down by the presence or absence of predisposing factors. The CAM-ICU score is associated with restraint use (Micek, Anand, Laible *et al*, (2005)

Intensive Care Delirium Screening Checklist

Roberts, Rickard, Rajbhandari *et al*, (2005) used the Intensive Care Delirium Screening Checklist of Bergeron, Dubois, Dumont *et al*, (2001) in a large Australian prevalence study of delirium in intensive care. This was originally developed in 93 intensive care patients, with a very high sensitivity but lower specificity against independent clinical assessment of delirium by psychiatrists. However they found a much lower incidence rate of 47% than the 83-87% found using the CAM-ICU in American work. They suggest a head-to-head comparison of these methods might be fruitful.

Delirium Rating Scale(DRS)

has been modified by Trzepacz, Mittal, Torres *et al*, (2001) (see correction Anonymous, (2001)), partly because of its inability to distinguish hypoactivity and hyperactivity. It appears to be better correlated with successful reporting of delirium in discharge summaries than its predecessor (van Zyl and Davidson, (2003).
It is available in Italian and Japanese (Grassi, Caraceni, Beltrami *et al*, (2001)

Comparison of DRS &CAM

In a head-to-head study our group has shown high levels of agreement between the two main delirium assessments used in research- the CAM and DRS (Adamis, Treloar, MacDonald *et al*, (2005). However, they were both administered by the same highly-trained researcher and it remains to be seen whether the CAM performs as well as the DRS when in less experienced hands

Memorial Delirium Assessment Scale

Is available in Japanese (Matsuoka, Miyake, Arakaki *et al*, (2001).

NEECHAM confusion scale

There has been further study of the predictive validity of the NEECHAM confusion scale (NCS) in patients with hip fracture by Johansson, Hamrin, & Larsson, (2002). Matsushita, Matsushima, & Maruyama, (2004)found it useful in improving recognition of delirium by medical staff. Milisen and colleagues have recently produced a Flemish version (2005)

Delirium Observation Screening Scale

A new nurse-observation scale for the detection of DSM-IV delirium -the Delirium Observation Screening Scale- has been developed by Schuurmans, Shortridge-Baggett, & Duursma, (2003) . It appears to be preferred by nursing staff to the NEECHAM (van Gemert and Schuurmans, (2004).

Cognitive Test for Delirium

has been validated against DSM-IV criteria in traumatic brain injury patients in a neurorehabilitation centre Kennedy, Nakase-Thompson, Nick *et al*, (2003)

Delirium Elderly At-Risk DEAR

Freter, Dunbar, MacLeod *et al*, (2005) have described a method of predicting post-operative delirium in elective orthopaedic patients . Using a simple checklist of risk factors (the DEAR: use of hearing aid or poor sight, ADL, MMSE, previous post-operative delirium, and substance misuse) they were able to predict the incidence of delirium in 132 patients undergoing elective orthopaedic surgery to hip or knee. Delirium occurred in 18 of these patients, with the best cut point on the DEAR scale having a sensitivity of 0.61 and a specificity of 0.76. This sounds promising, but may mean that as few as 30 percent of DEAR-positive patients became delirious in the development cohort. It is surprising that no test cohort was reported. Despite the authors optimism, this instrument cannot yet be recommended for everyday clinical use.

Strain of Care for Delirium Index

Milisen, Cremers, Foreman *et al*, (2004) have developed a questionnaire to measure the "strain" of care for delirium, to be used by nursing staff. They freely acknowledge the usual absence of all the aspects of good nursing care necessary to prevent and minimise the consequences of delirium. They are in agreement with the notion that while reducing strain for nursing staff cannot be an end in itself, an intervention which improved outcomes for patients at the expense of increased strain for nurses would be far less valuable than one that had no effect or even reduced it (personal communication).

The Delirium Index

McCusker and colleagues have reported on further development of the Delirium Index (DI: (2004). This is a severity measure based on the Confusion Assessment Method (CAM). They combined the data from 2 concurrent studies. Patients over 65 admitted to acute care hospital were screened using the Short Portable Mental Status Questionnaire (Pfeiffer, (1975). Those showing some impairment were then administered the CAM. A subsample of those with no impairment were also selected. Independent assessment using the DI was then carried out. Prior functional and health status data were collected. Inter- rater reliability assessment was carried out on a sample of 26 patients with 39 pairs of ratings. The internal reliability of the DI seems high; the intra-class correlation coefficient was98. The performance of the DI was assessed in patients with and without pre-existing cognitive impairment using the IQ code. Assessments were carried out every few days and then weekly during hospitalisation. Two different measures of fluctuation were derived from the DI and these correlated well with patients' independent diagnosis of delirium. There was also some correlation between fluctuation in the DI and patients without delirium but with dementia. However they were obliged to remove one item of the DI (perceptual disturbances) after their test of internal reliability. They also found that the DI was positively associated with measures of physical illness in delirium but this did not apply in patients with delirium and dementia. They suggest that aetiological factors in patients with delirium and no preceding dementia might be different from those with dementia. They also reflect on the possibility that the relationship between delirium and mortality is less in patients with pre-existing dementia than without.

Nursing Delirium Screening Scale (Nu-DESC)

Gaudreau, Gagnon, Harel *et al*, (2005b) have introduced a new rating scale: the Nursing Delirium Screening Scale (Nu-DESC). This has been derived from the Confusion Rating Scale (Williams,

Ward, & Campbell, (1988). They justify this because the confusion rating scale did not work very well with hypoactive patients - the majority of delirious patients, and the new scale include an item on psychomotor retardation. As with the parent instrument, they decided to maximise its sensitivity had the expense of specificity. The instrument takes just one minute to use, and is proposed as something that can be done regularly over long periods of time. During their study, 146 patients were admitted to the unit and screened using Nu-DESC. Fifty-two patients were assessed using the Confusion Assessment Method based on DSMIII-R. The Memorial Delirium Assessment Scale and DSMIV criteria were also applied. All the index assessments were applied independently of the Nu-DESC. Unfortunately, they do not described how they sampled those who ultimately received the validation assessments, and they also included data on seven patients who were assessed twice. The prevalence of CAM positive delirium was 35 percent of admissions to the combined oncology and internal medicine unit. The patient demographics are not described. The Nu-DESC performed very well against the CAM and achieved a positive predictive value of .77 and a negative predictive value of .91. However, the CAM itself is not a perfect predictor of delirium, and the relationship of the Nu-DESC to "gold standard" delirium remains unknown. Nevertheless this instrument does appear to have great promise by virtue of its brevity and accuracy. In the same study the authors compared the Nu-DESC and the CRS with the outcome being time to delirium recognition. Kaplan Meier curves showed a significant advantage of Nu-DESC over the CRS (Gaudreau, Gagnon, Harel *et al*, (2005a).

MMSE

O'Keefe and colleagues have described how using the MMSE at admission and six days later is highly predictive of the diagnosis of incident delirium (2005). A fall of two or more points had a sensitivity of 93% and specificity of 90%t against new delirium on the second occasion, and a rise of three points or more had a sensitivity of 77% and a specificity of 75% against improvement of prevalent delirium by the second occasion. They recommend routine MMSEs in acute and medical care of older people.

Chapter 3: The epidemiology of delirium

NB This chapter includes updates on predisposing risk factors for delirium but precipitating causes are discussed in the update for Chapter 6: The causes of delirium.

Emerging themes

Relationship between delirium and dementia

Lundstrom et al followed up those 78 patients without pre-existing dementia from 100 consecutive hip fracture patients for 5 years (2003). 38% were already delirious pre-admission or developed delirium during their hospital stay. All those with preoperative delirium developed dementia over the following 5 years. Post-operative delirium was also strongly associated with developing dementia. Unfortunately they did not use any more systematic method for the retrospective diagnosis of dementia than DSM-IV, and in their logistic regression poorer scores on cognitive tests was another independent factor predicting the development of delirium. It is possible that at least some cases of early dementia- itself a risk factor for delirium, were missed, and that this may explain some of their results. However, as they say, the possibility that delirium itself may be a risk factor for dementia remains. Duppils and Wikblad, (2004a) claim over a 6 months follow-up a difference in decline in MMSE between 115 delirious and non-delirious hip surgery (fracture and replacement) patients who completed follow-up, but also show an important difference in the impact of delirium on later quality of life. Lundstrom, Edlund, Bucht *et al*, (2003) have followed up 78 non-demented hip fracture for 5 years and report a strong association between the development of dementia and pre-operative and post-operative DSM IV delirium. In response to the evidence that delirium episodes are at least harbingers of dementia Meagher (2001) has suggested that post-delirium dementia may be mistakenly diagnosed because of the persistence of delirious symptoms rather than the onset of a different condition. However Gruber-Baldini, Zimmerman, Morrison *et al*, (2003) have abandoned the distinction between delirium and dementia in their study of cognitive impairment pre- and post-hip fracture and surgery in 674 patients and confirm the persistence of new impairment now found in many studies. Margiotta A, Bianchetti, Ranierei *et al*, (2005) have briefly presented data suggesting that the risk factors for delirium differ significantly between those who have dementia in those who do not. Further data are awaited.

Subsyndromal delirium

Marcantonio and colleagues have suggested that patients with some symptoms of delirium after hip fracture but who fall short of current diagnostic criteria may have similarly poor outcomes to those with definite but mild delirium (2002) . Recognition of just some delirious symptoms may be as important as that of the full syndrome.

Outcome: death

In contrast to what has been previously accepted, a careful and important study by McCusker et al (2002) has shown that delirium is associated with post-discharge mortality in medical patients independently of co-morbidity, physical function, and severity of illness. Interestingly the association seemed stronger for patients without dementia, which has led them to speculate whether delirium in dementia is different, although they also consider methodological possibilities for this. In a large study of patients admitted with community-acquired pneumonia, “altered mental state” was found to be an independent predictor of mortality by Waterer, Kessler, & Wunderink, (2004) along with age, cerebrovascular disease, cardiovascular disease and a haematocrit of <35%. Unfortunately, no more precise description was given.

Delirium in the ICU also seems to be associated with significant mortality controlling for severity of physical illness. (Ely, Shintani, Truman *et al*, (2004). 275 patients who were mechanically ventilated in ICU were studied, and only 18.3% never developed delirium during their time in the ICU. The duration of delirium had an interquartile range of one to three days. Dosage levels of medication were higher in the delirium group., but in only one drug (Lorazepam) was this significant. At six months 34 percent of the patients in the delirium group were dead versus 15 percent of those in the non delirium group. In a time-dependent multivariate survival analysis delirium was associated with a greater than three times higher risk of dying independently of the other covariates studied. The question of whether delirium is simply an epiphenomenon of non cerebral processes which are themselves largely responsible for excess mortality, or whether delirium represents a central process itself in hastening death is raised by a lot of the work in intensive care, and is the subject of a brief commentary by Ferreira and Trow, (2005). Indeed, evidence is mounting the delirium is itself a contributor to mortality in many settings independent of serious physical illness. Possible mechanisms for this are emerging (see Chapter 4).

The impact of delirium on survival after hip fracture (Nightingale, Holmes, Mason *et al*, (2001) has been confirmed.

Pitkala and colleagues examined the long-term outcome of delirium in acute wards of two geriatric hospitals and nursing homes (2005). All patients were over 70 years old and they were initially classified as either delirious or not delirious using DSMIV criteria. Prior dementia was assessed on the basis of history and clinical records. Outcomes under study were mortality, admission to hospital, and new admission to permanent residential care. In a logistic regression analysis prevalent delirium had an independent impact on mortality at one and two years, and an independent impact on a composite outcome of either deceased or in institutions at two years. They also found, interestingly, that the one-year mortality was lower in delirious patients with dementia than in delirious patients without dementia, although this was not statistically significant. They took this to mean that a more severe illness is required to "disturb a brain" without previous cognitive impairment but did not speculate as to how this "disturbance" would itself translate into mortality. Overall the outlook for patients with delirium was poor in this group of very frail old people, with nearly two-thirds dead within two years

Laurila and colleagues present data on the outcomes for patients with delirium diagnosed using the different criteria available (2004b). At baseline there were differences in the presence of pre-existing dementia, and whether or not living in permanent institutional care in a total sample of 425 patients. However, there were no differences in outcome between patients identified as delirious by the different criteria but they concluded that the DSM-IV has identified new subjects who would not previously have been identified as delirious but who shared the same dismal prognosis.

Outcome: Prolonged Hospital Stay

McCusker et al have carefully distinguished the contribution of incident and prevalent dementia to length of stay in a Montreal acute care hospital and found the former and not the latter was significant, and that dementia was less important (2003). Saravay et al (2004) have asked whether the association is related to the consequences of the illness causing the delirium rather than the delirium itself, or whether prolonged length of stay increases the chances of developing a delirium. Incidence studies which do not control for duration of exposure are open to this interpretation. However, in an attempt to determine how cognitive impairment (acute or chronic) is related to length of stay they did not attempt to distinguish dementia from delirium at admission but used a number of measures to derive the single factor of “cognitive impairment”, and related this to data, subsequently entered routinely on hospital charts, of two sorts- “mental manifestations” (e.g. cognitive impairment is noted) and “behavioural manifestations” (falls, need for restraints, pulling

IV out, incontinence and impaired decisional capacity) . They suggest their findings indicate that the former precede the latter but it is the latter that are related to increased length of stay. Interventions aimed at reducing lengths of stay might be better targeted at those showing "mental manifestations" before frank behavioural problems emerge. However, a means of determining incident events more robust than chart review is demanded before this interesting idea can be accepted.

Outcome: Institutionalisation

In a study of 477 patients mean age 82 admitted from home to hospital with hip fracture, only 20% returned home from hospital (Boockvar, Litke, Penrod *et al*, (2004). However at six months 58 percent of survivors had reached home, usually via a nursing home or rehabilitation facility. Moves to and from hospital and care home were common (average 3.5) in the six months after hip fracture, and significantly associated with, amongst other factors, delirium during the index admission. Interestingly, the presence of dementia was inversely associated with frequent relocation. Surprisingly, relocations were not significantly associated with worse outcomes at six months, once a raft of risk factors for poor outcomes had been controlled for, including delirium.

Delirium in special circumstances

Emergency room (A&E)

Many patients with delirium are seen in and not admitted- presumably because of less severe physical illness which may contribute to mortality- and so Kakuma and colleagues (2003) have studied mortality in this group to explore any independent contribution of delirium. They found only an 8.4% prevalence of delirium in 1268 patients, but an excess mortality at 18 months in delirious patients compared with non-delirious controls, particularly in the first 6 months after attendance. However, 72% of the delirious patients in this study were admitted. Importantly, they matched their controls for level of pre-existing dementia. Recognition of delirium by staff was inversely correlated with mortality, but the numbers were too small to assess the contribution of delirium to mortality in the delirious group who were not admitted. In another study in an emergency department Hustey et al found a similar prevalence (7%) of delirium in 271 emergency department attenders (Hustey, Meldon, Smith *et al*, (2003). Recognition rates by the physicians showed a sensitivity of 16% and a specificity of 98.4%. Over half the 19 delirious patients, of whom 3 were recognised, were planned to be discharged home. When CAM scores were revealed to physicians, no change in management plan resulted. The study was of a small proportion of attenders and was not a probability sample but the results are worrying.

Delirium in the ICU

Roberts, Rickard, Rajbhandari, Turner, Clarke, Hill, Tauschke C, Chaboyer, and Parsons, (2005) used the ICDSC in six intensive care units over six months, incorporated into routine observations. Of the 2568 patients admitted, 2383 were excluded, mainly because their stay in the intensive care unit was less than 36 hours. The average age of the studied group was 61 years and two-thirds of them had a medical diagnosis as reason for admission to the intensive care unit. Only 45 percent were rated as delirious using the ICDSC. They suggest that this low rate compared with N American studies may be related to them not using the CAM-ICU. Unlike Skrobic et al (2005) they found that psychoactive medication was significantly related to the presence of ICU delirium. McNicoll and colleagues have reported a prevalence of delirium of 31% in 118 intensive care unit patients aged 65 and over using the CAM (2003), but they also found a complex relationship between pre-existing dementia and the emergence and disappearance of delirium at various stages of the patients' trajectory through states of stupor in the ICU and later in other wards in the hospital.

The cumulative rate of delirium in those with dementia (i.e. developing delirium at any time after admission) was over 80% in those without pre-existing dementia and 63% in those without. In the latter group there was a significant incidence of delirium in the ICU.

Delirium after hip fracture

Bitsch, Foss, Kristensen *et al*, (2004) have carried out a semi - systematic review of the literature on risk factors for delirium and the consequences of interventions in patients experiencing hip fractures. Twelve studies published up until 2003 were included. Perhaps rashly, they concluded from the variance between these papers that "there is no common pathway leading to post-operative delirium". Less controversially, they concluded by recommending their own "multimodal" approach after Kehlet and Wilmore, (2002). Kaganski and colleagues have published a study of delirium in patients with hip fracture with a surprisingly low incidence rate of 11.4% of delirium (2004). However, they excluded patients with dementia, hearing loss and severe visual impairment and it has been suggested by O'Hanlon, (2005) that this was responsible for the low prevalence. Kaganski et al admit this, and go further to explain that they also excluded patients with "interval" delirium immediately postoperatively because "this type of delirium has less influence on the rehabilitation process" (Kagansky, (2005)- an opinion which will surprise many. Zakriya, Sieber, Christmas *et al*, (2004) have studied "Brief post-operative delirium"- lasting less than 6 weeks- and seem surprised to confirm the well-known association between delirium and institutionalization. It is clear that the exhortations of Segatore and Adams (2001) bears repeating: "Delirium is never a 'normal' or an acceptable response to acute surgical stress. Its presence may be the only indicator of a lethal co morbidity such as sepsis or myocardial infarction and the harbinger of irreversible neurological deterioration. The presence of delirium should prompt timely and scrupulous evaluation followed by thoughtful, targeted intervention."

The nature of delirium after hip fracture remains obscure. Apart from the Kagansky findings the incidence of delirium after emergency hip surgery in older patients is one of the highest. There is a suspicion that this is because many hip fracture patients are already cognitively impaired before their fall, or alternatively or additionally their fall is caused by a cerebral event, perhaps even including delirium itself. In a study of hip fracture patients from Sweden Olofsson and colleagues assessed 61 patients three or five days after surgery (2005). 38 (62%) were delirious. These patients suffered more complications during hospitalisation, were more likely to be depressed, and were also more dependent in activities of daily living before the fracture. 43% of the patients who developed delirium were suffering from dementia prior to admission. 40% of the delirious patients followed up at four months were still delirious, and there were continuing disabilities in this group. The prognosis of patients with delirium after hip fracture is very poor

Delirium in "post acute", rehabilitation or intermediate care facilities

Acute hospitals in the developed world increasingly make use of "post-acute" or "intermediate care" facilities, but because much delirium persists, it becomes a problem in these settings- in prevalence, incidence, recognition and management. The first published prevalence study at admission to these post-acute facilities found a rate of 16%, whilst more had sub-syndromal symptoms of delirium (Kiely, Bergmann, Murphy *et al*, (2003). A model including whether or not patients had all 8 symptoms of the Delirium Symptom Index (Albert, Levkoff, Reilly *et al*, (1992), pre-acute admission cognitive impairment, severe delirium and older age discriminated between those whose delirium persisted and those whose state did not (Kiely, Bergmann, Jones *et al*, (2004)

In an unusual observational study Marcantonio and colleagues have tracked delirium symptoms routinely reported by care staff in 85 "post-acute" facilities (i.e. taking patients from acute hospitals for rehabilitation or further assessment (2003). They used a variant of the Minimum Data Set system originally developed for long-term care containing the following six "delirium symptoms": "easily distracted, periods of altered perception, disorganized speech, periods of restlessness, periods of lethargy, and mental function varies over the course of a day". 23% of the 551 admitted patients who also had an MDS assessment a week later had at least one of these symptoms reported-episodes of disorganised speech being the most common. The majority had the same symptoms a week later. The study is flawed by the fact that many of these symptoms may be caused by dementia, and the MDS-PAC validation and inter-rater reliability data comes either from other raters in other institutions or does not exist at all. However, a Spanish study of a delirium in a similar facility have found a 22% rate of CAM delirium, nearly all in patients at transfer (Pi-Figueras, Aguilera, Arellano *et al*, (2004). This is a cause for concern, since moving delirious patients from one facility to another seems unlikely to be beneficial (though see Boockvar, Litke, Penrod, Halm, Morrison, Silberzweig, Magaziner, Koval, and Siu, (2004)).

Delirium in nursing homes

Cacchione et al (2003) report the prevalence of "acute confusion" as 39% in 74 residents of two community-based, for-profit long term care facilities for older people. However, it is not clear which of the methods used contributed to this diagnosis, and the univariate analysis of risk factors took no account of necessary corrections for multiple analyses. As dehydration is a known predisposing risk factor for delirium in hospital it was reasonable for Culp and colleagues to examine intensive measures of hydration in a large sample of nursing home residents to see whether it was predicted in this setting as well (2004). Using the Neecham scale, they identified 22 percent of the 313 residents as delirious during a period of study. Although patients with delirium had a higher blood urea nitrogen/creation in ratio, bioelectrical impedence analysis was not helpful in distinguishing delirium from non delirium.

Delirium after stroke

This is widely recognised clinically, but has not been studied systematically until recently. Caiero and colleagues have examined the impact of anticholinergic medications on the development of delirium after stroke in consecutive in-patients, matched by age and gender with non delirious patients after stroke (2004). 22 out of 190 consecutive acute stroke patients presented delirium, and these were more likely to show neurological neglect, have a higher Glasgow coma scale at admission, were less likely to have cerebral infarcts. Logistic regression revealed that intracranial haemorrhage and anticholinergics were amongst the most important independent predictors of delirium.

Delirium after vascular surgery

Bohner, Hummel, Habel *et al*, (2003) studied the incidence of delirium in 153 vascular surgery patients including an unknown number of older ones. 39% developed postoperative delirium

In a study of risk factors for delirium after coronary artery bypass surgery, Santos, Velasco, & Fraguas, Jr., (2004) found that age, hypertension, heart failure, renal function, atrial fibrillation, and pulmonary infection were, unsurprisingly, related to the emergence of delirium. However they were the first to directly associate smoking with delirium. These factors remained important after logistic regression analysis.

Rothenhausler, Grieser, Nollert *et al*, (2005) have reported a one-year follow-up of 34 patients undergoing elective cardiac surgery with cardiopulmonary bypass. Post-operative delirium developed in 11 of these patients but in all cases within three days of surgery. Delirium lasted up to seven days in this group: there were no prolonged episodes

Minden and colleagues have studied the incidence of delirium in 35 older patients undergoing aortic aneurysm surgery (2005). They use different methods of ascertainment of delirium to arrive at an incidence figure of 22.9%. Risk factors for delirium in this group were preoperative depressive symptoms, alcohol use and, inevitably pre-existing cognitive impairment. As might be expected delirium was associated with longer length of stay and poorer physical functioning, social functioning and energy at follow-up.

Rudolph, Babikian, Birjiniuk *et al*, (2005) have found a high correlation between atherosclerosis in the aorta and other arteries and post-operative delirium in 36 patients aged between 49 and 98 years undergoing coronary artery bypass surgery. The incidence of delirium was 41.7%.

Delirium after urological and thoracic surgery

In an intriguing study Hamann and colleagues have found a very low incidence of acute confusional state in 100 patients over 60 undergoing urological surgery (2005) . Using the CAM and ICD 10 criteria they found an incidence of only 7% in their sample -77% male, mean age was 71.9 years. These patients were referred to a university department and may not have been typical of all urological patients. However, their results are in keeping with other studies of urological surgery. It is possible that patients with dementia and other risk factors for delirium are specifically excluded from urological surgery, or it may be that urological surgery is particularly un- associated with systemic and cerebral vascular risk. Similarly, in a study of comprehensive geriatric assessment of 120 older patients undergoing thoracic surgery only 3 developed post-operative delirium (Fukuse, Satoda, Hijiya *et al*, (2005). Premorbid dementia predicted delirium, but it also predicted physical complications of surgery

Delirium in patients on long-tem Lithium

In an unusual population-based study Shulman and colleagues have reported on the association of lithium or sodium valproate dispensing with a new diagnosis of delirium one-year later (2005). As a reference they also examined this outcome in relation to prescription of benztropine. Using time to delirium as an outcome measure in over 10,000 patients with no previous history of mood disorder and a further 4000 with such a history, they found no relationship between the prescription of lithium and admission for delirium. . There was a trend for patients with sodium valproate prescriptions to be more likely to be admitted with delirium but this was not statistically significant. When they analysed the data for only patients in whom there was no documented history of dementia whatsoever they found the same result. This study relies on the recognition of recording of delirium in clinical records, a weakness that they freely admit Although the purpose of their article was to insist that lithium remains a preferable first line option over valproate, it also gives heart to those involved in the development of lithium is a treatment for dementia.

Table 1: Incidence studies in surgical patients published since manuscript submission of Delirium in Old Age

Study	Patients	No.	Age (years)	Delirium % (incidence)
Andersson, Gustafson, & Hallberg, (2001)	Hip surgery	505	65+	11
Litaker, Locala, Franco *et al*, (2001)	Major surgery	500	50+	11
Schneider, Bohner, Habel *et al*, (2002)	Vascular surgery	47	53-84	36
Marcantonio, Ta, Duthie *et al*, (2002)	Hip fracture	122	65+	40
Morrison, Sean, Magaziner *et al*, (2003)	Hip fracture	541	?	16
Milstein, Pollack, Kleinman *et al*, (2002)	Cataract	296	22-94	4.4
Bohner, Hummel, Habel, Miller, Reinbott, Yang, Gabriel, Friedrichs, Muller, Ohmann, Sandmann, and Schneider, (2003)	Vacsular surgery	153	?	39
Edelstein, Aharonoff, Karp *et al*, (2004)	Hip Fracture	921	65+	5.1 (post-op assessment only)
Kagansky, Rimon, Naor *et al*, (2004)	Hip Fracture	137	75+	11.4 (excluded ”interval” delrium)
Santos, Velasco, and Fraguas, Jr., (2004)	CABG surgery	220	60+	33.6
Fukuse, Satoda, Hijiya, and Fujinaga, (2005)	Thoracic Surgery	120	60+	2.5
Yamagata, Onizawa, Yusa *et al*, (2005)	Head & Neck cancer Surgery	38	mean 59.2	26
Olofsson, Lundstrom, Borssen *et al*, (2005)	Hip Fracture	52	70+	62
Hamann, Bickel, Schwaibold *et al*, (2005)	Urological surgery	100	60+	7
Rothenhausler, Grieser, Nollert, Reichart, Schelling, and Kapfhammer, (2005)	Cardiac surgery with CP bypass	34	mean 68	32
Rudolph, Babikian, Birjiniuk, Crittenden, Treanor, Pochay, Khuri, and Marcantonio, (2005)	Coronary artery bypass surgery	36	49-98	41.7
Minden, Carbone, Barsky *et al*, (2005)	Aortic aneurysm	35	46-88	23

Footnotes

McCusker et al (2001) have shown a deliriogenic effect of environmental factors in in-patient units.

Given that the majority of people with dementia, possible the biggest predisposing risk factor for delirium, live in developing countries, and that they may be subject o higher rates of incident physical (particularly infective) precipitating causes, studies in these countries are needed. The rate, associations and outcomes of delirium in older medical patients in Mexico has been established to be similar to those in developing countries (Villalpando-Berumen, Pineda-Colorado, Palacios *et al*, (2003), although the rate of immediate mortality was low.

The issue of delirium in learning difficulties/disabilities as then reviewed by van Waarde and van der Mast, (2004). These states appears to correspond to the model proposed by Inouye, (1999) in which learning disabilities, or their organic bases are strong predisposing factors.

Why risk factors for delirium after head and neck cancer surgery should be any different from any other major surgery is mysterious, yet Yamagata and colleagues have set out to examine this (Yamagata, Onizawa, Yusa, Wakatsuki, Yanagawa, and Yoshida, (2005). Unfortunately they use medical records to identify delirium, which makes it difficult to compare their result with those of others who have used more objective and reliable means of case identification.

Chapter 4: The neurophysiology of delirium

Emerging themes

EEG

In the first direct exploration of cerebral function in delirium since Engel & Romano's EEG studies (1959), Yokota et al (2003) have studied regional cerebral blood flow using xenon-enhanced computed tomography in 9 men and one woman in intensive care- all had clinically diagnosed hypoactive delirium and were seriously ill- none had head injury. They had apparently been psychiatrically well prior to their delirium and all subsequently recovered from it when they were re-investigated. The changes suggested hypo-perfusion throughout the cortex and subcortical areas during delirium. There seemed to be no lateralisation. The significance of this is unknown.

Neuroinflammatory markers

As discussed in the update for Chapter 1, Eikelenboom and colleagues have constructed a cogent neuroinflammatory hypothesis to explain both the genesis of delirium and depression in dementia (2002). They argue that the effect of acute phase reactants on pre-existing neurotransmitter deficits are responsible for a wide spectrum of behavioural disorders in dementia, and they include delirium in this category.

Uchikado and colleagues report on a method of assessing post-mortem brain tissue inflammation and applied this to 47 patients with a variety of pre-existing psychiatric illnesses including Alzheimer's disease and other forms of dementia and schizophrenias (2004). They found a good correlation between immunohistochemistry scores and pre-mortal C- reactive protein levels, and identified a correlation between systemic inflammation and activation of endothelial and perivascular cells; however, this did not apply well in patients without specific brain degenerative lesions. Their findings are highly relevant to delirium research, and in particular the permanent decrements found after delirium in patients with Alzheimer's disease, and the mechanisms of neuronal "devastation" that may be responsible.

There have been no prospective studies of the relationship between the inflammatory marker C-reactive protein and incident or prevalent delirium. However Belooesky has shown that complications of operative correction of hip fracture are independently associated with disturbed C-reactive protein kinetics. These complications include delirium and other adverse outcomes (Beloosesky, Grinblat, Pirotsky *et al*, (2004)

In their discussion about the apparent benefits of haloperidol in nearly 1000 patients who were mechanically ventilated Milbrandt, Kersten, Kong *et al*, (2005) postulate that haloperidol might work simply because it is less harmful than other sorts of sedation or that it may inhibit the release of pro-inflammatory cytokines and slow down what they described as the "cytokine storm" associated with critical illness. This is an important although uncontrolled cohort study, because it opens up the idea that treatment of delirium itself may improve mortality, even when there are few behavioural problems.

Given its importance in neuroinflammatory processes it is disappointing that perioperative plasma nitric oxide concentration changes do seem to reflect cognitive deficits, at least after coronary artery bypass surgery (Harmon, Eustace, Ghori *et al*, (2005). However, it is intriguing that in a small study which showed a surprising effect size Wilson, Broadhurst, Diver *et al*, (2005) have shown that low IGF-1 levels predicted incident delirium in 100 older medical inpatients.

Melatonin

In what appears to be only the second study of the role of melatonin in the genesis of delirium Balan and colleagues tested the hypothesis that high levels would be associated with hypoactive delirium and vice versa (2003). They measured urinary 6-sulphatoxymelatonin in 31 medical inpatients with delirium as assessed by DRS (Trzepacz, Baker, & Greenhouse, (1988) cut point. 7 were classified as hyperactive, 10 hypoactive and the remainder mixed. Using level after recovery as a comparator, they confirmed their hypothesis and raise some interesting questions about the mechanism. Following observations on the emergence of delirium after sleep deprivation by Shiihara, Nogami, Chigira, Tanno, Sakai, Takahashi, Kodama, and Kunimoto, (2001), a study of eight patients requiring ventilator therapy in intensive care, four of whom were over 65, is reported of melatonin levels in relation to sleep-wake pattern disturbances such as are found in delirium (Olofsson, Alling, Lundberg *et al*, (2004). They found a disturbed melatonin secretion rhythm in these patients, and suggested that bright light and medication may be responsible. Their findings supported a trial of melatonin in this situation in order to prevent delirium. It is interesting that Hobson, (2004) has drawn a parallel between delirium and dreaming, and suggests that some of the neurobiology of sleep might be studied with benefits in delirium research.

Footnotes

Flacker et al (2001) have reported a small but intriguing study of serum anticholinergic activity in medical inpatients who have not apparently taken any known anticholinergic medication. The issue of the assessment of anticholinergic activity has been critically reviewed by Carnahan, Lund, Perry *et al*, (2002) but the finding that serum anticholinergic activity in community based older people was strongly and inversely correlated with MMSE scores is of some importance in delirium research (Mulsant, Pollock, Kirshner *et al*, (2003).

Abnormal sodium levels and normal white counts in hip fracture patients appear to predict delirium (Zakriya, Christmas, Wenz, Sr. *et al*, (2002)- the latter supposed to represent failure to mount an effective stress response.

Nakamura and colleagues have extended their work on the utility of mianserin by showing that plasma free-3-methoxy-4-hydroxyphenyl (ethylene) glycol levels preoperatively may predict post-operative delirium while natural killer cell activity does not (2001).

Rudolph, Babikian, Birjiniuk, Crittenden, Treanor, Pochay, Khuri, and Marcantonio, (2005)have found a high correlation between atherosclerosis in the aorta and other arteries and post-operative delirium in 36 patients aged between 49 and 98 years undergoing coronary artery bypass surgery. The incidence of delirium was 41.7%. They speculate that the frontal lobes, which are particularly associated with inattention and thought disturbances are more susceptible to atherosclerosis. The anterior cingulate cortex was the focus of a study by Reischies, Neuhaus, Hansen *et al*, (2005) et al of delirium after ECT. Twelve patients with major depressive disorder with a mean age of 56.7 years were included. All patients received an anticholinergic drug as premedication; cognitive tests and EEGs were recorded at the beginning of the ECT course, shortly after the 6th session and 24 hours later. There was a significant improvement in cognitive tests between the last two assessments, which the authors took to indicate transient delirium. Impairment of orientation for time, episode memory and awareness of the environment were observed in all patients in the study. The study confirmed a significant increase of slow brain electrical activity during this period of impairment, and in a complex EEG source analysis they found that the most pronounced increase of Theta activity during this episode was in the anterior cingulate cortex

Gaudreau and Gagnon, (2005) have presented a hypothesis of delirium genesis in which the thalamus plays a central role., particularly in that caused by psychotropic drugs

Criticising Uchida, Aoki, & Ishizuka, (1999) hypothesis of delirium genesis involving serotonin and melatonin, Lewis and Barnett, (2004) suggest that this only explains hypoactive delirium. They have extended the construct to include a central role for tryptophan homeostasis which they suggest explains more of the delirium phenomenology

Miyamoto, Nakao, Tomimoto *et al*, (2004) have postulated that the basal ganglia are particularly effective by hypocapnia in a rat model of cerebrovascular disease and suggested that this may be related to long-term delirium. They found that the NMDA receptor their suggestion that ketamine might be used as a treatment for delirium flies in the face of its known propensity to cause delirium.

Chapter 5: Clinical assessment and diagnosis

Footnotes

Saito, Matsui, Otani *et al*, (2005) have described Liepmann's phenomenon in benzodiazepine withdrawal delirium. They described how a patient with delirium whose eyes were closed responded affirmatively to suggestions made to him about what he could see; whales, birds etc.

The use of skin potential measurement seems a simple non-invasive way of predicting delirium in a small series of intensive care patients (Shiihara, Nogami, Chigira, Tanno, Sakai, Takahashi, Kodama, and Kunimoto, (2001).

Anticholinergic delirium may be reversed by physostigmine injection and this is used as a diagnostic test in some centres in patients with altered mental states in emergency departments. Schneir and colleagues report a case-note (chart) review study, primarily focussed on safety, of 39 such tests over a period in excess of 6 years in a department with 37,00 visits per year (2003). Patients ranged in age from 18-68. In only one case was there a serious complication- convulsions- attributed to the injection; and even in this case, the patient had already had a convulsion before the administration of physostigmine. This does seem a safe procedure in the relatively young patients in this series, but its utility and safety in the recognition of and management of delirium more generally is not established.

In the assessment of delirious patients in which cerebral hypoxia is implicated, it might be thought that oximetry might not be feasible. However Bliwise and colleagues have shown that, at least in a dementia sample, overnight oximetry is feasible, even at home (Bliwise, Lee, Wood-Siverio *et al*, (2005)

Chapter 6: The causes of delirium

NB This chapter includes updates on precipitating causes for delirium but predisposing risk factors are discussed in the update for Chapter 3: the epidemiology of delirium

Emerging themes

Anaesthetics Of 921 hip fracture patients reported by Edelstein et al (2004) almost exactly half had spinal and half general anaesthetic and the latter, together with dementia and higher operative risk were independent risk factors for delirium. This was an observational finding, but surprising, since spinal anaesthetic may be reserved for patients with higher morbidity. Wu et al (2004) have systematically reviewed the evidence that general anaesthetics are more likely to be associated with cognitive dysfunction postoperatively than regional anaesthetics. 20 of the 23 studies tabled were RCTs. They could find no evidence for this. Many studies showed no difference, and in those that did the effect size were very weak. As usual, methodological differences played a huge role in the variance between the studies. Helpfully they list all the psychometric tests carried out in the various studies that they report.

Sleep-wake cycles and melatonin

Charlton & Kavanau (2002) agree with Fleminger, (2002) on the importance of sleep disturbance in the phenomenology of delirium and it may be a causal factor as well as a result. In what appears to be only the second study of the role of melatonin in the genesis of delirium Balan and colleagues tested the hypothesis that high levels would be associated with hypoactive delirium and vice versa (2003). They measured urinary 6-sulphatoxymelatonin in 31 medical inpatients with delirium as assessed by DRS cut point. 7 were classified as hyperactive, 10 hypoactive and the remainder mixed. Using level after recovery as a comparator, they confirmed their hypothesis and raise some interesting questions about the mechanism. Following observations on the emergence of delirium after sleep deprivation Shiihara, Nogami, Chigira, Tanno, Sakai, Takahashi, Kodama, and Kunimoto, (2001), a study of eight patients requiring ventilator therapy in intensive care, four of whom were over 65, is reported of melatonin levels in relation to sleep-wake pattern disturbances such as are found in delirium Olofsson, Alling, Lundberg, and Malmros, (2004). They found a disturbed melatonin secretion rhythm in these patients, and suggested that bright light and medication may be responsible. Their findings supported a trial of melatonin in this situation in order to prevent delirium. It is interesting that Hobson, (2004) has drawn a parallel between delirium and dreaming, and suggests that some of the neurobiology of sleep might be studied with benefits in delirium research.

Footnotes

It would seem from the lack of a co-ordinated approach to delirium in most healthcare settings that the economic costs of this disorder are not understood. The financial cost of delirium has been estimated in 500 surgical patients as an excess of almost $1000 per patient in nursing costs, around $1400 in technical costs, and around $400 in professional costs (Franco, Litaker, Locala *et al*, (2001). Leslie, Zhang, Bogardus *et al*, (2005) have examined the long-term economic consequences of preventing delirium in the Yale study. They compared total long-term nursing home costs in an economic analysis which suggested that, for long-term nursing home patients, a saving of 15.5% could be achieved by the intervention in hospital.

A debate about the use of antimicrobials in older nursing home patients broke out temporarily in the Canadian Medical Association Journal. The view that these are inappropriately prescribed (e.g. Walker, McGeer, Simor *et al*, (2002)) in the absence of urinary symptoms even when "confusion" is present (Nicolle, (2002) has been challenged by Miller, (2001) It remains the case that the association between delirium and urinary tract infection in the absence of urinary symptoms or signs (such as frequency) remains problematic.

Balas, Gale, & Kagan, (2004) have introduced the idea that doulas (unqualified assistants similar to those used in childbirth) could be very helpful in managing intensive care unit delirium. She lists the several domains of care in which such a person might be beneficial, and shows how the usual nursing and medical procedures leave scope for many common sense and humane interventions. As has been suggested elsewhere, the incidence, prevalence and complications of delirium are a manifestation of a whole system failure, and the role of the doulas may have become unfortunately vital given the withdrawal of most qualified nurses from a holistic approach to patient care.

Chapter 7: The management of delirium

NB Guidelines and their utility are discussed under Chapter 10: Education about delirium

Complex interventions- identification and treatment

Evaluation of complex interventions in complex systems by randomised controlled trials may never be satisfactory. This is exemplified by the failure of an important large RCT of systematic detection and multidisciplinary management of delirium to show any substantial difference in outcome compared with treatment as usual (Cole, McCusker, Bellavance *et al*, (2002). Apart from the eight methodological problems cited by the authors, the management protocol itself could not be as evidence-based as that of the Yale study of prevention (Inouye, Bogardus, Jr., Charpentier *et al*, (1999b). The failure to show an effect of this intervention has caused great concern in the world of delirium research (Rockwood, (2002), and led Anderson and Hewko, (2003) to challenge its findings.

A nurse-led intervention in hip fracture patients has been shown to reduce the severity and length of delirium but not to enhance functional recovery (Milisen, Foreman, Abraham *et al*, (2001). These results depart from those of the well-known Yale study, but there were methodological differences.

In an unusual study of aftercare for delirium, Rahkonen and colleagues have found that continuous nurse specialist attention and yearly spells in a rehabilitation centre significantly reduced increased the delay in admission to long-term care (2001) compared to those not followed up in this way.

The Cochrane review on multidisciplinary team interventions for delirium in patients with dementia has been revised, but its conclusions are the same. There is no evidence for these interventions, since the number of studies specifically aimed at delirium in dementia remains minimal Britton and Russell, (2004). They make the important point that since most cases of delirium occur in dementia, they should be specific attempts to examine the effectiveness of interventions in this group, rather than lumping together patients with delirium who lack this important predisposing factor with those that have it.

A specialist 4-bedded delirium unit in an acute geriatric unit has been described by Flaherty et al (2003) with good lighting, low sound levels and 24-hour presence of mostly specialist nursing staff. The approaches used sound like those of good nursing care, and what is striking is that this is considered so difficult to achieve in an acute geriatric inpatient unit that a special unit is required. This idea of isolating delirium from good general care has been challenged by Modawal, (2004).

Naughton, Saltzman, Ramadan *et al*, (2005) have evaluated the sort of whole-system intervention that is necessary to reduce the burden of delirium in acute medical facilities for older people. Having established the prevalence of delirium four days after admission in a pre-intervention cohort of 110 patients, together with data on outcomes, the authors reviewed the same data for a cohort presenting to the emergency department in which physicians and nurses had been specially trained to identify delirious or cognitively impaired older adults for selective admission to an acute geriatric unit which had just opened. Within the geriatric unit patients were monitored by nurses and physicians who had been exposed to an education programme about delirium -- its recognition, management and care. There were two post intervention cohorts studied -- one at four months and one at nine months after the intervention. 154 patients were admitted in the four-month cohort, and 110 in the nine months cohort. The cumulative illness rating scales (Linn, Linn, & Gurel, (1968) scores were similar in all cohorts. There was a dramatic shift towards delirious patients being admitted to the acute geriatric unit. The same patients in both cohorts received more antidepressants and neuroleptics, but fewer benzodiazepines. In the nine months cohort, patients

admitted to the geriatric unit hand higher levels of opiate treatment. Patients with delirium in the two post-intervention cohorts had significantly lower length of stay than those admitted to the general hospital unit.

Phy, Vanness, Melton, III *et al*, (2005) followed up 466 patients aged 65 or older admitted for hip fracture, and examined outcomes before and after the introduction of a "hospitalist" service. 236 patients were admitted before the new service started, the remainder after. In the normal treatment group emergency department doctors chose for clinical reasons to admit patients either to an orthopaedic service or a medical service if there were significant medical problems. In the intervention phase, a hospitalist (in the UK general internal physician) assessed all patients and coordinated their orthopaedic and medical care. However, they could not cope with all patients admitted during intervention period, and 10 percent were triaged in the normal way for this service. Although there was no difference in baseline characteristics between the control sample and intervention sample the outcomes for the latter were significantly better with shorter length of stay (both time to surgery and time after surgery to discharge). However, the diagnosis of delirium was more frequent in the intervention group. Since data was collected mainly from clinical records, this might represent a better outcome for the intervention group, since at least in this group delirium was recognised and recorded. There are of course many difficulties in interpreting studies attempting to evaluate complex interventions.

Inouye's study did not show any impact of the multicomponent intervention on length of stay (1999a). By contrast Lundstrom and colleagues have reorganised nursing care and instituted an education programme as an intervention for delirium recognition and management in one acute medical ward for older people ward. They compared a cohort of patients admitted to this ward with those admitted to another acute medical ward and found lower mortality and length of stay for delirious patients, and lower overall length of stay (Lundstrom, Edlund, Karlsson *et al*, (2005). An important part of their intervention was training in relationships with informal carers. Whereas Inouye's study was concerned with the prevention of delirium, this present study appeared to achieve its results by the rapid recognition and treatment of delirium. Neither study involved randomisation to treatment and control groups.

Simple interventions: treatment

A few more pharmaceutical and other simple intervention trials and case reports now grace the delirium literature. All show positive results with few adverse effects, but more formal RCTs are awaited.

Authors	Medication/intervention	Type of study	Notes
Breitbart, Tremblay, & Gibson, (2002)	Olanzapine	Open label non-controlled n=79	Cancer patients
Leso and Schwartz, (2002) .	Ziprasidone	Case Report	
Kim, Bader, Kotlyar *et al*, (2003)	Quetiapine	Open label non-controlled n=12	90mg a day for a mean of 6 days
Horikawa, Yamazaki, Miyamoto *et al*, (2003)	Risperidone	Open label non-controlled n=10	22–81 years old
Liu, Juang, Liang *et al*, (2004)	Risperidone & haloperidol	Retrospective observational n=77	
Mittal, Jimerson, Neely *et al*, (2004)	Risperidone	Open label non-controlled n=10	37-83 years old
Parellada, Baeza, de Pablo *et al*, (2004)	Risperidone	Open label non-controlled n=64	Mean age 67 SD 11.4 yrs
Sasaki, Matsuyama, Inoue *et al*, (2003)	Quetiapine	Open label non-controlled n=12	37-84 years old
Skrobik, Bergeron, Dumont *et al*, (2004)	Olanzapine & Haloperidol	Open label controlled quasi-randomised n=73	18=75 years old- in Intensive Care Unit.. Few differences in efficacy but olanzapine better tolerated (trial funded by makers of Olanzapine)
Dautzenberg, Mulder, Olde Rikkert *et al*, (2004a)	Rivastigmine added to antipsychotics	Observational study n=24 compared with 29 controls	Only in non-responders to antipsychotics. Seemed to lead to resolution in 15 patients
Schneider, (2005).	Intravenous Sodium valproate	Observational study n=4 "geriatric" patients	20mg/kg/day

Authors	Medication/intervention	Type of study	Notes
Han and Kim, (2004)	Haloperidol vs Risperidone	RCT n=28 of patients referred to psychiatrists	Mean age 65-66. Not much difference found
Gagnon, Low, & Schreier, (2005)	Methylphenidate	Case series n=14 with advanced cancer & hypoactive delirium	20-30mg per day; higher doses caused agitation. No delusion or hallucinations found.
Milbrandt, Kersten, Kong, Weissfeld, Clermont, Fink, and Angus, (2005)	Haloperidol	Retrospective observational cohort n=989 mechanically ventilated ICU patients. Mean age c 60 yrs	8% received haloperidol and had lower mortality (logistic regression)
Bourgeois, Koike, Simmons *et al*, (2005).	Adding sodium valproate	Case series n=6	

Simple interventions: treatment and prevention

O'Keefe and colleagues have described how using the MMSE at admission and six days later is highly predictive of the diagnosis of incident delirium (2005). A fall of two or more points had a sensitivity of 93% and specificity of 90%t against new delirium on the second occasion, and a rise of three points or more had a sensitivity of 77% and a specificity of 75% against improvement of prevalent delirium by the second occasion. They recommend routine MMSEs in acute and medical care of older people in an attempt to improve its recognition.

Footnotes

Mayo Smith and colleagues from the American Society Of Addiction Medicine have proposed a practice guideline on the management of alcohol withdrawal delirium in which they favour sedative-hypnotic agents over neuroleptic agents, based on a meta-analysis of nine prospective controlled trials (2004). However Klijn and van der Mast, (2005) in a thoughtful letter have challenged the established view the benzodiazepines are the first line of treatment for alcohol withdrawal delirium, pointing out that the Dutch guidelines van der Mast, Huyse, & Rosier, (2005) developed by themselves and colleagues determined that haloperidol should be the first line of treatment for suspected alcohol withdrawal delirium. They suggest that there is a danger that once alcohol withdrawal has been diagnosed, other additional causes of delirium in acute older medical in patients are ignored

It would seem from the lack of a co-ordinated approach to delirium in most healthcare settings that the economic costs of this disorder are not understood. The financial cost of delirium has been estimated in 500 surgical patients as an excess of almost $1000 per patient in nursing costs, around $1400 in technical costs, and around $400 in professional costs (Franco, Litaker, Locala, and Bronson, (2001). Leslie, Zhang, Bogardus, Holford, Leo-Summers, and Inouye, (2005) have examined the long-term economic consequences of preventing delirium in the Yale study. They compared total long-term nursing home costs in an economic analysis which suggested that, for long-term nursing home patients, a saving of 15.5% could be achieved by the intervention in hospital.

A debate about the use of antimicrobials in older nursing home patients broke out temporarily in the Canadian Medical Association Journal. The view that these are inappropriately prescribed (e.g. Walker, McGeer, Simor, Armstrong-Evans, and Loeb, (2002)) in the absence of urinary symptoms even when "confusion" is present (Nicolle, (2002) has been challenged by Miller, (2001) It remains the case that the association between delirium and urinary tract infection in the absence of urinary symptoms or signs (such as frequency) remains problematic.

Balas, Gale, and Kagan, (2004) have introduced the idea that doulas (unqualified assistants similar to those used in childbirth) could be very helpful in managing intensive care unit delirium. She lists the several domains of care in which such a person might be beneficial, and shows how the usual nursing and medical procedures leave scope for many common sense and humane interventions. As has been suggested elsewhere, the incidence, prevalence and complications of delirium are a manifestation of a whole system failure, and the role of the doulas may have become unfortunately vital given the withdrawal of most qualified nurses from a holistic approach to patient care.

Chapter 8: The prevention of delirium

NB Educational interventions are discussed in the update to Chapter 10: Education about Delirium

Complex preventative interventions

Further analysis of the costs of the Yale multicomponent intervention trial in the prevention of delirium showed that intervention protocol adherence was a crucial factor in its efficacy (Inouye, Bogardus, Jr., Williams *et al*, (2003). Overall, it was cost-effective in preventing delirium in those at moderate but not high risk (Rizzo, Bogardus, Jr., Leo-Summers *et al*, (2001). Conversely, 6-month follow-up of this sample showed few lasting benefits of this intervention for the group as a whole, but high-risk patients seemed to have better self-rated health and functional status in the intervention group compared with the control group (Bogardus, Desai, Williams *et al*, (2003). However Leslie, Zhang, Bogardus, Holford, Leo-Summers, and Inouye, (2005) have examined the long-term economic consequences of preventing delirium in this sample. They compared total long-term nursing home costs in an economic analysis which suggested that, for long-term nursing home patients, a saving of 15.5% could be achieved by the intervention in hospital. Marcantonio and colleagues (2001) have reported in a randomised double-blind trial that geriatric assessment and treatment successfully reduced the incidence of delirium (especially severe delirium) in hip fracture patients, but not its course or outcome.

Simple preventative interventions

Authors	Medication/intervention	Type of study	Notes
Dautzenberg, Mulder, Olde Rikkert *et al*, (2004b)	Rivastigmine	Retrospective cohort study n=11 compared with 29 controls	Patients on rivastigmine seemed less likely to develop delirium
Moretti, Torre, Antonello *et al*, (2004)	Rivastigmine vs Aspirin	Observational prospective cohort study n=246 with vascular dementia	Opaque methodology. 42% on rivastigmine developed delirium in 24 months, 62% on aspirin.
McCaffrey and Locsin, (2005)	Passive music therapy ("easy listening" type)	Non-blind RCT. Elective hip/knee surgery patients over 65 years n=66	Significant beneficial effect on no. of incident observed delirium episodes. Calmed staff and relatives too!

Footnotes

Adunsky et al (2002) studied the use of opiate analgesics in 302 patients admitted to an orthogeriatric ward with a hip fracture. Although pain is a known risk factor for delirium (Morrison, Sean, Magaziner, Gilbert, Koval, McLaughlin, Orosz, Strauss, and Siu, (2003), patients with cognitive impairment or delirium received significantly less analgesics than intact patients.

Adequate analgesia seems to be an important preventative factor in delirium, although the choice of analgesia may be as important (Adunsky, Levy, Heim *et al*, (2002)

An unusual means of preventing delirium is reported from Japan by Aizawa, Kanai, Saikawa *et al*, (2002). Possibly related to observations on the emergence of delirium after sleep deprivation (Shiihara, Nogami, Chigira, Tanno, Sakai, Takahashi, Kodama, and Kunimoto, (2001), they carried out a randomized controlled trial of a continuous intravenous infusion of benzodiazepines and, interestingly, pethidine (meperidene), overnight in 40 older patients for 3 nights after gastrointestinal surgery. Apart from morning drowsiness, there seemed to be few ill-effects. A significant reduction in the incidence of delirium was found. Given what is suspected about meperidene and delirium (Adunsky, Levy, Heim, Mizrahi, and Arad, (2002) perhaps even better results might have been achieved with a different analgesic.

In a German study ultrasound thigh muscle mass measurement came only second to immobility as an independent predictor of delirium risk (Weinrebe, Guneysu, & Welz-Barth, (2002) . In Adunsky et al's observational study poor mobility and previous cognitive impairment were the main risk factors for post-hip fracture pre-operative delirium (2003).

Chapter 9: The role of families, family caregivers and nurses

Emerging Themes

Involving the family caregiver in the management of in-patients In an important but underpowered trial of education of family caregivers, 49 care-giver/patient dyads were randomly allocated to receiving an educational programme plus a formalised agreement between the caregivers and nursing staff on key behavioural changes in patients (Li, Melnyk, McCann *et al*, (2003). "Acute confusion" was documented less often by the caregivers in the intervention than control group.

Distress in bystanders as opposed to sufferers? In a careful study of delirium in cancer patients on nurses and family caregivers Breibart & colleagues have quantified the distress felt by these groups, and related this to the phenomenology- particularly delusions and perceptual abnormalities (2002). They also found that, mercifully, later recall of delirium is inversely related to its severity. Distress in the patient is remarkable by its absence from a self-case-study of delirium by a retired British psychiatrist (Crammer, (2002)- perplexity was the most dominant affect, even when very alarming cognitions were experienced. The patient died the same year his account was published. A careful bedside study of 50 delirious patients using qualitative methods found high rates of post-recovery recall, and suggested that the meanings of the ideas expressed during the state might be helpfully considered by staff (Andersson, Hallberg, Norberg *et al*, (2002). The experience of nursing patients with delirium has now been reported by Andersson, Hallberg, & Edberg, (2003) including some graphic accounts of the subtlety of change in patients ("She had a darker look, she was aggressive and you could see it in her eyes. Her gaze was dark, black, more watery, more tense"). Accounts of how delirious patients respond to clear boundaries are also given:

> Then I said, 'It doesn't matter what you think or what you say, because you must lie down now or you'll get really sick.' He said 'bloody hell' and he
> swore and was really angry. Then I said, 'You can swear as much as you want for I'll swear back. Now you must lie down because you're not well, I can see
> by the way you look,' I said resolutely, almost angrily. Then he became quiet and I was even able to take his blood pressure."

The strains put on nurses caring for people with delirium is apparent from this important work, but whether a rating scale is for this will prove useful (Milisen, Cremers, Foreman, Vandevelde, Haspeslagh, Geest, and Abraham, (2004) remains to be seen.

Whole-system changes to nursing practice

Balas, Gale, and Kagan, (2004) have introduced the idea that doulas (unqualified assistants similar to those used in childbirth) could be very helpful in managing intensive care unit delirium. She lists the several domains of care in which such a person might be beneficial, and shows how the usual nursing and medical procedures leave scope for many common sense and humane interventions. As has the suggested elsewhere, the incidence, prevalence and complications of delirium are a manifestation of a whole system failure, and the role of the doulas may have become unfortunately vital given the withdrawal of most qualified nurses from a holistic approach to patient care.

Footnotes

Systemic approaches to the care of older people for whom multiple moves within hospitals are deliriogenic, quite apart from the extra toxicity cause by medication errors at each transfer, are reviewed by Gillick, (2002).

The British Association of Critical Care Nurses has issued guidance on the use of restraint in adult critical care units (intensive care units) (Bray, Hill, Robson *et al*, (2004). They do not confine their advice to physical restraints but include pharmacological and psychological methods. Their recommendations seem very reasonable and sensible, but interestingly they do not tackle the problem of capacity and consent in fluctuating states like delirium.

Chapter 10: Education about delirium

Emerging themes

The failure of guidelines?

There are now several sets of guideline for the recognition and management of delirium in medical settings. A guideline-driven intervention in British geriatric wards by Young and George, (2003) failed to show any response, although the cluster design was clearly underpowered. A similar "disconnect" between appreciation of the importance of delirium and actual practice is also manifest in Ely et al's study of intensive care staff (2004). One problem might be that apparent consensus may be illusory; in all such endeavour it is easier to retain something favoured by a colleague that you actually think is unimportant to ensure that something you think important is included without demur. Michaud has presented a study of expert views on the appropriateness of over 200 statements on risk factors, prevention, screening and diagnosis of delirium, using a formal method of iterative grading (Michaud, (2005). He found that 84 percent of the statements achieve significant agreement, but he found a lower rate of agreement about the feasibility of interventions to prevent delirium than about the appropriateness of these intervention. The usefulness of screening and the role of physical restraints in the development of delirium emerged as the most contentious. His full report has been submitted for publication but preliminary results support those of Carnes, Howell, Rosenberg *et al*, (2003). Variation in the management of delirium by 282 American physicians (including 14 psychiatrists) who are members of the American Geriatrics Society emerged from a vignette-based study of "best practice" in delirium after hip fracture surgery. Acknowledging the lack of an evidence base for the latter, the authors found wide variation in choice and dose of medications suggested. Interestingly, 15% of male respondents favoured the use of restraints (vest or wrist or both) compared with 3% of female ones. It is not clear how generalisable these results are- particularly to the surgeons who actually manage patients epitomised in the vignettes.

Mayo Smith and colleagues from the American Society Of Addiction Medicine have proposed a practice guideline on the management of alcohol withdrawal delirium in which they favour sedative-hypnotic agents over neuroleptic agents, based on a meta-analysis of nine prospective controlled trials (2004). However Klijn and van der Mast, (2005) in a thoughtful letter have challenged the established view the benzodiazepines are the first line of treatment for alcohol withdrawal delirium, pointing out that the Dutch guidelines (van der Mast, Huyse, and Rosier, (2005) developed by themselves and colleagues determined that haloperidol should be the first line of treatment for suspected alcohol withdrawal delirium. They suggest that there is a danger that once alcohol withdrawal has been diagnosed, other additional causes of delirium in acute older medical in patients are ignored

The British Association of Critical Care Nurses has issued guidance on the use of restraint in adult critical care units (intensive care units) (Bray, Hill, Robson, Leaver, Walker, O'Leary, Delaney, Walsh, Gager, Waterhouse, and British Association of Critical Care Nurses., (2004). They do not confine their advice to physical restraints but include pharmacological and psychological methods. Their recommendations seem very reasonable and sensible, but interestingly they do not tackle the problem of capacity and consent in fluctuating states like delirium.

Preconceptions of nursing staff

Low rates of recognition of delirium - especially of hypoactive symptoms, have been reported by Milisen, Foreman, Wouters *et al*, (2002) in a study of case-note recording by nurses in post-hip-fracture patients. Possible reasons behind this and other similar findings have been explored by McCarthy in an important qualitative analysis of nurse interviews (2003a). She found two main attitudinal perspectives on older medical and surgical patients, and an intermediary one. In the first, the "decline perspective", nurses expected all older people to be "confused", did not distinguish between acute and chronic cognitive decrement, and were most interested in the impact that patients with "confusion" would have on their working day or night. It is this attitude which Segatore and Adams so indignantly refuted: "Delirium is never a "normal" or an acceptable response to acute surgical stress" (2001). In the opposite "healthful perspective" nurses saw any cognitive impairment as unexpected and worthy of interest, distinguished between different causes, and were most interested in remediation or palliation. The intermediate perspective, which McCarthy called the "vulnerable perspective" nurses were unsure or vacillated between the other perspectives. She has refined this approach in a participant observation study and added that context was also important (2003b). She suggests 4 approaches to maximise the benefit to delirious patients: first, know the perspective of the nursing staff assigned to care for them, second, do not assign nurses with the "decline perspective" to this work, third, institute protocols that mitigate against this perspective, and only finally, education. If these findings could be developed, perhaps in a quantitative way if this was possible, it could lead to much better focussed management and educational interventions that could be validated against outcomes for patients..

Footnotes

The documentation of mental status in emergency department patients has been found deficient by Hustey and Meldon, (2002). suggesting yet another area for educational activity. The same team have later shown a very low rate of recognition of delirium in this setting (2003). They studied delirium in 271 emergency department attenders. Recognition rates by the physicians showed a sensitivity of 16% and a specificity of 98.4%. Over half the 19 delirious patients, of whom 3 were recognised, were planned to be discharged home. When CAM scores were revealed to physicians, no change in management plan resulted. The study was of a small proportion of attenders and was not a probability sample but the results are worrying.

Rockwood has criticised the tendency for teaching to be over-complex or remote and this may affect its efficacy (2004). We have recently shown that a simple educational package for staff on one ward was associated with a lower prevalence of delirium on that ward compared with the control ward (Tabet, Hudson, Sweeney *et al*, (2005). No causal connection can be made, but it does raise an issue about how complex interventions are evaluated- context is extremely important (Pawson and Tulley, (1997).

Mnemonics for teaching in delirium are offered by Flaherty and Morley (2004) and Crausman (2004).

The American Medical Association has produced a patient information leaflet about delirium (Torpy, Lynm, & Glass, (2004). It is not clear when it is to be used, but the language is clearly inaccessible to anyone with delirium, and most without.

Pun, Gordon, Peterson *et al*, (2005) have shown that with modest training it is possible to achieve very high rates of use of the CAM-ICU and compliance rates of 90 percent are possible. In addition, they were able to show agreement between the CAM-ICU and independent assessment could be sustained in routine use. This bodes well for all delirious patients if the results can be

generalised to general medical and surgical settings older people, but, as Riker and Fraser, (2005) have said, the benefits for all improved detection have to be judged against improved outcome for delirious patients in all settings.

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