**Editorials**

**Delirium and C-reactive protein**

Delirium is the most frequent complication of hospitalisation for older people affecting around one-third [1]. Despite its frequent occurrence, delirium is undetected or misdiagnosed by doctors or nurses in up to two-thirds of cases [2]. In hospitals it has a high mortality (around 25%), increased morbidity, functional decline, extended lengths of stay and an increased requirement for institutional care [1]. In the paper by McDonald et al. [3] in this issue, the authors investigated the value of C-reactive protein levels (CRP) in predicting the incidence and recovery from delirium in an acute medical unit. Ninety-four acutely ill patients aged over 70 years were included in the study. Patients were assessed for delirium using the Mini Mental State Examination (MMSE) on admission and the Confusion Assessment Method (CAM) every 3 days. The CAM score has been established as a reliable, simple method for detecting delirium [4]. Twenty-six cases of prevalent delirium (CAM positive on admission) and six cases of incident delirium (CAM positive during hospital stay, but negative on initial assessment) were detected. Despite these small numbers, it was possible to show a statistically significant relationship between CRP and incident delirium. Furthermore, a low CRP and a higher initial MMSE were shown to predict recovery from delirium during hospitalisation. This study raises two intriguing questions. First, is CRP a marker for delirium? Second, will this observation help our clinical practice and improve care for patients with delirium?

Ideally, a biomarker should be specific to detect a fundamental feature of neuropathology and this should be validated in neuropathologically confirmed cases. The disease-specific biomarker needs to be reliable, reproducible, non-invasive, simple to perform and inexpensive. In the case of delirium there is a fundamental problem: the underlying pathology in most cases is mixed and complex, involving many cellular systems, and not all of them will have the same markers to denote cellular dysfunction and damage. CRP is a marker of systemic inflammation and, as well as being a possible marker for delirium, may give us important clues as to the neuropathology of delirium.

A recent neuropathological study [5] found close correlation between the level of CRP and activation of vascular endothelial cells, and perivascular cells using immunochrom-istry. This would suggest that inflammatory stimuli activates vascular cells. In dementia, even low-grade inflammation can enhance inflammatory signalling, and this may explain the vulnerability of older people with cognitive impairment to delirium caused by systemic inflammatory conditions. Pre-existing brain degenerative changes, activated microglia and astrocytes produce a variety of pro-inflammatory molecules and these can raise the basal inflammatory level of brain parenchyma, and enhance inflammatory signalling to brain parenchyma from the periphery.

In the brain tissue, inflammatory responses are not restricted to astrocytes and microglia, but involve neurons too. Neurons not only respond to a number of inflammatory mediators but also produce many pro and anti-inflammatory molecules. Some inflammatory molecules are involved in the modulation of neuronal functions, such as neurotransmission. Interestingly, delirium is a frequent presentation in patients with senile dementia of the tangle type, characterised by an abundance of neurofibrillary tangles, in the absence of significant numbers of senile (amyloid) plaques [6].

A high CRP is very common in older patients admitted to hospital, and elevated levels have been associated with depression and pain as well as with dementia [7, 8]. It is far too non-specific to be considered as a marker for delirium, but nevertheless this study suggests that CRP has a role in monitoring progress and predicting recovery. In the real world, geriatricians and psychiatrists of old age often have difficulty convincing our colleagues and junior staff that patients with delirium are sick and require our full attention, [9] and an elevated CRP will help raise awareness. Obviously, further work needs to be done, but thus far the study by McDonald et al. [3] is the largest to be conducted in the elderly medically ill, in contrast to a previous study that was restricted to postoperative fractured hip patients [10].

Detection and management of delirium in acute hospitals is an important quality issue [11]. We are a long way from being able to recommend CRP as a specific marker for delirium. The diagnosis of delirium remains clinical, based on recognition of an acute change in mental state with impaired concentration or conscious level. Geriatricians need to promote the recording of a mental test score as a vital sign in older people with equal status to pulse, temperature and blood pressure. CRP may be clinically helpful in raising awareness, monitoring recovery and predicting outcome. Further studies are required to see if CRP can be used in identifying and treating delirium in the community, as well as in hospital settings.

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References


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Parkinson’s disease in Africa

In sub-Saharan Africa, in common with many developing countries, there is a perpetual shortage of health workers and resources. Social and economic effects and long-term conflict coupled with a high incidence of diseases such as HIV/AIDS and malaria stretch health systems to the limit and this is compounded by the loss of trained staff to more developed parts of the world [1].

The paper by Dotchin et al. [2] reminds us that Africa remains a dark continent in terms of our knowledge of neurological diseases and Parkinson’s disease in particular. Even in Europe, diagnosis of a disease with no biological markers, no specific imaging abnormalities and a variable presentation can be difficult, and given the compounding factors of vascular [3] and infectious disease any epidemiological study is going to be fraught with difficulties. One is struck by the relative youth of those affected by Parkinson’s disease in this study, and for the most part old people seem to be hardly visible in the studies that have been carried out. Most old people live in extended family structures in Tanzania and in 1988 only 4% of the 23.3 million population were over 60 [4]. The poverty is striking, with the choice patients must make between medication and food. The life expectancy for patients with Parkinson’s disease in Europe was severely limited before the introduction of levodopa, and that is essentially the situation that still exists in sub-Saharan Africa, so it is perhaps unsurprising that the truly elderly are unrepresented in the studies that do exist.

There have been major improvements in Parkinson’s disease care in the last 35 years in the developed world, including the introduction of levodopa and the dopamine receptor agonists as well as specialist nurses and a group of physicians who have developed a major interest in Parkinson’s disease. Levodopa is not regarded as an expensive medication in the United Kingdom but it is unaffordable in much of Africa, though one suspects its affordability could be increased by negotiation with pharmaceutical companies, similar to the successful arrangements that have brought about an improvement of access to anti-retroviral treatment in that population.

The theme that stands out in this paper is the different perception of illness in these societies where sufferers may be perceived as ‘bewitched’ or merely suffering from the effects of ageing. With treatment being unaffordable and unavailable, and with a complete discontinuity of medical care, it is unsurprising that patients turn to traditional healers.

Tanzania is one of the poorest countries in the world and faces overwhelming problems in health provision. Only 4.3% of gross domestic product is spent on health and almost half of this is private rather than government funded. Access to basic facilities such as clean drinking water remains a problem. While local resources and international aid are focussed on conditions such as infections and malnutrition, neurodegenerative disorders will not be perceived as a high priority. Life expectancy at birth is 46.5 years and