moclobemide and nortriptyline. *Biological Psychiatry*, **42**, 925–931.

Malhi, G. S. & Farmer, A. E. (1999) Drug therapy in treatment-resistant depression (letter). *British Journal of Psychiatry*, **175**, 390–391.

Mullen, P. E., Linsell, C. R. & Parker, D. (1986) Influence of sleep disruption and calorie restriction on biological markers for depression. *Lancet*, *ii*, 1051–1055.

Roose, S. P., Glassman, A. H., Attia, E., *et al* (1994) Comparative efficacy of selective serotonin reuptake inhibitors and tricyclics in the treatment of mania. *American Journal of Psychiatry*, **151**, 1735–1739.

A. R. Fraser Mood Disorders Service, Waitemata, Mental Health Services, Takapuna, New Zealand

Depression and interferon-alpha therapy

In their case report, McAllister-Williams *et al* (2000) hypothesise that recurrence of major depression following treatment with interferon-alpha (IFNα) is related to its capacity to impair serotonin synthesis by inducing enzymes that degrade tryptophan and they cite *in vitro* evidence in support of this. We suggest that there are other *in vivo* biological effects of this treatment, which may explain the association of IFNα with depression.

First, it is possible that the pathogenesis of depressive symptoms following treatment with IFNα is related to disturbance of the hypothalamic–pituitary–adrenal (HPA) axis. Overactivity of the HPA axis occurs commonly in people with major depressive disorder (Dinan, 1994), the rates of overactivity increasing with growing severity of depression. There is evidence to suggest that the effects of antidepressants on mood may be brought about by re-equilibration of the HPA axis (Barden *et al*, 1995). Exogenous IFNα therapy has been found to increase plasma adrenocorticotrophic hormone (ACTH) and serum cortisol in humans (Shimizu *et al*, 1995). The mechanism, however, does not appear to be a direct one as exogenous IFNα is a polypeptide that does not cross the blood–brain barrier and direct application of IFNα to cultured pituitary cells does not release ACTH. Indirect effects of exogenous IFNα on the HPA axis may occur through activation of endogenous cytokines, specifically interleukin-6 (IL-6) which is known to stimulate release of corticotrophin-releasing factor from rat hypothalamus *in vitro*. Furthermore, increase in serum IL-6 following *in vivo* IFNα is positively correlated with the IFNα-induced changes in serum cortisol (Shimizu *et al*, 1995).

Second, the possible effects of IFNα on tryptophan availability to which the authors refer may be a secondary effect of immune system activation. Major depression is associated with an activation of the immune-inflammatory response system, with cell-mediated increases in serum levels of pro-inflammatory cytokines including IL-6. Reduced availability of tryptophan in depression may be a result of this inflammatory response activation (Song *et al*, 1997). Exogenous IFNα also activates pro-inflammatory cytokines.

Paradigms about the aetiology of major depressive disorder are expanding beyond a narrow monoamine-centred concept. Clearly, stress, either medical or psychological, is important in the aetiology of depression. The major stress axis, the HPA, which is overactive in major depression, is potently activated by both exogenous and endogenous cytokines.

We suggest, therefore, that these biological pathways are important in the pathophysiology of depression during treatment with IFNα.

Barden, N., Reul, J. M. & Holsboer, F. (1995) Do antidepressants stabilise mood in depression through actions on the hypothalamic–pituitary–adrenal system? *Trends in Neuroscience*, **18**, 6–17.

Dinan, T. G. (1994) Glucocorticoids and the genesis of depressive illness. A psychobiological model. *British Journal of Psychiatry*, **164**, 365–371.

McAllister-Williams, R. H., Young, A. H. & Menkes, D. B. (2000) Antidepressant response reversed by interferon (letter). *British Journal of Psychiatry*, **176**, 93.

Shimizu, H., Ohtani, K., Sato, N., *et al* (1995) Increase in serum interleukin-6, plasma ACTH and serum cortisol levels after systemic interferon-α administration. *Endocrine Journal*, **42**, 551–556.

Song, C., Lin, A., Bonaccorso, S., *et al* (1998) The inflammatory response system and the availability of plasma tryptophan in patients with primary sleep disorders and major depression. *Journal of Affective Disorders*, **49**, 211–219.

E. M. Cassidy, V. O'Keane Beaumont Hospital, PO Box 1297, Beaumont Road, Dublin 9, Republic of Ireland

Sluggish economics affect health of Japanese 'business warriors'

Health among the Japanese people has been faltering since the 'bubble' economy burst in the early 1990s. The consequences of the recession are now visible. A middle-aged man committed hara-kiri, a ritual form of suicide often committed in the name of honour. In the past, samurai were willing to kill themselves to maintain the *oie* (the family which governed the territory inherited from the ancestor). The man appealed, at the expense of his life, to the company for which he had worked for decades, one of the most successful companies in Japan.

To survive the competitive business world, many Japanese companies have now embarked upon restructuring. It is those middle-age men, who contributed to the economic success of Japan since the Second World War, who are now, ironically, the target for restructuring. They have devoted almost all of their lives and often sacrificed their own family life for their companies. People have had the *aisha-seisin* (a deep spiritual attachment to their own company) exactly akin to that held by the samurai for the *oie*. The man who commited hara-kiri had trusted the company and believed that the company would not abandon the business warriors. He killed himself when he felt betrayed by the company.

There is evidence that the poor economic performance of Japanese business has affected the health of the nation. The number of deaths from suicide reached 31 734 (25.2 per 100 000 people) in 1998 (Statistical Information, Department of Health, Japan; further information available from the first author upon request); Japan's highest rate since statistics were first recorded in 1899. The rate of suicide has also risen after the end of the economic 'bubble', notably for middle-aged men, approaching 50 per 100 000 people (Taniguchi *et al*, 1998). An increase in the suicide rate, especially among middle-aged men, affected the estimate of life expectancy downward; as a consequence, the gap in expected longevity between men and women in Japan has become wider (6.85 years: Department of Health, Japan, August 6, 1999 (further information available from the first author upon request)).

Karoshi (early death due to overwork) (Lawlis, 1995) is also a result of *aisha-seisin*. These deaths can be avoided. People should realise that a strong worker–company bond and becoming a 'business warrior' is hazardous to health.

Lawlis, G. F. (1995) Alternative therapies in Japan: a prototype for conquering 'karoshi' and stress. *Alternative Therapies in Health and Medicine*, **1**, 28–29.

https://doi.org/10.1192/bjp.176.5.494-a Published online by Cambridge University Press