

on the main outcome measures, as we reported in the original paper, nor did the antioxidant supplementation modify the effect of serum total cholesterol on suicide.

Tanskanen *et al* (above) report in their letter that the risk of suicide was increased with higher serum total cholesterol levels in random samples of Finnish smokers. We do not have any obvious explanation for these conflicting findings, but study populations were rather dissimilar. Their subjects (aged 25–64 years) were mainly from eastern Finland, whereas our subjects (aged 50–69 years) were from south-western Finland. The results of other cohort studies investigating the association of serum total cholesterol levels with death from suicide have been inconsistent, since there has been no association or the association has been inverse in previous studies. Tanskanen *et al*, as well as Su *et al* (above), raise the possibility of dietary fatty acids affecting the occurrence of depressive disorder, which in turn is one of the strongest risk factors for suicide. Our aim is to analyse, in subsequent studies, the relationships between various dietary factors (fats, carbohydrates, and amino acids), depressed mood and suicide risk.

ATBC Cancer Prevention Study Group (1994) The alpha-tocopherol, beta-carotene lung cancer prevention study: design, methods, participant characteristics, and compliance. *Annals of Epidemiology*, **4**, 1–10.

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Motor responses to transcranial magnetic stimulation in schizophrenia

We read with interest the paper by Borojerdi *et al* (1999). Our group found a shorter latency for motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) in unmedicated people with schizophrenia of, on average, 2 ms compared with age- and gender-matched normal subjects (Puri *et al*, 1996). In contrast, Borojerdi *et al* (1999) reported no such latency difference (in their group

of medicated patients) and speculated that the presence of antipsychotic medication may have confounded their results. Indeed, our group has previously reported the effects of such medication on the latency and form of the inhibitory silent periods to TMS (Davey *et al*, 1997), which is known to occur as a result of activating superficial intracortical inhibitory interneurons, possibly GABAergic (Davey *et al*, 1994). Borojerdi *et al* (1999) found a longer latency of transcallosal inhibition to TMS in a group of medicated patients with schizophrenia but did not include a group of drug-naïve patients. It is clearly important to be able to differentiate between pathophysiological mechanisms resulting from schizophrenia and the actions of antipsychotic medication on the cortico-spinal system.

Borojerdi, B., Töpper, R., Foltys, H., et al (1999) Transcallosal inhibition and motor conduction studies in patients with schizophrenia using transcranial magnetic stimulation. *British Journal of Psychiatry*, **175**, 375–379.

Davey, N. J., Romaiguère, P., Maskill, D. W., et al (1994) Suppression of voluntary motor activity revealed using transcranial magnetic stimulation of the motor cortex in man. *Journal of Physiology*, **477**, 223–235.

—, **Puri, B. K., Lewis, H. S., et al (1997)** The effects of antipsychotic medication on electromyographic responses to transcranial magnetic stimulation of the motor cortex in schizophrenia. *Journal of Neurology, Neurosurgery and Psychiatry*, **63**, 468–473.

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Clozapine-induced thrombocytosis

Clozapine is known to cause blood dyscrasias, typically neutropenia and agranulocytosis. A raised platelet count, with clozapine as the sole implicated agent, had been reported to the Committee on Safety of Medicines in three cases. This is the first to be published.

A middle-aged male with ICD schizophrenia failed to respond to neuroleptic medication (haloperidol 25 mg/day, chlorpromazine 500 mg/day), or olanzapine at a dose of 20 mg/day for six weeks. He

was therefore started on clozapine. He continued to receive droperidol 20 mg/day and zopiclone 7.5 mg nocte.

Fifteen days after commencing clozapine he complained of nausea. His clozapine was increased the next day by 25 mg to 300 mg/day. He complained of arthralgia and became hypotensive (b.p. 90/60 mmHg). Clozapine was stopped and the symptoms subsided over 36 hours. Clozapine was then restarted at a dose of 100 mg twice daily. He re-developed hypotension, arthralgia, malaise and sweating after one dose. He was apyrexial. Five days after the onset of nausea, the platelet count was $454 \times 10^9/l$ (normal range: $150\text{--}450 \times 10^9/l$), the erythrocyte sedimentation rate (ESR) 70 mm/h and the C-reactive protein 103. Eight days later the ESR had fallen to <5 mm/h but the platelet count had risen to $774 \times 10^9/l$. Five days later the platelet count had fallen to $393 \times 10^9/l$ and subsequently returned to normal.

Muller *et al* (1991) reported fever 7–15 days after commencing clozapine in 12 patients with non-specific inflammatory parameters, including a raised white cell count, ESR and C-reactive protein. They did not comment on platelet changes. This case has similar symptoms but without pyrexia. The rapid re-emergence of symptoms on re-challenge suggests an immune response to the drug, and both thrombocytosis and thrombocytopenia are recognised features of such a reaction.

Muller, H., Manns, M., Hammes, E., et al (1991) Studies on inflammatory side effects of clozapine. *Biological Psychiatry*, **29** (suppl.) 415S–416S.

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Paternal age and schizophrenia in dizygotic twins

Crow (1999) reported that dizygotic twinning increases with parental age as does the incidence of schizophrenia. Our study of 574 patients with schizophrenia showed that the incidence of schizophrenia increases with paternal age (Raschka, 1998). Scientific publications reported increased incidence of at least 12 illnesses with increased paternal age. The rate of mutations in spermatogenesis increases with age (Penrose, 1955; Vogel & Motulsky, 1979; Raschka, 1995; Sankaranarayanan, 1998). Other age-related changes are also known

to occur in spermatogenesis. The study of the effect of paternal age could yield useful information regarding the reported greater occurrence of schizophrenia in dizygotic twins.

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Penrose, L. S. (1955) Parental age and mutation. *Lancet*, *ii*, 312–313.

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human populations: a 1998 perspective. *Mutation Research*, **411**, 129–178.

Vogel, F. & Motulsky, A. G. (1979) *Human Genetics: Problems and Approaches*. Berlin: Springer Verlag.

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One hundred years ago

The employment of the insane

The *Lancet* of 28th October refers to work done at the Wernersville State Asylum, Pennsylvania, where chronic patients considered fit to labour are received from the other State institutions. The results of five years' experience of agricultural labour are given as follows: – (a) Of the patients 6 per cent. can perform work equal to paid labour, 30 per cent. can perform labour equal to one half of paid labour, and 50 per cent. are equal to one fourth of the value of paid labour. The balance of 14 per cent. are non-working, and this includes those who are ill or are found on trial not to be able to work. (b) The estimated value of the gross amount of work done during the current year, on a basis of 400 men, is

\$29,000. The estimated cost of food per head is 20 cents per diem, or \$1.40 per week. (c) The health and welfare of the patients are medically attended to, and the medical reports regarding the health and mortality are found to be entirely satisfactory. Indoor work, e.g. brush-making, is now being introduced as an extension of the original industrial scheme, and it is believed that this also can be pursued with profit. These results are representative of our experience in asylums of this country where an adequate area of agricultural ground has been secured. It is somewhat surprising that the *Lancet* should go on to recommend that the example of Wernersville should be followed by other institutions in Britain and America. Old-established asylums such as Wakenfield

and Utica are veritable hives of industry; it is years since machinery was introduced in the shoemaking department at the former, and the old men were encouraged to make and repair stockings; while the useful trades at Utica are representative of the greatest possible variety, and would be still more efficient but for the interference of trades unions. Of course every asylum ought to have a farm proportionate to its size. It is late in the day to advocate that primitive measure.

REFERENCE

Journal of Mental Science, January 1900, **XLVI**, 208.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Epsom, Surrey.

Corrigenda

Acute manic symptomatology during repetitive transcranial magnetic stimulation in a patient with bipolar depression, *BJP*, **175**, 491. The authorship of this letter was reported incorrectly. The authors are: M. Garcia-Toro, A. González, M. Romera (Complex Hospitalari GESMA, c/Jesús no. 40, 07003 Palma de Mallorca, Spain) and A. Pascual-Leone (Laboratory for Magnetic Brain Stimulation, Beth Israel Deaconess Medical Center and Harvard Medical

School, Department of Neurology, 330 Brookline Avenue, Boston, MA 02215, USA).

Medial prefrontal glutamine and dreaming, *BJP* **175**, 288–289. The name and affiliation of the fourth author were omitted from the manuscript in error. R. S. Menon (Laboratory for Functional Magnetic Resonance Research, John P. Robarts Research

Institute, Box 5015, 100 Perth Drive, London, Ontario, Canada N6A 5K8) was a scientific advisor to the study team and helped collect the spectroscopic data reported.

Polydactyly and functional psychosis, *BJP*, **175**, 291–292. The author of this letter is M. S. Bhatia (not M. S. Shatia as originally reported).