broadly including combinations of inattention, recent memory impairment (with conspicuous preservation of immediate memory), retrograde loss of recall or recognition, and disorientation in time and space. The present trend is to confine 'Korsakov Syndrome' to amnesia combined with peripheral neuritis with or without cheerful confabulation and flight of ideas. Neural loss is not confined to the mammillary bodies (it should be remarked) but also involves the frontal lobes. When acute delirium with neurological signs indicating a brain stem lesion are added the disturbance is known as 'Wernicke's Encephalopathy'. In such cases an acute deficiency of thiamine (vitamin B_1) precipitates the dramatic onset; after replacement therapy the patient may be left with his 'Korsakov Syndrome'.

Using two high resolution protocols for imaging the human brain with magnetic resonance [MRI], it is now possible to distinguish anatomically between patients with diencephalic (mammillary nuclei) and medial temporal lobe (hippocampal formation) amnesia.[3] The mammillary nuclei may be severely shrunken or entirely absent in patients with Korsakov's psychosis. The development of these and other innovative techniques will serve to dispel the current ambiguity that bedevils classification of the amnesias and augurs well for the advancement of neuropsychiatry.

Eponymous remembrance is inclined to overshadow other important work. Korsakov was very clear in his mind about 'paranoia hyperphantastica' and helped to establish the concept of paranoia as a psychosis presenting clearly-defined delusions supported and defended by the patient (systematised delusions). His textbook Kurs Psychiatri became the standard in Russia soon after its publication in 1893. It compared favourably with contemporary works and a second edition [1901] kept it in useful circulation for a generation. His advocacy of freeing the patients from physical restraints including the straight-jacket was not popular with hospital staff. The principle of "less restraint for the patient the more restraint for the doctor" implied that the latter had to provide "more attention, affection and devotion to the patient".

In 1890 Korsakov helped to set up a Society of Neuropathologists and Psychiatrists in Moscow. Subsequently, after taking part in organising the International Medical Congress there in 1897, he saw the necessity of developing an Association of Psychiatrists and Neurologists on a national scale. Unfortunately the Russian Association he planned did not hold its inaugural meeting until 1901, the year after Sergei Korsakov died at the early age of forty-six.[1]

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LETTERS TO THE EDITOR

Lithium in resistant depression

Sir, – We would like to report the case of a 76 year old lady with recurrent major depression (DSM-III) resistant to a combination of dothiepin and electroconvulsive therapy (ECT), and also to fluoxetine but responding rapidly to the addition of lithium to fluoxetine.

Case Report

Our patient was admitted with a relapse of recurrent major depression (DSM-III) with stupor and mutism of 8 weeks duration. She had 3 previous episodes of major depression, 35, 30 and 15 years ago. The 2nd episode was treated with ECT in addition to drugs. She was normothymic between the episodes.

She was already on dothiepin 150 mg daily for the previous 8 weeks and improved minimally with 5 bilateral ECTs in 15 days at which time her relatives withdrew consent for further ECT and she was discharged on dothiepin 150 mg daily. She was readmitted two months later with an exacerbation of symptoms. On this occasion she showed a partial response to an increased dose of dothiepin of 225 mg daily and a second course of 8 bilateral ECTs over the following 6 weeks, when her relatives again refused further treatment. She failed to maintain the improvement and was readmitted six weeks later with an aggravation of her symptoms.

Her antidepressant medication was then changed to fluoxetine 20 mg daily which was increased to 40 mg daily after a fortnight. Since her depressive symptoms persisted, four weeks later she was commenced on lithium (Li) 600 mg daily. She made a complete improvement by the 4th day at a serum Li level of 0.89 mEq/l. Her Li was then reduced to 400 mg daily. She maintained her improvement throughout the 6 months at serum Li levels of 0.6 to 0.72 mEq/l.

Discussion

The rapid response to Li of depression resistant to tricyclic antidepressants (TCA) was first described by de Montigney et al[1] in 1981. They attributed this to Li enhancing serotoninergic neurotransmission in forebrain neurones already sensitized by TCA. Dinan and Barry[2] in a controlled study concluded that the Li is equally and more rapidly effective than ECT in TCA resistant depressives. Li has also been found to be effective in depression in the elderly resistant to TCA and ECT.[3] There has been one report each of the efficacy of Li in depression resistant to dothiepin (150 mg/day)[4] and to fluoxetine.[5] The literature on the efficacy of Li in TCA resistant depression has been reviewed recently.[6,7,8] This case would appear to describe the phenomenon previously reported, but this is the first report of the efficacy of Li in depression resistant to TCA, fluoxetine and two courses of ECT. The efficacy of lithium in depression resistant to combined ECT and dothiepin has not been reported before.

There has been a report[9] of neurotoxicity induced by

Prescribing information

Presentation Pale yellowish brown tablets containing 50 mg and 100 mg lamotrigine and coded 'LAMICTAL 50' and 'LAMICTAL 100' respectively. **Uses** Lamictal is an anti-epileptic drug, recommended for use as an 'add on' therapy for the treatment of partial seizures and generalised tonic-clonic seizures in patients not satisfactorily controlled with other anti-epileptic drugs. **Dosage and administration** *Adults, and children over 12 years of age:* The initial dose is 100 mg per day for the first two weeks in two divided doses. The usual maintenance dose is 200 mg to 400 mg per day given in two divided doses. In those patients taking sodium valproate, either alone or in combination with other anti-epileptic drugs, the initial Lamictal dose is 50 mg per day for the first two weeks. The usual maintenance dose is 100 mg to 200 mg per day given in two divided doses. *Children aged 12 years and under:* There is as yet insufficient information on the use of Lamictal in children aged 12 years and under. *Precautions:* Lamictal, as a novel agent, should only be used under the supervision of specialists. Adverse effects should be particularly noted. Lamictal exerts some inhibition of dihydrofolate reductase, hence, there is a possibility of interference with folate metabolism during long term treatment. The risk of rebound seizures may be avoided by tapering the drug off during a period of 2 weeks. Sodium valproate reduces metabolism of lamotrigine. Liver enzyme inducers (eg. carbamazepine, phenytoin) may increase dose requirements. Use during pregnancy or lactation should be avoided, unless considered essential by a physician. This product contains a novel active ingredient and is presently on intensive monitoring. Any side-effects or unusual response encountered with the drug should be reported immediately to the patient's consultant during the intensive monitoring period and thereafter to the National Drugs Advisory Board. *Side- and adverse effects:* Skin rash (usually maculopapular) occurs in up to 10% usually within the first month of therapy, resolving on withdrawal of drug. Stevens Johnson Syndrome has been reported. Adverse experiences normally associated with standard anti-epileptic drugs (including diplopia, dizziness, ataxia, etc.) have also been reported during trials of Lamictal when added on to such therapy. **Package quantities:** Blister Pack of 56 x 50 mg tablets (PA 17/99/2), 56 x 100 mg tablets (PA 17/99/3). **References** 1. Leach, M.J. *et al.*, (1986) *Epilepsia*, **27**/5, 490-497. 2. Jawad, S., Richens, A., Goodwin, G., Yuen, W.C., (1989) *Epilepsia*, **30**/3, 356-363. 3. Binnie, C.D. *et al.*, (1989) *Epilepsy Res.*, **4**, 222-229. 4. Sander, J.W.A.S. *et al.*, (1990) *Epilepsy Res.*, **6**, 221-226. 5. Loiseau, P., (1990) *Epilepsia* (In Press). Further information available on request from **Wellcome Ireland Limited**, Clonard Road, Dublin 12. Tel: 900666

Wellcome

Introducing Lamictal, a bright new prospect in epilepsy control.

Lamictal offers new prospects in the treatment of epilepsy. Chemically unrelated to existing therapies, Lamictal inhibits the release of those excitatory amino acids, principally glutamate,[1] thought to be responsible for generating epileptic seizures.

In four double-blind, 'add on', placebo-controlled, crossover studies[2-5] in patients with treatment-resistant epilepsy, Lamictal produced clinically significant reductions in both partial seizures and generalised tonic-clonic seizures. The incidence of side-effects observed with Lamictal in these studies was not significantly different from that with placebo.[2-5]

The clinical efficacy of Lamictal, combined with the low side-effect profile makes it an important advance in the treatment of epilepsy.

Lamictal*

lamotrigine

*Trade Mark

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combined fluoxetine and Li at a serum Li of 1.70 mEq/l, but in antidepressant and Li combination therapy a serum Li between 0.5 - 0.7 mEq/l is adequate,[2] although fluoxetine may have played a role in increasing the serum Li level.

This case highlights the opinion of Dinan and Barry[2] that in TCA nonresponders, adding Li to the TCA is a rapidly effective alternative to ECT. This is especially true when the poor patient acceptability of the latter is considered.[6]

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Psychiatrists' use of antidepressants: preferences versus toxicity

Sir, – O'Shea,[1] in an interesting paper, reported the results of a survey of psychiatrists on their use of and attitudes towards antidepressants. One of the reasons they cited for their preference for one antidepressant over another was the presence of a suicide risk in the patient.

Clarke and Lester[2] have argued that suicide is made more likely if the opportunities for suicide are made more available. There are data available on the likelihood of fatal overdoses by patients for most of the major antidepressants. It is interesting, therefore, to compare the psychiatrists' preferences as reported by O'Shea for the different antidepressants with the fatality rate of the antidepressants.

TABLE 1 – **Psychiatrists' preferences and fatality rates for antidepressants**

	preference			fatality rate/
	first	second	third	10^6 prescriptions
dothiepin	16	7	6	50.0
amitriptyline	10	6	8	46.5
lofepramine	10	10	8	0.0
mianserin	2	4	5	5.6
fluoxetine	2	*	*	not available
trimipramine	1	*	*	27.6
trazodone	1	*	*	13.6
clomipramine	1	*	*	11.1
tranylcypromine	1	*	*	58.1

* *not reported by O'Shea*

Table 1 presents the first, second the third choices of psychiatrists as reported by O'Shea and fatality rates (per 10^{16} prescriptions) in the United Kingdom for 1975-1984 as reported by Henry.[3] It can be seen that two of three most favoured antidepressants have much higher fatality rates than the third (lofepramine).

This information should be made available to psychiatrists when prescribing antidepressants, updating the fatality rates as more data become available. Use of this information might greatly reduce the incidence of fatal accidental and suicidal overdoses using antidepressants.

David Lester, PhD, Center for the Study of Suicide, RR 41, 5 Stonegate Court, Blackwood, New Jersey 08012, USA.

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Author's Reply

Sir, – I thank Dr. Lester for his thoughtful letter. It is certainly true that the older tricyclic antidepressants are more potentially lethal than are drugs such as lofepramine. However, there have been some deaths from lofepramine,[1] albeit much less than with other related drugs. Also, not all studies support the view that the availability of tricyclics promote suicide. There is even some evidence that they may reduce the suicide rate.[2] Thirdly, as a clinician, I have often been impressed by (a) the number of deaths from drugs which were not prescribed for the deceased, and (b) the paucity of information given to patients in receipt of a prescription. The danger is that we may throw out highly effective drugs without having used them properly, e.g. accurate diagnosis, estimation of suicidal proclivity, hospitalisation if necessary during the danger period, educational and supportive measures, adequate dosage, warnings re alcohol, and, essential in my opinion, evaluation of social status and personality variables.[3] The history of suicide during this century teaches us that the suicidal patient will shift to new agents/methods once former ones cease to be available.[4,5] This is an unfortunate but true fact of death. Newer tricyclics such as amoxapine may prove to be safer than their ancestors.[6,7] However, as Professor Cawley has said, "Whatever we see as the truth is always on probation".[8]

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