EDITORIAL

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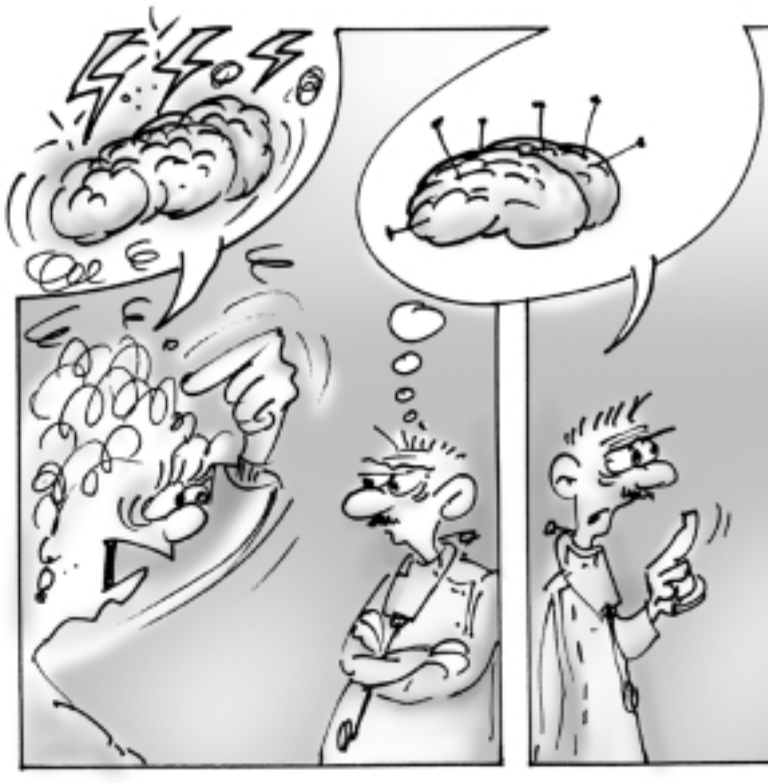
Adverse effects: direct reporting by patients is beneficial

Are suspected adverse drug effects described in the same way by patients and health professionals? Is the description modified by coding for inclusion in a pharmacovigilance database? And does patient reporting add anything useful to reports by health professionals?

British authors compared two sets of reports of adverse effects associated with paroxetine, a selective serotonin reuptake inhibitor antidepressant (SSRI) (a)(1,2).

The first set comprised 1374 e-mails that were sent spontaneously by patients or their relatives to BBC-TV in response to a documentary on the adverse effects of paroxetine (b), and 862 e-mails sent to an interactive discussion board (Adweb) for people taking SSRIs, placed online before the BBC programme was aired (3).

The second set was made up of 1555 case reports (Anonymised Single Patient Printouts or ASPPs) describing suspected adverse effects of paroxetine that had been transcribed from reports (Yellow Cards) by British health professionals to the Drugs and Health-Care Products Regulatory Agency (MHRA) (c). It was the first time the Agency had communicated to a third party data contained in the British pharmacovigilance database ADROIT (Adverse Drug Reaction Online Information Tracking database) (d).



Patients' reports drew attention to previously overlooked events. **In particular, there were 13 deaths by suicide considered surprising by the relatives, 47 suicide attempts, and 92 cases of self-harm or violent acts. This violent behaviour seemed to occur mainly at the beginning of treatment, after a change in the dose, or during weaning.**

As this link had not initially been spotted by the British agency, the authors analyzed 91 cases reported by health professionals describing suicides or suicidal behaviour by patients taking paroxetine. The authors found evidence to support the link in more than half the cases.

An "electric head" sensation during treatment withdrawal. **There were many reports of withdrawal symptoms after paroxetine treatment was stopped, both in the e-mails received by the BBC and Adweb. Even e-mails to the BBC from people with a positive opinion of paroxetine described problems on treatment withdrawal in 40% of cases. The authors discovered that the most common withdrawal symptoms included an electric head sensation, associated with sensations of whistling and dizziness. Patients reported that these symptoms were alarming and incapacitating.**

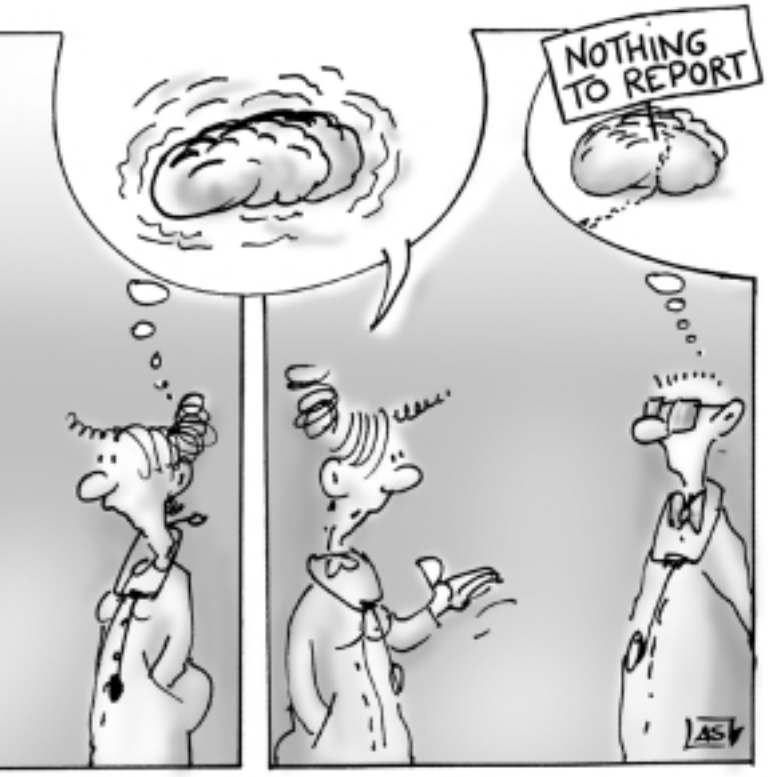
An inadequate coding system. **The authors looked for similar descriptions of "electric head" in the British agency's case reports (ASPPs). They found 52 such cases reported by health professionals, but these had been coded as "paresthesia". In the light of the e-mails sent to the BBC, the authors considered that this serious symptom, which many patients said made it difficult or impossible to stop taking paroxetine, should be given a more explicit code than "paresthesia".**

Numerous consistent patient reports must be taken seriously. **Independent patient reports, especially when numerous and consistent, must be taken seriously by health authorities.**

The British patients in this study described their behaviour and sensations more precisely than the health professionals. And an analysis of the reports received by the BBC-TV threw new light on information that was contained in reports by health professionals but that had been overlooked.

Patients reporting must be organised. **While the principle of patient reporting of adverse effects has been accepted by 23 countries (2), it is not covered by the new European legislative framework (4).**

An official British report published in May 2004 on providing access to pharmacovigilance (Yellow Card) data for researchers and public health bodies recommended creating a national system for collecting patient reports, within the British agency (5).



The agency agreed, announcing that it would launch pilot studies (6,7).

With some exceptions, such as collation of adverse events related to antiretroviral drugs and reported by HIV-infected patients to the French medicines agency (8), a few pilot trials (7), and the promising example of the British Drugs and Health Care Products Regulatory Agency, national health authorities in general appear to treat individual patient reports as barely credible and anecdotal (e)(2).

The British study of paroxetine reports shows that spontaneous reports from health professionals and patients are complementary. It should encourage all national health authorities to set up practical means (specific forms for consumers, pharmacovigilance consultations) by which patients can directly report suspected adverse effects. These reports should be treated transparently and rigorously, in the same way as all other pharmacovigilance data.

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a- *We have dealt with the adverse effects of paroxetine and other serotonin reuptake inhibitor antidepressants in several articles (refs 9-12).*

b- *13 October 2002, "The Secrets of Seroxat", a documentary on the adverse effects of paroxetine, was broadcast by the popular BBC-TV news magazine Panorama. After the programme, the BBC received nearly 65 000 telephone calls and 1374 e-mails. The authors classified the e-mails into two categories: those mentioning a positive global opinion of paroxetine ("very beneficial drug", "more advantages than disadvantages"); and those with a negative opinion ("more disadvantages than advantages", "no major benefit"). 48% of the e-mails gave a negative opinion (ref 1).*

c- *In the United Kingdom, health professionals report adverse effects on "Yellow Cards". The British system is described in detail on the "Adverse events: Drugs" page of the MHRA website (http://www.mhra.gov.uk). Anonymised Single Patient Printouts (ASPPs) are produced by MHRA staff from the Yellow Cards. Each adverse effect mentioned on a given Yellow Card is transcribed to a separate ASPP.*

d- *The extract from the ADROIT database, provided to the authors by MHRA, was restricted to four paroxetine adverse effect fields ("withdrawal reactions", "dependence", "injury and poisoning", and "suicidal behaviour"). By late 2002, 8625 Yellow Cards on paroxetine had been received by the British agency, generating 19 017 ASPPs (ref 2). The authors received from the British agency 1574 ASPPs coded under the field relating to increased suicide risk during treatment, or to withdrawal reactions (ref 2).*

e- *However, a joint taskforce of the European Medicines Evaluation Agency and patient groups concluded in favour of direct patient reporting and recommended a pilot study (ref 13)*

.Selected references from Prescrire's document watch.

1- Medawar C et al. "Paroxetine, Panorama and user reporting of ADRs: Consumer intelligence matters in clinical practice and post-marketing drug surveillance" *Int J Risk Saf Med* 2002; **15**: 161-169.
2- Medawar C and Herxheimer A "A comparison of adverse drug reaction reports from professionals and users, relating to risk of dependence and suicidal behaviour with paroxetine" *Int J Risk Saf Med* 2003/2004; **16**: 5-19.
3- Adweb discussion forum, http://www.socialaudit.org.uk/_disc//messages/boardtopics.html accessed on 27 May 2004.
4- Prescrire Rédaction "Europe et médicament: les succès obtenus par les citoyens" *Rev Prescrire* 2004; **24** (252): 542-548. [see printout of August 2004 issue "Medicines in Europe: the most important changes in the new legislation", and www.prescrire.org]
5- Independant steering committee "Report of an independent review of access to the Yellow Card scheme" The Stationery Office (TSO), London 2004: 214 pages. The TSO published most official British reports. Website: http://www.tso.co.uk
6- "Report of an independent review of access to the Yellow Card scheme: MHRA response to recommendations " Letter MLX 308 dated 4 May 2004. Website http://medicines.mhra.gov.uk consulted on 27 May 2004.
7- Williams K "Patients will be able to report drugs' side effects" *BMJ* 2004; **328** (7448): 1095.
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10- Prescrire Editorial Staff "Paroxetine withdrawal syndrome" *Prescrire Int* 2003; **12** (66): 141.
11- Prescrire Editorial Staff "Suicidal ideas with paroxetine or venlafaxine"" *Prescrire Int* 2004; **13** (69): 21.
12- Prescrire Rédaction "Actes suicidaires et antidépresseurs chez les enfants (suite)" *Rev Prescrire* 2004; **24** (251): 433.
13- EMEA/CPMP Working Group With Patients Organisations "Recommendations and proposals for action" Executive summary 20 April 2004: 21 pages. Website http://www.emea.eu.int accessed on 17 June 2004.