News Roundup [abridged Versions Appear In The Paper Journal]

More surveillance of drugs is needed to protect public

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Not just a moral imperative

This is a timely examination as we all witness the deleterious effect of the Vioxx episode on Merck. Your article says that pharmaceutical companies must have a moral imperative to do something about adverse reactions. I would however like to restate this.

Companies exist primarily to make profits, even though in case of pharmaceutical firms, they do so by serving an essential function of delivering healthcare related interventions.

Were firms to acknowledge to themselves the financial fall-out of failures to act upon known adverse reactions, they would address the problems quicker. In this time, when old-style blockbuster drugs are harder and harder to come by, firms would do well to focus on maintaining a revenue stream and doing so by addressing issues proactively. This goes beyond a moral imperative, which may be hard to translate to shareholder returns. It is pure existential logic for firms.

Competing interests:
None declared

Competing interests: No competing interests

17 November 2004
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Harm Reduction is a Noble Goal

Kudos to BMJ London reporter Lynn Eaton in her coverage of the timely November meeting of APRIL, otherwise known as the Adverse Psychiatric Reactions Information Link.(1) Likewise, congratulations to spokespersons Millie Kieve, Charles Medawar, Andrew Herxheimer, John Halliday, Keith Altman and Saad Shakin who were named in Eaton's article. Through their courageous efforts and the individuals and institutions they represent, consumers of medicines--psychiatric and non-psychiatric--might one day look forward to safer and more efficacious pharmaceuticals.

I am particularly delighted to see BMJ cover a story that never receives enough press: Psychiatric side-effects of non-psychiatric medicines. Except in a few obvious areas of clinical practice, like the 'black box' warnings for depression that appear on a drug like isotretinoin(Accutane) and similar warnings that now accompany antidepressants or the widely variable problems(i.e., confusion, delirium, paranoia, hallucinosis, agitation, mania and/or psychosis) that can accompany antiretrovirals(e.g., zidovudine), anti-inflammatories(e.g., sulfasalazine), antivirals(e.g., ganciclovir), dopaminergics(e.g., amantadine), antimicrobials(e.g., quinolones) and anabolic or corticosteroids, physicians and consumers are inadequately prepared to recognize medication side-effects and iatrogenic causes of psychiatric symptoms.

As has been said elsewhere, we as physicians can not 'do no harm' if we do not appreciate and understand the kind of harm that can be done.

1. Eaton L. More surveillance of drugs is needed to protect public. BMJ 2004; 329:1124

Competing interests:
None declared

Competing interests: No competing interests

16 November 2004
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Re: To Protect and To Serve. Are You kidding Yourselves and hope to infect others?

Dr. Herbert Nehrlich should not refer to himself as a "crackpot" for writing that, "What this world needs, and, more importantly, depends upon for its survival, is the drastic reduction in pharmaceuticals, a return to the family farm and the re-instatement of dignity in Joe Blow and myself." While "a return to the family farm" may not be an option for many of us, I am sure that there are many parents, doctors, and researchers etc. who would like to see a drastic reduction in pharmaceuticals which are in use today. For this reduction to happen, there would need to be greater understanding of the challenges faced by the individuals who are prescribed these pharmaceuticals, and also more information available about alternative strategies for dealing with their problems. Along with that, it would be helpful if more useful research were being conducted to uncover the causes or roots of these problems.

Last Thursday, I attended one day of the Geneva Centre for Autism's International Symposium on Autism 2004. When I emailed a friend (who has a son diagnosed with Asperger's Syndrome)that I had attended Dr. June Groden's presentation on "Autism and Anxiety: A Behavioral Approach to Assessment & Coping Strategies", she wrote back, asking whether Dr. Groden had mentioned anything about the use of medications to deal with anxiety. I was happy to reply that there had been no mention about the use of medications in Dr. Groden's talk. She focussed on the use of stress reduction techniques, picture rehearsal, using the stress survey schedule, assessing sources of stress, and teaching relaxation techniques. There was no discussion of using medications to help individuals with ASD reduce their levels of anxiety. As a parent, I would rather try these techniques first, before even considering whether medications would be of any use.

That same day, I also attended a presentation by Dr. Boyd Haley on the "Biomedical Aspects of Thimerosal Exposure". Dr. Haley told us that the CDC had issued an alarm that 1 out of 6 children in the United States have neurological disorders. He shared with us his dismay that the mainstream medical establishment believed it to be all right to medicate/drug these children so that they can attend better and behave more appropriately, without putting much effort into uncovering the causes of why so many children have these problems.

Here in Ontario, Canada, we have 1 out of 5 children who have a diagnosable mental health disorder, according to Children's Mental Health Ontario. A good number of them are being prescribed medications, even as toddlers, which have not been researched/tested with children. Personally, I would like to see more effort being put into eradicating the causes of these disorders, rather than more research into pharmaceuticals to "patch

the kids up" once the damage has been done.

Competing interests:
Some of my children have neurological disorders.

Competing interests: No competing interests

14 November 2004
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A lesson still not leant

Within a period of 20 years, only two physicians in New Zealand reported the addictive nature of the drugs in the benzodiazepine group.

Changes to the patient's behaviour along with other signs and symptoms of serious physical and mental adverse reactions including addiction, were routinely ignored. They were instead, and on the advice/instruction of the pharmaceutical industry, diagnosed as psychiatric disorders. This generally resulted in a cocktail of psychotropic drugs, thereby compounding the iatrogenic illness.

Although now restricted and under the supervision of the International Narcotics Control Board, millions of people on an international level have been affected. Many of those who got themselves through the prolonged and traumatic process of withdrawal and the post withdrawal syndrome, have been left with permanent neurological damage.

The medical profession is notorious for not learning the lessons arising out of history and experience - including the fact that the quickest way to kill off patients is by not listening to them.

Whether the current concerns are acted upon or whether they will once again be swept under the carpet, remains to be seen.

Competing interests:
None declared

Competing interests: No competing interests

14 November 2004
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Some pharmaceutical manufacturers ignore the signals

I am totally supportive of Professor D Moore in his call for good pharmacoepidemiology training and the need to identify signals.

However even when there is post-marketing follow-up of a drug, and when signals are spotted by regulators or following Prescription Event Monitoring studies, the pharmaceutical manufacturers do not always respond by amending the warnings on the patient information.

One example is the Drug Safety Research Unit mirtazapine study published in the Journal of Psychopharmacology 2003;17(1):121-126.

Mirtazapine is the first noradrenaline and serotonin specific antidepressant

The study found that more than 1 in 200 patients experienced agitation and aggression. There were reports of abnormal dreams and hallucinations. All were unlabelled adverse effects of mirtazapine. Abnormal behaviour is labelled.

The manufacturer has so far failed to alter the labelling following the PEM study on 13554 patients in England.

At a recent inquest of a man who had taken his own life. The coroner declared an open verdict due to the evidence of a possible link to the sudden change in personality and adverse effects of this drug. Another man is seriously injured due to a fall from a bridge, that occurred, he claims, due to the adverse effects of mirtazapine.

An elderly man described to me his inexplicable and thankfully unsuccessful attempt to kill himself, after being prescribed mirtazapine, not for depression but while his prostrate problems were being treated.

I hear directly from public about the sudden onset of suicidal feelings, due to akathisa or psychosis after suffering adverse effects or withdrawal effects of acne medication, anti-malarial, cortico-steroids, anaesthetics, antidepressants and other drugs. Their experience may throw light on the many unexplained suicides, deaths due to apparent careless accidents and motor vehicle accidents that occur.

It seems to take generations before the patients' experiences are acknowledged or their voices heard.

There is however, surely no excuse for ignoring the findings of the MHRA, FDA and DSRU. Suicide warnings will not cause suicides but may prevent them and if the manufacturers procrastinate for months, even years over labelling changes, other means must be found to warn the GPs,

psychiatrists, consultants, nurses and the public.

Competing interests:
Chair of APRIL charity
(Adverse Psychiatric Reactions Information Link)Organiser of the November 4th conference mentioned in the article.
www.april.org.uk

Competing interests: No competing interests

13 November 2004
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more surveillance or better analysis of data?

The editorial raises important questions, but should warn readers not to get
sidetracked:

- early detection of signals is feasible and done in the UK and elsewhere, with
the yellow-card type spontaneous reporting systems. These work to detect alerts. They are not conceived to confirm them, and exceptionally do.

- Premarketing safety data is just that. There is no way any data from clinical
trials can ensure drug safety, because clinical trials are so far removed from
real-life use of drugs. There is no way post-marketing real-life studies can
be done before a drug is put on the market. Million-patient clinical trials
cannot be done before the drug is on the market, and it is negation of common sense, and a proof of ignorance to even sugggest it.

- what is needed is good post-marketing follow-up of drugs, to first understand how they are used, and how this use possibly differs from clinical
trials, to know how much confidence one can have in the applicability of the
clinical trials.

- What is also needed is good pharmacoepidemiology training of regulators, academics, journalists and others to explore rapidly and efficiently

the signals that are identified from the spontaneous reporting schemes, and
to understand the reality of post-marketing surveillance and pharmacovigilance.

- What is especially needed is training of physicians and patients in proper
and safe use of medicines: the immense majority of adverse reactions are related to the pharmacological properties of older perfectly known drugs (1): Aspirin (the number 1 provider), NSAIDs, diuretics, anticoagulants,.
They have been known for years, and can usually be prevented or anticipated.
Drug-induced diseases are a clinical specialty like any other, and specialists
in these need to be trained to train the medical students. In some countries
these specialists are called clinical pharmacologists.(2)

- Physicians also need to be trained in taking proper drug histories (3), still
the best way to identify drug interactions, and taught pharmacology and the
effects of drugs, in medical school and afterwards.

- and the continued funding of such indispensible units as the Drug Safety
Research Unit in Southampton, the General Practice Research Database, an invaluable data ressource, or the Medecine Monitoring unit (MEMO) in Scotland, and other similar units worldwide which are a crucial part of rapid
exploration of emerging signals

Concerning the specific topic of the paper, that of the increased risk of
suicide in antidepressant users, I was taught that risk when I studied medicine 30 years ago. It seems to have been forgotten in the enthusiasm of
discovering "new" drugs.

Of course listening to the patients is indispensible, but in psychiatric patients
it is often difficult to know what comes from the disease and what comes from the drugs. Again it is not a problem of detecting problems, but assessing them properly, rather than howling with the wolves, first for the
drugs, then against the drugs.

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2. Moore N. The role of the clinical pharmacologist in the management of
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3. Moore N, Masson H, Noblet C, Joannidès R. What medicines do patients
really take? A comparison of free form vs oriented questionnaires. Post Marketing Surveillance 1993; 7: 355-362.

Competing interests:
None declared

Competing interests: No competing interests

13 November 2004
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To Protect and To Serve. Are You kidding Yourselves and hope to infect others?

Weekend is upon us and I am in a good mood but this article is like a cumulus cloud with promise.

What this world needs is not more monitoring or surveillance of drugs, not at all.

What this world needs, and, more importantly,depends upon for its survival, is the drastic reduction in pharmaceuticals, a return to the family farm and the re-instatement of dignity in Joe Blow and myself.

Those who have not seen this are to be pitied and castigated
- they are not the kind of people who will contribute to the welfare and quality of life - and sent to Baghdad, perhaps.

The public would do very well without the 'protection' of the Pharma-Clowns.
If some of us sound like crackpots it may be because we are.

Competing interests:
None declared

Competing interests: No competing interests

12 November 2004
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More radical approach needed

All medical doctors should consider all mental effects more seriously but whilst adverse reaction reporting is essential this and many recent articles on pharmaceutical "wrongdoing" are short-sighted. Simply increasing regulatory control costs money and as costs increase innovation and availability of treatments decrease. The solution is to leave R&D, clinical trial, data management and I suppose marketing with the pharmaceutical companies and to release data and statistical analysis to independant, possibly government, agencies. Open, anonymised, access to data reduces suspicion, is a gift to humanity, allows better monitoring of drug claims and effects and would not impact on ethical profits (synthesis patents and most intellectual property would or could remain protected).

Competing interests:
Probably none, but have worked for all - Government, academic, pharmaceutical, etc ...

Competing interests: No competing interests

12 November 2004
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