

"What they've done is just despicable ... "

Panorama ([BBC-TV](#)) last night broadcast its fourth programme on Seroxat® (paroxetine), a still deeper foray into the built-in nastiness of drug marketing and product promotion. All credit to the programme for sticking with the issue, if only to reveal how much more must be done to see this story through.

Thanks largely to *Panorama* and friends we now have a pretty clear picture of motive, opportunity, method and the sometimes awful consequences. Corrupting influence in pharmaceutical science has become almost natural and easy - the product not only of greed and self-interest, but of established professional and organisational practice. In some ways, collective lack of commitment and imagination seem to trump venality. Indifference rules, OK?

The more this story unfolds, the more scary seems the interdependence and over-connectedness of the three main powers. Between them, the Pharmas and their agents, governments and regulators, and doctors and research workers have constructed a 'health-care' system that now seems, almost routinely, to put health second and them on top.

Panorama of course illustrated the point in vivid microcosm and partly by reference to villains, heroes and victims. This was allegory, like John Le Carré's *The Constant Gardener*: how else does one encapsulate the wider point and bring it home? Only in human scale, with familiar dimensions, does full meaning begin to come clear. Statistics may point to part of the reality, but they don't bleed.

Now, in close-up, we see silky but sweaty denials from once trusted experts; they reveal not only grand arrogance, but also the crippling impact of institutional imperatives and their seductive, crushing effect on decent personal values. The human anguish that follows tops the iceberg that threatens to

sink us all. The sickness feels palpable: what is happening to humanity, honest science and real health?

These words, "*What they've done is just despicable*", were spoken by the mother of a 16-year old girl, when she later came to understand the cause of her loss. She had returned home to find her daughter hanging from the upstairs loft hatch; her body was still warm, but beyond revival. A packet of Seroxat tablets was next to the suicide note. That was in 2003, less than a month before the UK regulators published warnings about this drug – *don't* give it to under 18-year olds. This was on the basis of evidence from clinical trials that the manufacturers had held for several years.

In these circumstances, the word, 'despicable' seemed moderate. The case for meticulous investigation seems all the more compelling, when the victims include an eleven year old on paroxetine, who had used his puppy's leash to hang himself in a closet in the family home. There are too many tragic cases to mention: [Christopher Pittman](#) is another. He was prescribed paroxetine, then sertraline, and is now in the early stages of a 30 year prison sentence; he shot his grandparents aged 12 years old.

The focus in this programme was on Study 329, the centrepiece of a small series of clinical trials to investigate the effects of paroxetine on depressed adolescents and children. The scientific evidence available to SmithKline Beecham in 1998 suggested both lack of effectiveness and a possible excess risk of drug-induced self-harm.

The company held back the evidence, until the UK regulators chanced on it, in May 2003. They issued warnings soon after, estimating that the risk of drug-induced suicidality was three times greater with paroxetine than with no drug treatment (placebo). Later, the US Food & Drug Administration required a proper re-examination of the raw data: this established (2006), that the risk of suicidality, on-drug, was actually six times greater for children (three times greater for adults) than originally assumed.

Initially, the company decided not to publish the results of Study 329: memoranda now in the public domain record advice that it would be "commercially unacceptable" to disclose the facts, because it "would undermine the profile of paroxetine". Instead, the decision was "to effectively manage the dissemination of these data". This was so well managed that even sales representatives were led to believe that the drug "demonstrates remarkable efficacy and safety in treating the adolescent population". Sales (detail) people thus become potentially dangerous (if willing) victims, like the doctors who too willingly take their advice.

At this point in the programme, Shelley Jofre, the *Panorama* reporter, asked US attorney, Karen Barth Menzies what she made of that claim: "remarkable safety and efficacy". It was a lie, and fraud, she replied. The question seemed almost redundant, not just because of the weight of the evidence – but also because both of them have been chasing the truth on these issues for years. They are among the heroes, along with the brave, indefatigable Professor David Healy. He is *the* shining exception to the general rule, that these accusations have come from outside the establishment, not within.

How was all this achieved? It was of course the product of a complex collective effort, but *Panorama* could fairly point the finger at some especially conspicuous players. Two were influential and hitherto well-respected US academic psychiatrists, Drs Martin Keller and Neal Ryan. Both earned and gained very handsomely by touting the product and fronting for the manufacturers, (now GlaxoSmithKline, GSK). They too casually lent their names to misleading, fine-woven conclusions in prestigious publications, the product of assiduous ghost-writing and marketing steer.

Also conspicuous was the scarily brazen editor of a leading US psychiatric journal, *Child and Adolescent Psychiatry*. She emphasised she had "no regrets at all" about publishing the invisibly concocted and misleading version of Study 329, on the grounds that, "it generated all sorts of useful discussion".

Then there is Dr. Alastair Benbow, the Head of European Clinical Psychiatry at GlaxoSmithKline, who featured so prominently in two earlier *Panorama* programmes. Five years after the company's own evidence revealed no such thing, Benbow insisted that there was nothing to worry about. "The reality of the situation is that, in this trial (Study 329), Seroxat was generally well tolerated by this difficult to treat population," he claimed.

Meanwhile, GlaxoSmithKline has issued a bullish statement to *Panorama*: *"In developing Seroxat, GSK has always been strongly conscious of the duty it owes to the millions of patients who suffer from depression and refutes any allegation that it has failed in this duty. GSK utterly rejects any suggestion that it has improperly withheld drug trial information ..."* The statement does not specifically address *Panorama*'s concerns; the full text can be read [here](#).

So what is to be done? The short answer is almost everything, given that the so-called competent authorities have repeatedly failed to put their house in order. Previous episodes of *Panorama* have documented the grovelling impotence of the drug regulators (notably the MHRA and the FDA) and the passive connivance of the medical profession – of course with countless individual exceptions (no doubt including your doctor as well as mine).

Where do we go from here? In the immediate future, there is potential for progress on three main fronts – none politically attractive, though central to the future health and reputation of pharmaceutical medicine.

First, we need urgently to examine the meaning of personal responsibility in corporate settings: specifically, the General Medical Council (GMC) should now investigate and rule on the conduct of Dr Alastair Benbow. Both would in some way be on trial. The GMC is a professional court with feudal if honourable traditions, with still some way to catch up with the climate of the late 20th century. As for Dr. Benbow, he seemed so sincere in his advocacy for the drug, so replete with reassurance, that

his position must now be clarified. Did he critically review the relevant scientific evidence before making these claims? Was he a leader in some cynical process, or kept well ignorant and brilliantly coached in his denials? The latter seems much more probable, but we need to know for sure. Are these horrible and damaging drug disasters driven by knaves, fools, or victims - or some, none or all of the above? The GMC must now rise to the occasion: we need some definitive view.

Secondly, what of the proposed prosecution of GlaxoSmithKline by the UK authorities (led by the Medicines and Healthcare products Regulatory Agency)? In the USA, civil actions will progress later this year, seeking to link the now damning factual evidence with tragic human consequences. But in Britain, are we now due for a replay of Prime Minister Blair's recent decision to abort the bribery investigation into British Aerospace (BAE), on the grounds of national interest and security? What is the MHRA up to? Their [last word](#) (7 April 2006) was this – but [what's new?](#)

"The conduct of the investigation required the Enforcement Division of the MHRA to consider over a million pages of scientific and other documentation which comprised the factual background to the case. A team of medics and scientists from across the MHRA assisted with this. The process of considering documents is now completed and documents are only reviewed now if they come to light as new evidence. Potential witnesses from inside the MHRA have been interviewed and notes have been taken from them, from which statements will be drafted. These statements seek to convert the findings of the review of the scientific and regulatory documentation in to evidence suitable for the conduct of a criminal trial, if appropriate ... Once the criminal investigation has been concluded a file will be forwarded to prosecuting lawyers within the legal department of the Department of Health. They will apply the Code for Crown Prosecutors to decide whether or not there will be a prosecution."

Thirdly, we urgently need some proper enquiry into the conduct and effectiveness of the UK drug regulators themselves - the Medicines and Healthcare products Regulatory Agency (MHRA) - in line with the 2005 recommendations of the Parliamentary Health Committee, in

its report on '[The Influence of the Pharmaceutical Industry](#)'. The evidence from this and earlier *Panorama* programmes hugely underlines the importance of this main recommendation:

*"During this long inquiry we became aware of serious weaknesses in the MHRA. Worryingly, in both its written and oral evidence the Agency seemed oblivious to the critical views of outsiders and unable to accept that it had any obvious shortcomings, except those that could be remedied by more transparency. The Agency's attitude to its public health responsibilities suggested some complacency and a lack of requisite competency, reducing our confidence in its ability to undertake the reforms needed to earn and deserve public trust. Nor did we conclude that the MHRA provides the discipline and leadership that this powerful industry needs. **We recommend that there be an independent review of the MHRA ...**"*

This may seem a tall order, but so much seems badly wrong. This *Panorama* programme was a potent reminder of that – an emphatic, evidence-based and well-focused scream for medicines that honestly do work.

Declaration of interest: I have a critical, passionate and long-standing interest in the SSRI antidepressant story: see [Medicines out of Control?](#) I played no part in the making of this *Panorama*, but undertook (with Dr Andrew Herxheimer) an analysis of viewers' emails for the second programme in the series, for which I was paid about £1,350. I was also engaged (2004/5) as a specialist adviser on the Parliamentary Health Committee enquiry into [The Influence of the Pharmaceutical Industry](#).

Charles Medawar
30 January 2007