

REVIEW ARTICLE

Miriam Shuchman, The Drug Trial. Nancy Olivieri and the Science Scandal that Rocked the Hospital for Sick Children, Random House, Canada 2005, ISBN: 0-679-31084-3

The Drug Trial follows the synthesis of deferiprone in England in the 1980s, and growing hopes that it might replace the then standard treatment for thalassemia, deferoxamine, which was effective but inconvenient and uncomfortable. Thalassemia is the commonest single gene disorder in the world. Prior to deferoxamine, it led to disfigurement, early deaths, and social stigma. One of the standard bearers of deferiprone was Nancy Olivieri, who in the late 1980s and early 1990s was working at the Hospital for Sick Children, and the University of Toronto. Once an enthusiast for deferiprone, Olivieri became aware that it did not seem to work as well as deferoxamine. At this point in its evolution, the main deferiprone trial was sponsored by a pharmaceutical company, Apotex. Apotex neither welcomed Olivieri's growing suspicions nor shared her belief that the patients in the trial should be informed of emerging doubts about the new drug. Rather than warn, the drug was removed from Toronto overnight. When patients turned up for their treatment, they found a bewildered hospital staff, who had neither a treatment nor an explanation to offer. The deferiprone study continued elsewhere.

Many of the reviewers of this book have conflicts of interests, but have not always made them fully clear. Miriam Shuchman gives no indication about any conflicts she might have, other than what might be inferred between the lines. I have a bunch of conflicts that cannot be ignored. First, I think Nancy Olivieri is fabulously attractive, charming and a force of nature, just as this book makes clear many of her patients thought and continue to think and Miriam Shuchman appears to have once thought, and now portrays as a hazard for any of the men who come into Olivieri's ambit. Second, she's been sacked by the University of Toronto department head, as have I. Third she works clinically, as do I. Fourth she's been subject to what seems a highly personal attack, as was I.

Lets lay some of these conflicting forces out on the table. While lecturers and researchers perhaps risk something similar from disgruntled students or colleagues, clinicians are in a very tricky situation when it comes to 'whistle blowing'. People, at their most vulnerable, come to them with a myriad of anxieties and expectations, and some of these people are inevitably frustrated. They may be frustrated by a failure of communication or by the very real mistakes that happen when practice has to be conducted in situations of dangerous uncertainty. Bottom line is if you want to dig up dirt on even a sainted and fabulously wise clinician, there will always be patients happy to talk about simmering grievances, and colleagues who can point to 'errors'. It should be possible to get material like this with little risk of the patients writing in afterwards to

claim they have been misrepresented – as has happened following the publication of this book.

If you queer the pitch for some drug, from which a pharmaceutical company stands to make millions, and you later ask that company under freedom of information provisions for material they hold on you, or you have a chance to hunt through their archives, what might you find? You might find instructions to have people planted in the audience to challenge claims you make. You might find debates as to whether you can be sued for claims made. You might find efforts to target your junior staff. You might find policies to refuse funding for meetings you organise or in which you participate. You might find notes from phone conversations with people you thought were close friends and who you thought agreed with your point of view, and these notes seem to show them saying pretty much the opposite to some company person to what they may have said to your face only a few days before. Now why, when there is lots of material germane to the drug's hazards that probably should be in the archive but isn't, would something like this fall into your hands instead?

And what do colleagues, who of course are uninfluenced by pharma commercialism and deplore its influence on others daily before breakfast, and who think the industry is populated by scurvy knaves, do when one of their own blows the whistle on some industry practice? In most clinical settings, there are annual awards of good citizenship bonuses, designed explicitly to be given for standing up for patients' interests, or for discovering something or bringing it out in the open – awards that sound tailor made for a clinician who goes out on a limb. So does Nancy Olivieri get any awards of this sort? No whistle blower does. Pretty soon, you realise it's not just the things you know you're not getting that you're not getting, you're also not getting the things you don't know you're not getting.

Now if this isn't enough to induce paranoia, there are what might be termed the academic stalkers. For instance in my case, a series of letters to newspapers, and posts on listserves and finally an article on the martyrdom of DH. Some of the claims made in these pieces when first outlined were ones that I had only seen made by pharmaceutical companies before that, and it was difficult to see how they could be made without access to pharmaceutical company sources.

Since then I've come across emails from third parties claiming to know the truth about Healy, reiterating points made by Coyne (2005). I've had phone calls from friends in various parts of the world telling me they've had senior figures from world psychiatry pass through their institutes who warned them that Healy was trouble and would soon be in trouble – and this was even before I lost my job. The interesting thing about these figures was that none of them knew me or had ever heard me talk to the issues, on which I supposedly held dangerous views. And when invited to participate in debates, they balk, or if present at lectures I have given, none of it seems get round to pointing out any errors or even asking questions. How this all ties in to company PR documents that list Healy as a problem to be handled is anyone's guess.

Having investigated the Olivieri case, long before this book came out, I can say that there are lots of similar background events in this case that just do not feature in The Drug Trial. I can also say that again and again, the specific details outlined in this book seem to me simply wrong. But if we cut to what is a bigger issue - the biggest difference between Nancy Olivieri's case and mine aside from the fact that she was sacked more

than once – this lies in the extent to which she has been attacked personally. Nothing like this book by Miriam Shuchman has happened to me.

If you read this pacily written book without having first been beguiled by Nancy Olivieri, what are you likely to take out of it? Well given that even I with all my conflicts found myself thinking at times the author sounded pretty even handed, I can only imagine that someone much less biased than I but also less aware of some of facts would find it pretty persuasive. On this account, Nancy Olivieri in all likelihood got the science wrong, and her claims to be a heroine are based not on the science but on a stunning public relations coup that has fooled almost everyone, except a few Executives in the Hospital for Sick Kids, whose efforts to put the record straight have been thwarted at every turn.

Again and again the events are seen through a prism of sympathy for those who have been portrayed elsewhere as the villains of the piece. Take Gideon Koren, an early collaborator in the deferiprone trials, and in many respects Shuchman's hero in this tale. Until recently Koren had an unbelievable annual output of articles, some on issues that he had limited expertise in. For instance, on the basis of relatively small samples of pregnant women he claimed that there was little risk from taking SSRIs during pregnancy and it would be much worse to leave a depression untreated. Much larger samples now point to a significantly increased risk of birth defects from the drugs Koren endorsed. Shuchman touches on none of this.

In the midst of this saga, Koren sent a string of anonymous hate mails to Olivieri's colleagues. As Shuchman reports and is documented in Thompson et al (2001), Koren was the principal witness in proceedings against Olivieri while he simultaneously was sending anonymous harassing letters against her and her strongest supporters. His testimony against her was eventually proven incorrect and Olivieri was fully exonerated by independent inquiries. In contrast, Koren was disciplined by Sick Kids' Hospital and the University of Toronto for misconduct in sending the anonymous letters, and in then repeatedly denying responsibility until he was identified as author by DNA evidence. He was subsequently disciplined also by the College of Physicians and Surgeons of Ontario (CPSO) for his 'vicious diatribes against his colleagues ... His actions were childish, vindictive and dishonest.'

I'll leave it to the reader to guess how Miriam Shuchman might portray this episode in a manner that generates sympathy for Dr Koren.

In the case of the difficulties the leaders of the Hospital for Sick Kids and the University of Toronto had in getting to grips with the issues, Schuchman sets these in the context of a series of events that took place at a time when the interface between academia and industry was changing and new rules for regulating the interactions of academics and industry were being worked out. Now that the rules have been worked out, it's implied, nothing similar could happen again. You'd never guess from this book that other academic freedom cases blew up in Toronto after the Olivieri affair.

It is important that the author have sympathy for all parties as disputes like this will often be events that involve perfectly decent people making mistakes and getting caught up in new forces they only dimly understand rather than events that have been perpetrated by agents of outright evil. But the sympathy should be even-handed and in these pages Olivieri comes over as manipulative, mean and more concerned about her looks than anything else and her supporters seem like duped innocents. The least worst assessments are that driven people can be difficult, and the concession that she is a wonderful public

speaker – but so are many dangerous people. She is criticised for not recognising the hazards that others suspected before she used the drug and criticised for her later conviction there were hazards when others were less certain.

Olivieri is accused of having a PR agent, but there is no effort to record whether the Hospital or University had PR agents. The idea that Apotex might have any idea what a PR agency is as far off the radar of this book as mentioning Per Rectal examinations might be in polite company. Olivieri is portrayed as surrounded by lawyers, but there is little emphasis placed on the fact that she and her supporters and the Canadian Association for University Teachers had to fork out for substantial legal bills, while in contrast the Hospital for Sick Kids and the University retained some of the most expensive lawyers in Canada and in this case the fees came out of taxpayers' money.

But writing sympathetically should be just a first step to reaching the issues beyond the personalities, and the real problem with this book is that the author doesn't get to any issues. There is no questioning of what is happening in our universities, which were once places where poorly paid academics behind a bastion of tenure could question the power of Church or State. But our universities are no longer bastions of intellectual liberty. It is perilously easy for an academic to lose their post if they don't sign on to the new corporate agenda, while a growing string of exposures that academics from some of our most prestigious institutions have had their articles ghostwritten for them or been in receipt of up to a million corporate dollars per year has led to none of them being sacked or even censured. In fact it's difficult to think of anything that academics might do today in terms of working for business, short of a lengthy jail sentence, that might give them problems on our new corporate campuses. The current situation would have been unbelievable a few years ago, and is worsening, but there is not a hint of that from this book.

Starting right from the subtitle, *The Drug Trial* dodges the key issues by claiming that this is a scientific rather than an ethical scandal. If Olivieri got the science wrong, she ipso facto got the ethics wrong, and to say that she was right to speak out, that this was about academic freedom rather than scientific accuracy, is soft-headed. Pitching the issues this way pitches ethics against science. But in fact science is pretty well by definition never right - today's truth is tomorrow's shibboleth – and the ethical pressures get ever more intense the more ambiguous the details a scientist is faced with. If it turns out that Apotex's drug has some benefits for the heart in some patients with thalassemia, as the book suggests, this would no more invalidate the call that Nancy Olivieri made than recent findings that thalidomide is an excellent treatment for leprosy now invalidate the efforts of Siegfried Lenz to raise concerns about its teratogenic effects.

The key issue is whether in the face of ambiguous clinical trial data, a clinician treating patients should err on the side of the patient or on the side of the corporation that hopes to make money out of future patients. Shuchman glides over this by arguing we learn to live with the problems that many two-faced drugs cause by warning about hazards, but Apotex resisted warnings and recent experience with a range of drugs across all medical fields shows that corporations have to be dragged to court before they warn. From Chemie-Grunenthal, the makers of thalidomide, through to Apotex, it has always been possible to convene panels of experts who will come up with other explanations for inconvenient data, and will dismiss safety concerns as premature.

Shuchman cites Floyd Bloom, a former editor of Science and Chief at Scripps, as saying that researchers contracted the way Nancy Olivieri was handed over their rights. The company owns the data. But this is far from clear. This book offers no legal basis for saying Apotex in this case, or other companies in other cases, own the data. And there is a third party to these contracts, the patient. The consent form patients sign is a contract, but one that misses out a critical detail - namely that the company will seek to withhold all data from study participants, their clinicians or other clinicians in the future. The Drug Trial could have usefully asked a wider public what they think of this.

There are many compelling dilemmas that this book could have addressed. Instead it focuses exclusively on the swirling torrent of forces rushing through a particular controversy, the influences of money, power, fame and revenge. The facts, like rocks, occasionally protrude above the surface. With goodwill we might all agree on what's visible, but as outsiders we can only dimly make out or guess at what lies beneath. In the torrent that is the Olivieri case is it possible to hop from rock to rock and get to the far side? Not if you read this book. There have been two inquiries held, one instituted by the Hospital for Sick Kids, that found the Hospital and University blameless, and the other commissioned by the Canadian Association for University Teachers that found unequivocally for Olivieri. Shuchman passes both off as partisan, without rebutting any of the points made in the latter, leaving us stranded in mid-torrent. But Olivieri's case has also been reviewed by the College of Physicians and Surgeons of Ontario who found her behaviour 'exemplary', and this would seem to provide a bridge to the far side.

But if Olivieri's behaviour was exemplary, how come we now have a book casting doubt on this verdict? The field of bioethics focuses heavily on questions about the influence of private money and company corruption on research, and many ethicists back up tough talk by refusing to take a cent from company sources. But these are relatively straightforward and superficial issues. If bioethicists are going to get to grips with what's going on in science today, they will have to get down deep and personal. The field will need to have some method for taking into account the fact that everyone who has spoken out about a drug from Siegfried Lenz to Nancy Olivieri has had their public detractors who commonly rely heavily on unnamed sources. There are enough examples now that they cannot each be dismissed as *sui generis*. Maybe it's just my conflicts of interest acting up, but I'd like to know more about the ethics and motives behind an *ad hominem* academic mugging of this sort and what bioethicists plan to do about it.

References

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