BOOK REVIEW

Conflicts of interest

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Allison Bass. *Side effects: a prosecutor, a whistleblower, and a best-selling antidepressant on trial*. Chapel Hill, NC: Algonquin Books; 2008. 260 pp

Concepts such as conflict of interest and transparency could make for dense reading. In Side effects, Allison Bass shows that this needn't be the case.

Bass covers medicine, science and technology for the Boston Globe. Here, she knits together the stories of the people behind a path breaking campaign for transparency in the drug trial business. This is the story of how the New York State attorney general's office took GlaxoSmithKline to court for concealing information on the efficacy and safety of its drug Paxil - and won.

Among the lead characters in this book are a psychiatrist who tries to alert the medical profession to a drug's dangers, an administrator who blows the whistle on the chief of psychiatry for doctoring trial data, and a couple of gutsy lawyers ready to scrap with Big Pharma.

And on the other side are a profit-hungry drug industry, gaggles of researchers on the industry's payroll and ready to provide the right research findings, and a regulatory system that rushes through a drug's approval despite evidence that some patients would suffer serious side effects.

The practice of psychiatry was revolutionised by selective serotonin reuptake inhibitors (SSRIs), believed to be as effective as the older generation antidepressants but with none of the side effects. With aggressive promotion, SSRIs soon became top-selling drugs. Bass notes that in 2002, GlaxoSmithKline's Paxil was the world's best-selling antidepressant with $3.3 billion worldwide sales.

GSK also made huge profits through off-label marketing. As articles were published in respected journals establishing the drug's safety in children and adolescents, doctors started prescribing it as safe alternatives to the traditional anti-depressants. In 2002, GSK made $55 million through sales of Paxil in children and adolescents.

Assistant attorney general Rose Firestein was investigating off-label marketing when she stumbled upon a USFDA announcement: studies had found that Paxil did not work any better than placebo for children. And the UK health authorities issued a warning against the use of Paxil for children. Reports started coming in that these drugs sometimes triggered suicidal thoughts and behaviour. And such side effects were more common in children. But this was not reflected in the published literature.

Bass describes the unearthing of a nexus of multiple conflicts of interest behind the industry's market grab–a nexus entrenched in the drug industry, and not restricted to a few "bad apples". Is India any different?

The book talks about researchers who are paid to recruit their own patients into drug trials and publish only positive findings. Academic institutions rely on drug companies, compromising their independence in research. Doctors are paid handsomely to promote the drugs at conferences and in publications. When patient support groups get funds from drug companies they may choose industry interests over patients. (This is a new concern in India where support groups need to be watchful of their funding sources.) Then, the US FDA depends on industry funding (the drug review budget went from 7% in 1993 to 53% in 2004), making it reluctant to act against the industry even when it harms patients. Bass packs the book with such details to flesh out the larger picture.

Readers will be struck by the sheer guts of the fighters, given the odds that they face. Assistant district attorney Rose Firestein is losing her eyesight but refuses help reading hundreds of pages of documents for the lawsuit. Psychiatrist Martin Teicher testifies on Prozac's serious side-effects and has his reputation and his practice torn to shreds. Donna Howard is a single mother struggling to raise a child with bipolar disorder but this doesn't stop her from speaking out when she finds her senior fudging trial data.

Bass focuses on the harm caused by conflict of interest and the lack of transparency. The industry's drug promotion requires that it withhold publication of negative results. Indeed, this is a major ethical issue in industry-sponsored research today. Another related issue is the use of placebo controls, especially of psychiatric drugs. Seriously ill patients are harmed when they are given sugar pills to establish that a new drug works. However, this merits only a passing reference.

In August 2004, the attorney general of New York State arrived at a settlement with GSK. The deal included setting up a public registry with the results of all company-sponsored clinical trials–a requirement that was later extended by the government to all drug companies. Many other changes have taken place around this time. Public clinical trials registries have been set up and the major medical journals refuse to consider trial reports unless the trials were registered before they started recruiting patients.

From the little that we do know, the world of medical research and practice in India is rife with conflicts of interest. Do patients being recruited for a clinical trial know their doctor-researcher is paid to recruit them? No. Do doctors inform their patients if they've received a freebie from the company whose drugs they are prescribing? No. We can only guess that what we do see represents the tip of the iceberg.