Between two cultures: the expert clinician and the pharmaceutical industry

Edwin AM Gale

Author details
Edwin AM Gale
MA FRCP, Professor of Diabetes and Metabolism, Division of Medicine, University of Bristol

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ABSTRACT – Expert clinicians, valued for their academic status and independence, are used by the pharmaceutical industry for advice, for contract research, and as a means of conveying their message to other clinicians. Both academics and industry depend upon this interaction, but there is a fundamental clash of cultures at the interface between the two. Independence cannot be marketed for a fee, opinion too easily shades into advocacy, and secrecy and science do not mix. Formal guidelines and declarations of interest are inadequate as a means of policing an interface where undisclosed amounts of money change hands so freely. In the absence of effective sanctions, each of us must seek a personal solution to the professional and ethical issues involved.

KEY WORDS: conflict of interest, sponsorship

'The rich are not like other people,' said Scott Fitzgerald, 'they have more money'. So have the pharmaceutical companies. How much do *you* make from them? For most readers, probably not much – perhaps the odd 'free' lunch or sponsored trip to meetings. Your unit may have a nurse funded by a drug company; you may take part in a study in return for a bounty paid on each patient; or you may receive a fee for talking to local general practitioners. If you have been picked out as an opinion leader, your price tag will be higher. You may speak at drug company symposia (going rate £1,000–£6,000), be offered payment for writing a review, or participate in advisory boards at the local, national or international level. You may do occasional consultancy work, be paid a large retainer to act as an informal adviser to a company, perhaps with the muttered comment that such an arrangement could remain entirely private if you so wish, or you may act more formally as a consultant advising about the design of drug trials or preparing clinical expert reports for regulatory submission. The list does not stop there but I will, since this is the limit of my own experience. I enjoyed working with the companies, and stayed within the guidelines – so why the sense of relief when I decided to limit these activities?

Little attention has been paid to people like me and the role we play at the interface between industry, regulatory agencies, academia, and the health service in which we work. My own eyes were opened in 2000 when a friend asked me to review the thiazolidinediones at a European meeting. When I named others who knew more about the subject than I did, he surprised me by saying that all the experts he knew had funding from the companies, and that he wanted someone from outside the system. I thought this was carrying purity to extremes, but agreed to do the job. There was a lot to learn about the drugs themselves, but in the end it was the process by which they reached the hands of the prescriber that came to fascinate me most, together with the roles and responsibilities of the expert clinician.

When I arrived to give my talk, I was perhaps more sensitive than usual to the familiar format of all big scientific meetings. Centre stage were the stands of the drug companies; clinicians interested in unsponsored science had to seek it in the peripheries. The 'clinical interest' presentations were mostly in plush symposia sponsored by the drug companies. Meanwhile Disneyland reigned. Mickey himself was replaced by characters dressed up as Mr Muscle and Mr Fat, and clinicians could pose for photographs between them. A miniature Zeppelin zoomed overhead, tour buses came and went, and the stands were thronged with those wishing to enter a quiz, pick up a freebie or have their portrait taken in kindly caricature.

My talk described a system in which, despite the efforts and goodwill of many involved, expensive and potentially useful new drugs come to market without the evidence needed to use them effectively. Evidence-based medicine is the first casualty of drug development. Why? Because the pivotal studies are designed, analysed and presented in such a way as to favour the positive aspects of new drugs. The randomised controlled trial might seem an impartial oracle, but those who do not know how to set one up to bring in the desired result are probably not on a company payroll. When things go wrong, there is always the option of 'losing' a study or hiding it behind a misleading abstract that never sees full publication.[1] The conclusion seemed clear: evidence-based medicine was falling at the first hurdle when it came to the introduction of these important new drugs, and the gap had been filled with skilled misinformation.

Industry does what it must. A pharmaceutical company makes a profit or goes under. This is the system that brought us swift silent motor cars, mobile phones, personal computers, ACE inhibitors and statins. The problem, as always, is one of balance. The big companies have become victims of their own success, and the healthcare system suffers because expenditure on drugs is growing faster than the total healthcare budget, siphoning the money needed for growth into payment for drugs that could and should cost less. Meanwhile the traditional core business of developing and selling innovative drugs has fallen behind market expectations. The Food and Drug Administration approved 35 new molecular entities in 1999, 27 in 2000, 24 in 2001 and 18 in 2002.[2] We are locked into an unsustainable pattern of growth, the legal department is increasingly crucial to the survival of the pharmaceutical giants, and the battle for market share is set to become more ruthless. This is the world of big pharma, the first of our two cultures.

The second culture is our own, the world of clinicians who struggle to make sense of a flood of data and to use it for the benefit of their patients. Straddling the two cultures is the expert clinician.

Between two cultures

The transition can be abrupt. A friend met her manager on the day she started work for a company. 'Who are you working for now?' he asked. 'The patients?' she ventured. 'No,' he said, 'you are working for the shareholders.' A drug company obeys the law of the jungle. Its survival depends upon sales, which depend upon the doctors who prescribe its products, people who exist within a quite different culture. They can be reached by direct marketing, but we all know that the drug representative who befriends our secretary is paid to persuade. The expert clinician becomes a key intermediary.

Expert clinicians have two main roles: advice and advocacy. There are experts with special skills or knowledge, and experts needed for an opinion as to a therapeutic concept or research protocol. The invited expert should be on the alert for loaded questions; big companies are astonishingly insular, and boardroom power struggles influence major decisions. No-one knows this better than management consultants, who make their reputations by identifying what the most powerful faction within the client organisation wants and then endorsing it. In some environments no opinion is neutral, as I learned when I criticised a study design and someone got the sack. Fair enough, perhaps, except that those who invited the report probably knew what I would say.

Most expert clinicians are called upon late in the development pathway, and for advocacy rather than advice. The company with $100 million invested and reputations on the line has little interest in wise-after-the-event criticism, and nothing is more deaf than an organisation that has made the wrong decision. Experts are needed to create a climate of opinion favourable to the new agent. Respectability is conferred by senior physicians – known as 'silvertops' in the trade – whose knowledge is often remote from the subject area. Younger opinion leaders are sought according to their rank within the pecking order, but no-one is excluded, on the principle that the fairy not invited to the party is the one that causes all the trouble. So it is that experts who despise one another will be found on board, although at opposite ends of the ship.

Recruitment of centres for clinical trials requires tact. Few things in life are more boring than running someone else's drug trial, and leading academics are generally not very good at it. A common compromise is to associate one or two known names with the study with no expectation beyond authorship. Many academics steer away from drug trials, but others thrive upon them, and young investigators can rise on the back of a successful product. They have, for example, performed some of the initial studies and presented them well; from there they graduate to the status of spokesman for a brand, and – if successful – are now courted by its competitors. Soon no symposium is complete without them. Their risk becomes that of any media celebrity – memorably defined by Daniel Boorstin as 'someone who is famous for being well known'[3] – and they are fair game for any comer who sparkles more at the podium, writes a sharper review or, ironically enough, has not as yet acquired the reputation of a big pharma groupie. More routine is the role of the advisory panellist, whose opinions are respectfully noted and fed back to the marketing division whose task it is to modify them.

Whatever their category, the company needs acknowledged experts to present information about their products to national or international meetings, and to write reviews. But what motivates the expert clinician? Money does of course come into it, and some doctors exhibit a naive and bare-faced venality that is almost beyond belief. Emulation matters, since few academics will willingly cede a rostrum to one of their rivals. Flattery works well on those who suspect themselves of the highest motives. Self-interest and self-esteem are, however, only part of the story. Clinicians in the UK work within a grid-locked and dispirited healthcare system that accords them little respect, where even the simplest change requires endless time and patience to achieve. Would I choose to stand in some shabby clinical room watching yet another blood pressure cuff unpeel itself as I pump it up? Or would I rather be in a plane en route to a meeting where big decisions are made and funded with a clasp of the hand? It is both flattering and lucrative to attract this level of attention, and business class tickets can erode the sternest resolve. It is, for example, extremely galling for an invited speaker to fly to a scientific meeting in the economy section whilst his audience lives it up at the front of the plane.

Working with a company is, however, more subtle in its effects. The 'liar for hire' is of limited value compared with the individual whose integrity is respected and who speaks with conviction. The expert enters an exciting new subculture when he signs a confidentiality agreement. He now has access to privileged information, and meets a group of highly committed individuals whose lives revolve around a single product. These people are not cynical. Their intentions are good and their faith is genuine. The expert who stands up to represent this team at important meetings does not want to let them down. He falls victim to the effect

described by Machiavelli when he commented that 'it is of the nature of men to be bound by the benefits they confer as much as by those they receive'.[4]

The free lunch

On one side are large organisations with massive spending power; on the other are people willing to absorb some of the surplus. There is overwhelming evidence that financial links influence the opinion and behaviour of expert clinicians, as witnessed for example by the immense literature on the effects of drug company funding on the outcome of clinical trials. Others are prepared to lend their names to manuscripts ghosted by the medical writers employed by all companies, professionals who often write much better than the big names they support, and whose hand can be detected by standard phrases and references which recur in paper after paper regardless of authorship. Others again represent the product on the platform of symposia, or by going on lecture tours from one city to another. How much do experts earn for doing all this? Only the experts really know, and they are not saying. Not that I am against personal profit. Skill, judgement and hard work deserve their fee. The companies need expert clinicians, and clinical medicine would suffer if drug company support for education and research were to be withdrawn. Nor do I share the distaste one company doctor expressed to me as we watched clinical colleagues meeting up at the airport with cries of 'Who are you with?' and 'Where are they taking you?' The drug company junket is open and innocent enough, and the participants have after all (with some help from the taxpayer) earned their tickets. In my view, it is not the movement of money but secrecy that corrupts.

The role of an academic is to evaluate evidence, to dissect the soft from the hard, to identify gaps, and to present his findings without fear or favour. The role of a clinician is to identify and use the safest and most effective forms of treatment. Both these roles are compromised when every leading expert is on a company payroll. Authors of influential reviews are usually funded by the companies whose products they discuss, which may be why few reviews of new therapies offer serious criticism, demand better evidence, or fail to end on a favourable and optimistic note. Editors of medical journals seem to be losing the battle for open disclosure, a battle they cannot win so long as statements made by authors cannot be verified and there are no sanctions to enforce against those who transgress. There is a widespread assumption that you are not under oath when it comes to conflict of interest statements, and creative ways of navigating this obstacle have emerged. One ploy is to declare links to multiple companies, with no obligation to point out that company A pays me a handsome retainer, company B supports my research unit, and company C once took me out to dinner. Nor is there any obligation to declare anticipated future benefits, although expectation is a more potent motive than gratitude. The other tactic, used increasingly, is to deny everything. This I know, not just on the basis of privileged information, but also because of the publication record and speaking engagements of some authors. Why tell a lie that will be obvious to some at least of your readers? Only because you think that everyone else is doing the same, or, put another way, only because the currency of academic exchange has become so debased that honesty no longer matters.

Many benefits flow from the necessary interaction between academic doctors and the pharmaceutical industry, and from the new drugs themselves. There are many honest people on both sides, and there are many examples of good practice in this area. None of this I dispute. What must concern us all is the existence of a double standard in academic medicine. Like any other form of corruption, this is insidious in its effects, and flourishes in an environment of secrecy and acceptance. Secrecy is an essential part of the business world, and companies are under no obligation to produce an unedited version of the information at their disposal. In contrast, academics are accountable when they carry out non-commercial research. They are open to challenge and replication, and risk disgrace if they are found to be fiddling the results. The academic who moves from one culture to another is no longer accountable. He has no personal responsibility for the data he presents, typically unavailable to those who might wish to challenge it, and the money he receives from the company is regarded as his own private business. He looks sideways and sees his colleagues providing cosmetic accounts of competing products, and he begins to do the same. Bad science drives out the good.

Many of those involved in this type of work will insist that there are excellent guidelines to regulate our behaviour, and that any activity that is not forbidden is by definition legitimate. The latter claim may have some legal justification, but bad science is not illegal. The problem with regulation is that the smart money will always be one step ahead. The image that comes to mind is the situation in Germany immediately following reunification, when the lawbreakers drove BMWs and the East German police were expected to pursue them in the underpowered vehicles provided by state socialism. Regulation will always be ineffective where large amounts of money flow underground and its recipients are protected by secrecy, since effective safeguards could only be imposed at the cost of unacceptable intrusion into private life.

Is there any way back? The problem is that too many people benefit from the way things are. These benefits are not only at the individual level; academic institutions welcome the high overhead income generated by commercial contracts. Nowhere else in medicine is there quite such a stark contrast between the private and the public interest, or so much special pleading in place to deny it. The libertarian banner is waved vigorously by a profession that feels over-regulated in every other field of activity, but the more venal we appear, the less we will be believed, and the greater the restrictions that will be placed upon our freedom to prescribe the drug we consider most appropriate. Everyone suffers from a situation that benefits only a few.

An expert is hired for his opinion. The expert clinician moves too easily across the invisible divide between opinion and advocacy. His value lies in his reputation for independence and integrity, but these qualities cannot be marketed without the risk of compromising them. There is too much secrecy at the interface of industry and academic medicine, and too much

money going across it; the honest work done by the many is devalued by the dishonesty of the few. It is too easy to be drawn into this world by imperceptible degrees, bolstered by special pleading and fostered by the prevailing culture of secrecy, complicity and cheerful cynicism. Wriggle as we may, there is only one standard of honesty. The tough question for all who move between the two cultures is this: whose doctor are you, anyway?

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Conflict of interest statement

My current policy is to avoid all roles implying endorsement or advocacy, and my drug company income has fallen to £5–10,000 annually.

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