The Drug Industry

The public image

TONY SMITH

Ask the average, reasonably intelligent, literate Englishman, or indeed Western European for a snap reaction and he will say doctors are "good" but drugs are "bad." An American will probably add that doctors are too much concerned with making money.

The past 20 years have seen a gradual change in public attitudes to drugs, medicines, and vaccines from adulation to profound suspicion. In the immediate postwar years antibiotics dramatically cut deaths from tuberculosis, pneumonia, and eventually almost all bacterial diseases, while vaccines virtually eliminated poliomyelitis and controlled other virus infections. For a while drugs—and the pharmaceutical industry—rated high in public esteem and modern therapeutics was seen as one of the most worthwhile technical advances of the current century.

Disenchantment began with the catastrophic epidemic of deformities from thalidomide, compounded by the sorry tale of calculating pragmatism that emerged as the victims sought compensation. Next, critics such as Ivan Illich began to point to the failure of modern medicine to cure or even alleviate many of the non-infections, chronic disorders; and Thomas McKeown argued that most of the drop in mortality this century in Western countries was attributable to improvements in hygiene and not to any advances in clinical medicine. During the 1970s a series of reports linked first cyclamates and later saccharine with bladder cancer in rats; oral contraceptives were shown to cause thromboembolic disease and liver tumours; breast cancer was attributed to reserpine; and addiction to tranquillisers was portrayed as a major public health problem.

Changed views

The net effect of this tide of adverse publicity was that the public image of drugs changed. One of the characteristics of our society is the polarisation of attitudes, so that concepts (union closed shop, for example) and technical innovations (nuclear power stations) are seen as issues which have to be decided in Yes or No, black and white terms. They have supporters and opponents (and a silent majority who do not care one way or the other). Few people have thought about the issues and stayed in the grey areas of qualified approval or provisional rejection. Perhaps a midspectrum assessment which sees both faults and advantages is too difficult: for whatever reason the image of drugs and the pharmaceutical industry as projected by the press and television has switched from a belief that every new drug is a breakthrough to the sour certainty that drugs have dangerous (and possibly concealed) side effects and are also often ineffective.

This progressive change in public attitudes is, I believe, an important factor in determining the policies of drug regulatory agencies (whose scientific advisers may be independent, but whose secretariat take their cues from their political masters) and has been responsible for the low profile maintained by the pharmaceutical industry.

On the other hand, the informed critics of the pharmaceutical industry have valid targets at which to aim. In particular, some doctors in clinical practice complain that they are subjected to a sustained campaign of high-pressure advertising to persuade them to prescribe the newest (and, therefore, *prima facie* the least well clinically tested) representative of certain categories of drugs. Why is it, these sceptics ask, that after propranolol come another 20-odd beta-blockers—though propranolol remains in use as an effective, reliable drug? Why was it totally predictable that cimetidine should be followed by a whole range of look-alikes? Why does each decade see its new generation of minor tranquillisers and hypnotics, though chlordiazepoxide, nitrazepam, and diazepam are now so fully investigated?

Commercial realities

Part of the answer is that doctors who make these sorts of criticisms have no experience and no comprehension of the world of commercial realities. The top 20 or 30 pharmaceutical companies in the world—the major innovators—can stay in business only so long as they remain profitable. The consumer organisations and the general public seem unaware that pharmaceutical companies are going out of business, being merged and being absorbed into bigger companies. At least part of their ceaseless quest for new drugs is a frenetic attempt to maintain a share of the market and to maintain profitability in a hostile climate. How far regulatory agencies, governments, and other official bodies are justified in intervening in the activities of the drug industry is as much a matter of political as of scientific opinion.

"We need to remember," said Dr Smith (Director of Clinical Research and Drug Development with Hoffmann-La Roche, Basle), "that drug regulatory agencies were set up to assess the safety of each individual compound as it was presented to them. These committees were not set up to look at relative safety and efficacy nor at cost effectiveness. That seems to be changing. The individuals who serve on these agencies and committees tend to respond to different, newly fashionable notes in the songs of the watchdog groups and consumer pressures." One of these fashionable cries has become "Do we need another beta-blocker?" Whether or not to develop a drug is a commercial decision, and the regulatory agencies' duties should be confined to assessing its safety, argued Dr Smith. "All too often the critics assume that the 10th—or 21st—beta-blocker may be a straightforward 'me-too' with no significant clinical advantages. Yet in practice it may be quite

late in the development that unexpected—but very real—differences emerge that give a new drug substantial practical advantages over its predecessors. If a company could produce a new beta-blocker which had significant pharmacological benefits over its rivals, if it had clear advantages in convenience or cost, or if it was better tolerated by asthmatics, diabetics, or patients with heart failure, then it would be a valuable therapeutic advance. The pharmacology of beta-blockers is complex; but there is a hope that the 21st or 30th will provide a substantial further benefit to patients." He warned against crusades under the banner "Three drugs for each disease are enough"; such a policy would prevent the wider experience of drug usage after marketing, which often defined their true place.

Like Dr Smith, Dr Rondel (Director of Clinical Research (Europe) at Bristol-Myers) saw no reason for concern just because there are many beta-blockers on the market. "Ultimately physicians will choose the one or two that they want to use. There's always pressure when a new compound is first introduced to persuade everyone to use it; but doctors are inherently conservative and in time the medical and market forces reach an equilibrium. Furthermore, only with accumulated clinical experience do clinicians come to appreciate the range of individual variation in response to drugs, which help to justify the numbers of, say, minor tranquillisers that continue to be marketed.

Apparent affluence

Perhaps the indignation felt by many critics of the drug industry is fuelled by its apparent affluence. Doctors have become used to pharmaceutical companies acting as fairy godmothers—inviting them to lunches, weekend meetings, and international conferences and always picking up the bill. A mass of glossy advertising material and free journals supported by advertising pours through every medical letterbox. Some clinical pharmacologists and other physicians in academic environments are often genuinely shocked by this "conspicuous consumption." In the eyes of the pharmaceutical industry such critics make two fundamental errors. Firstly, they believe that doctors are rational beings and need only the facts to be placed before them to reach rational conclusions. "In reality," said Dr Janssen (President, Janssen Pharmaceuticals), "let us suppose the pharmaceutical industry had tried to use completely scientific methods of promotion. What would have happened? This promotional material would not have been read by more than one in a thousand and most of those who tried to read it would not have understood it. After 10 years of practice typical general practitioners are very far removed from the scientific world. Unless we use the right language, which I usually call slogans, they are not going to understand." Dr Janssen does not like what he sees: "It frightens me," he commented, "that the general medical community throughout the world is largely influenced by slogans and its convictions are based on slogans." But denial of that reality will not change it.

Secondly, the critics seem to expect pharmaceutical companies to solve medical problems; they do not acknowledge that the prime requirement of such companies must be to develop and market drugs. For example, the multinational companies have been widely criticised for giving too little attention to the medical problems of countries in the Third World. "This is an unfair criticism," says Dr Janssen. "These critics—and the public at large—do not realise that most of the parasitic infestations so common in tropical countries are treatable with cheap, safe drugs but that there is no distribution system to get these drugs to the villages where they are needed."

The fundamental problems, he explained, were lack of interest on the part of the local political leaders and ignorance and illiteracy on the part of the population. Many African countries have 90% of the population infested with roundworms;

treatment costs only a few pence. "It is technically feasible to do a great deal more for most tropical diseases," said Dr Janssen. "But very often what is needed is mass treatment of at least 80% of the population; and no way can yet be found to get that sort of commitment."

Public image

The most important misconception, however, is the public image of drugs as conforming to a stereotype of minor tranquillisers or sleeping pills taken for trivial reasons. Clearly drugs taken in these circumstances need to carry a copper-bottomed guarantee of safety—the sort of guarantee that can never be given with a new drug and hardly ever with a well-established one.

This unrealistic expectation of absolute safety has extended to all drugs and is reflected in the policies of drug regulatory agencies. "Some drug agency staff believe," said Dr Smith, "that they are open to criticism if they give approval to a new drug and there is a modest increase in adverse reactions. They do not seem to accept that whenever a therapeutic advance is made some new toxicity is also likely."

"For example, in the broad category of cardiovascular drugs we can contrast beta-blockers—where we can now predict the likely side effects—and the new growth area of converting-enzyme-inhibitors such as captopril, where the side effects cannot be fully foreseen in our present state of knowledge. I think the regulatory agencies should be prepared to say that in order to allow development in this area we have to accept that some unpredictable side effects may occur. Unfortunately society looks for reassurance and a lot of people—clinicians and members of regulatory agencies—try to convince the public that they have achieved the impossible goal of total safety."

Are changes either possible or likely in the way the drug regulatory agencies operate? These topics will be discussed in my final article next week.

What is the best prophylactic treatment for plant allergy?

There is no dependable prophylaxis for plant allergy apart from avoidance. Hyposensitisation may be carried out for poison ivy and ragweed dermatitis.¹ The practical management of suspected cases of plant dermatitis otherwise depends on accurate patch test diagnosis, followed by rigid avoidance of the species identified and often of closely related species. Topical steroids and oral antihistamines provide symptomatic relief. A short course of systemic steroid is useful in severe cases. Mitchell and Rook's book¹ is a unique recently published compendium of information on every aspect of plant dermatitis and is highly recommended.

¹ Mitchell J, Rook A. *Botanical dermatology: plants and plant products injurious to the skin*. London: Henry Kimpton, 1979.

It is recommended that certain drugs be stored within a certain temperature range, and a great many should ideally be stored below 15°C to prevent deterioration. Is storage below the recommended lower limit as detrimental as storing at too high a temperature? Some drugs have a recommended storage temperature of 10-15°C—for example, adrenaline solution BP.

Recommended storage temperatures are designed to maintain the optimum physical and chemical stabilities of drugs. Storage of drugs a few degrees below the recommended lower limit is not normally as detrimental as storage at raised temperatures. The stability of many dosage forms is influenced, however, by the effects of temperature on solubility, and low temperatures may produce crystallisation or precipitation. In suspensions crystal growth may occur which may affect the bioavailability of the drug, and in emulsion systems, such as creams for topical use, irreversible physical breakdown can occur.