Drug research: dead end or new horizon?

Industrial drug research is facing a crisis. Higher investments are necessary for the discovery of fewer drugs, and the return on investment shrinks.\(^1\) Regulatory constraints\(^2\) and financial pressures\(^3\) have been blamed for slowing the development of new drugs at a time when truly new discoveries have become rare events. Among the new drugs established in recent years are the histamine \(H_2\)-receptor antagonists, the angiotensin I converting-enzyme inhibitors, dopaminergics such as 2-bromo-criptine, the anthelminic praziquantel, and the monobactam antibiotics—not all that bad a record, and one that may well be compared with earlier periods considered teeming and prosperous. What has changed is the much larger expenditure, the incomparable higher cost, and the huge investments necessary to achieve these results.

One of the reproaches made to industrial drug research\(^4\) is that its efforts are concentrated on the common and chronic disorders while neglecting the rare diseases. Though understandable for economic reasons, such a one-sided research policy is medically undesirable. A second criticism is that drug research tends to be unimaginative, looking for quick results instead of waiting for the slowly ripening fruits of long-range projects. Both contain a core of truth. Drug research has arrived at a crossroads and has to decide where to go and how to proceed.

These matters were discussed at a recent symposium on “Decision Making in Drug Research” in Camogli, Italy, supported by the Fondazione Smith Kline, Milan. A group of research directors of multinational drug companies and representatives of universities and government institutions met for two days to discuss the problems of modern drug research. The methods of industrial drug research were seen to be in a state of fundamental change. Though not completely abandoned, the classical approach of screening of new chemicals now has only a small place. Chemical drug design has, however, not quite come up to expectations, its main shortcoming still being our modest insight into structure-activity relations.

One stimulating concept advanced at the meeting was an attempt to create new drugs by starting from a biological hypothesis and making use of new chemical substances to elucidate pharmacological or biological mechanisms. Such an integration of pathophysiological and pharmacological approaches may lead to new types of drugs. Systematic variation of known chemical structures should not, however, be depreciated as a means for the development of new drugs: talk of molecular manipulation or of me-too products is not justified in view of the advancements achieved by this approach.

One of the major problems for research-based pharmaceutical companies is attracting capable research people and keeping them intellectually satisfied. This is especially difficult when no products emanate from their efforts or when, for whatever reason, a research project or a whole section of research has to be abandoned. The answer may lie in close co-operation with university departments. A few examples have been encouraging, such as the one at Gothenburg, where local industry has supported the medical school and has been rewarded by efficient consultanship. The success of such ventures depends on an open-minded attitude from the company management and willingness from the academic partner.

External factors are having an increasing influence on decision making in drug research; political trends and government interventions, the power of press, television, and radio, and the attacks of pressure groups are directed not only against marketing and promotion but also against research activities. The drug industry has to face this challenge, even if the blame and accusations are often unjustified. Society is ready to condemn but reluctant to praise.

Meanwhile drug research continues to be productive. The opening of a new horizon makes us look for new ways and means to get there. We shall need to have the courage to undertake unorthodox procedures, to take responsibility for decisions, to assemble able groups of scientists, and to make proper use of their imagination and creativity. Efficient research will continue within the pharmaceutical industry, and important new drugs will be developed by systematic endeavour as well as by chance. The future cannot, however, be left to good fortune: it needs a comprehensive scientific approach to biomedical research.

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Choosing treatment for metastatic breast cancer

The choice of treatment for metastatic breast cancer is confusing and controversial and is made more difficult by the number of methods available. This wide choice reflects our failure to find any treatment that can cure established metastatic disease. (Though control of local recurrences may be a problem in some patients, in this article we look only at systemic treatments.)

Hormonal treatments have been used in breast cancer for nearly a century yet we still understand little of how breast cancer responds to hormones. The addition of oestrogens, progestogens, or androgens; the removal of hormones by ablation of the ovaries, adrenals, or pituitary; and the withdrawal of therapeutic doses of oestrogen may all cause regression of a tumour. In the past rules were drawn up for using these methods in a well-defined “cascade” of surgical and medical hormonal treatments. Yet the fact is that the addition or removal of oestrogens may cause the regression of a tumour in the same patient. The most useful innovation in recent years has been the introduction of hormone receptor assays.\(^1\) True, the results do not improve the survival of patients with breast cancer, but they are very helpful in selecting patients likely to respond to hormonal treatments.