



## The promise of molecular biology: Efficacy, safety, wallet depletion

The youthful scientific discipline of molecular biology is now evolving to its second phase of tangible clinical benefits.

The first phase, which began in the early 1990s, produced a spate of new diagnostic tests, using such tools as high-resolution gel electrophoresis, monoclonal antibodies, and polymerase chain reactions. For example, we can now accurately and reproducibly measure viral load for hepatitis viruses, and we can also detect HIV and other viral agents reliably with exquisite sensitivity. These tests, if not entirely routine, are now performed daily in many hospital laboratories around the world.

The second phase, just beginning, is the application of these and other techniques to develop novel treatments for some conditions for which the existing interventions have always been inadequate. These therapies are based on molecular medicines produced with recombinant DNA technology. Such technologies use either biological systems such as hybridomas to make therapeutic monoclonal antibodies, or more exacting in vitro splicing technologies to produce soluble receptors or other functional molecules. This development is revolutionizing the treatment of such recalcitrant diseases as rheumatoid arthritis and Crohn disease.

In this issue (page 585), Drs. Deal and Gideon discuss the recently introduced recombinant human parathyroid hormone, which can be used very effectively to treat osteoporosis, seemingly with infrequent side effects.

All such drugs, despite their efficacy and safety, have one important limiting side effect: extreme depletion of the wallet. These therapies are so much more expensive than the often less effective and often more dangerous "standard" treatments that we must consider the questions of how much are effectiveness and safety worth, and who should determine this in individual cases. Payers have been trying to influence such therapeutic decisions by making it inconvenient for physicians to order these medications.

These high costs will probably eventually come down as competitors introduce rival drugs because the manufacturing processes are not intrinsically expensive, although development expenses are high.

There is also the lurking worry that, although apparently safe in the short term, some of these drugs may turn out to have ominous late side effects that have not yet begun to surface, raising the specter of devastating liability issues down the road.

Nonetheless, it is clear that we are entering an exciting new era of medicine based on the concept of molecular medicine. The third phase of this era could well be the ability to alter the genome, for which we now have a road map. Whatever the pros and cons of actually doing this may be, one thing is certain: it will be even more expensive.

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