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THE HETEROCYCLIC SHAPE OF THINGS TO COME

The future, said E. B. White, is no unified dream but a mince pie—long in the baking, never quite done. And some of us feel that mince pie, like foreknowledge of the future, is something mankind was not meant to have. Trying to divine the future has usually meant trouble. Consider Agamemnon and Cassandra, Solomon and the Witch of Endor, Macbeth and the Weird Sisters, Mrs. Reagan and her astrologer. To peek behind the curtain is to court a pie in the face—which is why so much credit is due the five foolhardy prognosticators who sat in on the final panel of last month's "'Biopharmaceuticals Futures" conference, co-sponsored by PaineWebber and *Bio/Technology*. The panel on technical strategies included John Wilkerson, Paul Burnett, George Poste, Ralph Christofferson, and Michael Ross. Wilkerson is president of a top consulting group; Burnett, executive director for molecular and cell biology at Eli Lilly; Poste, president of research for Smith Kline & French Laboratories; Christofferson, vice president of discovery research at the Upjohn Company; and Ross, Genentech's vice president for medicinal and biomolecular chemistry. Ideas that might have seemed eccentric or iconoclastic took on the aspect of direct revelation when forcefully repeated by three or four research directors of notably forward-looking companies.

Wilkerson painted the backdrop against which tomorrow's pharmaceutical developments will be played out. Money will be tight: at current rates of increase, annual U.S. healthcare spending will equal the gross national product in 53 years. Increasing demands on the nation's financial resources mean, he said, that we are headed for a three-way civil war between the well, the sick, and the dying.

By 1995 more than 75 percent of the population will be getting their medical care through some sort of cost-containment program—a health-maintenance organization or whatever will succeed them. The other 25 percent of the population will bear the brunt of new healthcare R&D costs. Still, pharmaceutical sales should almost double by then, to some $42 billion. The complex peptides associated with biotechnology will account for only $3.5 billion of this.

Burnett, Poste, Christofferson, and Ross all agreed that the coming age of drug design will belong not to peptide therapeutics but to what Poste called "'an entirely new category of chemistry: the chemistry of macrocyclic structures." Ultimately, this will let us precisely assemble the familiar rings and chains of organic chemistry to mimic—or block—protein activity.

"'Products coming out in the late 1990s," Burnett said, "'Will have been dramatically impacted in the discovery and their development by the tools of biotechnology...whether they are proteins or not. And so we think that the true worth of biotechnology products can't be measured simply by adding up the sales of proteins."

While proteins, modified proteins, and the metabolite products of engineered physiological pathways will undoubtedly continue to hold considerable commercial interest, the greater contribution of biotechnology will come in the elucidation of a greater variety of physiological pathways—helping us to understand and intervene in the processes of health and disease.

This paean to synthetic organic chemistry was striking, especially in this age of excitement over polypeptides.

Almost as striking was the panelists near unanimity on the need for large-scale cooperative research. Poste called for consortia modeled after the European Airbus syndicate. We must go beyond the customary strategic alliances of big company with small company, to alliances between behemoths—building the big budgets and big teams needed to tackle the problems emerging from big biology. Christofferson and Ross echoed this call. Christofferson suggested that this might be the time to try to change the "'cottage industry" culture of commercial science.

All in all, it was surprising that the research directors agreed on so much, and that so little of it is yet conventional wisdom. It should be.

—Douglas McCormick