

Review of Experimental Reports and Discussions

HOWARD E. SKIPPER

Southern Research Institute, Birmingham, Alabama

The night of the 1st day's meeting I rushed to my room and wrote about 30 pages of review. Last night I wrote about 15 additional pages. This morning I waked up, tore up all I had written, and came prepared to test the thesis that a summary does not have to be eternal to be immortal.

I want to make 2 or 3 points and then shall leave the major chore of review to my friend and colleague, Dr. Zubrod.

This, to me, has been a good conference, which means that Dr. Farber and the Program Committee did a good job in selection of participants and that Dr. Wood and Dr. Serpick did yeoman service in organization. Also let me add that our colleagues from overseas have added greatly to the success of this conference: Dr. Jean Bernard, Dr. Georges Mathé, Dr. Laterjet, Dr. Franz Bergel, Dr. K. R. Harrap, and, of course, Dr. Joe Burchenal.

With 1 notable exception, the preclinical presentations were acute, astute, and erudite. The discussion was pertinent, critical, and constructive.

The possible obstacles to control of acute leukemia emphasized at this conference (as interpreted by me) were 4-fold:

Problem 1.—This problem was variously described, according to background and goals of the researcher. All were possibly saying somewhat the same thing.

a) Constant fractional survival of sensitive leukemic cells in spite of maximal dosage therapy (mathematically inclined chemotherapist).

b) Lack of drugs with sufficient cytotoxic specificity for neoplastic cells (cytologist and pathologist).

c) Lack of knowledge of exploitable biochemical differences between normal and neoplastic cells (biochemist).

d) Lack of drugs with sufficient therapeutic index (pharmacologist).

e) Limitation of host toxicity, making it necessary to produce toxicity in the patient in order to achieve temporary clinical remissions (clinician).

Problem 2.—*Meningeal leukemia*; failure of anti-leukemic agents to cross the "blood-brain barrier." There may be other anatomic compartments.

Problem 3.—*True drug resistance.* Drug selection and overgrowth of a drug-resistant population of leukemic cells in the face of continuous treatment (true drug-resistant variants in the biochemical sense).

Possible Problem 4.—"Cell cure" of leukemia but "survival" of a reinducing virus (or other "mutagen").

I cannot recall that any conference or committee meeting ever *solved* any major scientific problem; however, a small meeting with free discussion, such as has been held here during the past 3 days, can help to state the major problems and obstacles, place them in proper perspective, and possibly reveal areas of cross-discipline misunderstanding.

Unless I am mistaken, this conference has helped us focus on past failure phenomena and has revealed that basic knowledge regarding these obstacles is growing rapidly. I find it hard to believe that such knowledge will not catalyze progress toward better control of human leukemias.