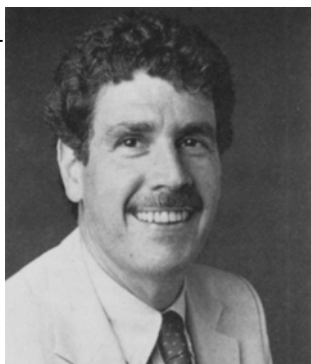


## The President's Corner. . .

### COMMUNITY INVOLVEMENT IN CLINICAL TRIALS: THE FIRST REPORT CARD



This is the time of year that parents look forward to and kids dread; it is report card time, when we get to assess how our children are coping in the real world. As one of the parents of CCOP, it is time for ACCC to take a first look at the performance of its offspring now that the second round of programs have been funded.

At the outset it is important to note that, like most parents, we had high expectations for the program and its potential benefits to the National Cancer Program. We hoped to change the pervasive attitude at NCI and the cooperative groups that practicing oncologists were academically and scientifically illiterate -- incapable of adequate care or recordkeeping and uninterested in clinical research. We hoped to bring oncology to the attention of our hospital administrators, to get additional resources, and to bring more prestige to our institution and staff. We hoped to help ourselves -- filling our own individual need to contribute to curing this dread disease and to help bring a better future for our patients.

We hoped for an A+ experience, but we are oncologists and naturally optimistic!

At the outset, it may be important to say the CCOP passes. The grade is not what we expected, but the effort has been enormous and the results are by no means modest. Indeed, when ACCC started pressuring NCI to consider this kind of program, perhaps five percent of all patients entered on formal NCI clinical trials were accessioned by community oncologists. Now the number is 60 percent! What a remarkable change. If only the rest of this child's potential could be tapped!

Let's look at usual report card categories: good work habits, knows subject, does homework, works with peers, and the three R's: reading, writing, and arithmetic. And, let's not forget that in these modern times, we need to evaluate the teachers as well as the taught.

**Good work habits:** Charles Coltman, M.D., Chairman of the Southwest Oncology Group forced CCOPs to meet the same standards as other group members. Indeed, Coltman reported recently that he expected his university institutions to live up to the standards set by many of his CCOPs. Sounds like this area is an A+.

**Knows subject:** The various cooperative groups treat their community participants in significantly different ways. Talking with CCOP investigators, one gets the impression that NCCTG, SWOG, and NSABP welcome, encourage, and even require involvement by community investigators in the science side of the groups. When this is done, just like with normal teacher-student relationships, you see the CCOP investigators living up (or down) to expectations established for their performance. Three groups A, most of the rest C+.

**Does homework:** Well sometimes. One way to evaluate this is the number of existing programs that were refunded in the second round, and the number of dropouts. It is important to note that the second round was tougher than the first round...because you had to show the reviewers your track record. About two-thirds of the initial class made it back, while only 10 to 12 percent of the large new group of competitors made the cut. There is some controversy about the review and at least one cooperative group chairman, who should know, says that some damn fine programs got "screwed" in the review. Thus, it sounds like many community programs that initially received awards were able to perform well when measured against the standards of the NCI and peer reviewers.

But, there are a number of ways of looking at this question. NCI wants to know why CCOPs are not putting more patients on trial. Quoting the infamous (and inadequate) patient log, NCI notes that many more eligible patients were ignored than put on trial. Of course, nobody mentions that most CCOP data managers could not handle an additional load even if these patients did match the criteria for real trials.

Another way to look at this question is whether the CCOP really helped galvanize the program at home. My assessment is that it did not, although it could, and this represents a "lost opportunity." Most citizens and patients do not realize that CCOP programs exist or bring them benefits because we do not advertise the advantage. If resources increased to support the cancer program, it was not from CCOP funding or presence, which in fact is a tremendous drain on personnel resources to keep up with the amazing quantity of federal bureaucratic entanglements. Where extra resources have emerged, they surfaced as a consequence of competition.

So for homework, the score should be: Performance: A-, Potential Performance: B+, Program Builder: C.

Continued on page 6

# WELLCOVORIN® TABLETS (leucovorin calcium)

Leucovorin in convenient  
5 mg and 25 mg tablets

Before prescribing WELLCOVORIN® Tablets, please consult complete prescribing information. The following is a brief summary.

**INDICATIONS AND USAGE:** Wellcovorin (leucovorin calcium) is indicated for the prophylaxis and treatment of undesired hematopoietic effects of folic acid antagonists (see WARNINGS).

**CONTRAINDICATIONS:** Leucovorin is improper therapy for pernicious anemia and other megaloblastic anemias secondary to the lack of vitamin B<sub>12</sub>. A hematologic remission may occur while neurologic manifestations remain progressive.

**WARNINGS:** In the treatment of accidental overdosage of folic acid antagonists, leucovorin should be administered as promptly as possible. As the time interval between antifolate administration (e.g. methotrexate) and leucovorin rescue increases, leucovorin's effectiveness in counteracting hematologic toxicity diminishes.

**PRECAUTIONS:**

**General:** Following chemotherapy with folic acid antagonists, parenteral administration of leucovorin is preferable to oral dosing if there is a possibility that the patient may vomit and not absorb the leucovorin. In the presence of pernicious anemia a hematologic remission may occur while neurologic manifestations remain progressive. Leucovorin has no effect on other toxicities of methotrexate, such as the nephrotoxicity resulting from drug precipitation in the kidney.

**Drug Interactions:** Folic acid in large amounts may counteract the antiepileptic effect of phenobarbital, phenytoin and primidone, and increase the frequency of seizures in susceptible children.

**Pregnancy: Teratogenic Effects:** Pregnancy Category C. Animal reproduction studies have not been conducted with Wellcovorin. It is also not known whether Wellcovorin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Wellcovorin should be given to a pregnant woman only if clearly needed.

**Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Wellcovorin is administered to a nursing mother.

**Pediatric Use:** See "Drug Interactions".


**ADVERSE REACTIONS:** Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

**OVERDOSAGE:** Excessive amounts of leucovorin may nullify the chemotherapeutic effect of folic acid antagonists.

**DOSAGE AND ADMINISTRATION:** Leucovorin is a specific antidote for the hematopoietic toxicity of methotrexate and other strong inhibitors of the enzyme dihydrofolate reductase. Leucovorin rescue must begin within 24 hours of antifolate administration. A conventional leucovorin rescue dosage schedule is 10 mg/m<sup>2</sup> orally or parenterally followed by 10 mg/m<sup>2</sup> orally every six hours for seventy-two hours. If, however, at 24 hours following methotrexate administration the serum creatinine is 50% or greater than the pre-methotrexate serum creatinine, the leucovorin dose should be immediately increased to 100 mg/m<sup>2</sup> every three hours until the serum methotrexate level is below  $5 \times 10^{-8}M$ .<sup>1,2</sup>

The recommended dose of leucovorin to counteract hematologic toxicity from folic acid antagonists with less affinity for mammalian dihydrofolate reductase than methotrexate (i.e. trimethoprim, pyrimethamine) is substantially less and 5 to 15 mg of leucovorin per day has been recommended by some investigators.<sup>3,4,5</sup>

1. Bleyer WA: The Clinical Pharmacology of Methotrexate. *Cancer*, 41(1):36-51, 1978.
2. Frei E, Blum RH, Pitman SW, et al: High Dose Methotrexate with Leucovorin Rescue: Rational and Spectrum of Antitumor Activity. *Am J Med*, 68:370-376, 1980.
3. Golde DW, Bersch N, Quan SG: Trimethoprim and Sulpha-methoxazole Inhibition of Haematopoiesis in *Vitro*. *Br J Haematol*, 40(3): 363-367, 1978.
4. Steinberg SE, Campbell CL, Rabinovitch PS, et al: The Effect of Trimethoprim/Sulfamethoxazole on Friend Erythroleukemia Cells. *Blood*, 55(3): 501-504, 1980.
5. Mahmoud AAF and Warren KS: Algorithms in the Diagnosis and Management of Exotic Disease. XX Toxoplasmosis. *J Infect Dis*, 135(3): 493-496, 1977.

 Wellcome | Burroughs Wellcome Co.  
Research Triangle Park, NC 27709

## Community Involvement in Clinical Trials...Continued from page 2

**Works with peers:** In some places we have been able to use CCOP as a way to get to some folks. Still, in most communities, it is only a few oncologists who put on the majority of patients. The "bandwagon" oncologist, who reads the latest journals but skips the methodology sections, still tends to ignore clinical trials participation. He cites a "newer" technology that will be abandoned next week when another journal reports another breakthrough.

There is also the "over-the-hill" oncologist who is burnt out and feels that "nothing works" and the "game of chance" oncologist who uses the last approach that someone, by chance, discussed with him. Participation in CCOP did not change their habits, even though we optimists thought it would.

Of course, there are a few who were affected and converts made among heathen referring physicians. But overall, one cannot say the program has done much to improve attitudes. Grade: D+.

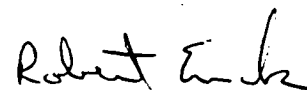
**The three R's:** Reading and writing by community oncology participants has increased. CCOP investigators and staff do get a chance to look at the science of groups much more frequently. But, the real reading and writing load comes with all the bureaucratic paperwork: the annual reports, the budget renewals and negotiations, the grant writing. Ugh!

And arithmetic! For the most part, CCOPs appear to be lower in unit cost than their university colleagues, but NCI clearly expects us to pick up part of the tab with hospital and physician resources. This is increasingly difficult in these tight economic times! So we get lots of practice at the three R's, but not much of value is produced. Grade: C-.

**The faculty:** Some good, some bad, some awful. The cooperative groups, like teachers, vary from open and progressive to stodgy and frumpy. Student response has been proportionate.

**The administration:** NCI leadership has displayed characteristic disorderly behavior. It has varied from the strong support by the (now absent) Bob Frelick, M.D., to the unrealistic gearing of the second round of competition toward cancer control clinical trials, which are then left unfunded, unapproved, and unloved by NCI staff. C+ for the cooperative groups. D- for NCI.

Overall CCOP gets a B- as an experience. Good, but room for improvement. ■



Robert E. Enck, M.D.  
President

### NOMINATIONS FOR ACCC OFFICERS AND TRUSTEES

The ACCC Nominating Committee is soliciting your nominations for the following Board positions:

- President-Elect
- Treasurer
- Three Trustees

The term of President-Elect is one year. The Treasurer and Trustee positions are two-year terms. While nominees are not required to be the voting representative from their institution, they must represent an ACCC Delegate institution.

Letters of nomination should be sent to the ACCC Executive Office citing the nominees' names, their respective Delegate institution, along with a copy of their curriculum vitae. **NOMINATIONS MUST BE RECEIVED NO LATER THAN JANUARY 15TH, 1988.**

Further information about the nomination process may be obtained from Lee E. Mortenson, Executive Director, ACCC Executive Office at (301) 984-9496. ■