DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20205

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Grace P. Monaco, Esq.
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Washington, D.C. 20006

Dear Grace:

Thanks for giving me a opportunity to comment on the IAT brochure produced by Dr. Burton's Immunology Researching Center. I have prepared a fairly lengthy commentary which is attached. I doubt that I have said anything that you didn't already know.

However, if I have raised a few issues or presented a few thoughts in a fashion that is helpful to you, I shall be satisfied.

Basically, the document has no substance. It uses some of the form but has none of the content of a technical document. It is pure promotion. Strictly speaking, it contains nothing that permits the analytic reader to conclude that IAT is either useful, inactive or anywhere in between. The ball remains in Burton's court. Although the siren song of this kind of promotion unfortunately continues to attract cancer patients, in a scientific sense Burton has made no case at all for IAT in this document.

Sincerely,

Bud

Bayard H. Morrison III, M.D.

IMMUNO-AUGMENTATIVE THERAPY

The basic question to be answered by IAT proponents is what objective evidence is there that IAT is effective. A careful reading of the brochure provides none. After reading of Dr. Burton's early work in which he demonstrated the literal melting of animal tumors by use of his methods and after reading that 1900 patients have been treated at the IRC since 1977, one would think that Dr. Burton would be ready and well equipped to make a well-documented case. Apparently not. On p. 14 of the brochure it is noted that Dr. Burton does not claim "cure". Instead he claims that many patients "prosper". However, in their forward Loupe and Cowles observe (after saying there is no cure for cancer) that Burton and staff believe that IAT is producing long term regressions- some complete - in almost 60% of the patients being admitted. This suggests that there may indeed be data to document the effects of IAT. In fact on pp. 10 and 11 one finds a table presenting trends in response of patients treated with IAT. Does this nail down the case for IAT? Alas, no.

His table of trends, which uses a "+" or "-" system, is almost useless for several reasons:

- the symbols reflect frequency of change in tumors and/or symptoms. Conceivably there might have been no tumor regressions.

- "+" indicates that 50-100% of patients with a particular diagnosis had a "long term" response. It is impossible to tell whether that response was objective or subjective, trivial or substantial. The"-" is equally imponderable and indicates that 0-49% of patients had some sort of objective or symptomatic response.

- "long term" regression or remission is not defined. Given some of the problems in followup alluded to by the writers, and the fact that the clinic has been operating for only 7 years, one wonders how many patients were followed up at 6 months, a year, 2 years, 5 years.

Other statements in the brochure may serve to explain the situation. We find that Burton's patients receive only a 6-8week course of treatment in the Bahamas; they are then sent home with enough material to provide them 13 weeks of treatment. Ideally they should then be reevaluated at the IRC in the Bahamas. However, one wonders how often this (or any) reevaluation takes place since on pg 2 the difficulty of patient followup, and the impossibility of statistical assessment are noted. Thus Dr. Burton has presented a report which suggests that IAT is producing marvelous results, but he has left an escape hatch available in case one questions the vague and unsubstantiated claims made in the report (e.g., table of trends). To fend off another possible criticism, Dr. Clement, Medical Director of IRC, explains why clinical trials of IAT have not been conducted. He says in essence it would be irresponsible to give one half of a randomized,

double-blind patient population an active principle, i.e., IAT, and the other half "water or something else totally inactive." In saying this, Dr. Clement has erected a strawman. In the first place it seems quite evident that patients have not gone to the Bahamas to take part in a clinical trial. They spend good money to receive a specific treatment, IAT. I would be surprised if Burton and his colleagues ever considered the possibility of setting up randomized, double-blind trials.

Second, and perhaps even more important, in raising the idea of a controlled clinical trial Dr. Clement is either unaware of or is ignoring the lessons learned in decades of clinical trials. That is, the randomized, double blind trial is generally reserved for use in Phase III trials in which a new active treatment is being compared with an existing standard treatment (or a new treatment is being used in a disease where there is no effective treatment). Such trials usually involve patients with one or a limited number of tumor types.

Tumor types, extent of disease, and symptoms are carefully recorded before treatment is started. During the treatment and followup period, objective and subjective changes (including treatment-induced toxicity) are recorded. The quality of such changes is evaluated in terms of pre-established criteria (e.g., partial and complete regressions).

The properties of the experimental treatment in such a trial are well-characterized since the material has usually undergone Phase I, II and even other Phase III studies before use in the study under consideration. The patients entered in such studies can expect to receive either a treatment of choice or an "experimental" treatment which is hoped to produce results equal to or, ideally, better than the standard treatment.

The purpose of the kind of controlled trial alluded to by Dr. Clement is to yield new information on therapeutic options and where possible effect therapeutic improvements.

The supreme irony of Dr Clement's remarks is not only that no element of the clinical situation at IRC (as it is described) lends itself to the kind of controlled trial mentioned, but also that the proponents have not provided in this brochure a shred of objective data (or references to such data) proving that IAT has undergone the rigorous preclinical and clinical testing (phase I, II, III trials) that could serve to support the proposition that IAT should be considered a treatment standard, i.e., the active principle, in a double-blind trial.

Having waded through this bit of misleading and irresponsible promotional fluff, a perceptive reader will realize that he has found none of the facts that would permit him to make any enlightened conclusions about the utility of IAT: patient numbers, histologic diagnoses, stage of disease, general clinical condition, details of previous treatment, all the details of the IAT period, evidence of tumor response, toxicity, results of periodic followups, subsequent treatment, etc., etc.

I think IAT can be faulted on other grounds. To illustrate, Dr. Burton has reduced antitumor immunology to a rather simple four element system. In the face of a dramatic increase in understanding of the complexities of the structure and function of the immune system attained during the past several years, Dr. Burton has not apparently proposed any modifications in his theories; neither has he tried to explain his concepts in the light of contemporary immunology. He has not even divulged enough information to enable anyone to accurately analyze or repeat the basic aspects of his work.

During the 6-8 weeks of treatment at IRC, a daily or twice daily assay in each patient of Dr. Burton's 4 immune factors is required to permit the necessary fine tuning of treatment required to restore the immunologic competence needed to effect maximum objective and symptomatic benefit. It is interesting that this need vanishes when the patient is sent home with the materials necessary to complete 13 additional weeks of treatment. Although the patient is urged to return to the care of a private physician, one can't help wonder what the physician is supposed to do since he can't monitor the factors deemed important by Dr. Burton and has no basis for knowing if or how doses of the material provided at IRC should be modified. He can, of course, replace or supplement IAT with conventional treatment or discontinue treatment entirely. We are given no idea of how often any of these things happen.

Followup visits at IRC are recommended, but the reader of the brochure is given no indication of the frequency, duration, indication of usefulness, and cost of such followups. Given the frequently observed fact that no two patients behave exactly the same, particularly when physiologic and emotional functions are perturbed by serious diseases (which themselves exert different effects), it seems amazing that Dr. Burton's therapeutic method can so predictably induce a state of such great clinical stability that home care can be carried out according to a routine formula and followup care by those who alone understand the system can be considered almost irrelevant. It is unfortunate that the data necessary to prove the value of this approach do not exist or have not been published.

It is said that this brochure is dedicated largely to laymen, but would be of interest to physicians and scientists. While the layman may find it appealing, most physicians and scientists will find it a pseudoscientific document, which in its appeal to a frightened patient offers a lot, guarantees nothing and, indeed, provides no evidence that anything has been delivered.

It is possible that IAT proponents will contend that this brochure is not intended to be a scientific document. Indeed, in the introduction they say that it is not intended to "emulate or take the place of clinical data". However, they play around with the forms of scientific reporting by citing some non-clinical literature references and devising their table of trends. If they chose to go that far and had the necessary data, they could have prepared some meaningful displays of objective information.

If they did not intend to provide hard data; it is only fair to ask them

why anyone should treat their unsubstantiated claims as though they were hard data or(in the absence of any clinical references), were backed by hard data.

They should be reminded that the conduct of clinical studies over the past decades has been marked by publication of thousands of papers in the formal biomedical literature. In reporting failures as well as successes, these papers trace the path of slow but remarkable progress that has resulted in the present state of the art of cancer management that Dr. Burton finds so easy to ignore.

Although his criticisms of conventional methods are somewhat muted, his denunciation of the "establishment" and the "conspiracies" that have hampered his efforts are not subdued.

This familiar technique is often used not only to explain why unorthodox practitioners have been forced out of the "system", but apparently is also expected to justify the use of non-scientific methods.

I think he realizes that he could get his work published if he were able or wished to present the data in the form needed to make his case. Nothing is required of him that is not required of others who wish to report their findings. If worst came to worst, he could as a start, publish and circulate the "clinical data" that he implies his promotional brochure is based upon just as easily as he published and circulated promotional material. He could also make available to the scientific community the laboratory and clinical records upon which his claims are based.

However, based on the testimony of the IAT brochure, as it stands now, he has provided only claims, and no evidence that he has or can contribute anything that will benefit cancer patients.