

# THE PROTOCOL:

(prōtə kôl/) a detailed plan of a scientific or medical experiment or treatment

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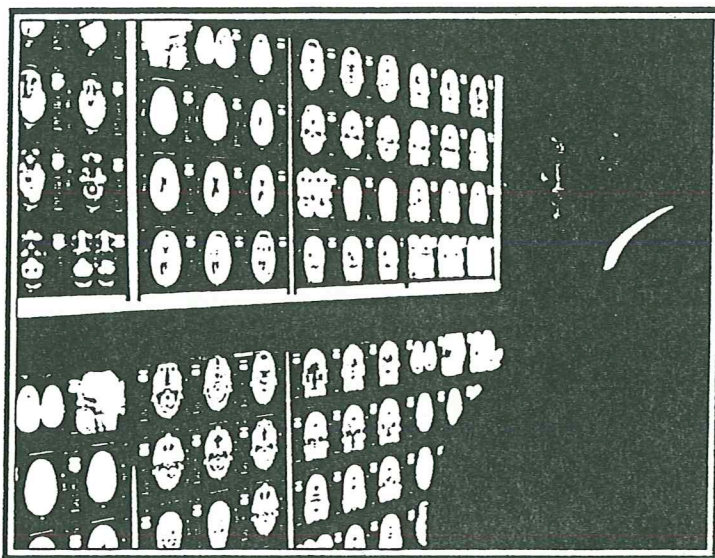
## A PROTOCOL EXCLUSIVE PHENYLACETATE: ADDING TO THE CANCER-FIGHTING ARSENAL

One of the best-accepted axioms of cancer research is that progress comes not in giant, news-making leaps but in modest, incremental steps that tend to miss the nightly news. By the time a new cancer therapy reaches the patient, its development has been so slowly progressive that little earth-shattering news remains.

Such steps are being taken at the National Cancer Institute in a research program involving phenylacetate, a promising cancer agent about to enter Phase II testing. Dvorit Samid, Ph.D. and Alain Thibault, M.D. head the project researching the benefits of phenylacetate and several of its analogs, such as phenylbutyrate. The purpose of these studies is to discover one or several non-toxic therapies for various cancers.

"Although chemotherapy has seen resounding successes with leukemia, lymphoma, and testicular cancer," says Dr. Thibault, "cancer remains the second leading cause of death in America today."

A major problem with cytotoxic chemotherapy, according to Dr. Samid and Dr. Thibault, is the seriousness



*Dr. Thibault examines MRI scans of a patient treated with phenylacetate*

of its side effects, which actually limits the full use of most anticancer drugs available today. To do its work conventional chemotherapy kills rapidly proliferating cells, but not just the tumor cells. This leads to toxicity, which may take the form of vomiting, hair loss, mouth sores, predisposition to infections, bleeding, and many other undesirable effects. For Drs. Samid and Thibault, the challenge now is to find non-toxic compounds that fight cancer cells biologically, finding the Achilles' heel in the cell in order to selectively destroy it.

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## NEW PROTOCOL FEATURE

*The Protocol* is written largely with the lay person in mind. As a continuing service to our physician members, *The Protocol* will add a periodic feature called "Physician's Broadsheet." This separate page will contain updates and articles geared exclusively to the technical oncologist and will be available only in copies of *The Protocol* mailed to MAOP members. MAOP members are encouraged to submit article ideas or complete articles to *The Protocol's* Editor Bob Jefferson, MACRF, 8811 Colesville Road, Suite G106, Silver Spring, MD 20910 or call 301/587-8362. **P**

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(Phenylacetate, continued)

"In the process, we're also trying to work for the patient by adding to quality of life," says Dr. Samid. She stresses that the aim of this research is not to replace cytotoxic chemotherapy, but to add to the cancer fighting options oncologists already have at their disposal.

### A NATURAL WAY

For several years, Dr. Samid has been looking for natural chemicals that control growth and are highly preserved throughout evolution. Both attributes describe phenylacetate, a molecule that occurs naturally in all living organisms. In plants, for example, phenylacetate controls growth and selectively blocks the growth of immature tissues. In laboratory models of cancer, phenylacetate makes tumor cells behave more normally. "We're not necessarily trying to kill (tumor) cells, but rather 'tame the shrew,'" says Dr. Samid.

### CLINICAL STUDIES

Phenylacetate and phenylbutyrate are currently undergoing Phase I studies at the Clinical Pharmacology Branch of the NCI, headed by Dr. Eddie Reed. These studies involve patients whose various types of cancers have not responded to conventional therapies and are at an advanced stage. Even with those low odds phenylacetate has shown promise, especially in patients with brain cancer and prostate cancer, two very

difficult cancers to fight. Researchers have been able to achieve the high blood levels of phenylacetate they believe are necessary to have an impact on the tumor, while keeping the side effects to a minimum.

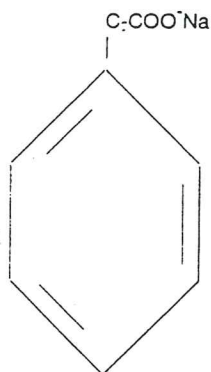
Phenylacetate enters Phase II trials this summer in patients with brain and prostate cancer. Trials of the drug in combination with other therapies are scheduled for 1995. Researchers must have a variety of compounds to study, because they still don't know which is most effective against what cancers or if various combinations will produce a greater impact.

"Oncologists must be optimists," says Dr. Thibault, "if one approach doesn't work, we move on to another until we find a solution."

The development of these new cancer therapies

has been a collaborative effort among the National Cancer Institute, university research centers, and research organizations such as MAOP. "At present we are offering experimental alternatives for MAOP patients here at NCI," says Dr. Samid. "At the same time, we are laying the groundwork toward moving this work to the MAOP clinics."

MAOP members who would like to sign up patients for the phenylacetate or phenylbutyrate studies should call Dr. Thibault or Dr. Samid (301/402-4681; fax: 301/402-1997). **[P]**



The Molecular Structure of Phenylacetate

(Past, continued)

motherapeutic agent is maintained with infusion therapy. This increases the likelihood that the cancer cell will die during its division phase and decreases the toxicity of some agents.

While MAOP is not the only group that has studied infusional chemotherapy, MAOP was one of the first groups to *focus* its efforts in this vital area, and is in the forefront of infusional research. MAOP currently has five clinical trials utilizing continuous infusion chemotherapy, studying its effect in colon, soft tissue sarcoma, renal, adenocarcinoma of unknown primary, and carcinoid tumors.

Growth has been good to MAOP, although many might say we've outgrown our "Mid-Atlantic" name. While our base of operations and majority of members are still in the Mid-Atlantic region, we also enjoy membership from clinics and hospitals in New England, Florida, Georgia, Ohio, California, and Oklahoma. If the last 13 years are any model, MAOP should enjoy more growth and greater insight into cancer treatment. **[P]**

(Countries, continued)

and Oceania (excluding Australia and New Zealand). The most surprising finding was that while the percentage of deaths due to cancer was lower in developing countries, the overall death rate (from all diseases) in developed countries was much lower, leading to a higher number of actual cancer deaths in developing countries.

The real cancer challenge to healthcare systems in developing countries is rapidly exploding and aging populations. As these populations become more urbanized and Westernized, doctors and other health care providers will have to develop new strategies for controlling malignancies through early detection and treatment. **[P]**

(Foundation, continued)

One of our newest Board of Advisor members, Dvorit Samid, Ph.D., of the National Cancer Institute, offered to give *The Protocol* an exclusive on her work with phenylacetate, which appears on the cover of this

season's issue. This is quite a coup for *The Protocol*, as several major newspapers and magazines have asked for this story but have not yet been offered the information. Thank you, Dr. Samid! **[P]**