

# Letters

## Radiation Therapy

Allen L. Hammond's Research News report "Cancer radiation therapy: Potential for high energy particles" (17 Mar., p. 1230) was of great interest to me. During the last 10 years, I have treated more than 500 patients for pituitary and other disorders with the Harvard proton beam. Proton beam therapy is of established value for the treatment of pituitary tumors producing acromegaly and Cushing's disease and is worthy of further study. From the point of view of a clinical research worker, I regard our work of the past decade as notably satisfactory. On the other hand, there has been little support of the enterprise.

In the 200 cases of acromegaly I have treated with the proton beam, the rates of remission and improvement far exceeded those for the cases treated with conventional x-ray therapy. There was no related mortality. Complications have almost vanished as a result of experience and improved technique. Cushing's disease can be reverted to normal without scars or posttreatment medication. About 50 percent of the patients have a remission, and an additional 35 percent experience significant improvement.

For several years, proton beam therapy at Harvard has been supported entirely by patient charges. Hospitalization costs are cheaper than with alternate modes of therapy. Patients are hospitalized for 6 to 8 days and may then return to work immediately.

In the early years of our project, we were warmly funded by the National Institutes of Health and NASA. Then for 3 years we received no funding. Two years ago, we obtained a grant to help us evaluate our cases and maintain the project. However, it appears that we enjoyed only a microscopic fraction of National Cancer Institute (NCI) support in 1971 for investigations of particle radiation.

We agree that a shortage of qualified radiotherapists interested in particle ra-

diation exists. We have been trying for 10 years to interest radiotherapists in proton beam therapy. The situation has been steadily improving. Now, in the past year, I have learned of one radiotherapist who has stated an interest in a proton project. Despite this shortage, when we spoke to two officials of the NCI, they declined to consider substantial support unless we located a radiotherapist.

While the value of radiotherapy and radiobiology skills to such a project is obvious, there are a few features of our application which have not been helped by conventional radiotherapy theory and practice. We usually seek to produce necrosis in our targets rather than arrest growth. Our dose rates are about 500 times greater than those normally used in radiotherapy, and the total doses are substantially different. Irradiation is conducted with the precision available from stereotactic technique, which, coupled with precise dosimetry, enables us to leave a thin shell of pituitary intact and thus preserve normal pituitary function.

Hammond strikes a sympathetic note when he says, "Instead of encouraging the use of available facilities for pre-clinical and clinical trials of protons or alpha particles, for example, the NCI has supported the development of new facilities for generating fast neutrons and for therapeutic applications of pions." The Harvard cyclotron is about 25 years old and is available to us for human therapy because it is obsolete for physics and would be expensive to tear down. The anticipated use of the machine in the fiscal year 1971-72 is 26 days. In the remaining time, it is idle.

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Hammond's discussion of cancer radiation therapy seems to miss a most important point: in localizing radiation dose to a certain volume, the therapist is never certain of the exact borders of

involvement. He makes an educated guess, the accuracy of which can be improved by various diagnostic procedures, such as lymphangiography and radioisotopic scans, but it is still a guess. Any experienced surgeon or pathologist can witness how often the surgeon, with the diseased area available for direct inspection and palpation, resects the cancer with "ample margins," only to have the pathologist report that he has cut through cancer. The surgeon can go back and remove more tissue, but the radiotherapist has a one-shot deal—either he guesses right the first time, or else.

It is unlikely that further sophistication of either radiation dosage or localization will result in an increased rate of cure (witness the rather disappointing gains in progressing from orthovoltage to the accelerator). . . . The only real hope for a breakthrough in the treatment of cancer lies in a full knowledge of its causes and mechanisms. Funding and efforts should be directed to this critical area, where there have been hopeful advances, rather than to the exploration of clinical treatment with what is, after all, only a refinement of existing methods.

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## Water Importation

In its report on water importation (11 Feb., p. 667), the AAAS Committee on Arid Lands concludes that "if there is a compelling reason for large-scale water importation, it is to prevent massive social and economic disruption in an established irrigated area." Certainly, we must always sympathize with the misfortunes of others, and it is important that society uses its resources to improve the circumstances of any unfortunate minority. However, when those circumstances are a direct result of the actions of a few who have created their own misfortunes by violating the limiting laws of nature, society may well be confronted with an impossible burden.

Water, because it is water, seems to be considered an everflowing renewable resource. In fact, there is no reason why the depletion of a geological deposit of groundwater should be treated any differently from that of any other non-renewable mineral resource. By analogy, to provide relief and subsidies to those

who continue to violate the inexorable laws of nature would be to allow the endless settlement and development of every floodplain on every river in the country, with the result that each stream could then be encased in concrete from its headwaters to its delta mouth, at public expense.

According to the same logic, we should import gold and ore-bearing rocks from elsewhere so that Montana's metal mines could continue to sustain the communities that are dependent upon them. It would also follow that the United States should be obligated to reimburse the untold thousands of homesteaders who failed in their attempts to establish 160-acre farms on the arid Great Plains.

I hope the AAAS Committee on Arid Lands will fully assume its social responsibilities by clearly defining the natural constraints to which our species must accommodate if we are ever to have a sustained and productive co-existence with nature.

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## Mercury Compounds

G. F. Wright (Letters, 19 Nov. 1971, p. 771) gives additional support—although uncontrolled—to the already well-known fact that monoalkyl mercury compounds behave differently from dialkyl mercury compounds and from the aryl mercury compounds (mentioned as diuretics) in biological systems.

The recalcitrant monomethyl mercury entity (present in fish and used as seed dressing) has a biological half-life of about 70 days in man, whereas mammals rapidly excrete dimethyl mercury and aryl mercury compounds when exposed to them. The distribution in the body as well as the biological effects are also very different.

It is not advisable to take a 1-gram intravenous injection (or oral dose) of monomethyl mercury if one wishes to enjoy a meaningful life.

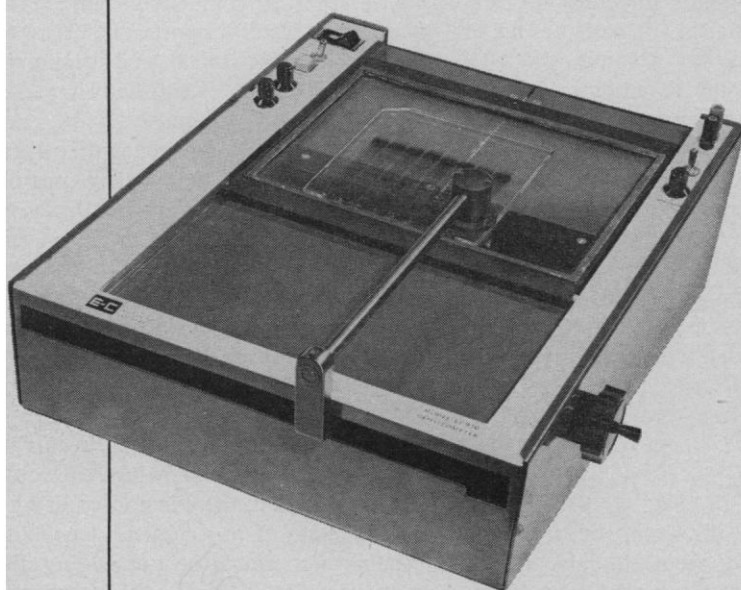
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I fully agree with George Wright. He has been extremely lucky. Of all the mercury salts he mentions, not one is outside the class of dialkyl mercury salts. It has been said for some time, for example, that dimethyl mercury is biologically inert (1). Monomethyl mercury, however, has been implicated as a deadly environmental poison. The metabolic conversion of dimethyl to monomethyl mercury in the mammalian organism is reported to be less than 10 percent. To my knowledge, only the higher monoalkyl mercury salts ethyl mercury and propyl mercury, are toxic. The body finds it easy to metabolize the dialkyl and higher monoalkyl salts, breaking the carbon-mercury bond and rendering these lipid-soluble agents harmless in the low concentrations of inorganic mercury presented to the brain. The body cannot, however, metabolize the lower monoalkyl mercury salts.

Undoubtedly there is an element of biological variability involved in susceptibility to these compounds, but it is not rational, in the face of overwhelming evidence, to consider individual susceptibility as large a factor in

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