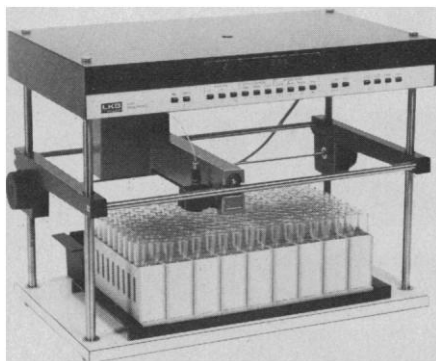


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## LETTERS

### Pontryagin's Article

In order that the readers of *Science* can assess correctly the reliability and veracity of the letter from Academician Pontryagin on page 1083 of the 14 September issue, they are invited to look at the third from the last paragraph of an autobiographical article by Pontryagin that has appeared in *Uspekhi Matematicheskikh Nauk* [33 (No. 6), (1978)]. A translation of this article, with a disclaimer and a rebuttal, will appear in *Russian Mathematical Surveys*, published by the London Mathematical Society, in November 1979.

ALEX ROSENBERG  
Department of Mathematics, Cornell  
University, Ithaca, New York 14853

### Treating Mental Disorders

Gina Bari Kolata reports (Research News, 5 Jan., p. 36) on the 1976 discovery by Wurtman and others that the rate at which the brain synthesizes acetylcholine can be increased by increasing the amount of choline in the blood and on the later observations that tardive dyskinesia, a side effect of antipsychotic drugs such as the phenothiazines and the butyrophenones, can be controlled by a high intake of choline or lecithin (which contains phosphatidylcholine). This article appears to indicate that the idea that dietary constituents can influence the functioning of the brain represents a new approach, discovered by Wurtman. In fact, there had been much earlier work in this field, which in recent years has been called orthomolecular psychiatry.

Kolata states that "It was thought that as long as the brain was supplied with oxygen and glucose it would make whatever it needed, independently of the metabolic and nutritional state of the body." It has, on the contrary, been known since long before 1976 that other exogenous constituents of the brain are required for its proper functioning and that, as I stated in my 1968 article (*Science*, vol. 160, p. 265), "Varying the concentrations of substances normally present in the human body may control mental disease." The most striking early work is that on the treatment of psychiatric patients with large doses of niacin, one of the B vitamins (1). A dozen other nutrients that affect brain function are also discussed in my 1968 article, which includes in addition a discussion of mechanisms such as increasing the rate of

formation of an important substance by increasing the concentration of a reactant. An example, not given in the article, is increasing the amount of the neurotransmitter acetylcholine by increasing the choline concentration.

I defined orthomolecular psychiatry therapy in 1968 as "the treatment of mental disease by the provision of the optimum molecular environment for the mind, especially the optimum concentrations of substances normally present in the human body." Wurtman has been quoted elsewhere as having said that the treatment of tardive dyskinesia by an increased intake of choline has nothing in common with orthomolecular psychiatry. It is clear, however, that it is a good example of orthomolecular psychiatry; especially interesting because the mechanism of its action is understood in greater detail than in the earlier examples.

LINUS PAULING  
Linus Pauling Institute of Science and  
Medicine, Menlo Park, California 94025

### References

1. V. P. Snyderstriker and H. M. Cleckly, *Am. J. Psychiatry* **99**, 83 (1941); A. Hoffer, H. Osmund, M. J. Callbeck, I. Kahan, *J. Clin. Exp. Psychopathol.* **18**, 131 (1957).

### Fetal Research Ethics

The 3 November 1978 issue of *Science* (p.540) contained another chapter in the long, unhappy history of the Philipson *et al.* fetal research study (1). This experiment led, at the state level, to criminal charges (eventually dismissed) of grave-robbing against the principal investigators, and, at the national level, to a scrutiny of fetal research that culminated in a research moratorium and creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

Throughout the debate on the Philipson *et al.* experiment, ethical questions concerning the fetal subjects of that research have preempted the attention of adversaries, advocates, and reporters like. Ethical questions concerning the *maternal* subjects of that research have not been raised but are just as important. Twenty-five of the 33 patient-subjects, 10 to 22 weeks pregnant, were aborted by hysterotomy (1). Hysterotomy is a major surgical procedure not normally used for abortion because it entails hospitalization, risk, discomfort, disfigurement, and because it precludes normal vaginal deliveries in future. From an investigator's point of view, however, hysterotomy as a method of

abortion has the advantage of yielding a live, intact fetus.

The doctrine of informed consent, originally put forth in the Nuremberg Code (2) and based on the principles of voluntariness, competence, and understanding, requires that the subject have sufficient knowledge and comprehension of the research "... to enable him to make an understanding and enlightened decision." This in turn requires disclosure of "... all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiments." Philipson *et al.* claim to have gotten informed consent from their subjects (1, p. 1219), but it is difficult to understand how 25 fully informed, competent people could have opted voluntarily to forego abortion by a simple, minimal risk procedure and submit instead to major surgery.

YVONNE BRACKBILL

*Departments of Psychology and  
Obstetrics and Gynecology, University  
of Florida, Gainesville 32611*

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1. A. Philipson, L. D. Sabath, D. Charles. *N. Engl. J. Med.* **288**, 1219 (1973).
2. *Trials of War Criminals before the Nuernberg Military Tribunals under Control Council Law No. 10: Nuernberg; October, 1946-April, 1949* (Government Printing Office, Washington, D.C., 1949), vol. 2, pp. 181-182.

Brackbill raises an appropriate aspect of patient informed consent in human studies. We fully agree that informed consent is essential in human studies.

In the particular study to which she refers, there was no need for either an intact fetus or "viable" tissue. The method of abortion was selected by a number of different surgeons, in each case on the basis of what would be best for the patient under the circumstances. Although it is correct that the different operative techniques have different risks and consequences, those matters had nothing to do with this study, since the procedure in each instance was selected entirely for the patient's benefit. In fact, the patients were not even invited to participate in the study until after the operative plan had been made.

L. D. SABATH

*Section on Infectious Diseases,  
Box 489, University of Minnesota  
Hospitals, Minneapolis 55455*

AGNETA PHILIPSON

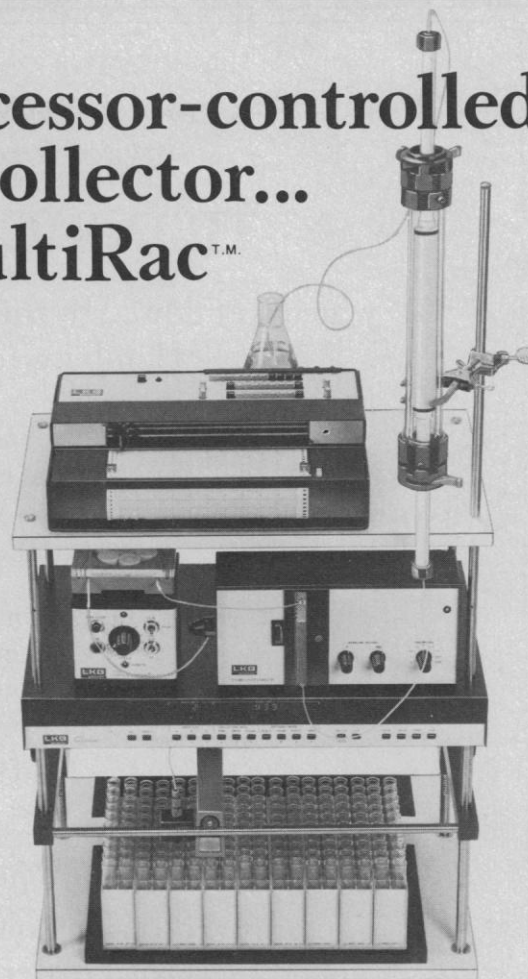
*Department of Infectious Diseases,  
Danderyd Hospital,  
S-182 03 Danderyd, Sweden*

DAVID CHARLES

*Department of Obstetrics and  
Gynecology, Memorial University,  
St. Johns, Newfoundland A1B 3V6*

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