Letters

Placebos for Relief of Pain

Beecher [*Science* **132**, 91 (1960)] presented a thesis that placebos are more effective for relieving pathological pain than for relieving experimental pain. The approach is very interesting, the data presented are clear-cut and convincing; however, I think that in interpretation one important factor is left out.

The data on pathological pain are based on observations in average, unsophisticated clinical patients. The subjects for the investigation of experimental pain are mostly medical or graduate students. As far as observation and interpretation of sensory phenomena are concerned, these students are surely in a different category from the average clinical patient. If, in addition, selection is limited to those volunteering for pain experiments, this puts the subjects in a very special class.

This was pointed out in several previous publications [*J. Appl. Physiol.* **8**, 630 (1956); *Science* **128**, 303 (1958)]. Beecher actually quotes from the second of these references, but he leaves out the main theme—the one indicating that the placebo effect becomes less pronounced with the greater ability of the subject to evaluate pain objectively.

I fully agree with Beecher's conclusions that placebos work on the anxiety component of pain and on anxiety-induced reflexes. However, I think that his own evidence indicates that this is largely due to differences in the psychological characteristics of the subjects—differences in degree of scientific understanding and in the ability to make objective evaluation.

FRED B. BENJAMIN
Republic Aviation Corporation, Farmingdale, New York

I am pleased, of course, that Benjamin found "the data presented . . . clear-cut and convincing" and that he "fully agree[s] with [my] conclusions that placebos work on the anxiety component of pain."

He is troubled, if I understand him, because the data on pathological pain are based upon the responses of "unsophisticated clinical patients," and those on experimental pain, on the responses of graduate students. He then makes a wholly unsupported statement; he says, "As far as observation and interpretation of sensory phenomena are concerned, these students are . . . in a different category from the average clinical patient."

But I am not at all sure that I know what Benjamin's real thesis is. He would not hold, presumably, that there are anatomical differences between the two groups, so he must believe that "conditioning" or "cultural" or economic differences make for different responses.

A great amount of effort has been devoted to demonstrating the presence or absence (according to the investigator's bias) of differences in pain threshold among Indians, Eskimos, Negroes, White subjects, North Europeans, South Europeans, men, women, the young, the aged, trained and untrained subjects, adapted and unadapted subjects, and so on. The enthusiast can "prove" about anything he wants to from this vast array of data [for references, see H. K. Beecher, *Measurement of Subjective Responses: Quantitative Effects of Drugs* (Oxford Univ. Press, 1959)]. It seems significant that no great differences have been uncovered and confirmed. Neither are the data as constant as others would like us to believe. Such differences as there are, are not great ones. In the study discussed in my report in *Science,* the difference between the two groups was tenfold. I am not at all certain how much familiarity Benjamin has with

"clinical patients" in a large American medical center of today. Certainly they are unlike those of his native Germany and unlike those of Kashmir, India, where he practiced (dentistry). Since those days he has largely spent his time in physiological laboratories (according to the recent edition of *American Men of Science*). This is by no means to question his scientific status. This information is merely relevant to the question he raised. If Benjamin is trying to imply that the clinical patients are insensitive peasant types (if such exist), he is quite wrong. They are familiar with life's advantages and "sensitive" to them. While economic brackets are only one item in placing a man, I can point out that these television-owning, automobile-driving clinical patients are charged $27.00 per day for their beds and they actually pay 70 percent of this, or $18.90 per day. It is impossible for me to believe that the *tenfold* difference I showed could be explained by any such nebulous possibility as suggested by Benjamin.

There is an extraordinary constancy in the average response to morphine and to placebos, for example, if one deals with rather large groups of patients, notwithstanding diverse backgrounds. Houde and Wallenstein, studying chronic pain in cancer patients, found in 67 patients that 10 milligrams of morphine satisfactorily relieved ("relief" was carefully defined) 65 percent. Lasagna and Beecher found in groups of postoperative patients of a similar size in different years that 65.8 and 69.3 percent, respectively, were relieved ("relief" was carefully defined here also) by 10 milligrams of morphine. Houde and Wallenstein found that a placebo satisfactory relieved 42 percent of their patients; Lasagna and Beecher's figure was 39 percent. Here are remarkably similar results in groups whose past experience, present situation, and future are highly different. If the response to "observation and interpretation of sensory phenomenon" are as labile as Benjamin believes, one would have expected the lability to show up in a comparison of these two disparate groups. It did not.

The "active" drugs aspect of my report is pertinent to the present discussion. The universal effect of morphine in relieving more or less completely the pain of a wound, in graduate students as well as in all others (sophisticated or unsophisticated, it makes no difference), has been demonstrated. But some 15 groups of investigators have now utterly failed to demonstrate any dependable effectiveness of morphine on the experimentally produced pain threshold in (usually) sophisticated subjects. Here we find effectiveness in one instance and lack of it in the other, in groups of graduate students, depending on whether or not the pain was of pathological origin or was experimentally contrived. Benjamin's thesis breaks down here, for the effectiveness of the morphine was not determined by "differences in the psychological characteristics of the subjects—differences in degree of scientific understanding and in the ability to make objective evaluation."

To turn to another aspect of the problem, Javert and Hardy found that pain thresholds in clinical patients were normal, in comparison with thresholds in volunteers in their experimental studies, for a group of women before labor, during labor, and *post partum*. Many other data could be cited to indicate that the difference postulated by Benjamin has no support.

Benjamin speaks of the "ability of the subject to evaluate pain objectively." Pain is a subjective experience, subjectively evaluated. He refers again to "the ability to make objective evaluation," in his last sentence. I do not know what he means by these statements and therefore cannot discuss them.

One can erect a thousand straw men in this field, but if the tenfold difference I showed in a very large number of individuals is to be explained on any such vague basis as "psychological characteristics of the subjects—differences in degree of scientific understanding and in the ability to make objective evaluation" (whatever that last phrase means), there must be more evidence than Benjamin has yet produced to show, first, that these characteristics exist as determinants and, second, that they are relevant to the present study. I have indicated above several kinds of data to indicate that they are not of much importance, if any, in the present connection.

HENRY K. BEECHER
Harvard Medical School,
Massachusetts General Hospital,
Boston, Massachusetts

Sterilization of Interplanetary Vehicles

The article by Phillips and Hoffman [*Science* **132**, 991 (1960)] about the sterilization of interplanetary vehicles poses some interesting and difficult problems as regards one "component" that will be engaged in space travel—namely, man himself. Perhaps it is time that thought and investigation be given to the production of germ-free human beings.

JACK DE MENT
De Ment Laboratories,
Portland, Oregon