

## Human experiment

SIR — The relative rarity with which the results of experimental work in human beings are reported in *Nature* must be the excuse, if not a good one, for the publication of a study on pain in which (1) no indication of whether consent was sought is given (and the study design probably excludes the possibility); and (2) pain experienced by individuals was increased by the experimenters' hidden actions. ("Placebo and naloxone can alter post-surgical pain by separate mechanisms", by R.H. Gracely *et al.*, *Nature* 306, 264-265; 1983). Although dental pain may be regarded as trivial, I, and I am sure many of my colleagues, would regard this study as unethical by any standard.

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● R.H. GRACELEY REPLIES — Professor Dudley's letter challenges whether consent was obtained and the ethics of giving a drug that may increase pain. It is unfortunate that the consent procedure was not described in the text. Human research protocols at the National Institutes of Health (NIH) must be approved by a formal review process that includes written informed consent. In this case, the consent form indicated that "withdrawal from the study may be accomplished at any time without jeopardy or prejudice" and informed the subjects that they may receive "a maximum of 10 mg naloxone — a drug that may be less effective than placebo in pain relief and that theoretically may increase any pain". Professor Dudley is correct in citing this omission from the manuscript but he inappropriately suggests that this study could be performed without consent.

His description of this study as unethical is a more serious matter. He criticizes not only our ethics, but those of other investigators. A dose of 10 mg naloxone has been administered to dental patients after third molar extractions in several highly publicized studies, including one published in *Nature* (272, 826-827; 1978). The increase in pain after naloxone administration was slight and caused no excessive discomfort in these experiments. Our use of naloxone was accompanied by knowledge of its effects in previous studies and by an informed consent procedure that included termination at any time. Patients not only completed this study (involving extraction of third molars on one side) but returned for a similar extraction of their contralateral third molars. They described the naloxone experiment as uncomfortable but tolerable.

Professor Dudley is apparently unaware of the previous studies assessing the effects of naloxone on postoperative dental pain or of the magnitude of the naloxone effect. Naloxone causes a minimal and temporary

increase in discomfort in this situation. However, a great majority of human medical research involves discomfort and risks. It is not the presence of these factors but their magnitude, along with important issues of consent and voluntary termination, that are of ethical concern. The discomfort and risk in this experiment were considerably less than those experienced in many routine medical studies. Unfortunately, Professor Dudley has not addressed previous studies (cited in our article) or the relative magnitude of the discomfort, and has also questioned the research policies at NIH.

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## Placebo defect

SIR — A recent light-hearted account of the banning of urea foam insulation in Canada (*Medical Post*, 15 November 1983), has drawn attention to the lack of a word in the English language to describe the opposite of a placebo. A placebo may be defined as something which, in itself, is inactive, such as a simple lactose pill. However, a placebo has been found to be effective therapeutically in about 30 per cent of patients suffering from a wide spectrum of diseases.

Little attention has been paid to the possibility that a harmless substance produces harmful effects when the patient believes it to be toxic. The author of the article in *Medical Post* suggests the word "garblow". The urea foam insulation was banned precipitately by the Government of Canada after a media crusade against the "dangerous" formaldehyde gas which the insulation may emit. Of about 80,000 households which had installed foam insulation, about 10 per cent developed symptoms which they were encouraged to attribute to the formaldehyde vapour. The English have learned to live with the particular peril of foam insulation but there must be many examples of garblow in our own press threatening our health and sanity.

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## Not by corn alone

SIR — With reference to J. R. S. Fincham's interesting article "Transposable elements and plant gene structure" (*Nature* 306, 425, 1983), I write to point out that P. A. Peterson is a member of the faculty of Iowa State University and not, as the article states, of our sister institution, the University of Iowa.

Incidentally, D.S. Robertson, mentioned in the article as the discoverer of the *Mu-1* transposable element, is also a member of our faculty.

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## Homer's wine

SIR — Wright and Cattley's chemical hypothesis about Homer's "wine-dark sea" (*Nature* 303, 568; 1983) is both interesting and evidence of a commendable piece of interdisciplinary cooperation.

But the topic of Homer's epithet is many-sided. Any "solution" of the "puzzle of the wine-dark sea" will be a function of one's particular couching of the question. The chemical hypothesis would certainly be appropriate to the question "Why did Homer call the (Mediterranean) sea wine-coloured (he mentions only red wine in his epics) when it is celebrated for its blueness?" The hypothesis that adding alkaline water to the wine of Homer's time and region turned it from red to blue complies with the scientific requirement of being empirically verifiable, in principle if no longer in practice. Yet a positive test result would not solve, or even invariably be appropriate to, other aspects of the puzzle unless one asserted reductionistically that a scientific answer is the "one proper" one.

Among the many other equally tantalizing aspects of the sea/wine topic are:

(1) Irrespective of the actual colour of the wine, should not the phrase "wine-dark sea" be seen purely or primarily as a formulaic device of the oral Homeric tradition, a recurrent epithet or a fixed metaphor? Homer uses it many times in diverse contexts in both the *Iliad* and the *Odyssey*.

(2) Should we doubt that the Mediterranean sea can look wine-red? The classicist Stanford and others have noted that it is at times a "deep purple crimson" or "mulberry" in places. So "wine-dark" could in fact mean "wine-red".

(3) How adequate, in aesthetic and/or other respects, are the various translations of Homer's original Greek phrase, namely *οινοπα ποντον*, to quote one inflexion? Down the ages it has been translated into several languages and with divergent meanings. Examples are "wine-dark sea" (Rieux, Shewring), *les vagues vineuses* (Bérard), *weinrote Meer* (Schadewalt), and *wijnkleurige zee* (Boutens). Among English translations, we have variations such as "wine-coloured sea" (Simcox), "wine-faced sea" (Cook) and even "the gloomy flood" (Cowper). The translator Cook, in fact, sees no colour connotation whatever in the original Greek phrase.

(4) If we focus on just one English translation, say "wine-dark sea", and consider it simply as an aesthetically piquant English phrase, then what is its poetic merit as such? This question entails the usual multiplicity of considerations of imagery, associations, allusions, euphonics, and phonetic symbolism, and decisions made in terms of facets of these criteria may scarcely be a function of what colour the wine was.

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