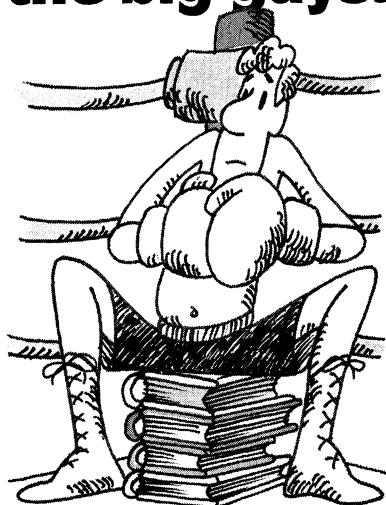


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frequency of SCE's increased with acoustic power in a critical range (3).

Free radicals are generated in aqueous solutions by pulsed ultrasound (5); their products have also been identified in the DNA thymidine of animal cells exposed to continuous wave insonation (6). The bioeffects of ultrasound responsible for the increased SCE frequency and some of the other findings described in more than 700 publications since 1950 (7) may well be the result of free radical release.

The failure of Ciaravino *et al.* to confirm our results (15 Mar., p. 1349) might be accounted for by many factors. Among these are the high degree of inter-observer variation in their SCE scoring, their high SCE baseline values, and the fact that their critical acoustical power range was not verified and was not systematically varied. These and other variables may account for the failure of some laboratories to reproduce results of others, leading to the confusion in this field.

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The following points are pertinent to Bases' letter.

1) Interobserver variation in SCE scores is expected and is the reason why controls were included. The SCE rate in our experiments did not increase above control values for any of the three independent scorers.

2) SCE baseline values vary considerably from laboratory to laboratory; for example, they were 3.28 for Kakati *et al.* (1), 16.3 for Lambert *et al.* (2), and 27.33 for Dutrillaux *et al.* (3). Our SCE baseline values were well within this range.

3) The dosimetry for our experiments was accomplished by Paul Goodwin, staff physicist at Albert Einstein College of Medicine, who also was involved in making dosimetric determinations for Liebeskind *et al.* (4). The intent of our experiments (5) was to duplicate exactly the experimental conditions of the Liebeskind *et al.* study (4) with a well-defined, nonvarying field from a specific diagnostic ultrasound device. Our earlier

attempts to verify their results with our equipment had been unsuccessful (6).

4) The Albert Einstein group declined to score the slides that we made on their premises with their equipment.

5) Bases suggested that we undertake "independent double-blind scoring by recognized experts . . ." of our slides (7). The coded slides were sent to William Morgan (at the University of California Medical Center, San Francisco); his evaluation agreed with ours.

6) Bases then suggested (8) that we send the slides to David Jacobson-Kram (George Washington University) for evaluation. His scoring agreed with ours.

7) The results of Martin *et al.* (9) are negative [χ^2 tests . . . were not significant. . .] (9, p. 993), as are the results of most of the studies in this area (10).

8) Makino *et al.* (11) used a Bransonic 12 cell disrupter that produces a continuous sound wave at a frequency of 20 kilohertz; their study thus has little relevance to diagnostic ultrasound.

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Murine Retroviral Vectors and Human Gene Therapy

In his excellent and timely article, "Prospects for human gene therapy" (26 Oct. 1984, p. 401), W. F. Anderson discusses some of the possible difficulties surrounding the envisaged future use of retroviral vectors in attempts to correct human genetic defects. Such vectors unfortunately appear to have a strong propensity for deleting or rearranging their own sequences. One way in which such structural alterations might arise is through recombination events with homologous endogenous viruses already present in the cellular genome. In addition to the possible loss of vector-born

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sequences, such events could lead to the potentially harmful production of packageable infectious recombinant virus. Since avoidance of any homology with endogenous retroviruses is thus desirable, Anderson suggests using mouse retroviral vectors as a delivery system. However, quite apart from the putative inherent instability of recombinant retroviruses, this proposal is probably insufficient to overcome the recombination problem. This is because sequences with homology to mouse mammary tumor virus (1), Moloney murine sarcoma virus (2), Abelson murine leukemia virus (3), and Moloney murine leukemia virus (4) have recently been found in the human genome. Indeed, sequences containing murine retrovirus long terminal repeats (LTR's) have been employed in the screening of human genomic libraries (5).

There would appear to be two alternative means of circumventing this problem which would eventually enable murine vectors to be used in human gene therapy. Every such attempt would have to be preceded by a search for vector-homologous sequences in the patient's genome by Southern blotting. If sequences homologous to murine retroviral vectors currently in use are indeed found to be common in human genomes, as suggested by the work of Repaske *et al.* (4), alternative vectors derived from more distantly related species would have to be considered. Clearly, considerable attention will have to be directed toward the construction and experimental trial of appropriate retroviral vectors in order to optimize any future gene delivery system for use in humans.

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David Cooper raises a legitimate concern regarding possible recombination between murine leukemia virus (MuLV)-based viral vectors and endogenous retroviral sequences present in the human genome. In fact, recombination between a deletion mutant of Moloney MuLV and homologous sequences in mouse DNA involving a 400-base-pair segment that was 78 percent homologous

has recently been demonstrated (1). To evaluate possible recombination between MuLV's and human endogenous retroviral sequences, mouse cells have been cotransfected with defined *gag* and *pol* deletion mutants of Moloney MuLV (2) and cloned *gag* and *pol* segments of endogenous human retroviral DNA's. In no case could recombination be demonstrated. Although the deduced amino acid sequences comprising the *gag* and *pol* regions of endogenous human retroviral sequences are evolutionarily related to comparable segments of MuLV's (3), the extent of polynucleotide sequence identity may be too low for homologous recombination. For example, the *gag* and *pol* regions of human endogenous MuLV sequences are only 35 percent and 44 percent, respectively, related to analogous segments of MuLV. Furthermore, nucleotide sequencing of several different human endogenous retroviral clones (4) has indicated the presence of point mutations, inappropriate terminator codons, and deletions of various sizes, any one of which could render recombinants that might be generated replication defective.

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Erratum: The name of M. Wallroth was omitted as the fourth author of the report "A simple and general method for transferring genes into plants" by R. B. Horsch *et al.* (8 Mar., p. 1229).

Erratum: In the legend for figure 2 of the report "Plasmodium falciparum malaria: Band 3 as a possible receptor during invasion of human erythrocytes" by V. C. N. Okoye and V. Bennett (11 Jan., p. 169), a reference for the use of metrizamide to purify schizonts was inadvertently omitted after the fifth sentence. It should have read, "Following the method of C. S. Pavia *et al.* [*Am. J. Trop. Med. Hyg.* **32**, 675 (1983)], as modified by Lyons."

Erratum: In figure 1 of the report "How bees remember flower shapes" by J. L. Gould (22 Mar., p. 1492), the results shown for the 24-element patterns (K₁ and K₂) should have been $P > 0.05$.