PAI 00958

Ann Arbor, MI, March 26, 1986

Dear Editor.

My participation in a recent mini-symposium on ethical issues in pain research (Fifth annual meeting, American Pain Society, October 20, 1985, Dallas, TX) led me to formalize some thoughts regarding animal models of chronic pain. I wish to present a very brief summary of my arguments to readers of *Pain* in the hope that this action will lead to a serious reconsideration of the issue. I believe that such a reconsideration is timely because we now have some results from experiments that have used chronic pain models and because of the increasing need for scientific societies to address the ethical concerns of those within and outside the biomedical community.

'Chronic pain' is almost never defined, but I am referring to pain that may be intermittent but present during most waking hours for at least 1 week and usually much longer. Given that definition, my review of the available evidence and my personal clinical experience lead me to conclude that there are neither clinical nor scientific reasons for conducting experiments in which the animal subject experiences chronic pain. This conclusion could be challenged seriously if it could be shown, in humans, that chronic pain was effective uniquely in producing a clinically significant condition for which other probable causes had been ruled out. This requirement eliminates depression and various treatment failures as possible justifications for animal models of chronic pain. The most common experience, in fact, is that effective treatment of a chronic painful condition eliminates the pain and the associated depression without leaving in its wake a chronic neurologic disorder attributable to prolonged nociceptive input.

Pathological conditions of peripheral nerve or of innervated tissue have been shown to produce changes in the responsiveness of peripheral receptors, nerve fibers, and of central neurons. The pathological changes in peripheral tissue could be the cause of various painful conditions and clearly deserve serious investigation. Such studies do not, however, require that the experimental animal experience chronic pain. Depending on the focus of the study, local or systemic analgesics or even pain-preventing surgery can be and, in some laboratories, is used. This would not compromise scientific design or significance because there is no evidence that the pain of arthritis or chronic neuropathy, for example, produces central nervous system changes that alone are painful, debilitating, or even recognizable clinically. Central changes certainly do occur in the widely recognized central pain syndromes, and probably in phantom limb pain, but the development of animal models of these conditions requires, in my opinion, a more precise description of the clinical pathologic anatomy and physiology than is available now. But even animal models of central pain syndromes, if necessary and possible, need not require that the subject experience chronic pain because there is no clinical evidence that pain causes or even facilitates the development of these syndromes. Euthanasia could and should be performed as soon as there is evidence that the clinical condition has been established.

For the present, all of what needs to be learned about pain mechanisms requires only that the animal subject experience brief and relatively infrequent exposure to noxious stimuli that are under the animal's control and that would be tolerated by humans. In my opinion, the burden of proof falls upon those who argue otherwise.

University of Michigan Medical Center, Chief, Neurology Service, Veterans Administration Medical Center, Ann Arbor, MI (U.S.A.) KENNETH L. CASEY