

TABLE 1. Pharmacokinetic Analysis of Recovery from the Neuromuscular Blocking Effect of Succinylcholine

| Patient Group | 25-75% Recovery Time (s) | 25-75% Rate of Decline (R) (% min ⁻¹) | t × R | Injection-25% Recovery Time (s) |
|---------------------|-----------------------------------|--|--------|---------------------------------------|
| Term-pregnant | 83 | 1.66 | 137.78 | 470 |
| Postpartum | 95 | 1.90 | 180.50 | 685 |
| Control subjects | 102 | 2.04 | 208.08 | 501 |
| Oral contraceptives | 104 | 2.08 | 216.32 | 499 |

t = duration.

Based on mean data from Leighton *et al.*¹

Leighton *et al.*¹ are summarized in table 1 in order of increasing duration and rate of decline of effect. Control and oral contraceptive users have similar t × R values that differ from those in term-pregnant and postpartum patients, which in turn differ from each other. Thus the observations of Leighton *et al.*¹ are due to differences in m and/or A_{min} and/or k₁₀. Because equivalent (rather than equipotent) doses were administered, a difference in m could be the result either of a shift in the dose-response curve resulting from a pharmacokinetic perturbation (for example a change in the volume of distribution or clearance of succinylcholine), or of a change in succinylcholine pharmacodynamics, *per se* (i.e., a change in cholinergic receptor sensitivity to a given concentration of succinylcholine). These changes may occur simultaneously, with the observed effect being the net result of either two opposing or additive effects. A change in m due to a pharmacokinetic perturbation will cause a resultant change in A_{min} but not C_{min} (threshold or minimum effective concentration), the latter reflecting a true change in pharmacodynamics. The longer injection -25% recovery time in postpartum patients reflects either a decreased volume of distribution (resulting in higher initial

concentrations and thus a longer time period for decline to the threshold for start of recovery) or to a change in C_{min} such that recovery now starts at a different concentration. Clearance and elimination processes (as opposed to distribution) probably play a somewhat minor role in the injection -25% recovery times. On the other hand, the differences (albeit not statistically significant), in the rate of decline of effect (R) in the linear 25-75% effect range are more a reflection of changes in the elimination of succinylcholine, presumably due to differences in serum cholinesterase activity if this is assumed to be the major pathway of succinylcholine clearance from the body. The point to be made from the data of Leighton *et al.*¹ is that oral contraceptives and the physiologic perturbations of pregnancy and the postpartum period may modify not only the pharmacokinetics but also (and perhaps predominantly) the pharmacodynamics (concentration-effect relationship) of succinylcholine. Unfortunately, separation of these two effects must await the development of a sensitive and selective assay for succinylcholine in biologic fluids.

IQBAL M. RAMZAN, PH.D.

Assistant Professor

Department of Pharmaceutical Sciences

School of Pharmacy

University of Pittsburgh

Pittsburgh, Pennsylvania 15261

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Animal Welfare and Biomedical Research

To the Editor:—Shapiro's otherwise excellent editorial, "Animal rights and biomedical research: No place for complacency,"¹ calls for additional comment.

The fact that research using animals has benefited mankind does not justify abuses that have occurred. In addition, Shapiro's point that nature itself is inhumane is not justification for cruelty.

The major humane groups are not antivivisectionist, but they do want to reduce pain and suffering in exper-

imental animals as much as possible. Scientists should want to do this also. A scale of pain and suffering has been devised by the Scientists Center for Animal Welfare.* This scale, together with peer review for importance, can be used to determine the ethical cost of most experiments

* Scientists Center for Animal Welfare, 4805 St. Elmo Avenue, Bethesda, MD 20814.

and whether approval should be granted. In addition, an extremely painful experiment, regardless of importance, should not be approved. A change in method, involving less pain, may make the experiment acceptable. A similar concept has long been used in Sweden and England.

The use of pound animals in research is a complicated issue. Scientists say that it does not make sense to euthanize pound animals and also breed animals for research. It is not that simple. First and foremost, *it is not a question of death but of suffering*. Purpose-bred animals, because of their genetic and environmental background, suffer less distress and fear than pound animals, when used in research,² and fewer can be used to obtain statistical significance.

Some scientists use pound animals because they cost less. However, hidden costs are high. In 1973, the National Heart and Lung Institute reported that between 1966 and 1970, 43% of pound animals were rejected. Of those animals that were accepted, 53% became ill and 13% died. If this happens during an experiment, from causes not related to the experiment, it can be expensive. If, as a result, the data are misinterpreted, it can be disastrous. The cost of animals is only a small part of the total cost of an experiment, and today the National Institutes of Health uses purpose-bred animals only.

The pound or shelter is a place where lost, stray, or unwanted animals can be brought to be reclaimed by their owners, adopted, or euthanized. If shelter animals are experimented on, many people who consider this inhumane will no longer support the shelter or bring in animals.†‡ This contributes to the stray-animal population. Finally, scientists should not base their research on the existence of a permanent stray-animal population. This is a conflict of interest for the scientist who also should want to see the stray-animal population brought to zero.

† ASPCA Letter to Members, December 28, 1972.

‡ Anchel M: Statement for the Committee on the Use of Laboratory Animals in Biomedical and Behavioral Research of the National Research Council and Institute of Medicine of the National Academy of Sciences, February 11, 1986.

§ Hearings before a Subcommittee of the Committee on Interstate and Foreign Commerce, House of Representatives, on H.R. 1937 and H.R. 3556, September 28 and 29, 1962.

Rapid-sequence Induction: Vecuronium versus Pancuronium versus Succinylcholine?

To the Editor:—A recent publication by Lennon *et al.*¹ seems a rather straightforward, simple description of the clinical use of vecuronium and/or atracurium in doses far exceeding the ED₉₅. However, I believe that the conclusions and experimental protocol deserve comment:

Shapiro writes that “steady progress in the welfare of laboratory animals has been occurring quietly.” But this progress was made *in spite of the opposition of essentially the entire scientific community*. When an Animal Welfare Act was proposed in 1962 and again in 1966, the record shows an overwhelming percentage of statements by the scientific community to be against passage.§¶ On what basis should animal-welfare groups trust the scientific community?

Shapiro writes that his Institutional Animal Care and Use Committee was able to make minor and easily achieved alterations in 30–40% of submitted protocols, which would reduce stress to experimental animals. This is a splendid achievement that demonstrates what can be done when there is concern.

The recently enacted Dole–Brown bill (1985) provides that an Institutional Animal Committee be formed at each facility that uses animals. Among other concerns, the Committee is “to provide representation for general community interests in the proper care and treatment of animals.” If this is carried out conscientiously, it should greatly allay the mistrust and frustration that was the basis of many laboratory break-ins. The new law also should help prevent abuses and expose those that do occur.

HERBERT RACKOW, M.D.
Professor Emeritus, Anesthesiology
147-01 Third Avenue
Whitestone, New York 11357

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¶ Hearings before the Subcommittee on Livestock and Feedgrains of the Committee on Agriculture, House of Representatives, March 7 and 8, 1966. Hearings before the Committee on Commerce, United States Senate, S 2322, S 3059, S 3138, March 25, 28, and May 25, 1966.

1. Lennon *et al.* concluded that “vecuronium may be preferred for situations in which succinylcholine is contraindicated and in which rapid paralysis is mandatory.” The quality of intubation conditions during a rapid-sequence induction could be critical for patient survival (*e.g.*,