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EDITORIAL VIEWS

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Who's Afraid of Blaise Pascal?

Undoubtedly many of our readers are already aware that some changes in Journal policy have occurred as detailed in the Guide for Authors published in the January 1982 issue. If you are not in the habit of reading that scintillating section of the Journal then you likely would not recognize all of the changes until the June or July 1982 issues. The changes are small ones. After thirteen years, pressure measurements no longer will be reported in torr units. Authors instead may use mmHg, cmH_2O, or kPa. If they choose the latter, then pressure measurements must be reported parenthetically in mmHg or cmH_2O also. Another change will be even less noticeable; references will provide the names of all of the authors and not just the first three.

Why discard torr? Pick up any nonanesthesia journal of medical science and the units for pressure measurements will be mmHg, cmH_2O, or kPa. In the Common Market countries the International System of Units (SI) is required and kPa is the standard unit of pressure. In the United States those SI units which are considered to be entirely foreign to the clinician's ear (and eye) are rejected. Thus, although molar units for reporting concentrations or amounts may be preferred scientifically and/or called for by SI, reporting drug doses or laboratory measurements in molar units rather than in the familiar units of mass could introduce unnecessary risk factors in patient care. In the same way vascular pressures, partial pressures, and airway pressures reported only as kPa would cause confusion and increased risk in clinical application. Thus, we are dropping torr, which is not a familiar unit to physicians other than anesthesiologists, but we are not embracing the SI unit for the reasons given.

In a recent informal (and therefore anecdotal) survey of over a dozen editors of prominent medical and scientific journals in this country, I requested information concerning their use of SI units—present and future. The response was predictably quite variable, ranging from those who rejected the concept of ever accepting SI units (in their entirety) to those who viewed this as inevitable but worth resisting. None were actively pursuing the forced use of "undesirable" SI units. I was particularly attracted to the response of one of these editors. It was his view that the stimulus to change units should come from the authors and readers, not the editors, of journals. Your Editorial Board agrees. Accordingly, the unit torr, introduced by editorial fiat in 1969,[1] will be abolished and pressure units in common usage will be adopted again. We will not deny the author his right to use kPa but we will not impose this on the reader without accompanying familiar units.

Regarding the policy of listing authors in references, those journals such as ANESTHESIOLOGY which adopted the "three-authors-only" policy created a minimonster. Once upon a time the second most prestigious position for listing one's name on a multiauthored publication was not second author but rather last author. More often than not, the senior author in whose laboratory the work was done, was the last author and with this knowledge the interested reader could identify quickly the source (and possibly the quality) of the work. With a "three-authors-only" policy this convenient identification process often is short-circulated and one must go to the full

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published work. The minimonster created is that in the minds of some, the second most prestigious position today for listing one's name on a multiauthored publication is now neither second nor last but rather third. This, along with hula hoops and pet rocks, will be difficult to explain to the next generation.

Whether these small changes can be considered progress is debatable, rather they are made in the interest of uniformity and common sense. If those interests are served, our purpose is accomplished.

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Reference

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Opiate Receptors and Their Definition by Antagonists

THAT RECEPTORS EXIST as a physical entity is in no doubt. Nevertheless, the term "receptor" more often than not is a hypothetical construct used to describe drug effects vis-a-vis a given physiologic endpoint. As such, the receptor represents an operationally defined entity through which agents are able to exert a powerful effect on cellular function.

The relative potency of a series of structurally related agonists which produce a given physiologic or biochemical effect define a structure-activity relationship that is *characteristic* for that receptor. Thus, a receptor is defined in the same way one would define a lock by the set of keys that operate it. A particularly valuable paradigm for studying receptors has been the development of agents with high affinity for a particular receptor and low efficacy, *i.e.*, antagonists. Thus, an antagonist will recognize a given receptor conformation and, while occupying that receptor, prevent activation by an agonist that would otherwise act on that receptor. Thus, it is possible in a shorthand fashion to "define" the nature of the receptor with which some novel agonist interacts by determining whether a receptor-selective antagonist is able to effectively block the effects produced by the novel agonist.

Receptor interactions of particular agonists and antagonists are characterized by certain quantifiable parameters; one of these is the pA_2. *In vitro*, the pA_2 is the negative log of the concentration of antagonist that doubles the concentration of agonist necessary to produce a particular level of response. If experimental conditions are appropriate, the pA_2 is the negative log of the antagonist-receptor equilibrium dissociation constant.[1] If a series of agonists act on the same receptor, then, though different concentrations of each agonist may be required to produce the *same* physiologic or biochemical effect, the pA_2 of the antagonist will be the same no matter which of the agonists is employed to determine it.

In vivo, dose must be substituted for concentration since it is usually not possible to adequately determine the tissue concentration of antagonist and, therefore, the pA_2 can no longer be strictly identified with the negative log of the dissociation constant. However, it is often reasonable to assume that dose is proportional to concentration, and the criterion that if two agonists are acting on the same receptor they should yield similar antagonist pA_2 values is still valid.

Studies examining the antagonism by naloxone of the analgesia produced by a wide variety of systemically or intrathecally administered opiate alkaloids and peptides including morphine, levorphanol, ethylketocyclazocine, [d-ala^2-met^5]-enkephalin, and β-endorphin, have uniformly provided pA_2 values of approximately 7.[2,3] That the naloxone pA_2 obtained in the presence of these structurally diverse agonists is the same suggests that each of these agonists is producing its effects by an action on the same receptor. In contrast, the pA_2 value of naloxone obtained in the presence of [d-ala^2-d-leu^5]-enkephalin is approximately 6, suggesting that naloxone has a lesser affinity for the spinal receptors acted upon by this peptide to produce analgesia.[4]

Further definition of a receptor population can be achieved by comparing the affinities of a number of antagonists for a pharmacologically similar population of receptors. If the same receptor population is acted upon by a series of agonists, then the relative ordering of the pA_2 values for the several antagonists vis-a-vis these different agonists should be the same. Thus, the pA_2 of naltrexone in the presence of morphine is 8.[5] It would be predicted that those agonists for which naloxone has

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