

Limitations of the Effective Dose Equivalent

TO THE EDITOR: It was disappointing to read Dr. Poston's paper and his outline of the MIRD committee's view that the application of the effective dose equivalent in nuclear medicine is inappropriate (1). Clearly there are limitations to the use of the effective dose equivalent as summarized in Dr. Poston's paper. However, there has been a growing need in the medical field for simple expressions of the risks associated with ionizing radiation. The public's general perception that ionizing radiation is dangerous is well known. In addition, there is growing awareness of the need to educate medical staffs in the risks associated with ionizing radiation.

The problem is how to explain such risks. Organs receiving significant levels of radiation vary from study to study and, as noted by Dr. Poston, the underlying associated risks depend on the organ. Therefore, individual organ absorbed doses are clearly the fundamental structure for risk assessment and must always be considered in any review of medical procedures. The effective dose equivalent should be regarded as a derived parameter that gives a first order approximation to the risks associated with radiation exposure.

There are limitations to the accuracy of the effective dose equivalent, as outlined by Dr. Poston. However, we do not believe that these are severe enough to condemn its use. Indeed, the ICRP indicates in *ICRP Publication 53* that the effective dose equivalent can be used for medical exposures as long as its limitations are understood (2). Considering the limitations noted by Dr. Poston, the revised weighting factors have been increased in number in *ICRP Publication 60* (3), taking into account both fatal and nonfatal effects of radiation. The ICRP recognized that weighting factors are imprecise and therefore proposed a banding of weighting factors of similar values for simplicity. Other aspects of risk mentioned by Dr. Poston such as cost of ill health, loss of income, etc., can be considered separate issues of cost-benefit analysis (4) generally only appropriate for consideration of groups (i.e., when seeking ethical committee approval).

Applying appropriate age- and sex-related risk factors to the effective dose equivalent (or effective dose) (5) for patients enables comparison of techniques from a dosimetric view. Effects of both variations on anatomy and stages of disease are likely to produce errors at least as great as in the calculation of organ dose. Dr. Poston quotes from the 1977 ICRP statement regarding medical exposure. It is right and proper that medical exposures are not considered in terms of the ICRP limits for occupational exposure. However, this does not preclude the use of the effective dose equivalent as a guide to associated risk. These guidelines can be weighed against the benefits that accrue from exposure. It would be inappropriate to consider such benefits in any calculation of risk. The balance of risk and benefit should remain a separate consideration.

The risks and hazards associated with radiation are never going to be an exact science. The effective dose equivalent can be a useful parameter to indicate risk and has gained general acceptance in the European nuclear medicine community (6, 7). As long as its limitations are recognized, it can provide a useful yardstick for assessing risk, particularly in situations where individual organ doses can vary and for comparing risk associated with different tests. Abandoning the effective dose equivalent, or the effective dose as it is now defined in *ICRP Publication 60*, would be a retrograde step and difficult to justify on the basis of the arguments put forward by Dr. Poston.

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REPLY: The MIRD Committee read with interest the letters submitted by Shields and Lawson; Harding, Elliott and Shields; Clarke; and Thomson, Chandler, and Griffiths. Nevertheless, it is the opinion of the MIRD Committee that its concerns regarding the application of the effective dose equivalent are clearly expressed in the April 1993 editorial (1).

The Committee's objections are not with the concept of comparing risks associated with different kinds of radiation exposures, but rather with the use of the effective dose equivalent in estimating individual patient risk in light of the way the tissue-weighting factors were developed by the ICRP (2,3). The tissue-weighting factors developed in both *ICRP Publication 26* (2) and *Publication 60* (3) were derived from Japanese A-bomb survivor data. These exposures involved high dose, high dose rate and relatively uniform whole-body irradiation. In contrast, exposures from the internal emitters used in nuclear medicine are typically low doses delivered at low dose rates, and the activity distributions are usually nonuniform within organs and tissues of the body. Since each of these factors affects the relationship between the absorbed dose and the biological effect, extrapolations that do not include corrections for differences in these factors can be unreliable.

Usually the absorbed dose calculation in nuclear medicine is made to provide a basis for estimating the effect of radiation exposure on a particular patient or class of patients. For this purpose, we recommend the estimate of the absorbed dose to specific organs while acknowledging that in some cases other physical factors may need to be considered. For a comparison of the risk to a collective population for various kinds of radiation exposures, the effective dose equivalent may be useful. Its use in evaluating the actual risk to a particular patient, however, is questionable. Consistent with discussion in *ICRP Publication 60* (3), the Committee emphasizes the fundamental importance of the absorbed dose and the mean absorbed dose to the organ in estimating the effects of exposure on individual patients or classes of patients.

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Latex D-Dimer for Diagnosing Pulmonary Embolism

TO THE EDITOR: We read with interest the article by Harrison et al. in which the usefulness of a latex D-dimer assay in the exclusion of pulmonary embolism was emphasized (1). We too are very interested in using the D-dimer assay in the diagnostic work-up of patients with suspected pulmonary embolism, but feel that a few comments are in order.

First, as discussed by the authors, several reports have shown that ELISA D-dimer assays may be of potential use in the exclusion of pulmonary embolism (2-4). The only problem is that to date, no management studies have been published which show the safety of withholding anticoagulant therapy in patients with normal D-dimer results. This makes the suggestion that it is now safe to use D-dimer assays in the clinical practice premature, and may cause readers to believe that such a practice is definitely established.

The most important point of interest, however, is the fact that this report is the first one to advocate the use of a latex method for the exclusion of pulmonary embolism. Many reports, using various latex methods, have shown that latex tests are not sensitive enough for screening in suspected venous thromboembolism (4-6). Although the detection limit of the latex technique used in the study by Harrison et al. may be better than previous assays, a sensitivity of 94% in 16 patients with proven pulmonary embolism results in a 95% confidence interval with a lowest value of 70%. This means that up to 30% of patients with proven pulmonary embolism may remain undetected when relying on a normal latex D-dimer result alone. Furthermore, in a recent study of 151 consecutive patients with suspected pulmonary embolism, we found that latex tests were normal in 7%-15% of patients tested, while at the same time the same manufacturers (ELISA) showed elevated values (4). This could easily lead to pulmonary embolism to be missed by latex tests in a substantial number of patients.

Therefore, we would like to conclude that D-dimer should presently only be considered a research tool and should be used with great caution in the routine management of patients with pulmonary embolism until careful clinical studies have proven its reliability.

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Negative Predictive Value of C-Reactive Protein Testing

TO THE EDITOR: In a 1989 article, Drs. Thomas and Cobby (1) reported on the negative predictive value of the C-reactive protein test in patients with clinical suspicion of deep venous thrombosis. We wanted to see if this observation would be applicable to the detection of pulmonary embolism.

We asked our colleagues in the emergency department to request a C-reactive protein test in patients referred to us for lung scans for possible pulmonary embolus. This was no small undertaking in a private hospital practice, but eventually we were able to collect data on 47 patients. The C-reactive protein test was performed in a clinical laboratory and reported as positive if the serum level equaled or exceeded 6 µg/ml. A discharge diagnosis of pulmonary embolus was supported by clinical and laboratory data including mismatched perfusion/ventilation defects in a lung scan, angiography in three cases and clinical grounds in all. A discharge diagnosis excluding pulmonary embolus was supported additionally by no hospital readmissions or significant clinical events during a follow-up period of 6 mo. The C-reactive protein test was positive in 20 patients including 15 with a discharge diagnosis of pulmonary embolus. The C-reactive protein test was negative in 18 patients, none of which had a discharge diagnosis of pulmonary embolus.

In this small series, a negative C-reactive protein test has a high negative predictive value for pulmonary embolus. Given the simplicity and low cost of the test, it might be a good idea to start a multi-institutional prospective study of the C-reactive protein test in patients suspected to have pulmonary embolus.

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