genase (ADH) (*4*). The findings can be explained adequately by differences in hepatic first-pass metabolism related to the rate of delivery of alcohol to the liver: with more rapid delivery, more alcohol bypasses hepatic alcohol dehydrogenase. This explanation is supported by the finding that famotidine, which is not believed to have an appreciable effect on gastric ADH, can increase apparent alcohol absorption, and that a similar effect can be demonstrated in animals that lack gastric ADH (*5*).

We would, therefore, disagree with the final suggestion of the authors: that the effect of erythromycin on alcohol absorption might be of more concern in individuals with low gastric alcohol dehydrogenase activity, including those taking cimetidine. First, the effect of erythromycin in the subjects studied by Edelbroek et al. (*1*) was to make alcohol *fully* bioavailable. The volume of distribution of ethanol has been shown to be equivalent to total body water (~0.64 liter/kg) (*6*), so that the theoretical Cmax in this study resulting from complete distribution of the dose of 0.5 g/kg in 0.64 liter/kg would be 78 mg/dl, almost identical to the peak alcohol level observed −77 mg/dl. How could alcohol be made any more than fully bioavailable in selected populations? That would require *de novo* synthesis of alcohol! Second, the incremental increase in alcohol bioavailability with erythromycin is likely to be diminished, rather than enhanced, in those with low first-pass metabolism (an effect previously attributed to diminished activity of gastric ADH), such as females, fasting males and patients taking H2-receptor antagonists. In these subjects, alcohol is already more "fully" bioavailable, so that there is less alcohol remaining, out of the amount ingested, to become available for enhanced absorption due to accelerated gastric emptying. Third, the effect of H2-receptor antagonists is only demonstrable with very low alcohol loads (0.15 g/kg, compared with the 0.5 g/kg used by the authors), where even complete bioavailability would not raise Cmax alarmingly. In contrast, the motility effects of erythromycin, as shown nicely in this study, have an effect even with substantial alcohol loads.

REFERENCES

1. Edelbroek MAL, Horowitz M, Wishart JM, Akkermans LMA. Effects of erythromycin on gastric emptying, alcohol absorption and small intestinal transit in normal subjects. *J Nucl Med* 1993;34:582–588.
2. Burnham D, Miller D, Karlstadt R, Friedman C, Palmer R. Famotidine increases plasma alcohol concentration in healthy subjects. *Aliment Pharmacol Ther* 1993: in press.
3. Burnham D, Miller D, Karlstadt R, Friedman C, Palmer R. Effect of famotidine on alcohol absorption: a re-evaluation [Abstract]. *Am J Gastroenterol* 1993;88:1503.
4. Levitt MD. Do histamine-2 receptor antagonists influence the metabolism of ethanol [Editorial]? *Ann Int Med* 1993;118:564–565.
5. Batra SC, Mirmiran-Yazdy A, Gentry RT, Korsten MA, Lieber CS. First pass metabolism of ethanol persists in hamsters despite the absence of gastric alcohol dehydrogenase. *Gastroenterology* 1993;104:A875.
6. Wagner JG, Wilkinson PK, Ganes DA. Parameters of V_m and K_m for elimination of alcohol in young male subjects following low oral doses of alcohol. *Alcohol Alcohol* 1989;24:555–564.

Robert H. Palmer
Daniel Burnham
SmithKline Beecham Pharmaceuticals
King of Prussia, Pennsylvania

REPLY: Drs. Palmer and Burnham are correct in that, if our data are pooled (which would be statistically incorrect), about 70% of the variance in peak blood alcohol concentrations is accounted for by the rate of gastric emptying. In view of recent observations, including those made by the authors, the relative importance of hepatic and gastric alcohol dehydrogenase in first-pass metabolism of alcohol is contentious and dependent on the alcohol load (*1,2*).

We therefore agree that the impact of either reduced levels of gastric alcohol dehydrogenase, or decreased exposure to gastric alcohol dehydrogenase as a result of more rapid gastric emptying after erythromycin is uncertain.

Our study confirms that first pass metabolism of alcohol (either gastric or hepatic) is significant, in that the area under the curve (AUC) for alcohol was substantially greater after erythromycin.

REFERENCES

1. Levitt MD. Do histamine-2 receptor antagonists influence the metabolism of ethanol [Editorial]? *Ann Intern Med* 1983;118:564–565.
2. Lewis JH, McIsaac RL. H_2 antagonists and blood alcohol levels [Letter]. *Dig Dis Sci* 1993;38:569–572.

M. Horowitz
M. Edelbroek
J. Wishart
L. Akkermans
Royal Adelaide Hospital
Adelaide, Australia

Application of the Effective Dose Equivalent to Nuclear Medicine Patients

TO THE EDITOR: The international nuclear medicine community has cause to be extremely grateful to the MIRD Committee for its seminal work on internal dosimetry and for the magnificent service it has provided over the years in tabulating invaluable basic data. We read the recent article on the application of effective dose equivalent (*1*) with great interest, but find it necessary to express serious concern. The opinions expressed therein on behalf of the MIRD Committee could unfortunately be described as ill-founded and unhelpful. They threaten to set back progress made in comparison of potential hazard from different medical procedures by ten years or more.

The effective dose equivalent (now known as effective dose) is indeed a weighted sum of doses to individual organs where the weighting factors are based upon estimates of relative risk of stochastic effects from irradiation of the different tissues. The concept was introduced by the ICRP as a means of relating inhomogeneous irradiation of the human body to a comparable whole-body radiation and its purpose was indeed initially to facilitate the protection of workers occupationally exposed to radiation. Its use has since been widely recommended for comparison of doses to patients from medical diagnostic procedures (*2–5*) and it has been found to be very useful for this purpose (*6,7*). It is accepted that its use is not appropriate for therapeutic procedures, where deterministic (nonstochastic) processes predominate.

Dr. Poston and the MIRD Committee now pronounce that use of this quantity for individual patients undergoing diagnostic nuclear medicine procedures is "inappropriate." They cite four reasons and we shall deal with each in turn:

1. It is stated that the effective dose equivalent was intended for radiation protection purposes and that the risks were to be compared with mortality in safe industries. This is not an argument against using the effective dose equivalent as a single figure indicator of hazard. The fact that a quantity is

used to compare risks in one sort of situation does not invalidate its use in another.

2. Dr. Poston reminds us that the risk coefficients assigned to individual tissues (and thus the tissue-weighting factors) were assumed to be independent of the age and sex of the exposed individual. The pattern of coefficients might be very different for an individual patient than for the average occupationally exposed adult. This point was recognized by the ICRP in 1980 when they observed that the accuracy of the risk estimates themselves did not justify the use of different weighting factors for workers as distinct from the population as a whole. Age-specific and sex-specific risk coefficients have been developed in some detail by the National Radiological Protection Board (NRPB) (*7*). They conclude that, bearing in mind the large uncertainties in the analysis, it is reasonable to take one set of tissue-weighting factors for the whole population but to apply a different estimate of detriment to each of three broad age bands. (See our recommendation below.)
3. Dr. Poston notes that the calculation of EDE as originally recommended by the Commission only involved six different tissues with all others lumped into a category called "remainder." This is true. The new definition of effective dose involves 13 tissues. Clearly this is an area in which refinements will be made as knowledge advances. We cannot see this as an argument against the use of the concept for nuclear medicine patients. Perhaps the authors have in mind the idea that in some nuclear medicine applications an individual organ dose may be notably high and that this fact would be lost within the weighted calculation of an EDE. We would agree that in such cases the notably high individual organ dose should be quoted additionally.
   Stabin et al. (*8*) point out that the use of effective dose is certainly preferable to "total body dose, which is quite useless in almost all situations in medicine." However, they also recommend consideration of individual organ absorbed doses and we would not disagree. In any scientific assessment of dosimetry, it will always be important to define the model used, the methodology and the resulting calculations of individual organ doses. This does not detract from the advantages of a single figure when comparing risks from different procedures.
4. Dr. Poston states incorrectly that the ICRP has given little guidance on the use of effective dose equivalent as an indication of risk in medical exposures, and he quotes an irrelevant paragraph from ICRP 26 which refers to dose limits. In fact, the ICRP has stated clearly in its publication no. 52 (page 23):

   > "In order to facilitate a comparison between different types of radiological investigations, the effective dose equivalent is a convenient measure."

   On the same page, the Commission notes the dependency of risk coefficients on age and sex but concludes,

   > "However the weighting factors assigned are probably not very sensitive to changes in age of the population. Therefore the effective dose equivalent can be used in comparisons of the radiation exposure to a patient from different procedures used in diagnostic nuclear medicine and in research."

In summary, we conclude that Dr. Poston and the MIRD Committee have unfortunately failed to appreciate the significant advantages to be gained from the use of the concept of effective dose equivalent for nuclear medicine procedures. Furthermore, they have misrepresented the position of the ICRP.

We consider that the concept of representing nonuniform dose distributions by a single figure is invaluable in comparing different radiological procedures. We continue to recommend its use for medical diagnostic procedures and find an increasing general awareness of effective doses in millisieverts. For those who are not specialists in the science of radiation protection there really is no practical alternative. The conversion of effective dose values to risk estimates (essentially the concern of your correspondents) is rarely necessary. If, however, this is required, then we suggest the use of the ICRP's figure for detriment of 73 per million per mSv for the general population, applying a factor of 2 for pediatric patients and a factor of 0.2 for geriatric patients.

REFERENCES

1. Poston JW for the MIRD Committee. Application of the effective dose equivalent to nuclear medicine patients. *J Nucl Med* 1993;34:714–716.
2. Johansson L, Mattsson S, Nosslin B. Effective dose equivalent from radiopharmaceuticals. *Eur J Nucl Med* 1984;9:485–489.
3. Huda W, Sandison GA. The use of effective dose equivalent, H_E, as a risk parameter in computed tomography. *Br J Radiol* 1986;9:1236–1238.
4. Shields RA, Lawson RS. Effective dose equivalent [Editorial]. *Nucl Med Commun* 1987;8:851–855.
5. ICRP Publication 52. Protection of the patient in nuclear medicine. *Annals of the ICRP, volume 17.* Oxford: Pergamon Press; 1987.
6. UK Department of Health, ARSAC. Notes for guidance on the administration of radioactive substances to persons for purposes of diagnosis, treatment or research. January 1993.
7. National Radiological Protection Board. Occupational, public and medical exposure. *Documents of the NRPB.* 1993.
8. Stabin M, Stubbs J, Watson E. Recent Controversy in Radiation Dosimetry. *Eur J Nucl Med* 1993;20:371–372.

L.K. Harding
A.T. Elliott
R.A. Shields
Administration of Radioactive Substances Advisory Committee
London, U.K.

Use of the Effective Dose Equivalent

TO THE EDITOR: We were disappointed to read that the MIRD Committee believes that it is inappropriate to use the concept of the effective dose equivalent for patients undergoing nuclear medicine procedures (*1*). In the U.K., the use of the effective dose equivalent has been advocated for the intercomparison of the relative risks involved in nuclear medicine and radiological procedures (*2*). Over the last few years, the nuclear medicine community has made great progress in educating its users to put the risks of nuclear medicine procedures into perspective by the use of the effective dose equivalent. While understanding that the tissue-weighting factors may not be strictly accurate for a patient population and that the overall risk will depend on the age, sex and reproductive status of the individual patient, we do not believe that this invalidates the use of the effective dose equivalent in this context. We think that this point can be illustrated by an analogy with automobile fuel consumption.

Fuel consumption will obviously depend on the manner in which a car is driven, and so in the U.K. manufacturers quote figures for several stated conditions; such as a constant 56 miles