Letters to the Editor

Irradiation of Volunteers in Nuclear Medicine

TO THE EDITOR: We have read with considerable interest the recent article by W. Huda and J.W. Scrimger on "Irradiation of Volunteers in Nuclear Medicine" (*1*). We have recently been preparing, for issue to Ethics Committees, a document on the exposure of humans to ionising radiation in research projects. Although we are pleased to see the question of irradiation of volunteers addressed in the Journal of Nuclear Medicine, we must disagree with the authors' approach and are disturbed by their use of data from ICRP 26 to support a dose limit of 50 mSv.

All radiation exposures for research purposes must be justified by the benefit produced, taking into account the risks involved. In specific terms this means that (a) the exposures must provide some benefit or perception of benefit, (b) the benefit must outweigh the risk, which itself should be known, and (c) the risk should be acceptable to those exposed regardless of benefit. With the available evidence it is possible to estimate the risk from radiation. It is much more difficult to estimate benefit, especially in research where any benefit is likely to be to the overall population rather than the volunteer. Therefore, this requires a value judgement. The problem of weighing up the perceived benefits and the estimated risks must be similarly approached and, in defining an acceptable level of risk, which must surely depend on the particular group of volunteers, a value judgement is again required.

The responsibility for making such judgements falls on the Ethics Committee although of course the final decision must rest with the volunteers. It is essential that they are supplied with sufficient details of the risks and potential benefits to allow them to come to a decision.

With so much depending on value judgements it makes no sense to define a formal dose limit for medical research just as it makes no sense to define one for medical diagnosis. If such a limit was set it would lead investigators into the same trap as the authors have fallen in their paper, that is, making the assumption that the "dose can be considered safe up to a maximum of 50 mSv per year." It would therefore encourage the use of high doses in projects with only minimal merit. A strict dose limit also fails to take account of variations in the risk-dose relationship, for example, with age. More fundamentally it completely ignores the role of value judgements in deciding what is acceptable in widely different patient groups.

The absence of a dose limit does not prevent us from giving advice to an Ethics Committee and many decisions will be clear-cut. For example it would be unlikely that approval would be withheld on the grounds of radiation dose for exposures of 1 mSv in subjects over 70 years of age; it would be unthinkable for doses of 50 mSv to be used in young adults unless for the most compelling of reasons.

Clearly most decisions will be more complex than this, yet such decisions are made daily in medicine. A properly constituted Ethics Committee, with its mix of medical, scientific and lay members, and drawing on advice from experts and national bodies, is ideally suited to such a task. Perhaps more effort should be made to aid such committees instead of drawing up yet more rules.

In defining a dose limit the article bases its assessment of risk on ICRP 26, now more than eleven years old and in urgent need of revision. Recent re-assessment of the Hiroshima and Nagasaki survivors (*2*) has suggested that the risk factor for fatal cancer may be an order of magnitude higher than the ICRP 26 estimate.

The radiation exposures at Hiroshima and Nagasaki were of course over very short time periods, and for low LET radiation it is usually assumed that irradiation at low dose rates will be less carcinogenic than at high dose rates, for a given total dose. According to the National Radiological Protection Board in the UK (*3*):

"The majority of the available animal data indicate a dose rate effectiveness factor (DREF) of between about two and four for the induction of cancer at low dose rates compared with that calculated at high dose rates. The figure that has been adopted by NRPB is three for all cancers except breast cancer for which a DREF of two is more appropriate."

Using these values of DREF, NRPB obtain a total lifetime fatal cancer risk in the UK population of 4.5×10^{-2} Gy^{-1} for low LET radiation following whole body irradiation. This is almost four times the corresponding risk factor from ICRP 26.

In the light of these increased risk estimates NRPB has recommended that the dose limits for workers occupationally exposed to radiation should be lowered from 50 mSv to 15 mSv (*4*). Using a risk factor of 4.5×10^{-2} Sv^{-1}, a radiation dose of 50 mSv would give a lifetime risk of 1 in 450 for fatal cancer and more than double this for non-fatal cancer. By any measure this is not an insignificant level of risk (*5*) and is likely to be unacceptable to many groups of well-informed volunteers.

In summary, therefore, we feel that the adoption of strict dose limits is wholly inappropriate in medical research; Ethics Committees should make informed judgements based on the available evidence of risks and benefits. The use of doses as high as 50 mSv should be discouraged except for the most compelling of reasons.

References

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REPLY: The letter by Dr. Patterson represents the type of discussion of this important topic which we were hoping to generate. It contains a number of interesting perspectives with which we are essentially in agreement, and which are contained in the article (*1*).

We are not advocating a dramatic move towards higher doses to volunteers, but rather indicating an upper boundary to such doses. As is pointed out in the article, average doses from nuclear medicine procedures are typically around 5 mSv, and will likely remain at that value if the proposals made in the paper are accepted. Furthermore, we do not advocate that the careful judgement of an ethics committee be eliminated, but rather that we provide more reasoned guidelines when deliberations on the subject of administered activity to volunteers take place.

Reference

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Hyperthyroidism After Head and Neck Irradiation

TO THE EDITOR: I question the conclusions of the article published in the Journal of Nuclear Medicine entitled "Hyperthyroidism with Low Radioiodine Uptake After Head and Neck Irradiation for Hodgkin's Disease (*1*)".

This is a situation in which *hypothyroidism* is common and deserves no comment. On the contrary *hyper*thyroidism has not been described. However the Petersen, Keeking and McDougall description is suspect because of the recognized iodine excess mainly from lymphangiography. Due attention to this iodine excess has not been made and no total iodine in the serum or urine of the patients is shown.

For us these observations are typical of the effect of excess iodine on thyroid hormonognesis (*2*).

Hyperthyroidism is but an example of what can happen after iodine excess (*3*).

References

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REPLY: In response to Dr. Savoie's comments, it has not escaped our attention that hypothyroidism is common after head and neck irradiation. Indeed, we have published data concerning this, Constine et al. (*1*). Dr. Savoie states that hyperthyroidism has not been described, but indeed it has. First, by my colleagues, Wasnich et al. (*2*) and it has been described by us following hypothyroidism (*3*).

The reason for our current communication was to present three patients who became hyperthyroid and subsequently hypothyroid after head and neck irradiation. Two of the patients have remained permanently hypothyroid for several years at this juncture. We accept that hyperthyroidism can occur after iodine loading, but it is quite unusual in the West Coast of the United States where iodine in the diet is substantial. We believe this sequence of events and the time course in our patients were such that it is unlikely that iodine played a role, although in our original discussion we acknowledge that this probably was not excluded entirely.

We have recently seen a woman with Hodgkin's disease who had mantle radiation. She had a similar history of general malaise, palpitations, and sweating. Thyroid function tests drawn to exclude what was thought to be a low probability of thyroid dysfunction showed a high FT4, suppressed TSH, and radioiodine uptake at 24 hr of less than one percent. The patient had not had an iodine load for more than 1 year. This strengthens our view that this is an important entity which should be looked for in patients who have had mantle radiation.

References

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2. Wasnich RD, Grument FC, Payne RO, et al. Graves' ophthalmopathy following external neck irradiation for nonthyroidal neoplastic disease. *J Clin Endocrinol Metab* 1973; 37:703–711.
3. Constine LS, McDougall IR. Radiation therapy for Hodgkin's disease followed by hypothyroidism and then Graves' hyperthyroidism. *Clin Nucl Med* 1982; 7:69–70.

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