not result in a referral to hospital. These approaches, if extended to other disciplines, may prove to be better for assessing the quality of 90% of patient contacts in the NHS.

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1 NHS Executive. *The new NHS: a national framework for assessing performance*. London: Department of Health, 1998.
2 Bindman A B, Grumbach K, Osmond D, Komarony M, Vranizan K, Lurie N, et al. Preventable hospitalisations and access to health care. *JAMA* 1995;274:305-11.
3 Reid FDA, Cook D, Majeed FA. Variation in hospital admission rates between general practices: cross sectional study. *BMJ* 1999;319:98-103.
4 Giuffrida A, Gravelle H, Roland M. Measuring quality of care: performance indicators should not be confused with health outcomes. *BMJ* 1999;319:94-8.
5 Coulter A, Seagratt V, McPherson K. Relation between general practices' outpatient referral rates and rates of elective admission to hospital. *BMJ* 1990;301:273-6.
6 Coulter A. Managing demand in the interface between primary and secondary care. *BMJ* 1998;316:1974-6.
7 Fertig A, Roland M, King H, Moore T. Understanding variation in rates of referral among general practitioners: are inappropriate referrals important and would guidelines help to reduce rates? *BMJ* 1993;307:1467-70.
8 De Marco P, Cain C, Lockwood T, Roland M. How valuable is feedback of information on hospital referral patterns? *BMJ* 1993;307:1465-6.
9 Jankowski RF. Performance indicators in general practice. *BMJ* 1993;307:1356.
10 Campbell SM, Roland MO, Quayle JA, Buetow SA, Shekelle PG. Quality indicators for general practice: which ones can general practitioners and health authority managers agree are important and how useful are they? *J Pub Health Med* 1998;20:414-21.
11 Roland M, Holden J, Campbell S. *Quality assessment for general practice: supporting clinical governance in primary care groups*. Manchester: National Primary Care Research and Development Centre, University of Manchester, 1998.
12 Howie JGR, Heaney DJ, Maxwell M. A comparison of the Patient Enablement Instrument (PEI) against two established satisfaction scales as an outcome measure of primary care consultations. *Family Practice* 1998;15:165-71.

Radioiodine and thyroid eye disease

Use with caution

Ophthalmopathy is a characteristic feature of Graves' disease, although it is usually mild or subclinical. Enlargement of the extraocular muscle can be shown by computed tomography or magnetic resonance scanning in most patients with autoimmune hyperthyroidism, but only in 10-25% of cases does this result in clinically important problems such as proptosis, conjunctival oedema, or ophthalmoplegia—and the dreaded complication of optic nerve compression is mercifully rare.[1] When it does occur, however, severe thyroid eye disease is difficult to treat and may result in disfigurement, diplopia, or visual loss. Radioactive iodine (I-131) is widely used to treat the thyrotoxicosis of Graves' disease, but, despite its demonstrable efficacy and safety,[2] there have long been concerns about its possible adverse effect on thyroid eye disease. Recently definitive evidence for this link has been presented.[3] As a result, all doctors should now be aware that radioiodine should be used with caution in patients with ophthalmopathy.

In their large, well designed study Bartalena et al treated 443 patients with Graves' hyperthyroidism and mild or no ophthalmopathy with methimazole until euthyroid, then randomly allocated them to continued methimazole treatment, radioiodine, or radioiodine with adjuvant corticosteroid therapy.[3] The groups were well matched at baseline, and hypothyroidism or persistent hyperthyroidism after radioiodine treatment was corrected promptly. The results of the study were clear cut. After radioiodine treatment 15% of patients developed new or worsened ophthalmopathy, whereas this occurred in only 3% of patients treated with methimazole and in none treated with radioiodine plus prednisone. In the radioiodine group 24% of those with pre-existing ophthalmopathy suffered an exacerbation, whereas only 8% of patients without eye disease at baseline developed it.

In most cases the adverse effect was transient, lasting two to three months, but eight patients, seven of whom had ophthalmopathy at baseline, required orbital radiotherapy and high dose corticosteroids. The trial excluded patients with pre-existing moderate or severe eye disease, in whom such an exacerbation could have been disastrous. The study conclusively shows an adverse effect of radioiodine on thyroid eye disease compared to methimazole. It confirms the results of a previous randomised trial,[4] which was criticised on methodological grounds.[5]

The mechanism by which radioiodine exacerbates ophthalmopathy is poorly understood, as is the pathogenesis of thyroid eye disease in general. Two plausible theories have been advanced.[1] The first is that radiation induced thyroid damage releases one or more antigens which are shared by thyroid and retro-orbital tissues, resulting in immune mediated ophthalmopathy. Putative antigens include a 64 kDa protein which has been isolated from eye muscle and thyroid[1 6] and the receptor for thyroid stimulating hormone, which is expressed in retro-orbital tissues as well as in thyrocytes.[7] Recently an animal model for thyroid eye disease has been developed in mice treated with syngeneic lymphocytes sensitised to the human thyroid stimulating hormone receptor.[7] This strengthens the role of the receptor in thyroid eye disease and should lead to further productive research. The second mechanism by which radioiodine may exacerbate ophthalmopathy is by the rapid induction of hypothyroidism, causing increased secretion of thyroid stimulating hormone.[1] This in turn may stimulate antigen production by thyrocytes or induce proliferation or differentiation in retro-orbital preadipocytes which express the receptor for thyroid stimulating hormone.

We believe that the study by Bartalena et al[3] has important implications for clinical practice. Firstly, since radioiodine treatment carries a substantial risk of exacerbating pre-existing thyroid eye disease it should be avoided as far as possible in patients with active or severe ophthalmopathy, in whom medical therapy with a thionamide drug such as carbimazole is preferable. Radioiodine may be used in patients with mild eye disease but adjuvant corticosteroids should be prescribed.

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Oral prednisone at a dose of 0.4-0.5 mg/kg daily for one month, tapered over the following two months, was effective in this study; lower doses may also be effective but have not been tested.

Secondly, patients without clinical evidence of thyroid eye disease have a small risk (8% in this study) of developing ophthalmopathy and a very low risk (< 1%) of developing severe eye disease. It may be prudent to warn all patients of this possible complication, but the risks do not justify denying most patients the benefits of definitive treatment with radioiodine when indicated. In addition, the risks do not justify the routine use of corticosteroids in patients without ophthalmopathy.

Finally, it is known from previous research that smoking, a raised serum tri-iodothyronine concentration, and uncorrected hypothyroidism are also risk factors for thyroid eye disease after radioiodine.[1 4] To minimise the risk of thyroid ophthalmopathy as far as possible, patients should therefore be advised not to smoke, be rendered euthyroid with a thionamide before radioiodine, and be followed closely to detect and correct early hypothyroidism or persistent thyrotoxicosis.

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1 Burch HB, Wartofsky L. Graves' ophthalmopathy: current concepts regarding pathogenesis and management. *Endocr Rev* 1993;14:747-93.
2 Lazarus JH, on behalf of the Radioiodine Audit Subcommittee of the Royal College of Physicians Committee on diabetes and Endocrinology, and the Research Unit of the Royal College of Physicians. Guidelines in the use of radioactive iodine in the management of hyperthyroidism: a summary. *J R Coll Physicians Lond* 1995:29:464-9.
3 Bartalena L, Marcocci C, Bogazzi F, Manetti L, Tanda ML, Dell'Unto E, et al. Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy. *N Engl J Med* 1998;338:73-8.
4 Tallstedt L, Lundell G, Tørring O, Wallin G, Ljunggren J-G, Blomgren H, et al. Occurrence of ophthalmopathy after treatment for Graves' hyperthyroidism. *N Engl J Med* 1992;326:1733-8.
5 De Groot LJ, Gorman CA, Pinchera A, Bartalena L, Marcocci C, Wiersinga WM, et al. Therapeutic controversies: radiation and Graves' ophthalmopathy. *J Clin Endocrinol Metab* 1995;80:339-49.
6 McGregor A. Has the target autoantigen for Graves' ophthalmopathy been found? *Lancet* 1998;352:595-6.
7 Ludgate M, Crisp M, Lane C, Costagliola S, Vassart G, Weetman A, et al. The thyrotropin receptor in thyroid eye disease. *Thyroid* 1998;8:411-3.

Reasons for not seeing drug representatives

Lightening workload, cutting costs, and improving quality

Many doctors—both hospital doctors[1] and general practitioners[2]—feel that their workloads are increasing. There is a sense that we are being overwhelmed by a multitude of calls on our time, fitting in management and administration, continuing medical education, teaching, audit, and appraisals over and above our basic clinical work. Why then do so many doctors still find time to see drug company representatives?

Most doctors still see them regularly and a few (perhaps about 10%) see them quite often (M Butterfield, personal communication: unpublished data from *BMJ* readers). Lexchin noted that representatives have traditionally been seen as the most important source of information about new drugs.[3 4] There may have been a time when representatives were the easiest source for finding out about pharmaceutical developments, but now there is ready access to a plethora of non-promotional, evidence based information in simple and digestible form on all the major therapeutic advances. Drug information departments additionally supply detailed advice on such matters as new formulations and interactions. There seems little or no need to see representatives in order to keep abreast of drug developments.

Indeed, strong reasons exist for *not* seeing representatives. Their job is primarily to sell their company's product. They are an important part of the pharmaceutical industry's promotion methods, and they are highly successful in altering doctors' prescribing habits. Work in Northern Ireland showed an increase in prescribing of various drugs that appeared to be greater than could be accounted for by an increase in patients with specific indications for these drugs.[5] The authors suggested that the profession may not have instituted effective checks to ensure that the promotion of new products did not lead to inappropriate or wasteful use. Not surprisingly, there is also evidence that the more reliant doctors are on commercial sources of information the less rational they are as prescribers.[3] This may mirror the circumstance, recently discussed in the *BMJ*, of conflict of interest in relation to review articles written by people with drug company links.[6] Such people are more likely to be sympathetic to the drug in question. Similarly, doctors are more likely to be supportive of—and prescribe—a drug promoted to them by a representative.

Drug companies might point out that their representatives provide information to clinicians faster and at an earlier stage than other sources. This may be true sometimes but does not of itself lead to good practice. Indeed it may have the opposite effect. At the time that new drugs are licensed there are often no published comparisons with existing standard treatments and rarely any economic evaluations. Thus the really useful information is often unavailable at this stage, and by the time it is, the sales force has moved on to talk about other, newer products. Rather than rushing to know the latest on every new drug, we should perhaps be more concerned about why some proved worthwhile treatments are so slow to be taken up, even when the evidence has been widely publicised.

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