

Radioiodine in the management of benign thyroid disease

Clinical guidelines

Report of a Working Party 2007



**Royal College
of Physicians**
Setting higher medical standards

The Royal College of Physicians of London

The Royal College of Physicians plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the UK and overseas with education, training and support throughout their careers. As an independent body representing over 20,000 Fellows and Members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

Citation of this document: Royal College of Physicians. Radioiodine in the management of benign thyroid disease: clinical guidelines. Report of a Working Party. London: RCP, 2007.

Copyright

All rights reserved. No part of this publication may be reproduced in any form (including photocopying or storing it in any medium by electronic means and whether or not transiently or incidentally to some other use of this publication) without the written permission of the copyright owner. Applications for the copyright owner's permission to reproduce any part of this publication should be addressed to the publisher.

Copyright © 2007 Royal College of Physicians of London

ROYAL COLLEGE OF PHYSICIANS OF LONDON

11 St Andrews Place, London NW1 4LE

www.rcplondon.ac.uk

Registered Charity No 210508

ISBN 978-1-86016-297-8

Review date: 2015

Typeset by Dan-Set Graphics, Telford, Shropshire

Printed in Great Britain by The Lavenham Press Ltd, Sudbury, Suffolk

Contents

Preface	v
Members of the Working Party	vi
Evidence and recommendations grading criteria	vii
Glossary	viii
1 Overview of radioiodine therapy	
Indications	1
Factors determining whether radioiodine treatment is appropriate	1
Causes and severity of hyperthyroidism	2
Euthyroid goitre	3
Treatment selection	4
Safety of radioiodine therapy	4
Cost of radioiodine therapy and effect on quality of life	5
2 Administration of radioiodine	
Regulations	6
Strategy for administration in hyperthyroidism	7
Recommended activity	8
Antithyroid drug administration	9
Contraindications to radioiodine therapy	9
Duties of the clinician assessing the patient	10
Patient information and consent	11
Subclinical hyperthyroidism	11
Euthyroid goitre	12
Thyroid eye disease	12
3 Management of the first year following radioiodine therapy for thyrotoxicosis	
Symptoms	13
Use of antithyroid drugs	13
Follow-up	13
4 Monitoring and follow-up after the first year	
Rationale	15
Communication between specialist, general practitioner and patient	15
Monitoring methods	16

Appendices

A	Special precautions	17
B	Information for patients having radioiodine treatment for thyrotoxicosis	19
C	Sample consent form to be used for patients for whom radioiodine therapy has been prescribed	24
D	Sample patient information card	26
E	Elements of a system to support long-term follow-up of patients treated with radioiodine	27
	References	29

Preface

This report updates guidelines published in 1995 by the Royal College of Physicians (RCP) of London and has been written by a working group representing the several bodies involved in the administration of radioiodine for hyperthyroidism. Regular revision of guidelines is essential to ensure best practice, and the present working group has included developments in the past ten years in the legislation relating to radioiodine treatment, as well as advances in our understanding, such as the effect of radioiodine on thyroid eye disease. We have also extended the scope of the guidelines to incorporate information on the treatment of subclinical hyperthyroidism and non-toxic goitre. This in turn led to the change in the report's title, to encompass this range of benign thyroid disease, rather than hyperthyroidism alone.

The practice of guideline writing has also moved on, with the expectation that evidence is assessed and recommendations are made according to established criteria (see [Table 1](#)).

Unfortunately, much of the evidence supporting the way we give radioiodine is derived from custom and practice, and many of the fundamental principles we use are unlikely ever to be subject to controlled trial. This document is intended primarily to be a practical guide to the use of radioiodine for specialists who will be familiar with the previous guidance.

We have therefore chosen to keep the same format as the 1995 guidelines and to grade recommendations where we feel these can be estimated from the available evidence, without a wholesale revision and exhaustive review of the older literature. Where recommendations are made without a statement of the level, these can be taken as level [4]. Finally, we are grateful to the many individuals who have commented on drafts of this document, in particular to Michael Waller for his help with [Appendix A](#), and to the staff of the RCP who have helped in the production of the final version.

March 2007

Tony Weetman
Chair, Working Party

Members of the Working Party

Tony Weetman (*Chair*)

Dean, School of Medicine and Biomedical Sciences, University of Sheffield; British Thyroid Association

Mary Armitage

Consultant in Endocrinology, Royal Bournemouth Hospital; Clinical Vice President, Royal College of Physicians of London

Sue Clarke

Consultant Nuclear Medicine Physician, Guy's Hospital; Joint Specialty Committee on Nuclear Medicine

John Frank

Consultant in Nuclear Medicine and Radiology, Charing Cross Hospital; British Nuclear Medicine Society

Jayne Franklyn

Professor of Medicine, University of Birmingham; British Thyroid Association

Peter Lapsley

Patient and Carer Network Representative, Royal College of Physicians of London

John Lazarus

Professor of Clinical Endocrinology, Cardiff University; British Thyroid Association

Val Lewington

Consultant Nuclear Medicine Physician, Royal Marsden Hospital; Joint Specialty Committee on Nuclear Medicine

Susan Owens

Consultant Clinical Scientist, Christie Hospital, Manchester; Institute of Physics and Engineering in Medicine

Evidence and recommendations grading criteria

Table 1 Levels of evidence grading criteria

Levels of evidence	
Level	Type of evidence
1a	Evidence obtained from meta-analysis or randomised control trials
1b	Evidence from at least one randomised controlled trial
2a	Evidence obtained from at least one well-designed control study without randomisation
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study
3	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
4	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities
Grading of recommendations	
Grade recommendations	
Evidence levels 1a, 1b	Requires at least one randomised controlled trial as part of the body of the literature of overall good quality and consistency addressing the specific recommendations
Evidence levels 2a, 2b, 3	Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation
Evidence level 4	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Glossary

Activity: the amount of radioactivity administered or prescribed, measured in MBq.

ALARP: as low as reasonably practicable

Antithyroid drugs (ATD): carbimazole, propylthiouracil

ARSAC: Administration of Radioactive Substances Advisory Committee

Comforter and carer: any individual who (other than as part of their occupation) knowingly and willingly incurs an exposure to ionising radiation resulting from the support and comfort of another person who is undergoing or has undergone any medical exposure.¹

Destructive thyroiditis: transient inflammation of the thyroid caused by viral infection, autoimmune damage or drugs (such as amiodarone), typically resulting in a phase of thyrotoxicosis followed by a phase of hypothyroidism.

EA: Environment Agency

EHS: Environment and Heritage Service (in Northern Ireland)

Euthyroid: the state of an individual with normal thyroid hormone levels.

Exemption limits: maximum activity of radioiodine that may be present in and disposed of from a specific area (such as a hospital) without the need for registration and authorisation under the Radioactive Substances Act.²

Graves' disease: hyperthyroidism due to thyroid stimulating antibodies directed against the TSH receptor. Associated with clinical evidence of thyroid eye disease in around 50% of patients.

Gy: gray; the international system unit of absorbed dose of radiation.

HSE: Health and Safety Executive

Hyperthyroidism: clinical state produced by excessive activity of the thyroid gland leading to thyrotoxicosis; common causes are Graves' disease and toxic nodular thyroid disease.

Hypothyroidism: clinical state produced by thyroid hormone insufficiency; common causes are autoimmunity and ietrogenic damage to the thyroid from radioiodine or surgery. Treatment is usually with levothyroxine tablets.

IRMER: Ionising Radiation (Medical Exposure) Regulations 2000

IRR99: Ionising Radiations Regulations 1999

MARS: Medicines (Administration of Radioactive Substances) Regulations 1978

MBq: megabecquerel: a measure of the amount of radioactivity ($1 \text{ MBq} = 1 \times 10^6$ disintegrations per second).

MDGN: Medical and Dental Guidance Notes 2002

mGy: milligray; a measure of the absorbed dose of radiation ($1 \text{ Gy} = 1 \text{ Joule/kg} = 100 \text{ rad}$)

MHRA: Medicines and Healthcare Products Regulatory Agency

MPE: medical physics expert

mSv: millisievert; a measure of effective dose to the body which is used for radiation protection purposes.

Ophthalmopathy: also known as thyroid eye disease; clinically evident as lid retraction, periorbital oedema, proptosis and/or diplopia in around 50% of patients with Graves' disease.

QA: quality assurance

RPA: radiation protection adviser

SEPA: Scottish Environment Protection Agency

T3: tri-iodothyronine

T4: thyroxine

Thyroid crisis (or storm): severe exacerbation of thyrotoxicosis often resulting in death if inadequately treated.

Thyroid eye disease: see ophthalmopathy.

Thyrotoxicosis: a state produced by elevated thyroid hormone levels in the blood; may be due to hyperthyroidism, excessive ingestion of thyroid hormone or destructive thyroiditis.

Toxic (nodular) goitre: hyperthyroidism produced by a nodular enlargement of the thyroid with autonomous function of one or more nodules.

TSH: thyroid stimulating hormone

¹³¹I: radioiodine

I Overview of radioiodine therapy

Indications

1.1 Radioiodine (^{131}I) has been used in therapy for hyperthyroidism for more than 60 years. Radioiodine is indicated in cases of hyperthyroidism due to Graves' disease or toxic goitre (solitary toxic adenomas or multi-nodular goitre) and is effective in curing hyperthyroidism in virtually all patients who are given single or multiple doses.^{3,4} [2a] There is an emerging role for ^{131}I in the treatment of subclinical hyperthyroidism, at least in the USA.⁵ [2b] Radioiodine is also indicated for treatment of euthyroid goitre in selected cases.⁶ [2a] Radioiodine is not an appropriate treatment for thyrotoxicosis secondary to thyroiditis or for thyrotoxicosis associated with iodine excess. A European Association of Nuclear Medicine survey for 2002 indicated that approximately 6,000 doses were administered in the UK that year.

1.2 In Graves' disease, radioiodine may be administered as first-line treatment, or may be given if treatment with an antithyroid drug (ATD) has failed to result in long-term remission. This may be due to difficulty with patient management, unacceptable or serious side effects, resistance to drug therapy (a very rare occurrence) or, most commonly, the relapsing nature of the underlying disorder. Radioiodine is also indicated if hyperthyroidism is not controlled or recurs after thyroid surgery.

1.3 For persistent hyperthyroidism due to toxic nodular goitre, radioiodine represents the treatment of choice since ATDs are not curative in this condition.^{3,4} [2b] In euthyroid subjects with diffuse or nodular goitre, surgery has been the treatment of choice to reduce goitre size and relieve compressive symptoms. Recently, it has been shown that radioiodine is effective in reducing goitre size by 50% at one year,⁶ accompanied by a significant reduction in associated symptoms and signs.⁷ [2a]

Factors determining whether radioiodine treatment is appropriate

1.4 Factors that influence the decision to proceed to radioiodine therapy in hyperthyroid subjects include patient age, gender, diagnosis, severity of hyperthyroidism, the presence of other medical conditions, access to radioiodine, and patient and doctor preference. In euthyroid subjects with goitre, similar factors are relevant to the decision-making process, especially pertinent being goitre size, availability of surgery and likelihood of surgical complications. All patients considering radioiodine treatment should be counselled regarding treatment options by an accredited specialist in the treatment of thyroid disease.⁸ [4]

1.5 Most hyperthyroid patients aged less than 40 years have Graves' disease. In this group it is common practice in the UK to administer a course of ATD treatment, although many clinicians prescribe radioiodine as a first choice because of the relatively low rates of long-term remission associated with ATD alone.⁹ [2b] Failure to control hyperthyroidism with carbimazole or propylthiouracil, due to difficulties in management or, more commonly, recurrence of hyperthyroidism after withdrawal of an ATD, are indications for radioiodine therapy in view of

the long-term morbidity and potential mortality associated with poorly controlled thyrotoxicosis.^{10,11} [2a] Serious side effects such as agranulocytosis and hepatic dysfunction are contraindications to further ATD treatment; such patients should proceed to radioiodine therapy as soon as possible. Relapse of hyperthyroidism after withdrawal of an ATD is an indication for surgery or radioiodine in Graves' disease since further courses of drug therapy rarely result in long-term remission once relapse has occurred. If there are features suggestive of a malignancy, surgery is indicated.

1.6 Although ATDs and surgery are generally regarded as the treatments of choice in childhood Graves' disease, radioiodine is effective in this age group. A recent retrospective study of 116 subjects treated with radioiodine at under 20 years old revealed cure of hyperthyroidism without any increased incidence of thyroid cancer, leukaemia or congenital abnormalities in offspring.¹² [3]

1.7 Pregnancy and breast feeding represent absolute contraindications to radioiodine treatment. In patients of reproductive age, their plans for pregnancy, including assisted conception, must be taken into consideration in planning the timing of therapy. It may also be necessary to postpone radioiodine treatment (and continue with medical treatment), even in relapsed disease, until breast feeding has ended and the age of the child is sufficient to allow compliance with radiation protection regulations. Further information on pregnancy and breast feeding is given in [section 2.17](#).

Causes and severity of hyperthyroidism

Graves' disease

1.8 Although radioiodine therapy is effective in patients with Graves' disease, those with large goitre, patients with more severe biochemical disease and possibly men and younger patients are less likely to respond to a single dose of radioiodine.¹³ [2a] The effect of such treatment on thyroid eye disease (ophthalmopathy) is still uncertain (see also [sections 2.28–2.30](#)). A large retrospective study revealed no difference in the development or worsening of thyroid eye disease in patients treated with an ATD, thyroid surgery or radioiodine.¹⁴ In contrast, a prospective study comparing the risk of development or worsening of eye disease after treatment with radioiodine, surgery or an ATD suggested a greater risk with radioiodine.¹⁵ Others have shown the development or worsening of thyroid eye disease to be more frequent in those treated with radioiodine than with an ATD, although worsening of eye disease can be prevented by administration of steroids for a few weeks after treatment.¹⁶ [1b] Early administration of thyroxine for hypothyroidism following radioiodine is also important to reduce the occurrence or worsening of thyroid eye disease.¹⁷ [1b]

Toxic nodular goitre

1.9 Radioiodine is the treatment of choice for toxic nodular goitre.^{3,4} Goitre size is a determinant of clinical outcome in patients treated with radioiodine, but a reduction in goitre size can be expected in most patients. In patients with very large goitre and upper airways obstruction there is a theoretical risk of worsening airways obstruction following radioiodine treatment, although in practice this complication is rarely seen. In the longer term, radioiodine represents a successful means of reducing goitre size.

1.10 Patients with toxic nodular goitre tend to be older than those with Graves' disease and to have milder disease, but they often manifest cardiovascular complications. For patients in atrial fibrillation, consideration should be given to warfarin therapy before radioiodine is administered, in order to prevent embolic complications. Higher activities of radioiodine may be indicated in this group in an effort to achieve a rapid resolution of hyperthyroidism depending on goitre size, although overall a similar response to radioiodine is observed to that in the treatment of Graves' hyperthyroidism.¹³

1.11 Patients with severe hyperthyroidism due either to Graves' disease or toxic nodular goitre should be treated with an ATD before and after radioiodine therapy to prevent significant clinical and biochemical deterioration (and the rare complication of thyrotoxic crisis or storm) associated with ATD withdrawal for treatment¹⁸ [2a] (see also [sections 2.15–2.16](#) and [section 3.2](#)). Pre-treatment of patients with propylthiouracil, as well as resumption of propylthiouracil after radioiodine therapy, may be associated with relative radioresistance and hence the possible need for further (or larger) doses of radioiodine.¹⁹ Carbimazole pre-treatment, in contrast, does not affect outcome.²⁰

Toxic adenoma

1.12 Radioiodine is an appropriate treatment for patients with solitary toxic adenoma since the radioiodine is concentrated by the toxic nodule, thus theoretically sparing the surrounding thyroid tissue from radiation-induced change.

Subclinical hyperthyroidism

1.13 It is presently uncertain whether subjects with persistent subclinical hyperthyroidism (defined biochemically as a reduction in serum thyroid stimulating hormone (TSH) associated with normal serum free T4 and T3 concentrations) should receive antithyroid treatment with an ATD or radioiodine. Based largely on evidence that subclinical hyperthyroidism is associated with increased risk of development of atrial fibrillation²¹ and increased vascular mortality,²² a recent consensus statement from the USA has suggested that treatment should be considered for those patients with persistent suppression of serum TSH below 0.1 mU/L, especially in the presence of symptoms or signs suggestive of cardiac disease, and with evidence for underlying thyroid disease on clinical examination or imaging of the thyroid.²³ [4] One small study has shown that radioiodine reduces bone loss in postmenopausal women with subclinical hyperthyroidism.²⁴ To date, there have been no randomised controlled trials evaluating the effect of radioiodine treatment (or ATD treatment) on long-term morbidity or mortality in subclinical hyperthyroidism (see also [section 2.26](#)).

Euthyroid goitre

1.14 Radioiodine is being used increasingly, especially in continental Europe, for the management of euthyroid goitre once malignancy has been excluded.⁶ For subjects with goitre of sufficient size to produce significant cosmetic complaints or symptoms or signs of obstruction of the upper airways or oesophagus, surgery is considered the treatment of choice, but radioiodine should be discussed as an alternative treatment, especially in those patients with significant comorbidity in whom surgery may be high risk. In those with small to medium sized goitres (<100 ml in volume) there is an approximate 50% reduction in goitre size following radioiodine

treatment, half of the effect being evident within the first three months.²⁵ [1b] A second dose of radioiodine may cause an additional reduction in volume comparable to that achieved with the first dose.²⁶

1.15 Radioiodine has been shown to be effective in those with retrosternal goitre; in those with diffuse goitre, a greater size reduction may occur than in those with multinodular goitre. The relative reduction in goitre size following radioiodine treatment is inversely related to the size of the goitre.²⁷ Therefore this treatment is relatively contraindicated in those with very large goitre because of the need for high or repeated doses. Concerns about a transient increase in goitre size, and hence compression of airways, in the short term following radioiodine have not been realised in practice, even in those with large multinodular goitre.^{27,28} Radioiodine treatment may trigger the onset of Graves' disease in approximately 5% of cases.²⁸ Hypothyroidism may also ensue in about 20% of patients by one year and occurs at a lower rate thereafter³⁰ (see also [section 2.27](#)).

Treatment selection

1.16 Surveys of thyroid specialists have revealed marked differences in doctor preference for ATD or radioiodine therapy in different parts of the world,³¹ in part due to differences in regulations regarding radiation protection. However, there has been no large-scale randomised trial comparing the three modes of treatment (ATD, surgery and radioiodine therapy) over the long term. Older surveys revealed a preference for drug therapy or surgical treatment for young female patients with hyperthyroidism. This preference for forms of treatment other than radioiodine in part reflected concerns about the safety of radioiodine, especially in terms of perceived long-term cancer risk and risks of infertility and teratogenicity.³² ATD treatment is also associated with a much lower risk of permanent hypothyroidism. These concerns are frequently expressed by patients, but are readily addressed by counselling and patient information literature. Doctor preference is also influenced by ease of access to radioiodine therapy and administrative arrangements. It is essential that patients are given clear advice regarding the timing of therapy, omission of any ATD, contraception and thyroid eye disease, and that details of follow-up arrangements can be agreed. This requires close liaison between the endocrinologist, or other thyroid specialist who is licensed to administer radioiodine, and the nuclear medicine department.

Safety of radioiodine therapy

1.17 Increased long-term vascular mortality has been described after treatment of hyperthyroidism with radioiodine, a finding which probably reflects the underlying disorder (and its vascular complications) rather than radioiodine treatment itself.^{10,11} A small increase in relative risk of diagnosis or death from thyroid cancer after radioiodine treatment (standardised mortality ratio up to 3.9) has been reported in large epidemiological studies carried out in the UK, the USA and Sweden.^{33–35} Comparison of risk in those treated with other modalities suggests that this small increase in risk is associated with the underlying thyroid disease rather than treatment with radioiodine;^{34,35} the absolute risk of thyroid cancer is low in all of these studies. There is no evidence for an increase in the incidence of leukaemia or solid tumours in those given radioiodine, with the possible exception of small bowel cancer and gastric cancer in single

cohorts.^{33,36–38} It should be noted that few studies have included large numbers of patients treated at less than 40 years of age, making it important to continue long-term follow-up of populations treated with radioiodine to ensure the accumulation of further evidence in support of its safety. A recent retrospective analysis of 116 subjects treated at less than 20 years old and followed for 36 years, showing no excess of adverse effects, provides the best available evidence of safety in children and adolescents.¹²

1.18 Less direct information than for cancer risk is available regarding radioiodine and subsequent risks of congenital abnormality. There is no evidence of increased congenital abnormality in small studies of the offspring of women treated with radioiodine. The theoretical risk of genetic abnormality resulting from radioiodine treatment in women and men has been estimated at 0.003%;³⁹ not surprisingly, such a risk has not been identified in clinical studies.

Cost of radioiodine therapy and effect on quality of life

1.19 Because radioiodine therapy for hyperthyroidism does not require the patient to be hospitalised, the cost is relatively low and comparable to that of ATD therapy. This cost is substantially less than that of surgical treatment which usually requires a stay of 2–4 days in hospital. Quality of life assessment has indicated similar responses regardless of treatment administered (ATD, surgery or radioiodine).^{40,41}

2 Administration of radioiodine

Regulations

2.1 The Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER)¹ define four main levels of responsibility for those involved in the conduct of medical exposures, namely the employer, referrer, practitioner and operator. The duties of the 'employer' include ensuring that appropriate written procedures and protocols exist for every aspect of work relating to the exposure of patients to ionising radiation, that staff are appropriately trained and that equipment undergoes quality assurance and is fit for purpose.

2.2 Those clinically managing hyperthyroid patients may refer them for radioiodine treatment. In this context, a 'referrer' is 'a registered healthcare professional'... entitled [under local procedures] to refer individuals for medical exposure to a practitioner'. The main duty of the referrer is to provide the practitioner responsible for radioiodine treatment with sufficient clinical data to enable a judgment to be made that there will be an overall benefit from the treatment.

2.3 The practitioner for radioiodine treatment takes the responsibility for an individual administration. This practitioner must hold a license granted by the health ministers, according to the Medicines (Administration of Radioactive Substances) (MARS) Regulations 1978,⁴² following application to the Administration of Radioactive Substances Advisory Committee (ARSAC). Certificates are granted only to those who can show training, experience and competence in the administration of radioactive substances relevant to radioiodine treatment in hyperthyroidism. A certificate is specific to the practitioner, the type of treatment and the location where the treatment will be administered. The ARSAC certificate holder, as practitioner, is responsible for justification of the exposure to radiation and for authorising the radioiodine treatment. It is possible for the referrer and the practitioner to be the same person, for example, if an endocrinologist who refers the patient also holds the relevant ARSAC certificate.

2.4 An 'operator' is any person who undertakes a task which is part of, or affects, the patient's radioiodine exposure. This therefore includes:

- ▶ calibration of the activity of the radionuclide (¹³¹I)
- ▶ carrying out quality assurance of equipment, such as a radionuclide calibrator
- ▶ confirming that the patient is suitable for treatment, including assessing:
 - ability to swallow
 - suitable home circumstances
- ▶ undertaking the task of prescribing
- ▶ explaining the procedure
- ▶ giving the radioiodine to the patient.

Therefore, operators may include the person giving the radioiodine, the medical physics expert (MPE) or the ARSAC certificate holder.

2.5 The IRMER regulations require an MPE to liaise with the certificate holder to ensure that radioactive substances are administered safely with regard to their use in patients. This function is distinct from that of radiation protection adviser (RPA), who deals with the safety of staff and the public, although it may be carried out by the same person. Local procedures and protocols must be drawn up to demonstrate compliance with the IRMER and MARS regulations.

2.6 Radioiodine may be stored and dispensed only in premises that have registration and authorisation from the appropriate regulatory body under the Radioactive Substances Act, 1993.⁴³ The regulatory bodies are the Environment Agency (EA) in England and Wales, the Scottish Environment Protection Agency (SEPA) in Scotland and the Environment and Heritage Service (EHS) in Northern Ireland. Registration covers the keeping and use of radioactive materials on those premises and authorisation covers the disposal of such materials. The Ionising Radiations Regulations 1999 (IRR99)¹ require a suitable and sufficient prior risk assessment to be undertaken so that each department can identify the measures needed to restrict exposure of employees and other persons (excluding patients) to radiation. One conclusion of this will be that the administration of radioiodine should take place within a controlled area, for which the requirements are set out in the IRR99¹ and the Medical and Dental Guidance Notes (MDGN).⁴⁴

2.7 If in-patients from another hospital are to be treated, notification of the administered activity should be sent to the RPA of the referring hospital; this is to ensure that each hospital remains within exemption limits or within any authorisation granted by the EA, SEPA or the EHS. IRR99¹ will apply if a patient is to be treated and then return to any premises where radioactive materials are not normally used, but where others will be employed to care for them, such as a nursing home or to their own home where they receive support from a district nurse. IRR99 will apply to their work and their respective employers will need to complete their own prior risk assessments and notify the Health and Safety Executive of their intention to undertake this work at least 28 days before it starts. This is necessary the first time such work is undertaken and, as identifying and contacting employers can become quite time consuming, it is essential to involve the RPA or MPE as soon as possible. Hospitals that discharge patients in this way should cooperate with any local employer whose employees will be at risk of radiation exposure as a result of their care of the patient. Examples include by providing them with information about the radioactivity of the patient and the precautions to be taken in handling any body fluids with which they may come into contact.

2.8 Radiation risk assessment must be performed before radioiodine treatment. This is done with guidance from the RPA or MPE and may be a generic radiation risk assessment, using assumptions for a typical patient (IRR99;¹ paragraphs 15 and 19). However, if assessment of a patient shows that they do not conform to the generic assumptions, an individual risk assessment is necessary.

Strategy for administration in hyperthyroidism

2.9 The intention of radioiodine treatment is to cure hyperthyroidism. Historically, UK prescribing has varied widely according to local custom and practice.⁴⁵ Low activity radioiodine administration leads to a delayed, often inadequate response. This is undesirable, particularly

in the elderly, given the adverse cardiovascular effects of persisting hyperthyroidism. Conversely, routine administration of high activities that would necessitate thyroxine replacement therapy for the majority of patients is unjustified, as many patients achieve euthyroidism with smaller activities.

2.10 Treatment of children must always be performed in conjunction with a paediatric endocrinologist.

2.11 There is no evidence that precision dosimetry leads to improved outcome.^{46,47} [1b] Our recommendation is to prescribe sufficient radioiodine to cure hyperthyroidism with the acceptance that hypothyroidism will occur in a significant number of patients.

2.12 This approach would be expected to restore euthyroidism in 50–75% of patients within six to eight weeks of radioiodine administration. Persisting hyperthyroidism is usually treated by further radioiodine (see [section 2.14](#)). Hyperthyroidism that has been adequately treated with radioiodine seldom recurs.

2.13 Compounds that contain iodine, such as amiodarone and radiographic contrast agents, may block iodine uptake for up to a year following drug withdrawal. Iodine uptake measurements are helpful in this instance to determine the activity required and optimal timing of radioiodine therapy (see [section 2.20](#)). Lithium carbonate may enhance the effectiveness of radioiodine when given for a few days immediately after treatment, but the clinical significance of the effect is unclear and side effects may be experienced by 10% of patients.^{48,49} Lithium is not recommended for routine use.

Recommended activity

2.14 The range of activities currently prescribed varies between 200–800 megabecquerel (MBq), with the majority of patients receiving 400–600 MBq. The following activities are recommended for guidance:⁵⁰ [4]

- ▶ Uncomplicated Graves' disease
Guide activity: 400–600 MBq
- ▶ Uncomplicated toxic multinodular goitre
Guide activity: 500–800 MBq
- ▶ Toxic adenoma, usually mild hyperthyroidism
Guide activity: 500 MBq
- ▶ Ablation therapy may be required for patients with severe co-morbidity such as heart failure (New York Heart Association grades 3/4), malignancy or psychosis. Ablation therapy may also be appropriate for patients who are intolerant of ATDs or with thyroid eye disease to reduce the need for a second dose of radioiodine.
Guide activity: 500–800 MBq
- ▶ Re-treatment after six months is indicated for persisting hyperthyroidism. The re-treatment activity is usually the same as or higher than that prescribed previously. Individual risk assessments for close family are indicated if a patient receives more than one treatment in a year.

- ▶ The maximum activity per administration for outpatient treatment is 800 MBq. If there is a clinical need to prescribe a higher activity, the radiation protection implications should be discussed with the MPE.

Antithyroid drug administration

2.15 An ATD is commonly used to treat symptomatic hyperthyroidism at presentation, although practice varies widely. Subclinical hyperthyroidism or hyperthyroidism associated with mild symptoms in otherwise healthy patients is often managed using radioiodine alone, accepting that biochemical and symptom control may be delayed for up to three months. Beta adrenergic blocking agents (such as propranolol 20–40 mg tds) may be helpful for interim symptom relief, provided that there are no contraindications. Patients with severe hyperthyroidism due to Graves' disease or elderly patients with signs of cardiac failure should be treated with an ATD to restore normal circulating thyroid hormone levels before radioiodine treatment. Depletion of thyroidal hormone stores in this way reduces the likelihood of symptom exacerbation early after radioiodine administration and decreases the low risk of thyroid storm.^{51,52} [4]

2.16 Evidence that pre-treatment using an ATD may lead to relative radioiodine resistance is conflicting. ATD prescription may, therefore, be determined pragmatically according to symptom severity. Carbimazole should be withdrawn for at least two days before planned radioiodine administration. Propylthiouracil has a radioprotective action which may reduce the effectiveness of radioiodine, even if the drug is stopped several weeks before radioiodine treatment. This protective effect may be overcome either by stopping propylthiouracil for a minimum of two weeks before the administration of radioiodine or by giving a larger dose of radioiodine.^{19,53,54} Patients needing an ATD before radioiodine may require the same drug again after treatment, sometimes in combination with a beta adrenergic blocking agent to prevent symptom recurrence before the radioiodine has taken effect. Where necessary, ATDs can be recommenced seven days after radioiodine administration without affecting the radiation dose delivered to the thyroid significantly.⁵⁴

Contraindications to radioiodine therapy

2.17 Radioiodine treatment should **not** be given under the following circumstances:

Pregnancy

- ▶ Pregnancy is an **absolute contraindication** to radioiodine therapy because it will damage the fetal thyroid. If necessary, a pregnancy test should be performed to confirm that the patient is not pregnant at the time of radioiodine administration. Women are advised not to become pregnant for six months and men are advised not to father children for a period of four months after receiving radioiodine.⁵⁵
- ▶ If pregnancy occurs within six months of radioiodine treatment, the advice of the MPE should be sought to provide an estimate of fetal radiation dose. If conception occurs within a few weeks of treatment, the fetal dose is usually not considered sufficient to justify termination. However, this does not obviate the need to advise every woman of childbearing age to avoid becoming pregnant for six months after treatment, which is intended to eliminate any unnecessary radiation dose to the fetus and to reduce risk to the population as a whole.

- ▶ There is no evidence of any fetal or maternal risk in pregnancy or its outcome in women who receive radioiodine provided the above guidelines are followed. A person living in the same house as a pregnant woman may receive radioiodine provided there is no close or prolonged contact with the pregnant woman.

Breast feeding

- ▶ Breast feeding must be discontinued permanently through a pregnancy when radioiodine is given as iodine is concentrated in milk, but is safe in subsequent pregnancies.

Other

- ▶ Situations where it is clear that the safety of other persons in relation to exposure to radiation cannot be guaranteed.

2.18 Additional care should be taken in patients who are incontinent of urine; they should be catheterised before radioiodine administration to allow safe disposal of urine containing radioiodine, and MPE advice should be sought. [Sections 2.28–2.30](#) set out precautions in those with thyroid eye disease.

2.19 Even in cases of known iodine sensitivity, radioiodine administration is very unlikely to precipitate a hypersensitivity reaction. The elemental iodine content of radioiodine preparations is 0.05–0.18 µg. This is very significantly lower than average daily iodine intake (>150 µg/day) in the UK.

Duties of the clinician assessing the patient

2.20 At the initial consultation, the clinician should record the following:

- ▶ clinical data relevant to the prescription of radioiodine or to the outcome of treatment, particularly regarding:
 - aetiology: diagnostic biochemistry, clinical features and ultrasound usually differentiate Graves' disease from nodular thyrotoxicosis. Perchnetate or ¹²³I thyroid imaging is useful to identify patients with acute thyroiditis, factitious hyperthyroidism and unsuspected non-functioning nodules, as well as to exclude recent exogenous iodine administration (for instance, amiodarone or intravenous contrast media), which would impair radioiodine uptake by the thyroid
 - drug history: ATDs; beta adrenergic blocking agents
 - history of significant heart disease
 - heart rate and rhythm
 - thyroid size
 - goitre type
 - signs of thyroid eye disease
 - recent thyroid function tests.
- ▶ personal or social factors that would determine the need for special radiation protection advice, or plans for conception that would preclude radioiodine.

Patient information and consent

2.21 At the initial consultation patients should be advised of what the treatment consists of and its effectiveness, with particular regard to:

- ▶ the slow onset of action of radioiodine
- ▶ the possibility of persistent or recurrent hyperthyroidism and what may be done about it
- ▶ the possibility of hypothyroidism and its symptoms, implications and treatment
- ▶ the need for regular follow-up to detect hypothyroidism.

2.22 Before treatment, patients should be advised of recommendations with regard to radiation protection and informed of the implications of radioiodine treatment in relation to work, travel and contact with the family (Appendices A and B).

- ▶ The patient may need to take time off work for a period related to the activity of radioiodine received and the nature of their work.
- ▶ The patient should avoid prolonged close contact with children and with pregnant women for a period of time related to the activity of radioiodine received.
- ▶ There may be restrictions on travel related to the activity of radioiodine received.

Premenopausal women should be advised to avoid pregnancy within six months of radioiodine administration (see [section 2.17](#)).

2.23 An information sheet should be given to patients following the initial consultation (the information it should include is detailed in [Appendix B](#)). This will summarise information contained in [sections 2.21–2.22](#) and contain a contact telephone number in case of problems. Close communication with the GP is essential and is covered in detail in [sections 3–4](#).

2.24 Before radioiodine administration, patients should sign a consent to treatment form using the current NHS template ([Appendix C](#)), indicating that they understand the advice concerning radiation protection, the outcome with regard to risks of hypothyroidism and (where appropriate) that they are neither pregnant nor breast feeding.

2.25 Following radioiodine administration, patients should be given an information card clearly stating the date on which the radioiodine was taken, the total activity, and the duration for which special precautions are necessary (the information it should include is detailed in [Appendix D](#)). The card should be carried by the patient during the time special precautions are necessary. A telephone contact number should also be given on the card. Patients should be informed that some screening procedures at ports and airports may detect residual radioactivity several months after radioiodine administration, and the card should be carried on all commercial flights for six months after treatment.

Subclinical hyperthyroidism

2.26 There is little evidence to indicate the activity of radioiodine that should be administered in treating this condition. If a patient has subclinical hyperthyroidism associated with a clinically

significant multinodular goitre, a guide activity of 600 MBq is appropriate, while in those without moderate or large goitre, a lower activity of around 400 MBq is reasonable.²³ [3] The patient should be followed up clinically and biochemically at intervals similar to those indicated for treatment of hyperthyroidism.

Euthyroid goitre

2.27 Most trials to date have undertaken individual dosimetry studies to estimate the amount of radioiodine that needs to be given, based on the aim of administering 100 Gy absorbed dose.^{6,27} In the trial situation this has generally been achieved by giving 3.7–5.5 MBq/g thyroid tissue, corrected for the 24 hour ¹³¹I uptake. If such an approach is adopted in the UK, this would require inpatient admission if the total dose exceeds 800 MBq. An alternative would be to give a single fixed dose of 400–600 MBq for small to medium sized goitres and 800 MBq for large goitres. These doses can be given in the outpatient setting but some patients may require repeated treatment to have a significant effect on goitre size. These practical issues determine that the treatment may be difficult in those with very large goitres. It is possible that recombinant TSH may improve the efficacy of radioiodine treatment⁵⁶ [1b] but further trials are necessary before its use can be recommended. After radioiodine treatment, the patient should be followed clinically and biochemically at intervals similar to those indicated for treatment of hyperthyroidism.

Thyroid eye disease

2.28 Radioiodine treatment for Graves' disease is followed by the appearance or worsening of thyroid eye disease in more patients than after treatment with ATDs,^{13,14} although there is still controversy over the importance of radioiodine as a risk factor.⁵⁷ This effect is often transient and can be prevented by the administration of prednisolone. Smoking increases the risk of progression of thyroid eye disease up to four-fold.⁵⁸ Early treatment with thyroxine reduces the risk of thyroid eye disease deteriorating after radioiodine,^{17,59} suggesting that careful avoidance of hypothyroidism is worthwhile, particularly in patients with existing eye disease.

2.29 Radioiodine should be avoided if possible in newly diagnosed patients with Graves' disease who have active eye disease and an ATD is the best first-line treatment in this setting. Consideration should be given to referral to an ophthalmologist at this stage. Long-term ATD treatment and surgery are alternatives to radioiodine which should be discussed with patients with eye disease whose hyperthyroidism relapses after ATD treatment and the additional risk of deterioration in smokers should be taken into account.

2.30 Many endocrinologists prefer to use prophylactic glucocorticoids in patients who have significant eye disease and require radioiodine for treatment of Graves' disease which has relapsed after an ATD.⁶⁰ One regimen which avoids worsening of eye disease¹⁴ is to give 0.4–0.5 mg of prednisolone per kilogram of body weight starting two to three days before radioiodine therapy and continuing for one month; the dose is then tapered over a period of two months, and the drug discontinued. [1b] The usual advice regarding the precautions necessary for steroid treatment must be given and the side effects of treatment discussed with the patient.

3 Management during the first year following radioiodine therapy for thyrotoxicosis

Symptoms

3.1 In the first two weeks following the administration of radioiodine therapy, patients should be warned that palpitations or exacerbation of other thyrotoxic symptoms may be experienced, especially if he or she is not euthyroid at the time of treatment. This is particularly relevant in the elderly and patients with cardiac disease, for whom admission to hospital for a period after the radioiodine therapy may be considered.

Use of antithyroid drugs

3.2 In patients who have been rendered euthyroid with an ATD before therapy, medication after radioiodine treatment will usually not be necessary. In patients with poorly controlled hyperthyroidism, carbimazole may be recommenced seven days after radioiodine administration without affecting the long-term outcome of treatment.⁶¹ [1b] For those patients with mild to moderate thyrotoxic symptoms persisting after radioiodine and no contraindications, a beta adrenergic blocking agent (such as propranolol 20–40mg tds) may be used.

Follow-up

3.3 Before treatment, patients should be made aware of the importance of follow-up thyroid function tests. These tests may be carried out at the hospital where the radioiodine therapy has been administered or by the referring clinician. If a patient subsequently becomes hypothyroid and is then rendered biochemically euthyroid on thyroxine, follow-up by the patient's GP may be considered. If a patient remains biochemically euthyroid after one year of follow-up in the appropriate hospital clinic, then continued follow-up is normally transferred to the GP. Clear guidance for follow-up should be given to the GP and to the patient.

3.4 If the patient is not receiving an ATD, it is rare for hypothyroidism to develop within the eight weeks following radioiodine treatment; the first blood test should therefore be carried out about six weeks after radioiodine therapy. Serum free T4 and TSH levels should be measured to determine accurately the results of therapy. Persistent suppression of the TSH level may continue for several months following radioiodine therapy. Rising levels of TSH suggest the development of hypothyroidism; this finding will be useful in determining the frequency of further follow-up. In patients who are biochemically euthyroid at six to eight weeks a further set of thyroid function tests should be performed at 12 weeks after radioiodine therapy.

3.5 Patients should be advised to report recurrence of thyrotoxic symptoms or alternatively the development of symptoms of hypothyroidism to their GP or to the follow-up clinic. New symptoms should be reported as soon as they occur, rather than waiting for their planned appointment, as hypothyroidism may sometimes develop rapidly following radioiodine

treatment. In patients who remain hyperthyroid following therapy, and in whom an ATD is recommenced, the drug should be gradually withdrawn over a period of three to five months after initial radioiodine therapy to assess the late efficacy of treatment. If thyroid hormone levels become elevated on withdrawal of an ATD, repeat radioiodine therapy should be given six months after the initial treatment.

3.6 Hypothyroidism in the first six months after treatment may be transient in over half of the patients and long-term thyroxine replacement should not be given unless it is clear that hypothyroidism is permanent.⁶² [2b] A continuing rise in TSH levels and a fall in free T4 levels indicate developing thyroid failure. Thyroxine replacement should be commenced and the dose titrated to ensure euthyroidism. There is no evidence of benefit from a combined replacement regime with thyroxine and liothyronine.⁶³ [1b]

3.7 Follow-up should be continued in patients who remain euthyroid, with measurement of thyroid function (TSH and free T4) at six, nine and twelve months following radioiodine therapy. Thereafter, annual testing of thyroid function is essential to detect late onset hypothyroidism⁶⁴ (see [section 4](#)).

4 Monitoring and follow-up after the first year

Rationale

4.1 Regular review of thyroid function tests in patients who have undergone radioiodine treatment for hyperthyroidism is essential to assess the efficacy of the treatment and for timely detection of changes in thyroid status. Initial follow-up is usually conducted by the consultant who has clinical care of the patient, with subsequent monitoring in general practice (see [section 3](#)). The main consequence of radioiodine therapy is the development of hypothyroidism, but a small number of patients (around 10–20%) will require a second or rarely a third or even fourth dose of radioiodine because of continuing hyperthyroidism. The prevalence of hypothyroidism following treatment has been estimated to be 90% over a typical patient's lifetime. Therefore all patients should have thyroid function tests followed up indefinitely.

4.2 It is recommended that a fail-safe monitoring system be adopted to support regular patient monitoring with standardised follow-up. This may best be facilitated using a computer-based system. The extremes of unnecessary follow-up and of patients 'dropping through the net' will thus be minimised. Such a system will also provide information in an auditable format for the assessment and maintenance of the quality of patient care. The responsibility for life-long follow-up should not rest solely with the GP; patients have an important role to play, and specialists have a legitimate interest in long-term follow-up. Shared care is a management strategy that facilitates joint responsibility between general practitioners, consultants and patients in cost-effective follow-up.

Communication between specialist, general practitioner and patient

4.3 In keeping with best practice and Department of Health guidelines, copies of clinic letters should be routinely copied to the patient. After leaving the clinic, patients may well think of additional questions they would like to have asked, or find that concerns subsequently arise. Patients should be provided with details of someone they can contact following the consultation if they have any further questions or concerns. Since patients may turn to their GPs for advice, the GP should be sent a copy of the information sheet ([Appendix B](#)) given to the patient (including any standardised information regarding restrictions to which the patient will be subjected), in addition to the clinic letter outlining the proposed treatment.

4.4 Following the administration of radioiodine, a letter indicating the date of treatment and the activity given should be sent to the general practitioner and copied to the patient. This letter should include an indication of when the patient is to be reviewed at the hospital clinic and the duration of hospital visits (usually one year). Patients must be made aware of the need for regular review of their condition.

4.5 We recommend that initial follow-up of patients who have received radioiodine therapy is conducted by the medical team under the supervision of the consultant who has clinical care of the patient. This should normally include an arrangement to identify and recall non-attendees. The cooperation of the GP in helping to trace non-attendees should be obtained. The role of

patients (or, where appropriate, their carers) in being responsible for their own well-being should not be overlooked; support and advice may be needed to ensure this involvement. The recommendation from the British Thyroid Association, British Thyroid Foundation and Association of Clinical Biochemists is indefinite surveillance.⁶⁴ [4] Follow-up arrangements in the first year are detailed in [section 3](#).

4.6 Patients requiring life-long follow-up should be aware of the need for regular review of their condition. They should be provided with an information sheet indicating the frequency of review appropriate to their condition, and the appropriate content of such a review. This may form part of a summary record or cooperation card, held by the patient, containing summary medical history, review dates, review results, general information and advice.

Monitoring methods

4.7 Patients who are euthyroid after radioiodine treatment require annual thyroid function testing (TSH and free T4).⁶⁴

4.8 Computerised clinical systems may improve records and communication, provide useful clinical and administrative information, create organisational structure, assist quality assurance and support long-term follow-up.^{65–67} Such systems have been used for a number of years in the care of radioiodine treated patients and have provided the basis for the development of shared care. The advantages of shared care for thyroid disease are reduced loss to follow-up, improved adherence to therapy, improved detection of hypothyroidism, cost-effectiveness compared with alternative methods of follow-up and increased opportunity for audit and evaluation of care. The way forward is an integrated approach which links general practice and specialist records and which encourages a greater role for patients in their own care. A manual system could be used if a computerised system is not currently considered feasible, but both should have similar characteristics (see [Appendix E](#)).

4.9 There should be an effective audit procedure to ensure quality of both the information and the follow-up care provided by the system used. Indicators of data quality are described in [Appendix E](#).

Appendix A

Special precautions

As part of good radiation protection practice, it is necessary to place some restrictions on normal activities to ensure that those coming into contact with patients who have undergone treatment with ^{131}I do not receive inappropriate levels of radiation dose.

Patient-specific advice regarding radiation doses should always be sought from the local medical physics expert (MPE) and/or radiation protection adviser (RPA). However, it is possible to provide some general guidance on behaviour restrictions which may be used when planning treatments with ^{131}I .

In formulating advice on such restrictions, three groups of individuals are considered:

- ▶ comforters and carers
- ▶ children for whom the patient is responsible
- ▶ others (both children and adults).

Within the UK's radiation protection framework, comforters and carers are those who are knowingly and willingly exposed to ionising radiation as the result of the treatment of another person. Such people must be given advice on, and agree to the level of, radiation exposure. They are subject to a dose constraint, normally set at 5 mSv. Those in the other two groups, as members of the public, are normally subject to a dose limit of 1 mSv in any calendar year.

In all cases, the Ionising Radiations Regulations 1999¹ (IRR99) impose a duty to restrict doses to be as low as reasonably practicable (ALARP). This necessitates a risk assessment for each patient, although a generic one often suffices in the absence of problems such as incontinence of urine, or residence in a nursing home.

In the majority of cases it is practicable to restrict doses to others to 1 mSv. However, it is recognised that occasionally a more flexible approach is needed. The IRR allow a cumulative dose limit of 5 mSv in any five consecutive calendar years when members of the public are exposed to ionising radiation resulting from the medical exposure of another. This limit can be particularly useful when considering cases where the patient is the principal carer for children within the household.

Table A1 provides periods of restriction for a range of commonly administered activities. The times are based on the results of studies in which the radiation dose to other people from patients receiving ^{131}I treatment for thyrotoxicosis has been measured. In each case, the longer time is designed to restrict the radiation dose to 1 mSv and the shorter time, which is in brackets, should restrict it to 5 mSv.

Table A1 Behaviour restriction periods.

Behaviour restriction	Activity of ¹³¹ I administered in MBq			
	200	400	600	800
	Period of restriction in days			
Stay at least 1 m away from children under 3 years*	15 (2)	21 (8)	25 (11)	27 (14)
Stay at least 1 m away from children between 3 and 5 years of age*	11 (0)	16 (3)	20 (6)	22 (9)
Stay at least 1 m away from children over 5 years of age and adults who are not comforters and carers*	5 (0)	11 (0)	14 (1)	16 (3)
Sleep separately from comforters and carers ⁴⁴	–	–	4	8
Avoid prolonged close contact (more than 3 hours < 1 m) with other adults [one-off exposure] ⁴⁴	–	–	–	1

* The restrictions in the first 3 rows of this table have been taken from the Medical and Dental Guidance Notes⁴⁴ for the 1 mSv periods of restriction and from ICRP Publication 1994 (ICRP 1994),⁶⁸ which in turn references O'Doherty et al,⁶⁹ for the 5 mSv periods. In order to merge these, there has been a modification, in that ICRP 1994 cites children of 2 years of age, rather than 3 years, in the first two rows. However, the periods of restriction for 1 mSv are almost identical in the sources referenced.

- ▶ The 1 mSv dose constraint will apply to the majority of patients. The 5 mSv in five years limit may be used as the basis of advice in **exceptional circumstances** following consultation with the MPE or RPA, provided that the patient is unlikely to require further ¹³¹I treatment within five years.
- ▶ Due to the pattern of clearance of radioiodine from the body, it is not possible simply to extrapolate between the days in the table of precautions, such as precautions to restrict the dose to 3 mSv will not be half-way between 1 mSv and 5 mSv. The MPE or RPA can advise on the dose consequences of particular patterns of close contact.
- ▶ It is important to advise the patient of the importance of keeping as much distance as possible between themselves and others, including children, and of keeping contact times as short as possible (that is, to exploit the dose-saving potential of the inverse square law).

In most cases, it should be possible for arrangements to be made so that children cared for by patients undergoing radioiodine therapy are not subjected to unnecessary stress resulting from behavioural modifications. In extreme circumstances, where separation from their parents/carers is necessary, adequate notice and sensitive scheduling of treatment will allow arrangements to be made for alternative childcare for the periods indicated above. These periods are usually manageable where there is a developed support network.

There will remain circumstances – such as when a patient is the sole person responsible for the care of a child – where these restrictions provide difficulties, particularly for very young children. In these cases, options include prolonging the patient's medication until the child is over 3 years old or considering admission of the mother to hospital for radioiodine treatment.⁷⁰

Appendix B

Information for patients having radioiodine treatment for hyperthyroidism

What is hyperthyroidism?

Your thyroid gland is in your neck, in front of your windpipe. It produces a hormone called thyroxine which acts as your 'body clock', keeping your body working properly. Thyroxine has a direct effect on your heart rate, bowel activity, skin and organs. Hyperthyroidism (also known as Graves' disease, thyrotoxicosis and overactive thyroid) develops when your thyroid gland produces too much thyroxine, making your body clock run too fast.

What is radioiodine treatment?

Radioiodine treatment uses radioactive iodine to cure hyperthyroidism. The radioactivity destroys the overactive thyroid tissue and slows down the production of thyroxine. The thyroid gland uses most of the iodine, so only a small amount of radioactivity is needed.

What about my tablets?

If you have been given tablets to control your hyperthyroidism, you will need to stop taking them before your radioiodine treatment starts. The letter giving you your appointment for radioiodine treatment will tell you when to stop taking your tablets. You can only have radioiodine treatment after you have stopped taking your tablets, so please follow the instructions carefully.

Also, if you are taking any tablets which contain iodine or kelp (a seaweed which contains iodine), such as vitamin or mineral supplements, you will need to stop taking them at least a week before being treated with radioiodine. (If you have thyroid problems it is best not to take any tablets or vitamin supplements which contain iodine or kelp.)

How is the radioiodine given?

The radioiodine is given either as a drink or as a capsule. The drink tastes just like water and only contains a small amount of radioiodine. The capsule looks like those used for many other medicines and you swallow it whole with a drink of water.

How long does the radioiodine take to work?

It can take between a few weeks and several months for the treatment to work. Most people with hyperthyroidism (80–90% of people) are cured by a single dose of radioiodine. If the treatment has not worked within six months, it can be repeated.

Is radioiodine treatment dangerous?

No, its safety record is excellent. Radioiodine treatment has been given to millions of people since it was introduced in the early 1940s.

Where else in the body does radioiodine go?

Most of the radioiodine goes to the thyroid gland within a few hours. The rest will pass out of your body in your urine during the first few days after treatment. How long this will take depends on how much you are given.

Can I have the treatment if I am pregnant or breast feeding?

No. Radioiodine can harm unborn babies and babies that are being breast fed. You will not be given radioiodine treatment if you are pregnant or wish to continue breast feeding. You should avoid getting pregnant for six months after your treatment.

Are there any risks in having children afterwards?

No effects on the unborn babies of women who have been treated with radioiodine more than six months before they got pregnant, or on the health of those children, have been shown in over sixty years of experience in using radioiodine treatment. The treatment does not affect a woman's fertility.

Can I father children after radioiodine treatment?

Men should be careful not to father children for four months after radioiodine treatment. The treatment does not affect a man's fertility.

Will there be any danger to my family or friends?

After your radioiodine treatment, your body will contain some radioactivity, which will decrease every day. If you follow the advice you are given, other people may receive only an insignificant radiation dose from you. You will be able to continue shopping, cooking and doing other day-to-day household activities as normal. However, you will need to take some simple precautions for some time after your treatment to stop your family, friends and other people coming into contact with too much of the radiation.

How long you will need to do these things will depend on the amount of radioiodine you have been given. Your specialist will give you advice on the precautions at least a week before your treatment.

If you are given a large dose of radioiodine, you may have to stay in hospital for a few days after the treatment to reduce the risk of other people coming into contact with radiation.

You can travel home by public transport as long as you do not spend more than one hour sitting next to the same person on the bus, train or tube. You can drive yourself home. If someone else is driving you home, you should sit on the back seat, as far away from them as possible.

Hygiene

- ▶ Most of the radioiodine leaves your body in your urine and sweat during the first few days after your treatment. Drinking plenty of fluids and going to the toilet a lot will speed this up process.
- ▶ Men should urinate (wee) sitting down on the toilet to avoid getting radioiodine on the edge of the toilet.
- ▶ After going to the toilet you should flush it twice.
- ▶ Always wash your hands well after going to the toilet.
- ▶ Make sure that no one else uses your towels and face cloths.
- ▶ Wash all your crockery and cutlery thoroughly.

Other precautions

Your specialist will advise you about the following activities at least a week before your treatment is given. How long these precautions will apply for will depend on the amount of radioiodine you receive. Different precautions may apply for different lengths of time, but some may be for up to two to four weeks.

For the time advised:

- ▶ Limit your contact with children, especially children under 3 years of age. If you have your own children or have a job where you have contact with children, it is important to talk to the specialist about this as soon as possible.
- ▶ Stay more than an arm's length away from other people.
- ▶ Sleep alone.
- ▶ Take a few days off work if your job brings you into close contact with other people.

- ▶ Avoid going to places like cinemas, theatres, pubs and restaurants, where you may be in close contact with other people.
- ▶ Avoid travelling on public transport, apart from your journey home from hospital.

Carry the card

Your specialist will give you a card with the details of your treatment. You should carry this with you until you no longer have to follow any of these instructions. You should also carry the card with you if you are travelling through ports or on international flights for six months after treatment. Some security devices at airports are so sensitive that they may detect that you have had radioiodine treatment even after this length of time.

Will I need to see a doctor after the radioiodine treatment?

Yes, you will need to see either the doctor you saw at the clinic or your family doctor. You will have to have regular blood tests to monitor how the treatment is affecting your thyroid gland.

Are there any short-term side effects?

Most people notice no side effects from the treatment. A few people develop symptoms of an overactive thyroid (such as palpitations and sweating), usually five to ten days after the treatment. For this reason, your doctor may tell you to take a tablet called a beta-blocker for a few weeks after the treatment, and they may tell you to start taking your antithyroid tablets again.

Your thyroid gland may become underactive at a time ranging from a few months after treatment to many years later, causing 'hypothyroidism'. In a small number of people, this happens quite soon after radioiodine treatment. The blood tests will show whether this has happened.

If your thyroid gland does become underactive, your doctor will give you thyroxine tablets to replace the thyroxine that your thyroid gland is no longer producing. The tablets are very safe and contain a man-made version of the natural thyroxine that your body is unable to produce enough of. It may take a little time to find the right dose of thyroxine for you. You will not have to pay prescription charges for thyroxine tablets.

Thyroid eye disease (which can develop in Graves' disease) may get worse after the treatment. The doctor will discuss this with you before you have the treatment and may suggest that you take a steroid called prednisolone for a month or two after the treatment.

More information

You can get more information about radioiodine treatment and thyroid disease from:

The British Thyroid Foundation
PO Box 97
Clifford
Wetherby
West Yorkshire
LS23 6XD

Phone or fax: 01423 709707 or 01423 709448

Website: www.btf-thyroid.org

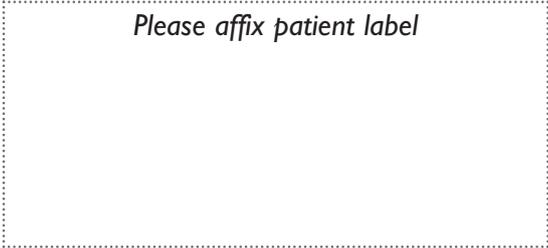
If you have any questions or you need more advice, please call the following number.

Phone:.....

Appendix C

Sample consent form to be used for patients for whom radioiodine therapy has been prescribed

Please affix patient label



INSERT HOSPITAL DETAILS

Patient/parental agreement to investigation or treatment

¹³¹I Radioiodine treatment for hyperthyroidism or non-toxic goitre

Statement of health professional (to be filled in by health professional with appropriate knowledge of proposed procedure, as specified in consent policy).

The intended benefits: I have explained the procedure to the patient/parent. In particular, I have explained that this treatment is being proposed to treat the thyroid gland which has become overactive and/or enlarged.

Serious or frequently occurring risks: Several radioiodine treatments may be required. There may be a short period of thyroid overactivity following the radioiodine treatment. The thyroid gland may stop working completely after this treatment and regular blood tests will be required to check the functioning of the gland. Thyroxine treatment may become necessary. In patients with thyroid eye disease, the possible risks of radioiodine treatment have been discussed. I have satisfied myself that the patient, if female, is not pregnant and that she is aware that pregnancy must be avoided for six months. Male patients should not father children for four months.

I have also discussed what the procedure is likely to involve (including the specific written requirement to avoid contact with children and pregnant women and to take time off work), the benefits and risks of any available alternative treatments (including no treatment) and any particular concerns of those involved. I have informed the patient/parent that they can withdraw their consent for treatment at any time.

Radioiodine activity to be administered
 MBq ¹³¹I (±10%)

The following leaflet/tape has been provided:

'Thyrotoxicosis and its management' and 'Radioiodine treatment instructions'

Signed Date
 Name (PRINT)..... Job title

Statement of interpreter (where appropriate)

I have interpreted the information above to the patient/parent to the best of my ability and in a way in which I believe s/he/they can understand.

Signed Date
 Name (PRINT).....

Statement of patient or person with parental responsibility for patient

- ▶ I agree to the procedure described above.
- ▶ I understand that you cannot give me a guarantee that a particular person will perform the procedure. However, the person will have appropriate experience.
- ▶ I confirm that I am/the patient is not pregnant or breast feeding.

Signed Date
 Name (PRINT)..... Relationship to patient.....

Confirmation of consent (to be completed by a health professional when the patient is admitted for the procedure, if the patient/parent has signed the form in advance)

- ▶ I have discussed relevant written radiation protection advice.
- ▶ I have confirmed that the patient/parent has no further questions and wishes the procedure to go ahead.

Signed Date
 Name (PRINT)..... Job title

Copy accepted by patient: yes / no (please circle)

Appendix D

Sample patient information card

Radionuclide instruction card

Patient name

Patient address

Registration number

Consultant name

Radionuclide ¹³¹I MBq

Administered on

Signed

Hospital address

Please observe the following instructions

Avoid prolonged close contact (a distance of less than 1 metre) with children and pregnant women for the following number of days:

.....

Sleep apart from your partner for the following number of days:

.....

Do not return to work for the following number of days:

.....

Avoid close contact (less than 1 metre) with any other person for more than three hours for the following number of days:

.....

Please carry this card with you at all times for 4 weeks after your treatment and for 6 months when travelling through ports and airports, and if travelling abroad.

Appendix E

Elements of a system to support long-term follow-up of patients treated with radioiodine

Structured systems (computerised or manual) are important to ensure long-term follow-up of patients treated with radioiodine, specifically to prompt regular biochemical testing to detect the onset of hypothyroidism and to ensure that any subsequent treatment with thyroxine is correctly adjusted to achieve biochemical targets.⁶⁵⁻⁶⁷

Ensuring long-term follow-up is an important and intrinsic component of the care provided by the thyroid specialist. Such follow-up is facilitated by the presence of a computerised system linked to details of radioiodine treatments, and should ideally be compatible with both hospital and primary care IT systems. Long-term follow-up may be undertaken in primary care, in agreement with the specialist, GP and patient, and is again facilitated by the presence of a computerised system.

Characteristics of follow-up systems

- ▶ All patients treated with radioiodine should be identified. Mechanisms should be in place to capture all patients, such as through links to radioiodine prescribing records.
- ▶ All relevant data should be collected, and should comprise:
 - patient demographic details and identifiers (hospital/NHS numbers)
 - details of thyroid specialist and GP
 - date(s) and dose(s) of radioiodine treatments
 - dates and results of serial thyroid function tests
 - date of initiation of thyroxine therapy.
- ▶ Additional data may be recorded, especially to facilitate long-term audit of outcomes and research. These data may include:
 - aetiology of hyperthyroidism
 - presence and severity of thyroid eye disease
 - and details of ATD therapy.
- ▶ Data collection should fit easily into a normal clinical routine. Data may be managed in such a way as to facilitate updating of general hospital and/or primary care records and/or to generate routine correspondence.
- ▶ The system should provide useful information. Data should be used:
 - to inform day-to-day care
 - for quality assurance of patient care

- for long-term patient follow-up
- for the review of treatment practices and outcomes.
- ▶ The system must ensure regular recall of patients for biochemical testing (typically at annual intervals):
 - systems must be in place to identify defaulters from follow-up and to prompt further recall
 - systems should be sufficiently flexible to allow recording of biochemical data from several laboratory sources
 - systems should ideally highlight abnormal results in order to facilitate clinical intervention when appropriate.
- ▶ Procedures must be in place to ensure complete and accurate data collection and overall implementation of effective follow-up.

Indicators of data quality

Regular data validation should include the following indicators of quality:

- ▶ completeness – are data available for all radioiodine treated patients?
- ▶ consistency – are findings recorded consistently throughout the patient record?
- ▶ accuracy – is there variation between observers?
- ▶ face validity – would an alternative method for collecting data give similar results?
- ▶ relevance – do the data as recorded allow prediction of those at risk?

References

- 1 Her Majesty's Stationery office. *Ionising Radiation Regulations 1999* (No. 3232). London: HMSO, 1999 and *Ionising Radiation Regulations (Northern Ireland) 2000* (No. 375). London: HMSO, 2000.
- 2 Her Majesty's Stationery Office. *Ionising Radiation (Medical Exposure) Regulations 2000* (No 1059). London: HMSO, 2000 and *Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006* (No. 2523). London: HMSO, 2006.
- 3 Cooper DS. Hyperthyroidism. *Lancet* 2003;362:459–68.
- 4 Franklyn JA. The management of hyperthyroidism. *N Engl J Med* 1994;330:1731–8.
- 5 McDermott MT, Woodmansee WW, Haugen BR *et al*. The management of subclinical hyperthyroidism by thyroid specialists. *Thyroid* 2003;13:1133–9.
- 6 Hegedus L, Bonnema SJ and Bennedbaek FN. Management of simple nodular goiter: current status and future perspectives. *Endocr Rev* 2003;24:102–32.
- 7 Le Moli R, Wesche MF, Tiel-Van Buul MM *et al*. Determinants of long-term outcome of radioiodine therapy of sporadic non-toxic goitre. *Clin Endocrinol (Oxf)* 1999;50:783–9.
- 8 Vanderpump MP, Ahlquist JA, Franklyn JA *et al* on behalf of the Research Unit of the Royal College of Physicians of London, the Endocrinology and Diabetes Committee of the Royal College of Physicians of London, and the Society for Endocrinology. Consensus statement for good practice and audit measures in the management of hypothyroidism and hyperthyroidism. *BMJ* 1996;313:539–44.
- 9 Allahabadia A, Daykin J, Holder RL *et al*. Age and gender predict the outcome of treatment for Graves' hyperthyroidism. *J Clin Endocrinol Metab* 2000;85:1038–42.
- 10 Franklyn JA, Maisonneuve P, Sheppard MC. Mortality after the treatment of hyperthyroidism with radioactive iodine. *N Engl J Med* 1998;338:712–8.
- 11 Franklyn JA, Sheppard MC, Maisonneuve P. Thyroid function and mortality in patients treated for hyperthyroidism. *JAMA* 2005;294:71–80.
- 12 Read CH Jr, Tansey MJ, Menda Y. A 36-year retrospective analysis of the efficacy and safety of radioactive iodine in treating young Graves' patients. *J Clin Endocrinol Metab* 2004;89:4229–33.
- 13 Allahabadia A, Daykin J, Sheppard MC *et al*. Radioiodine treatment of hyperthyroidism-prognostic factors for outcome. *J Clin Endocrinol Metab* 2001;86:3611–7.
- 14 Sridama V, DeGroot LJ. Treatment of Graves' disease and the course of ophthalmopathy. *Am J Med* 1989;87:70–73.
- 15 Tallstedt L, Lundell G, Torring O *et al*. Occurrence of ophthalmopathy after treatment for Graves' hyperthyroidism. The Thyroid Study Group. *N Engl J Med* 1992;326:1733–8.
- 16 Bartalena L, Marcocci C, Bogazzi F *et al*. Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy. *N Engl J Med* 1998;338:73–8.
- 17 Tallstedt L, Lundell G, Blomgren H *et al*. Does early administration of thyroxine reduce the development of Graves' ophthalmopathy after radioiodine treatment? *Eur J Endocrinol* 1994;130:494–7.
- 18 Andrade VA, Gross JL, Maia AL. The effect of methimazole pretreatment on the efficacy of radioactive iodine therapy in Graves' hyperthyroidism: one-year follow-up of a prospective, randomized study. *J Clin Endocrinol Metab* 2001;86:3488–93.

- 19 Bonnema SJ, Bennedbaek FN, Veje A *et al.* Propylthiouracil before ¹³¹I therapy of hyperthyroid diseases: effect on cure rate evaluated by a randomized clinical trial. *J Clin Endocrinol Metab* 2004;89:4439–44.
- 20 Braga M, Walpert N, Burch HB *et al.* The effect of methimazole on cure rates after radioiodine treatment for Graves' hyperthyroidism: a randomized clinical trial. *Thyroid* 2002;12:135–9.
- 21 Sawin CT, Geller A, Wolf PA *et al.* Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. *N Engl J Med* 1994;331:1249–52.
- 22 Parle JV, Maisonneuve P, Sheppard MC *et al.* Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. *Lancet* 2001;358:861–5.
- 23 Surks MI, Ortiz E, Daniels GH *et al.* Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA* 2004;291:228–38.
- 24 Faber J, Jensen IW, Petersen L *et al.* Normalization of serum thyrotrophin by means of radioiodine treatment in subclinical hyperthyroidism: effect on bone loss in postmenopausal women. *Clin Endocrinol (Oxf)* 1998;48:285–90.
- 25 Wesche MF, Tiel V, Lips P *et al.* A randomized trial comparing levothyroxine with radioactive iodine in the treatment of sporadic nontoxic goitre. *J Clin Endocrinol Metab* 2001;86:998–1005.
- 26 Nygaard B, Hegedus L, Gervil M *et al.* Radioiodine treatment of multinodular non-toxic goitre. *BMJ* 1993;307:828–32.
- 27 Bonnema SJ, Bertelsen H, Mortensen J *et al.* The feasibility of high dose iodine 131 treatment as an alternative to surgery in patients with a very large goiter: effect on thyroid function and size and pulmonary function. *J Clin Endocrinol Metab* 1999;84:3636–41.
- 28 Nygaard B, Faber J, Hegedus L. Acute changes in thyroid volume and function following ¹³¹I therapy of multinodular goitre. *Clin Endocrinol (Oxf)* 1994;41:715–8.
- 29 Nygaard B, Knudsen JH, Hegedus L *et al.* Thyrotropin receptor antibodies and Graves' disease, a side-effect of ¹³¹I treatment in patients with nontoxic goiter. *J Clin Endocrinol Metab* 1997;82:2926–30.
- 30 Bonnema SJ, Nielsen VW, Hegedus L. Long-term effects of radioiodine on thyroid function, size and patient satisfaction in non-toxic diffuse goitre. *Eur J Endocrinol* 150:439–45.
- 31 Wartofsky L, Glinoe D, Solomon B *et al.* Differences and similarities in the diagnosis and treatment of Graves' disease in Europe, Japan, and the United States. *Thyroid* 1991;1:129–35.
- 32 Baxter MA, Stewart PM, Daykin J *et al.* Radioiodine therapy for hyperthyroidism in young patients – perception of risk and use. *Q J Med* 1993;86:495–9.
- 33 Franklyn JA, Maisonneuve P, Sheppard M *et al.* Cancer incidence and mortality after radioiodine treatment for hyperthyroidism: a population-based cohort study. *Lancet* 1999;353:2111–5.
- 34 Ron E, Doody MM, Becker DV *et al.* Cancer mortality following treatment for adult hyperthyroidism. Cooperative Thyrotoxicosis Therapy Follow-up Study Group. *JAMA* 1998;280:347–55.
- 35 Dobyns BM, Sheline GE, Workman JB *et al.* Malignant and benign neoplasms of the thyroid in patients treated for hyperthyroidism: a report of the cooperative thyrotoxicosis therapy follow-up study. *J Clin Endocrinol Metab* 1974;38:976–98.
- 36 Hall P, Berg G, Bjelkengren G *et al.* Cancer mortality after iodine-131 therapy for hyperthyroidism. *Int J Cancer* 1992;50:886–90.
- 37 Hall P, Boice JD, Jr., Berg G *et al.* Leukaemia incidence after iodine-131 exposure. *Lancet* 1992;340:1–4.
- 38 Holm LE, Hall P, Wiklund K *et al.* Cancer risk after iodine-131 therapy for hyperthyroidism. *J Natl Cancer Inst* 1991;83:1072–77.

- 39 Robertson JS, Gorman CA. Gonadal radiation dose and its genetic significance in radioiodine therapy of hyperthyroidism. *J Nucl Med* 1976;17:826–30.
- 40 Ljunggren JG, Topping O, Wallin G *et al.* Quality of life aspects and costs in treatment of Graves' hyperthyroidism with antithyroid drugs, surgery, or radioiodine: results from a prospective, randomized study. *Thyroid* 1998;8:653–9.
- 41 Abraham-Nordling M, Topping O, Hamberger B *et al.* Graves' disease: A long-term quality-of-life follow-up of patients randomized to treatment with antithyroid drugs, radioiodine, or surgery. *Thyroid* 2005;15:1279–86.
- 42 Her Majesty's Stationery Office. *Medicines (Administration of Radioactive Substances) Regulations* 1978 (No 1006). London: HMSO, 1978.
- 43 Her Majesty's Stationery Office. *Radioactive Substances Act* 1993. London: HMSO, 1993.
- 44 *Medical and dental guidance notes: A good practice guide on all aspects of ionising radiation in the clinical environment.* York: Institute of Physics and Engineering in Medicine, 2002.
- 45 Hedley AJ, Lazarus J, McGhee SM *et al.* Treatment of hyperthyroidism by radioiodine. Summary of a UK national survey prepared for the Royal College of Physicians Committee on Endocrinology and Diabetes. *J R Coll Physicians Lond* 1992;26:348–51.
- 46 Jarlov AE, Hegedus L, Kristensen LO *et al.* Is calculation of the dose in radioiodine therapy of hyperthyroidism worthwhile? *Clin Endocrinol (Oxf)* 1995;43:325–329.
- 47 Leslie WD, Ward L, Salamon EA *et al.* A randomized comparison of radioiodine doses in Graves' hyperthyroidism. *J Clin Endocrinol Metab* 2003;88:978–83.
- 48 Bogazzi F, Bartalena L, Brogioni S *et al.* Comparison of radioiodine with radioiodine plus lithium in the treatment of Graves' hyperthyroidism *J Clin Endocrinol Metab* 1999;84:499–503
- 49 Bal CS, Kumar A, Pandey RM. A randomized controlled trial to evaluate the adjuvant effect of lithium on radioiodine treatment of hyperthyroidism. *Thyroid* 2002;12:399–405.
- 50 Lazarus JH. Guidelines for the use of radioiodine in the management of hyperthyroidism: a summary. 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. *J R Coll Physicians Lond* 1995;29:464–9.
- 51 McDermott MT, Kidd GS, Dodson LE Jr *et al.* Radioiodine-induced thyroid storm. Case report and literature review. *Am J Med* 1983;75:353–9.
- 52 Cooper DS. Antithyroid drugs and radioiodine therapy: a grain of (iodized) salt. *Ann Int Med* 1994;121:612–3.
- 53 Santos RB, Romaldini JH, Ward LS. Propylthiouracil reduces the effectiveness of radioiodine treatment in hyperthyroid patients with Graves' disease. *Thyroid* 2004;14:525–530.
- 54 Bonnema SJ, Bartalena L, Toft AD *et al.* Controversies in radioiodine therapy: relation to ophthalmopathy, the possible radioprotective effect of antithyroid drugs, and use in large goitres. *Eur J Endocrinol* 2002;147:1–11.
- 55 Administration of Radioactive Substances Advisory Committee. Notes for guidance on the clinical administration of radiopharmaceuticals and use of sealed radioactive sources, March 2006 (www.arsac.org.uk/notes_for_guidance/index.htm).
- 56 Silva MN, Rubio IG, Romao R *et al.* Administration of a single dose of recombinant human thyrotrophin enhances the efficacy of radioiodine treatment of large compressive multinodular goitres. *Clin Endocrinol (Oxf)* 2004;60:300–8.

- 57 Gorman CA. Therapeutic controversies. Radioiodine therapy does not aggravate Graves' ophthalmopathy. *J Clin Endocrinol Metab*. 1995;80:340–2.
- 58 Bartalena L, Marcocci C, Tanda ML *et al*. Cigarette smoking and treatment outcomes in Graves' ophthalmopathy. *Ann Intern Med* 1998;129:632–5.
- 59 Kung AW, Yau CC, Cheng A. The incidence of ophthalmopathy after radioiodine therapy for Graves' disease: prognostic factors and the role of methimazole. *J Clin Endocrinol Metab*. 1994;79:542–6.
- 60 Weetman AP, Wiersinga WM. Current management of thyroid-associated ophthalmopathy in Europe. Results of an international survey. *Clin Endocrinol (Oxf)* 1998;49:21–8.
- 61 Bonnema SJ, Bennedbaek FN, Gram J *et al*. Resumption of methimazole after ¹³¹I therapy of hyperthyroid diseases: effect on thyroid function and volume evaluated by a randomized clinical trial. *Europ J Endocrinol* 2003;1409:485–92.
- 62 Aizawa Y, Yoshida K, Kaise N *et al*. The development of transient hypothyroidism after iodine-131 in hyperthyroid patients with Graves' disease: prevalence, mechanism and prognosis. *Clin Endocrinol (Oxf)* 1997;46:1–5.
- 63 Escobar-Morreale HF, Botella-Carretero JJ, Escobar del Rey F *et al*. Treatment of hypothyroidism with combinations of levothyroxine plus liothyronine. *J Clin Endocrinol Metab* 2005;90:4946–54.
- 64 Association for Clinical Biochemistry, British Thyroid Foundation and British Thyroid Association. UK guidelines for thyroid function tests (first draft www.british-thyroid-association.org/TFT_guidelines_consultation_10_05.pdf).
- 65 Jones SJ, Hedley AJ, Curtis B *et al*. Do we need thyroid follow-up registers? A cost-effective study. *Lancet* 1982;1:1229–33.
- 66 Jung RT, Scott A, Chong P *et al*. A new Pick-based computer thyroid register based on the national SAFUR requirements for local usage. *Health Bull (Edin)* 1991;49:244–9.
- 67 Flynn RWV, Morris AD, Jung RT *et al*. Does an automated thyroid register improve the clinical management of hypothyroid patients? An observational study. *Clin Endocrinol (Oxf)* 2005;63:116–8.
- 68 International Commission of Radiological Protection. Release of nuclear medicine patients after treatment with unsealed sources. *Annals of the ICRP*. Oxford: Elsevier, 2004.
- 69 Doherty MJ, Kettle AG, Eustance CNP *et al*. Radiation dose rates from adult patients receiving ¹³¹I therapy for hyperthyroidism. *Nucl Med Commun* 1993;14:160–8.
- 70 Barrington SF, O'Doherty MJ, Kettle AG *et al*. Radiation exposure of the families of outpatients treated with radioiodine (iodine-131) for hyperthyroidism. *Eur J Nucl Med* 1999;26:686–92.