Personal Practice

Management of Graves' Disease in Children and Adolescents: Should Radioiodine Treatment Be Given?

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Abstract

The large published literature on the management of Graves' Hyperthyroidism reflects the persisting controversies regarding optimum management of this common condition. This was highlighted in surveys of the European and American Thyroid Associations in 1986 and 1990 in which expert opinion differed in many areas. Few subjects raise greater controversy than the treatment of Graves' disease in children and adolescents. There is no specific cure for the illness, and potential complications are associated with each therapeutic option. Antithyroid drug therapy with thionamides is associated with side-effects and a high relapse rate even after prolonged therapy. Thyroidectomy achieves high rates of remission, yet is a complex surgical procedure that can result in hypoparathyroidism or dysphonia due to damage to the recurrent laryngeal nerves. Radioiodine therapy achieves high rates of remission, yet the long-term safety of iodine-131 in children and adolescents has been evaluated in fewer than 1000 individuals. Concerns also linger about the oncogenic potential of radioiodine and the potential risks of genetic damage to offspring after radioiodine treatment. In this article, I would review the information about the risks and benefits of current treatments for hyperthyroidism in adult and childhood Graves' disease with special emphasis on children and adolescents and the safety of radioiodine therapy in the paediatric population. I aim to highlight areas in which the literature does, I believe, provide guidance in the management of Graves' disease, and summarise the state of knowledge in those areas in which the data remain inconclusive.

Key words

Children and adolescents; Graves' disease; Radioiodine; Treatment

Introduction

Graves' disease is the most common cause of thyrotoxicosis in children and adults. It is an autoimmune disorder characterised by diffuse goitre, hyperthyroidism and ophthalmopathy. In Graves' disease, the spontaneous development of antibodies (thyroid-stimulating antibodies – TSAbs) that mimic thyrotropin (TSH) action leads to the excessive production and release of thyroid hormone, resulting in thyrotoxicosis. Untreated, thyrotoxicosis can have pernicious physical and behavioural effects on growing children and adolescents. As Graves' disease is a protracted disorder with rare spontaneous resolution,[1-4] treatment is essential for the well-being of the child and adolescent. Currently, antithyroid drug, thyroidectomy and radioiodine are the three main therapeutic options for Graves' disease.

Problems in Management of Graves' Disease

Despite the long history of this common condition, there are persisting controversies regarding its optimum management. This was highlighted in surveys of the European and American Thyroid Associations in 1986 and 1990 in which members were asked questions regarding the investigation and treatment of a 43-year-old female with moderate hyperthyroidism, a diffuse goitre and minimal eye signs. Results are shown in Table 1.[5,6] In Hong Kong, currently we have no consensus protocol of medical treatment (including investigations, choice of medication,

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Table 1 Comparison of the management of Graves' disease in Europe and the USA[5,6] (Adapted from surveys of the European and American Thyroid Associations)

Treatment	Europeans (%)	Americans (%)
Standard case		
Surgery	1	1
Thionamides	77	30
Radioiodine	22	69
Duration drug treatment		
<6 months	5	0
<12 months	90	90
Age <19 years		
Surgery	3	4
Thionamides	93	63
Radioiodine	4	33
Large Giotre		
Surgery	51	7
Thionamides	32	18
Radioiodine	17	78

starting dose, maintenance regimen, prognostic factors, and duration of treatment). There is also no consensus on referral for ablative therapy (surgery or radioiodine therapy). Many patients are followed up for a long period of time as the chance of remission is less compared with the adults.

Therapeutic Controversies

Few subjects raise greater controversy than the treatment of Graves' disease in children and adolescents. There is no specific cure for the illness, and potential complications are associated with each therapeutic option. Antithyroid drug therapy with thionamides is associated with side-effects and a high relapse rate even after prolonged therapy. Thyroidectomy achieves high rates of remission, yet is a complex surgical procedure that can result in hypo-parathyroidism or dysphonia due to damage to the recurrent laryngeal nerves. Radioiodine therapy achieves high rates of remission, yet the long-term safety of iodine-131 (I-131) in children and adolescents has been evaluated in fewer than 1000 individuals. Concerns also linger about the oncogenic potential of radioiodine and the potential risks of genetic damage to offspring after radioiodine treatment.

In this article, I would review the information about the risks and benefits of current treatments for hyperthyroidism in adult and childhood Graves' disease with special emphasis on children and adolescents and the safety of radioiodine therapy in the paediatric population. I aim to highlight areas in which the literature does, I believe, provide guidance in the management of Graves' disease, and summarise the state of knowledge in those areas in which the data remain inconclusive.

Antithyroid Drug Therapy

This was introduced in the early 1940s by Astwood.[7] Current mainstays of antithyroid therapy include the thionamide derivatives propylthiouracil (PTU), methimazole (MMI), and carbimazole (CBZ). They reduce thyroid hormone synthesis by inhibiting oxidation and organic binding of thyroid iodide. PTU has a short-half life (4-6 h) and is typically given every 8 h, starting dose 5-10 mg/kg/day (usually 400-600 mg/day). MMI has a longer half-life (12-16 h), dose is 0.5-1.0 mg/kg/day given QD to tid (usual starting dose 30-40 mg/day). CBZ is metabolised to MMI *in vivo* but is less potent gram for gram. Initial improvement occurs in 2-4 weeks. Ninety percent can be rendered euthyroid or hypothyroid by 4-6 weeks. Before that time signs and symptoms of hyperthyroidism may be controlled with β-blockers. In patients with thyroid storm or requiring surgery, thyrotoxicosis can be rapidly controlled with saturated potassium iodide (or Lugol's solution). They block the release of thyroid hormones and reduce the vascularity of the thyroid gland.

Which Drug

So far, there is no data directly comparing the long-term remission rates of one drug vs another. The choice of drug is largely determined by local practice – PTU is more commonly used in US, while MMI in UK and CBZ in Europe and Asia. CBZ/MMI have the advantage of single daily dosing with increase in patient compliance and a larger body of literature on their use. PTU is more protein-bound with reduced passage into placental tissue and breast milk, justifying its use in pregnancy and lactation, and it is additionally able to inhibit T4 to T3 conversion. However, the value of these effects on clinical outcome has not been compared and at present individual variation in the choice of drug used remains justified.

What Initial Dose

A high starting dose is recommended to render patients euthyroid as quickly as possible. CBZ 30-40 mg, MMI 30-40 mg or PTU 400-600 mg are commonly used.[8-10] However, doses higher than these should not be used

routinely because of the associated increase in incidence of serious side-effects.[11-13]

High or Low Dose Maintenance Therapy

The remission rates in adults were found to be similar with the '*titration regimen*' (i.e. tapering the dose of thionamides to the lowest level to maintain euthyroidism) or the '*block and replace regimen*' (i.e. with the addition of thyroxine to allow maintenance of high thionamide doses) (Table 2).[13-21] Studies in adults have also found little evidence for an independent beneficial effect of thyroxine on the relapse rates nor the level of TSAbs.[15,20-24]

Maintenance Therapy – How Long

Prospective randomised controlled trials (RCT) in adults have shown extending treatment beyond 6 to 18 months to be beneficial when titration regimen is used but courses over 18 months confer no additional benefit.[25,26] One RCT using block-replace regimen in adults has found treatment beyond 6 months conferred no additional benefit.[27] No large RCT has been done in children. Most of the paediatric patients in Hong Kong are maintained on antithyroid drugs for a much longer duration as this is the preferred therapeutic option of both the paediatricians and the patients.

Long Term Remission Rates and Outcome Predictors

Previous studies of adult patients reported remission rates of 40-50% after prolonged therapy.[28] However, these have fallen considerably over the past few decades,[29] possibly due to the well-documented increase in mean dietary iodine intake.[30] In children, the best remission rates are 50-60%[2,31] but are usually less than 30-40%,[2,32-37] being considerably less in prepubertal (17%) than in pubertal children (30%).[37]

There are no reliable markers to predict the outcome after treatment. Large goitres (>40 ml), ophthalmopathy, young age, high titres of TSAbs (>30 U/L) are associated with poor remission rates (9% vs 80%).[38-42] A recent meta-analysis of 18 studies between 1975 and 1991 confirmed an association between the absence of TSAbs at end of treatment and increased chance of long-term remission (P<0.00001).[43] It has also been suggested that the long-term remission rate can be predicted from the response to short term (4-6 months) antithyroid drug therapy.[44,45] Long-term remission is less likely if high levels of TSAbs are present or if hyperthyroidism persists after short-term drug treatment.[42,44,45]

Side-effects of Antithyroid Drug Therapy

They are more common in children than adults.[46,47] It can be idiosyncratic or dose-related. Thirty-six serious complications and 2 deaths in children have been reported to the FDA MedWatch Program.[48] Published studies show that 20-30% patients will develop complications (Table 3),[2,32-36] among these 1/3 to 1/4 require discontinuation of all thionamide drugs and for the remaining, complications may resolve after switching to alternative thionamide.

The incidence of serious haematological side-effects (agranulocytosis, aplastic anaemia) has been reported to be 0.17% to 2.8%.[11,13-14,17,19,49-51] Most occur at high doses and within 3 months of therapy but cases have been reported with doses as low as 10 mg MMI,[17] and as late as 12 months or more after starting treatment.[49] Hence, all patients must be advised to stop the drug promptly and have a white cell count checked if sore throat, fever or mouth ulcers develop. Hepatotoxicity (acute hepatic necrosis or cholestatic hepatitis) can continue despite discontinuation of drug

Table 2   Trials comparing the effect of high and low dose thionamide maintenance treatment on relapse rates[14,16-19,21]

Reference	Treatment groups	Number studied	Duration (months)	Follow-up (months)	Relapse (%)	Significant difference?	
Romaldini, et al (1983)[14]	MMI 60 mg + T3	65	12	24	25	Yes	*P<0.001*
	MMI titrated	48			58		
Jorde, et al (1995)[19]	MMI 60 mg + T3	19	6	24	58	Yes	*P<0.02*
	MMI titrated	22			77		
Reinwein, et al (1993)[17]	MMI 40 mg + T4	153	12	12	35	No	
	MMI 10 mg + T4	156			37		
Lucas, et al (1997)[21]	CBZ 30-45 mg + T4	30	18	60	67	No	
	CBZ titrated	30			60		
Meng, et al (1991)[16]	MMI 40 mg + T4	41	12	12	54	No	
	MMI titrated	68			53		
Edwards & Tellez (1994)[18]	CBZ 60 mg + T4	34	12	24	50	No	
	CBZ titrated	36			66		

Table 3   Complications of antithyroid drug therapy in more than 500 children[4,35,36]

Complication	Incidence (%)
Mild increases in liver enzymes	**28**
Mild leucopenia	**25**
Skin rash[a]	**9**
Granulocytopenia[b]	**4.5**
Arthritis[b]	**2.4**
Nausea[a]	1.1
Agranulocytosis[b]	0.4
Hepatitis[b]	0.4
Loss of taste	Rare
Hypothrombinemia[b]	Rare
Thrombocytopenia[b]	Rare
Aplastic anaemia[b]	Rare
Nephrotic syndrome[b]	Rare
Death	Rare

[a] May respond favourably to substitution of an alternative thionamide drug; [b] Necessitate discontinuation of all thionamide drugs

therapy and may be fatal. It is more common with use of higher drug doses.[12,13] Minor side-effects such as rash, pruritus, arthralgia and gastritis occur in 10-25% children and they are more clearly dose-related.[11,13-14,17,19,27]

Risk of Cancer

The incidence of developing thyroid cancer in one's lifetime is 1 in 400 for males and 1 in 300 for females.[52] Several reports show that patients with Graves' disease have a higher incidence and more aggressive thyroid cancer. The Collaborative Thyrotoxicosis Study Group revealed that the incidence of thyroid carcinomas over 10-20 years of follow-up (not lifetime incidences) is 5-fold higher in adults with Graves' disease treated with thionamide drugs than in patients treated with I-131 and 8-fold higher than in patients treated surgically.[53] Rates of thyroid adenomas were also 10 and 20 times higher among the adults treated with antithyroid drugs than in patients treated with I-131 or surgery respectively.[53] Rather than reflecting a causative role for medical therapy in the pathogenesis of thyroid neoplasia, these observations may reflect the persistence of more thyroid tissue in patients treated with drugs than in those treated with radioiodine or surgery.

Surgery

In the first prospective RCT comparing the three treatment modalities, surgery was shown to be quicker than

either thionamides or radioiodine in establishing euthyroidism and to have the lowest 2-year failure rate (6% vs 21% for radioiodine and 40% for drugs).[54] After subtotal thyroidectomy, relief of hyperthyroidism is achieved in about 80% of children and adults, hypothyroidism develops in about 60% of individuals, risk of recurrence occurs in 10-15% of patients.[36,55,56] In comparison, hyperthyroidism recurs in <3% of children and adults who undergo total thyroidectomy, but hypothyroidism is nearly universal.[55-59] Table 4 showed the complications of thyroidectomy in children.[36,55,58-61] With advances in anaesthesia, surgery, and postoperative care, it is possible that complication rates have decreased. However, with increasing use of radioiodine, less thyroid surgery is now performed, and fewer surgeons are able to develop and maintain their skills than in the past.[62]

Radioiodine

Radioiodine therapy for Graves' disease was introduced nearly 60 years ago.[63,64] After an oral dose of I-131, most radiation is localised in the thyroid gland leading to destruction of follicular cells followed by fibrosis. Due to individual variation in the sensitivity of the thyroid to radioiodine, most oncologists prefer to give fixed doses of 5-15 mCi (185-555 MBq) on the basis of thyroid size assessed by clinical exam or ultrasound.[65] The effective half-life of I-131 is 7 days. Transient hyperthyroid may occur 4-10 days after I-131 therapy. This can be controlled by β-blockers or Lugol's solution without adversely affecting the outcome of treatment. A second dose of I-131 is recommended if hyperthyroidism persists beyond 2 months of therapy.[7,28] Patients as young as 1 year old have been treated with I-131.[66] The reported doses in children and adolescents have ranged from 100-250 μCi/g (5.5-7.4 MBq/g) thyroid tissue.[32,66-72] Table 5 shows a literature review on

Table 4   Complications of thyroidectomy in more than 2000 children[36,55,56,60,61]

Complication	Incidence (%)
Pain	100
Transient hypocalcaemia (1-7 days)	10
Keloid	2.8
Permanent hypoparathyroidism	2
Vocal cord paralysis	2
Transient hoarseness	1
Temporary tracheostomy	0.7
Haemorrhage / haematoma	0.2
Death	0.08

Table 5   Literature review on radioiodine studies in children and adolescents with number of patients   30[32,66-69,72,73,75,76]

	No. of patients	Age	Follow up	Radiation activity	Hypothyroid	Retreated
	n	yr	yr	mCi	%	%
Chapman & Maloof (1955)[67]	30	1-18	1-23	#	27	#
Crile, et al (1965)[72]	30	7-15	3-15	9.9*	53	40
Starr, et al (1968)[69]	73	2.5-18	10-18	#	#	42
Hayek, et al (1970)[73]	30	8-18	9.2*	6.6*	27	17
Safa, et al (1975)[66]	87	3-18	12.3*	9.8*	46	24
Freitas, et al (1979)[68]	51	6-18	14.6*	14.1*	92	23
Hamburger, et al (1985)[32]	191	3-18	#	10	86	#
Clark, et al (1995)[75]	33	6-19	0-5	7.7*	88	17
Nebesio, et al (2002)[76]	40	8-19	#	15*	100	2.5

*mean; #not clearly stated

studies of I-131 therapy in children and adolescents with number of patients 30 or more.[32,66-69,72-76]

Long-Term Cure Rates

Long-term cure rates are higher in patients treated with high dose (370 MBq) than low dose (185 MBq) I-131.[28] The risk of recurrent hyperthyroidism is 5-20% for high dose vs 25-40% for low dose while the risk for hypothyroidism is 60-90% vs 40% respectively.[7,66,73,77] Responses to I-131 therapy are lower in patients with larger goiter size (>80 g), high TSAbs, more severe pre-treatment hyperthyroid state and pre-treatment with antithyroid drugs.[78-83] Failure rate is 9% with no thionamide; 17% with thionamide withdrawn >7 days before; and 29% with thionamide withdrawn 4-7 days before.[81]

Complication Rates

Acute complications of I-131 have been reported to be low (Table 6).[28,84,85] In children, very few acute adverse responses to I-131 therapy have been described.[32,68-74] Some children experience vomiting and enuresis, mostly

related to the hyperthyroid state. Some have mild pain over the thyroid gland, reflecting radiation thyroiditis. These side-effects are self-limited and respond to treatment with antithyroid drugs or nonsteriodal anti-inflammatory agents. Severe neck swelling and tracheal compression have been reported rarely in patients with very large goitres and can be controlled with large doses of corticosteroids.[84] Vocal cord paresis occurs very rarely.[77,86] Thyroid storm has been reported in a 7 1/2-year-old boy 4 days after I-131 therapy and 13 days after stopping thionamide.[87] Patients with severe thyrotoxicosis and very large goiters may be at higher risk for thyroid storm. Thionamides can be given for several weeks to ensure that the thyroid is depleted of stored hormones and withdrawn 5-7 days before I-131 therapy.

Does Radioiodine Worsen Ophthalmopathy

Controversy remains surrounding the effects of radioiodine on Graves' eye disease. In adults, exacerbation occurs in 1/4 of patients after I-131 therapy vs 1/8 after surgery.[88] It is related to the destruction of thyroid cells leading to release of antigens and activation of autoimmunity. Both hypothyroidism and smoking are known to be independent risk factors for ophthalmopathy. Most recently, a RCT of 450 patients has confirmed that prednisone 0.4-0.5 mg/kg begun 2-3 days post-I-131 therapy, continued for one month and then tailed off over 2 months, improves existing ophthalmopathy in the majority of patients and appears to completely prevent the development of new eye disease.[85] In contrast to adults, children rarely develop severe ophthalmopathy.[7,46,89] Thus, eye disease worsens in only a small percentage of children after medical, radioiodine, or surgical therapy.

Table 6   Complications of I-131 therapy in adults[28,84,85]

Complication	Incidence (%)
Worsening of eye disease	3-5
Transient thyroid pain	5
Nausea	Rare
Thyroid storm	Rare
Transient hypocalcaemia	Rare
Hyperparathyroidism	Rare

Hypothyroidism

Hypothyroidism occurs in nearly 100% of patients at a mean of 1-2 months post I-131 therapy. Monthly free T4 should be checked and T4 replacement given promptly to prevent carcinogenesis from prolonged TSH stimulation.

Thyroid Cancer Risks

The increased risk of thyroid cancer after thyroid irradiation in childhood has been recognised for nearly 50 year.[90] Thus a major concern of I-131 therapy relates to the risks of thyroid and nonthyroid cancers. Studies show that the risk of thyroid cancer is increased with exposure to low or moderate levels of external radiation. In contrast, the risks are much lower after high level irradiation that results in thyroid cell death or reduced capacity of cells to divide.[91,92] Thus, low doses of I-131 are associated with increase incidence of thyroid nodules and neoplasms.[53] Large epidemiological surveys showed no increase rates of thyroid cancer nor thyroid cancer mortalilty in adults.[53,93-96] Outcomes have been reported for about 1000 children and adolescents showing no increase risk of thyroid malignancy. The duration of follow-up ranged from <5 years to 15 years, with only some >20 years.[32,68,69-74] Patients with Graves' disease are at higher risk for developing thyroid cancer than the normal population. In adults, thyroid cancer developed in about 1 in 2000 patients during a 10- to 20-years follow-up period after radioiodine therapy in the Collaborative Thyrotoxicosis Study Group.[53] The most common tumour type after thyroid irradiation is papillary carcinoma (90%), which is a slow growing tumor treated by thyroidectomy and adjunctive I-131 therapy.[97-99] The prognosis of papillary carcinoma in children is excellent, and fatalities from papillary carcinoma occur rarely.[97-99] Thus, in the unlikely event that thyroid carcinoma develops after childhood I-131 therapy, the prognosis should be excellent.

Nonthyroid Malignancies

In adults, studies show no significantly increase nonthyroid cancer (including leukaemia, salivary gland, breast, stomach, and bladder cancer) mortality after I-131 therapy.[96] Among I-131-treated children, a comprehensive follow-up study of nonthyroid cancer risks has yet to be performed.

Is Developing Child at Higher Risk for Developing Cancer after I-131 Therapy

The risk of thyroid cancer in children treated with I-131 is unknown. Studies of external thyroid irradiation, nuclear disaster and atomic bomb survivors showed that the cancer rates are higher at progressively younger ages.[100-103] Thus there is a theoretical risk of a small increase in thyroid cancer with radioiodine therapy in children. The potential risks is probably greatest in children <5 years and progressively lower in 5-10 and 10-20 years. The risk of increase nonthyroid cancers is likely to be very small.

Health of Offspring

The radiation exposure of the gonads during I-131 therapy is comparable to that from a barium enema or an IV pyelogram.[104] Data on 500 offsprings born to 370 subjects treated with I-131 for hyperthyroidism during childhood and adolescence showed no increase congenital anomalies.[32,66,68-70,72,73] There were also no increase birth defects in survivors of atomic bomb blasts exposed to higher external irradiation of gonads than associated with I-131 therapy.[105]

I-131 Therapy – Summary

Radioiodine is a convenient and cost-effective therapy for childhood Graves' disease. The efficacy is dose-related. 5.5-7.4 MBq/g (150-200 µCi/g) can achieve >90% long-term cure rate. 85-90% patients only require a single dose to cure the hyperthyroidism. There may be a small increase risk of thyroid cancer. This theoretical risk is probably highest in children <5 years and progressively lower at 5-10 and 10-20 years. Children should receive higher doses of I-131 (5.5-7.4 MBq/g) to minimise residual thyroid tissue and decrease the tumour risk. Post-I-131 therapy, thyroxine should be used to treat hypothyroidism and prevent raised TSH.

There are no increase birth defects in offspring of patients treated with I-131. Careful follow-up is needed for all patients treated for Graves' disease and should include regular examination of the thyroid gland. All newly developed thyroid nodules should be biopsied or excised. Radiation-related thyroid tumours more typically appear 10-20 years after exposure, long term follow-up beyond paediatric age is essential.

Conclusion: Recommendations for Clinical Practice

All 3 treatment modalilties for Graves' disease have their advantages and disadvantages (Table 7).[106] Absolute contraindications for each modality are few. Patient preference and local expertise are therefore important factors and Table 6 may prove useful in guiding patient

Table 7   Advantages and disadvantages of the 3 treatment modalities[106]

Treatment	Cannot use in	Advantages	Disadvantages
Tablets (thionamides)	Patients with severe reaction to these drugs	Quite rapid (4 weeks) Predicable initial response Sudden swings in T4 rare Painless Safe in unfit patients	2 years of tablets 60% relapse after Px 20% risk of rash, minor SE 0.2% risk serious bone marrow SE
Radioiodine	Pregnancy Breast feeding	Painless Low chance of relapse (once if works) – permanent effect	Slow action (1-3 m or more) High chance of hypothyroid requiring T4 tablets Sudden T4 swings possible May worsen eye problems ? thyroid cancer risk
Surgery	Patients unfit for operation Uncontrolled thyrotoxicosis	Rapid (days) Low chance of relapse – permanent effect	Risk of GA 2% parathyroid or nerve to vocal cords damage Discomfort / neck scar 0.08% death

choice. Thionamides are the treatment of choice for initial therapy especially for those with mild hyperthyroidism, small goitre and low TSAbs. Time to euthyroidism and risk of side-effects can be minimised by commencing therapy with carbimazole 0.5 to 1.0 mg/kg/day with reassessment of thyroid function at 4-6 weeks. Long-term remission rates of 30-40% should be achievable using at least 12 months and preferably 18-24 months of therapy. Block-replace/continued high dose therapy is convenient and may shorten the period of treatment required but has not been shown to improve long-term outcomes. The addition of thyroxine alone confers little benefit. Surgery has very good cure rates (90%) and reverses the hyperthyroid state rapidly. Total thyroidectomy is the preferred operation but is a complex surgical procedure with definite surgical risks, including death in about 1 in 1000 operations in children. Of concern is the fact that the number of skilled thyroid surgeons has declined over the past several decades.[58] Surgery may be preferable when the thyroid gland is very large (>80 g) or in the rare few with profound ophthalmopathy. Radioiodine is associated with high cure rates (>90%). It is the simplest and least expensive treatment option and rarely associated with acute side-effects. Studies of children with Graves' disease treated with radioiodine have not revealed increase risk of thyroid neoplasia. However, as only several thousand children have been treated and not all have been followed long term, it is only possible to conclude that radioiodine is not associated with moderate or large increases in the

incidence of thyroid cancer. A long-term study of larger population is needed to define the true incidence. So far we do not know whether there is an age below which high dose I-131 should be avoided. It may be preferable to consider radioiodine for those 15 years or older, at least 10 years old but never below 5. So far in Hong Kong, radioiodine therapy is not the choice of option for Graves' disease among the paediatric and adolescent patients. The small risk of an increase in the rate of thyroid cancer after radioiodine therapy needs to be balanced against the known complications of drug therapy or surgery. Perhaps it is now the right time that we need to reconsider this treatment option especially for those older than 15. Selection of a treatment modality for the child with Graves' disease is often a difficult and highly personal decision. Discussion of the pros and cons of each therapeutic option by the paediatrician is therefore essential to help the patient and the family select a treatment option.

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