

# Thyroid Cancer Canada Wally Patching Memorial Lecture 2008

In 2004, the Board of Directors of Thyroid Cancer Canada announced the creation of the annual **Wally Patching Memorial Lecture** to honour one of our most vibrant and determined founding members and to help contribute to his vision of improved Canadian thyroid cancer patient information, support and access to qualified thyroid cancer specialists. The first memorial lecture was given on May 14th, 2005 in Ottawa by Dr. Irving B. Rosen.

Wally was diagnosed with a rare and aggressive variant of papillary thyroid cancer in 1998 at age 58. At the time of his diagnosis, his cancer had already spread beyond his neck and he died in January 2004. Wally often joked that being 'advanced' meant that he had a lot more experience on how to live while battling thyroid cancer. Wally and his wife Diane shared their experiences, strength and vision with TCC members and their determination inspired us all.



Diane and Wally Patching

The *Wally Patching Memorial Lecture 2008*, was given by Dr. Vladimir Milosevic MD. FRCPC, as part of the Thyroid Update Lectures at Humber College, May 31/08

# Update on Thyroid Cancer

Dr. Vladimir Milosevic MD. FRCPC

Endocrinology

Credit Valley Hospital

# Overview

- Epidemiology
- Diagnosis
- Management
  - Surgical
  - Radioiodine ablation
  - Thyroid hormone suppression
- Follow-up
- Current issues and controversies

# Epidemiology of Thyroid Nodules

- Prevalence of palpable nodules is approximately 5% in women and 1% in men living in iodine-sufficient parts of the world<sup>1</sup>
- Only 10% of nodules are clinically apparent<sup>1</sup>
- Framingham database: 4.2% (6.4% in women, 1.5% in men)<sup>2</sup>
- Using 10-MHz transducer ultrasound (U/S), 67% prevalence (72% in women, 41% in men)<sup>3</sup>

1. Singer et al. *Arch Intern Med* 1996;156:2165-2172.

2. Vander et al. *Ann Intern Med* 1968;69:537-540.

3. Ezzat et al. *Arch Intern Med* 1994;154:1838-1840.

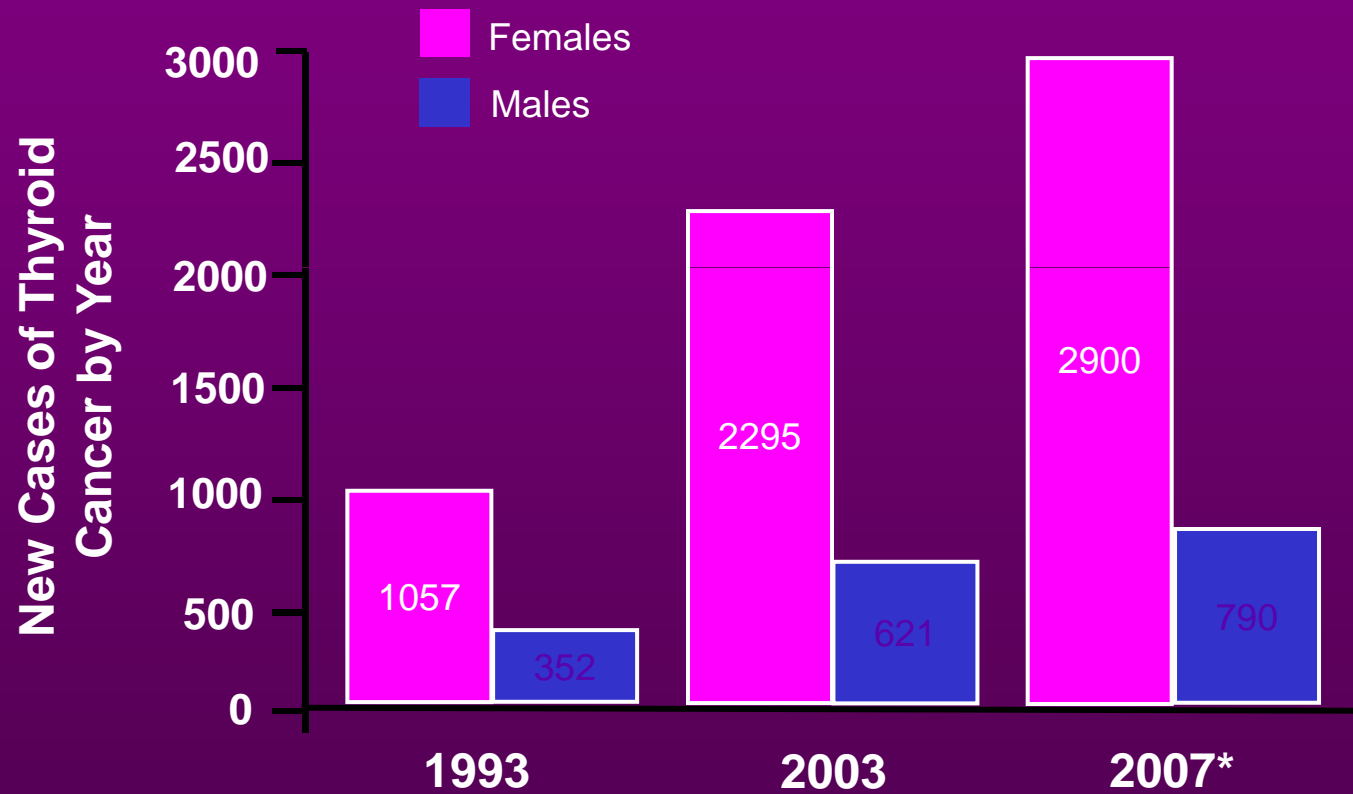
# Epidemiology of Thyroid Cancer

- 33,550 new cases of thyroid cancer are expected to be diagnosed in the U.S. in 2007<sup>1</sup>
  - 25,480 are expected to occur in women and 8,070 in men
  - New cases are increasing at a rate of 2% per year<sup>1,2</sup>
- Thyroid cancer is 2 to 3 times more prevalent in women<sup>2</sup>
  - The number of expected new cases in women in 2007 exceeds new cases of ovarian cancer by 2500<sup>1</sup>
- Thyroid cancer prevalence in the U.S. is estimated at over 350,000 people living with a diagnosis of thyroid cancer<sup>†</sup>

*†estimated prevalence based upon NIH SEER data on prevalence from 2002 coupled with new incidence and low 5 year mortality rate*

1. American Cancer Society. [www.cancer.org](http://www.cancer.org).  
2. National Cancer Institute. [www.nci.nih.gov](http://www.nci.nih.gov).

# Epidemiology of Thyroid Cancer in Canada



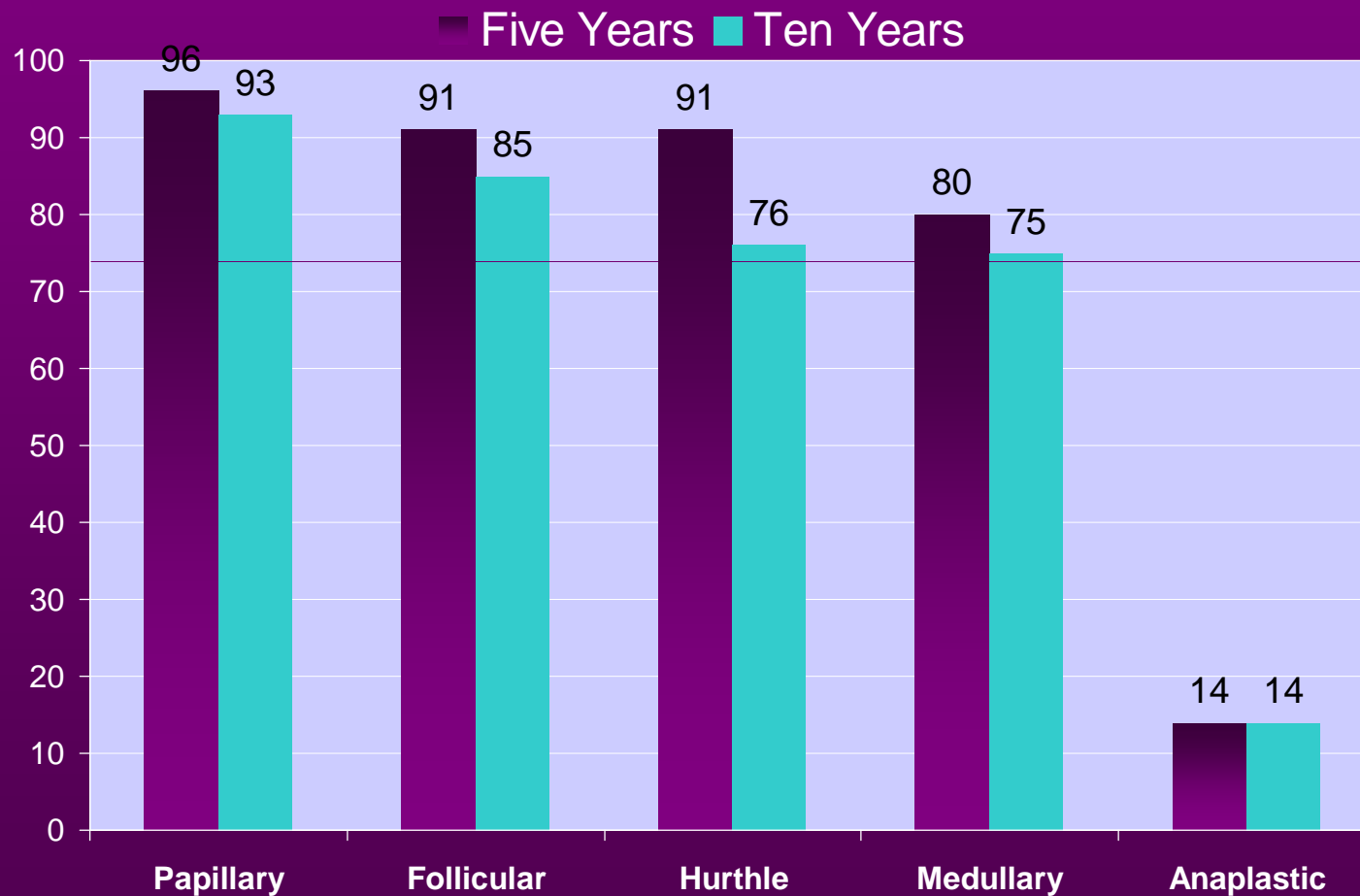
\* 2007 data are estimated new cases of thyroid cancers

# Top 10 Cancers Among Women 2002 US incidence rates per 100,000

	All Races	White	Black	Asian/Pacific Island	Hispanic
1	Breast - 124.9	Breast - 126.8	Breast - 110.1	Breast - 79.8	Breast - 88.7
2	Lung & Bronchus - 53.7	Lung & Bronchus - 54.9	Colon & Rectum - 51.8	Colon & Rectum - 34.3	Colon & Rectum - 34.9
3	Colon & Rectum - 44.9	Colon & Rectum - 43.9	Lung & Bronchus - 50.3	Lung & Bronchus - 26.7	Lung & Bronchus - 25.2
4	Corpus & Uterus, NOS - 23.6	Corpus & Uterus, NOS - 24.1	Corpus & Uterus, NOS - 19.8	Corpus & Uterus, NOS - 14.5	Corpus & Uterus, NOS - 17.9
5	Non-Hodgkin Lymphoma - 15.5	Non-Hodgkin Lymphoma - 16.0	Pancreas - 12.9	Thyroid - 12.4	Non-Hodgkin Lymphoma - 13.7
6	Melanomas of the Skin - 13.6	Melanomas of the Skin - 15.2	Cervix Uteri - 12.4	Stomach - 10.0	Cervix Uteri - 13.1
7	Ovary - 13.1	Ovary - 13.5	Non-Hodgkin Lymphoma - 10.5	Non-Hodgkin Lymphoma - 9.8	Ovary - 11.0
8	Thyroid - 12.1	Thyroid - 12.5	Kidney & Renal Pelvis - 10.0	Ovary - 9.5	Thyroid - 10.6
9	Pancreas - 9.5	Urinary Bladder - 9.8	Ovary - 9.8	Cervix Uteri - 7.5	Pancreas - 9.4
10	Urinary Bladder - 9.4	Kidney & Renal Pelvis - 9.2	Stomach - 8.6	Liver & IBD - 7.4	Kidney & Renal Pelvis - 9.0

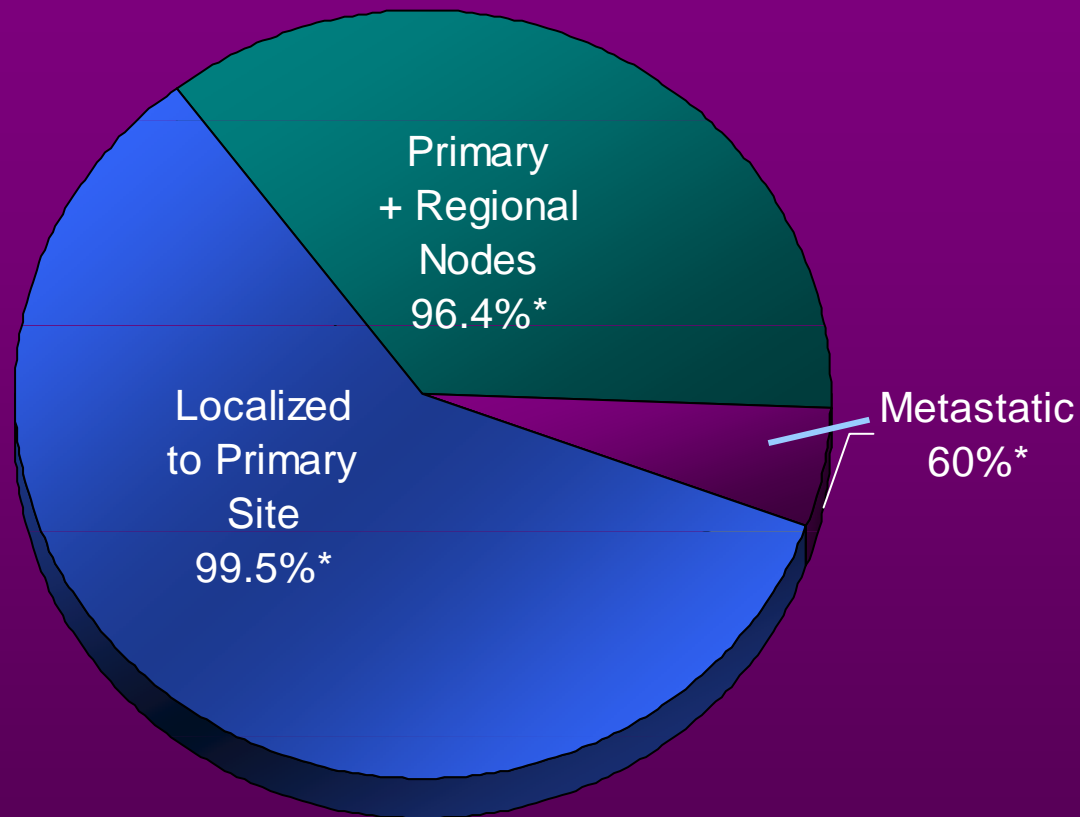
Source: Center for Disease Control, National Program of Cancer Registries.

# Five and 10-year Survival Rates by Thyroid Cancer Histology



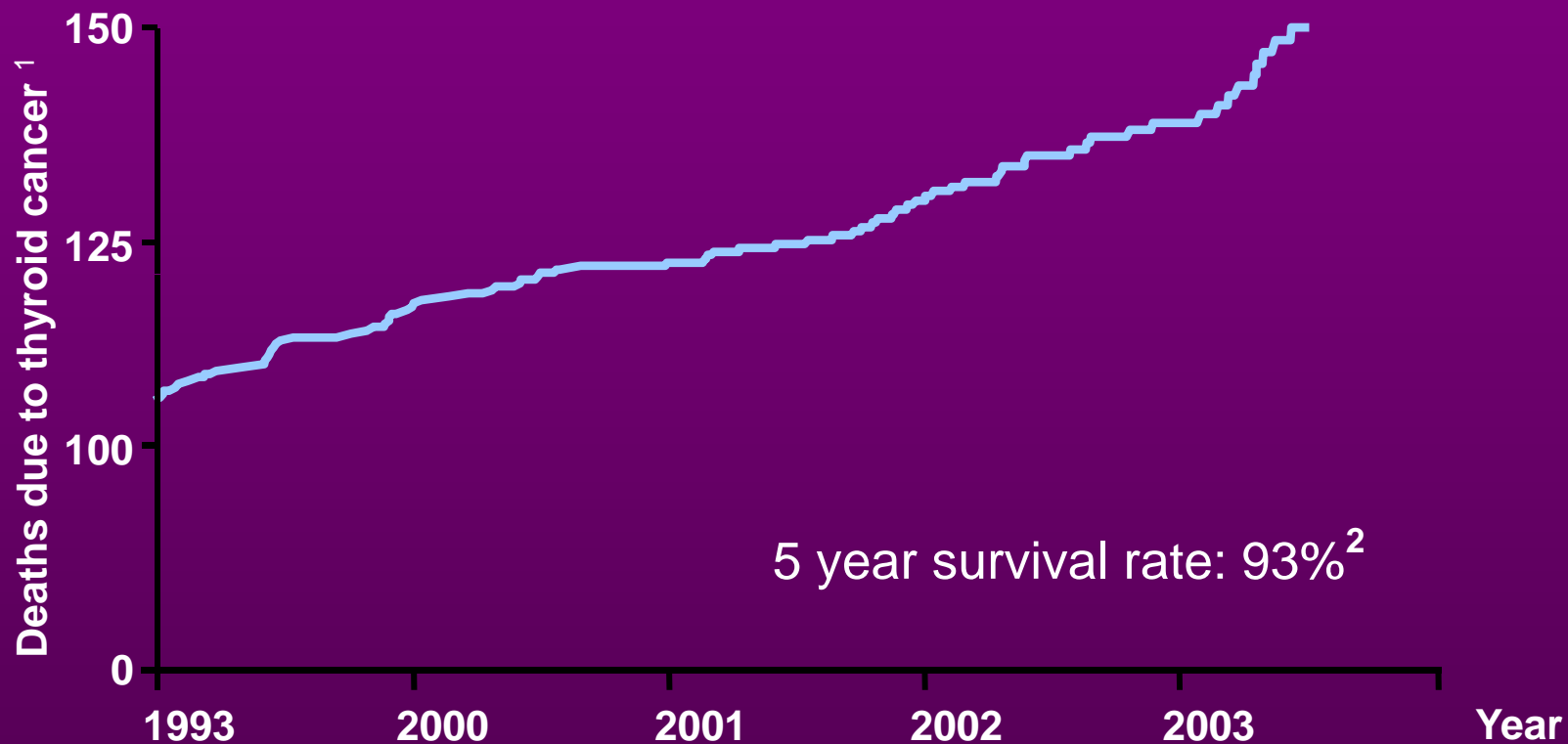
Adapted from: Hundahl et al. A National Cancer database report on 53,856 cases of thyroid carcinoma treated in the US, 1985-1995. *Cancer* 1998;83:2638-2648.

# Thyroid Cancer Relative Five-Year Survival Rates



*\*percent surviving at five years*

# Thyroid Cancer Mortality: Canada



1. Statistics Canada, Canadian Vital Statistics, Death Database.  
2. Statistics Canada, Canadian Cancer Registry, August 2006.

# Diagnosis

- Current gold standard for diagnosis is fine needle aspiration biopsy (FNAB)
- Thyroid scan has a poor predictive value
- Ultrasound cannot distinguish benign from malignant nodules but certain features are worrisome; irregular border, punctate calcifications, increased vascularity, absence of a “halo”
- Surgical pathology is the final word

# Current Guidelines

- European Thyroid Association Guidelines
- British Thyroid Association Guidelines
- ATA Guidelines
- NCCN Guidelines
- Society of Ultrasound Radiologists

# Initial Treatment of Well-Differentiated Thyroid Cancer

- **Treatment**
  - Surgery: near total or total thyroidectomy
  - Radioiodine (RAI) remnant ablation
  - Thyroid hormone suppressive therapy

# Surgical Treatment

- For most patients with thyroid cancer, the initial surgical procedure should be a near-total or total thyroidectomy.
- Thyroid lobectomy alone may be sufficient treatment for small, low-risk, isolated, intrathyroid papillary carcinomas in the absence of cervical nodal metastasis, however the patient will have to be monitored regularly on a long-term basis.

# TNM Staging For Thyroid Cancer

<b>(T)</b>	Primary Tumor*	<b>(N)</b>	Lymph Node Metastases	<b>(M)</b>	Distant Metastases
<b>TX</b>	Cannot be assessed	<b>NX</b>	Cannot be assessed	<b>MX</b>	Cannot be assessed
<b>T1</b>	≤ 2 cm limited to the thyroid	<b>NO</b>	Not present	<b>MO</b>	Not present
<b>T2</b>	> 2 to 4 cm limited to thyroid	<b>N1a</b>	Metastasis to level IV (pretracheal/ paratracheal/ prelaryngeal LN)	<b>M1</b>	Present
<b>T3</b>	> 4 cm or minimal extrathyroidal extension	<b>N1b</b>	Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal LN		
<b>T4a</b>	Any size that extends beyond capsule to subcutaneous soft tissue, larynx, trachea, esophagus or recurrent laryngeal nerve				
<b>T4b</b>	Tumor beyond thyroid tissue; invades pre-vertebral fascia or encases carotid artery or mediastinal vessels				

\* Any anaplastic carcinomas considered T4 tumors

# TNM Staging Chart

	Papillary or Follicular Thyroid Cancer	
STAGE	<45 yr	>45 yr
I	Any T, any N, M0	T1, N0, M0
II	Any T, any N, M1	T2, N0, M0
III	-	T1 or T2, N1a, M0 T3, N0 or N1a, M0
IVA	-	T1 or T2 or T3, N1b, M0 T4a , N0 or N1a or N1b, M0
IVB	-	T4b, Any N, M0
IVC	-	Any T, Any N, M1

# Objectives For Radioiodine Remnant Ablation

- Eradicate all thyroid cells
- Reduce risk of local and distant recurrency
- Provide undetectable serum Tg and negative iodine scan
- Prolong survival
- Increase sensitivity of follow-up tests
- Promote earlier detection of recurrent or metastatic disease

# Radioiodine Remnant Ablation

- Recommended for patients with:
  - stages III and IV disease
  - all patients <45 years old with stage II disease
  - most patients >45 years old with stage II
  - selected patients with stage I, especially those with multifocal disease, nodal metastasis, extrathyroidal or vascular invasion, and/or more aggressive histologies<sup>1</sup>
- Best definition of successful ablation is an undetectable serum Tg level following TSH stimulation and normal neck ultrasound<sup>2</sup>

1. ATA Guidelines 2006.

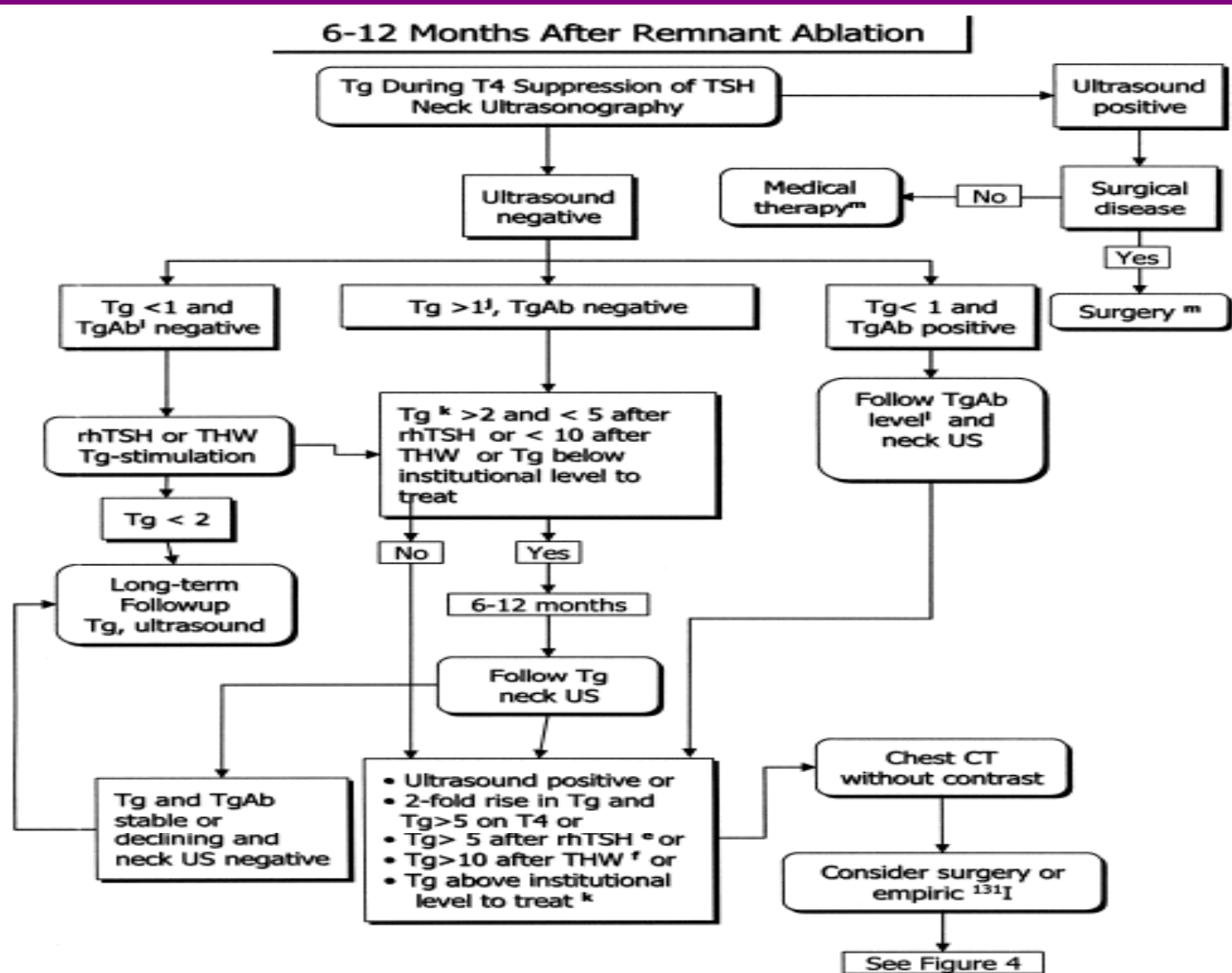
2. European Guidelines 2006.

# Thyroid Hormone Suppression

- Levothyroxine is recommended for long-term suppression<sup>1</sup>
- TSH measurement should be done after 6 weeks if change in dosage (dosage is highly variable among individuals)
- TSH <0.1 mU/L in high risk patients and 0.1-0.5 mU/L in low risk patients

1. British Guidelines 2006  
2. ATA 2006 Guidelines.

# ATA 2006 Guidelines for WDTC Follow-up



# TSH Stimulation and Testing Following Initial Treatment

- **Thyroid hormone withdrawal**
  - LT4 treatment is withdrawn for 4-5 weeks. To reduce symptoms of hypothyroidism, patients may switch from T4 to T3 for 3 weeks, then T3 is withdrawn for 2 weeks
- **rhTSH injections**
  - rhTSH is injected for 2 consecutive days and  $^{131}\text{I}$  is administered on the day after the second injection (day 3), serum Tg is measured on the third day after the second injection (day 5)
- **Restricting iodine in diet**
  - Induce iodine depletion and increase avidity of thyroid to take RAI

# rhTSH Schedule

- Recommended dose: 0.9mg IM q24 hr x 2 doses
- Serum Tg protocol is identical for both Tg alone testing and when combined with WBS
- 4 mCi <sup>131</sup>I should be used for scans; which should be acquired for ≥ 30 minutes and/ or ≥ 140,000 counts

Day 1	Day 2	Day 3	Day 4	Day 5
rhTSH 0.9 mg	rhTSH 0.9 mg	<sup>131</sup> I (if WBS is performed)		Serum Tg with or without WBS
<i>Monday</i>	<i>Tuesday</i>	<i>Wednesday</i>	<i>Thursday</i>	<i>Friday</i>

# Advantages of rhTSH (Thyrogen)

- No need for a 4-6 week plan undergo testing
- No hypothyroidism
- Normalization of TSH may require up to 8 weeks post-testing
- Whole body radioactive iodine retention is half that of hormone withdrawal

# 2006 ATA Guidelines: Recurrence Risk After Initial Treatment

- **Low-risk patients:**
  - no local or distant mets;
  - all macroscopic tumor resected;
  - no tumor invasion of loco-regional tissues or structures;
  - tumor does not have aggressive histology and,
  - if  $^{131}\text{I}$  given, no uptake outside the thyroid bed on RxWBS
- **Intermediate risk patients:**
  - microscopic invasion of tumor into the perithyroidal soft tissues at surgery; or,
  - tumor with aggressive histology or vascular invasion
- **High-risk patients:**
  - macroscopic tumor invasion or incomplete tumor resection;
  - distant metastases; or,
  - $^{131}\text{I}$  uptake outside thyroid bed on post-ablation RxWBS

# Importance of Long-Term Monitoring

- Up to 30% of patients will develop recurrent cancer
  - 1/3 of these patients will have recurrences decades after initial therapy<sup>1</sup>
- Delay in the diagnosis of recurrent cancer significantly increases mortality
- Bulk of metastatic disease is a strong predictor of death from thyroid cancer
- There is definitive evidence that anaplastic carcinoma can result from the transformation and de-differentiation of WDTC<sup>2</sup>

1. Mazzaferri and Kloos. *J Clin Endocrinol Metab* 2002;87:1490-1498.

2. Hunt et al. *Am J Surg Pathol* 2003;7(12):1559-1564.

# Monitoring Patients for Metastatic Disease

- Disease can be cured as even patients with poor radioiodine uptake may have a long-term survival
- Management of a rising serum Tg and negative diagnostic radioiodine scans should be tailored to the individual
- Investigations include neck ultrasound, CT scan of the lungs, FDG-PET scan

# Utility of PET-FDG Scanning in Evaluating Metastatic Thyroid Cancer

- Increasingly important imaging modality
- This method may be considered in all patients of differentiated thyroid cancer with suspected recurrence and/or metastasis<sup>1</sup>
- Coregistered 18F-FDG PET/CT can provide precise anatomic localization of recurrent or metastatic thyroid carcinoma, leading to improved diagnostic accuracy, and can guide therapeutic management<sup>2</sup>

1. Khan et al. *Br J Radiol* 2003;76:690-695.

2. Shamma et al. *J Nucl Med* 2007;48:221-226.

# Managing Patients with Metastatic Disease

- Surgical excision
- Radioiodine therapy
- External beam radiation, rarely chemotherapy
- Eventually use of new molecules such as anti-VEGF
- Watchful waiting

# Current Issues and Controversies

# Surgical Controversy

- Total thyroidectomy vs. lobectomy for low risk patients

# Diagnostic Accuracy: WBS vs. Stimulated TG

Published data from retrospective study

Whole Body Scan			Thyroglobulin Testing*		
	rhTSH	Withdrawal		rhTSH	Withdrawal
Sensitivity	0.69 (43/62)	0.80 (53/66)	Sensitivity	0.86 (54/63)	0.79 (56/71)
Specificity	1.0 (47/47)	0.93 (26/28)	Specificity	0.82 (36/44)	0.89 (24/27)
PPV	1.0 (43/43)	0.96 (53/55)	PPV	0.87 (54/62)	0.95 (56/59)
NPV	0.71 (47/66)	0.67 (26/39)	NPV	0.80 (36/45)	0.62 (24/39)

\*Based on a Tg cutoff of 2 ng/mL

PPV = Positive Predictive Value  
NPV = Negative Predictive Value

Robbins et al. *J Clin Endocrinol Metab* 2001;86:619-625.

# rhTSH-Stimulated Detection of Metastatic Disease

## Detection Rate of Metastatic Disease in Patients with Thyroid Cancer

Clinical Study	rhTSH-stimulated Tg $\geq$ 2 ng/mL % [N]	rhTSH-stimulated Tg $\geq$ 2 ng/mL and Dx WBS	Comment
Vitale <sup>1</sup>	100% [14/14]	100% [14/14]	Prospective Study
Haugen <sup>2</sup>	100% [7/7]	100% [7/7]	Retrospective Study
Mazzaferri <sup>3</sup>	100% [9/9]	100% [9/9]	Retrospective Study
Robbins <sup>4</sup>	85% [145/169]	93% [158/169]	Retrospective Study
Pacini <sup>5</sup>	100% [11/11] *	100% [11/11]	Prospective Clinical Trial
Robbins <sup>6</sup>	86% [54/63]	98% [62/63]	Retrospective Study
Haugen <sup>7</sup>	100% [30/30]	100% [30/30]	Genzyme-Sponsored Prospective Clinical Trial

\* PrThyrogen<sup>®</sup> stimulated Tg  $\geq$  1 ng/mL used in this study

1. Giovanni et al. *Clin Endocrinol* 2002;56:247-252.

2. Haugen et al. *Thyroid*. 2002;12:37-43.

3. Mazzaferri and Kloos. *J Clin Endocrinol Metab* 2002;87:1490-1498.

4. Robbins et al. *J Clin Endocrinol Metab* 2002;87:3242-3247.

5. Pacini et al. *J Clin Endocrinol Metab* 2001;86:5686-5690.

6. Robbins et al. *J Clin Endocrinol Metab* 2001;86:619-625.

7. Haugen et al. *J Clin Endocrinol Metab* 1999;84:3877-3885.

# Remnant Ablation

- The use of rhTSH for remnant ablation is not approved in Canada yet
- It has been studied and proven as good as thyroid hormone withdrawal

1) Robbins RJ, J Nucl Med 2002

2) Pacini F, JCEM 2002

# PET Scanning

- Used to identify metastases that are not seen on the post treatment WBS
- Most studies indicate that treatment with radioiodine in these lesions is not useful
- These patients need treatment with other methods such as external beam radiation
- rhTSH and CT fusion may enhance the FDG-PET scanning

# Conclusion

- Thyroid cancer is on the rise in Canada
- We need to raise awareness with regards to screening and diagnosis
- Well differentiated thyroid cancer is treatable and has an overall good prognosis
- The most important issue is ongoing follow-up

QUESTIONS