

# Laryngeal Cancer

Dr Jeeve Kanagalingam

TTSH

# Overview

- History
- Epidemiology
- Biology
- Assessment
- TNM
- Treatment
  - Early stage disease
  - Advanced disease
- Voice restoration

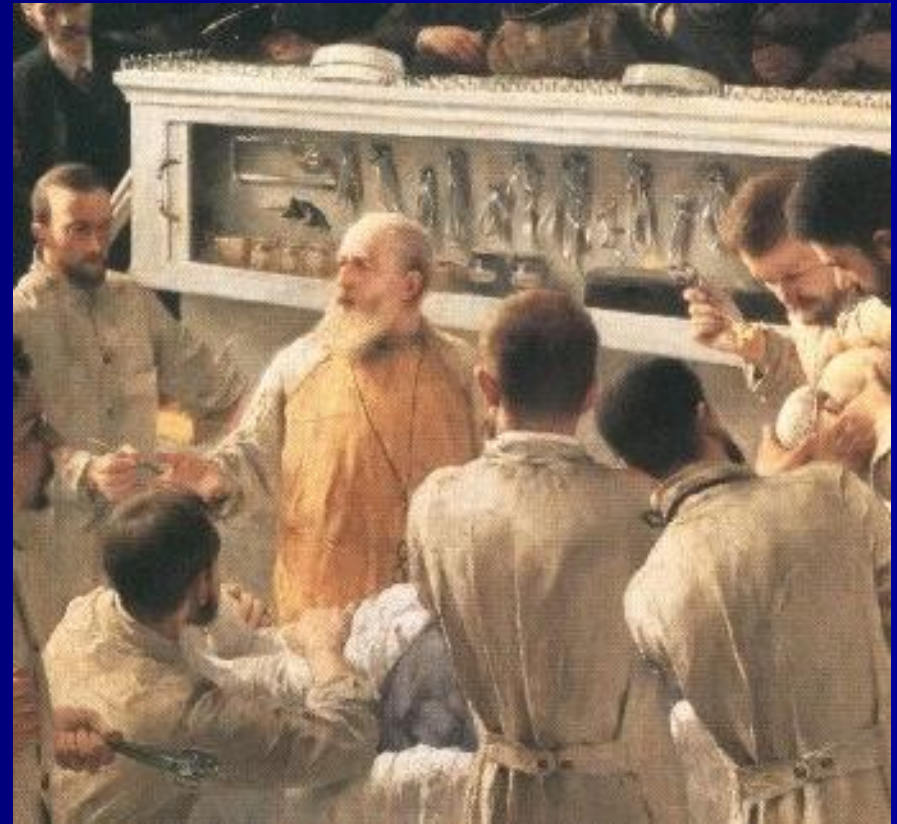
# Treatment of laryngeal cancer

Patrick Watson in Edinburgh did first laryngectomy in 1866 for syphilis. Pt died after 8 weeks

Billroth in 1873 performed first for cancer. Pt survived 1 year

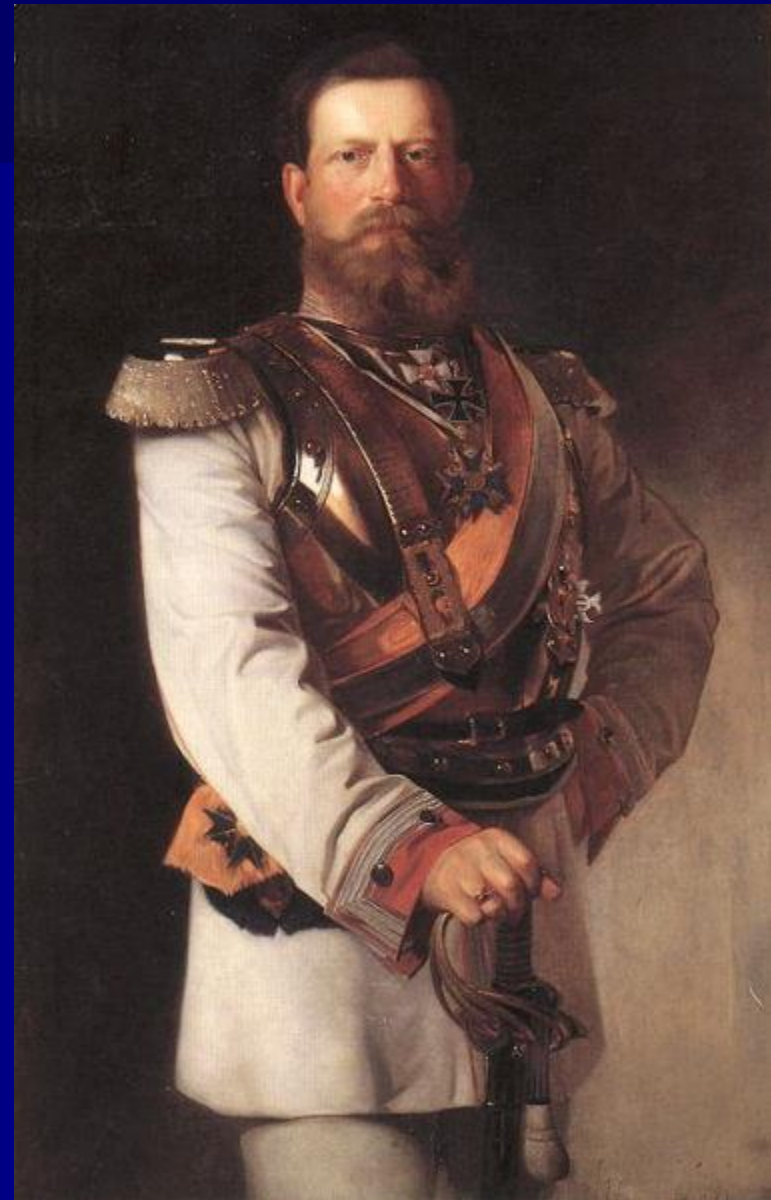
First 103 cases, only 9 survived > 1 year

Closure of pharynx and separation from trachea introduced by Langenbach



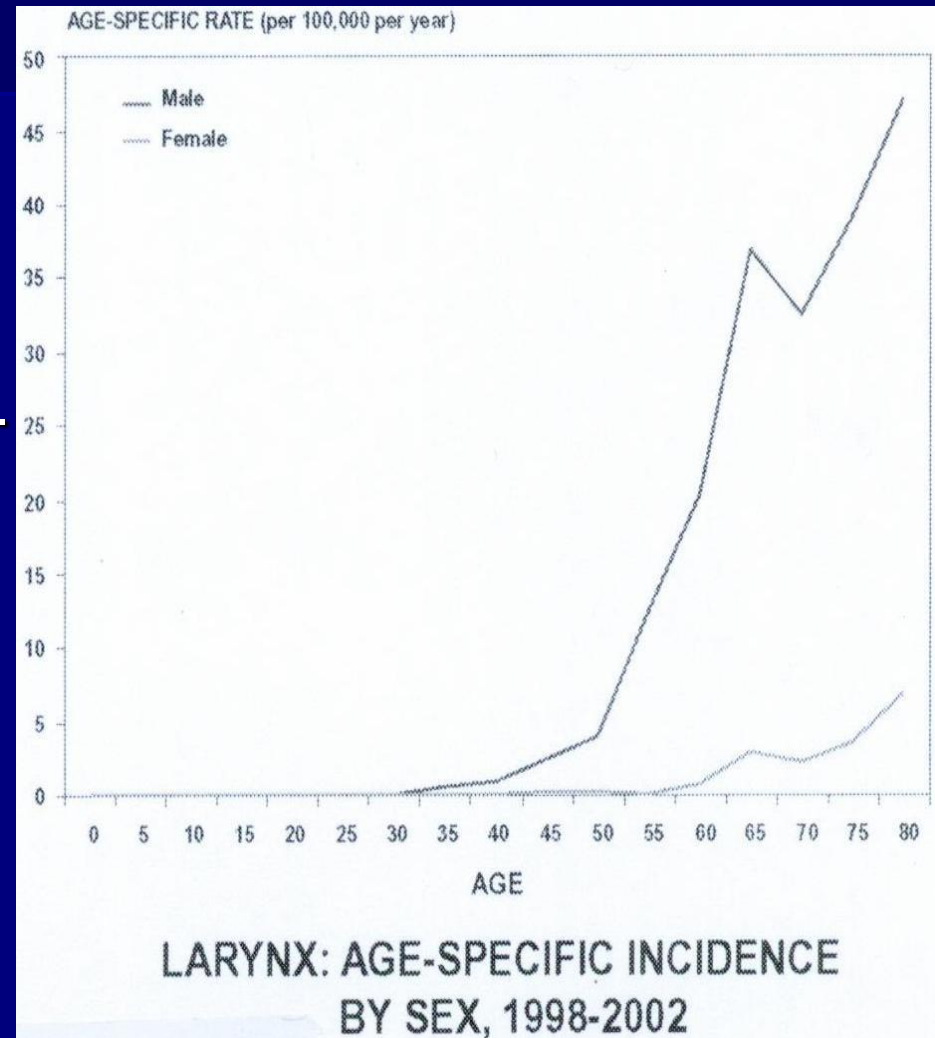
**Theodor Billroth (1829-1894)**

# Laryngectomy could have saved us a world war!



# Laryngeal cancer in Singapore

- Incidence of 4.4 per 100,000 (1998-2002) down from 6.8 (1968-1972)
- 75 cases a year
- Male to female ratio 12.3:1
- 97.3% are SCC
- Ratio of glottic:supraglottic is 5:2



# Smoking, alcohol and laryngeal cancer

- RR of laryngeal ca between smokers and non-smokers is 15.5 in men, 12.4 in women
- Drinking 100g alcohol per day (7 standard drinks) confers an RR of 15
- Using an additive risk model, combined use increases risk by 50%



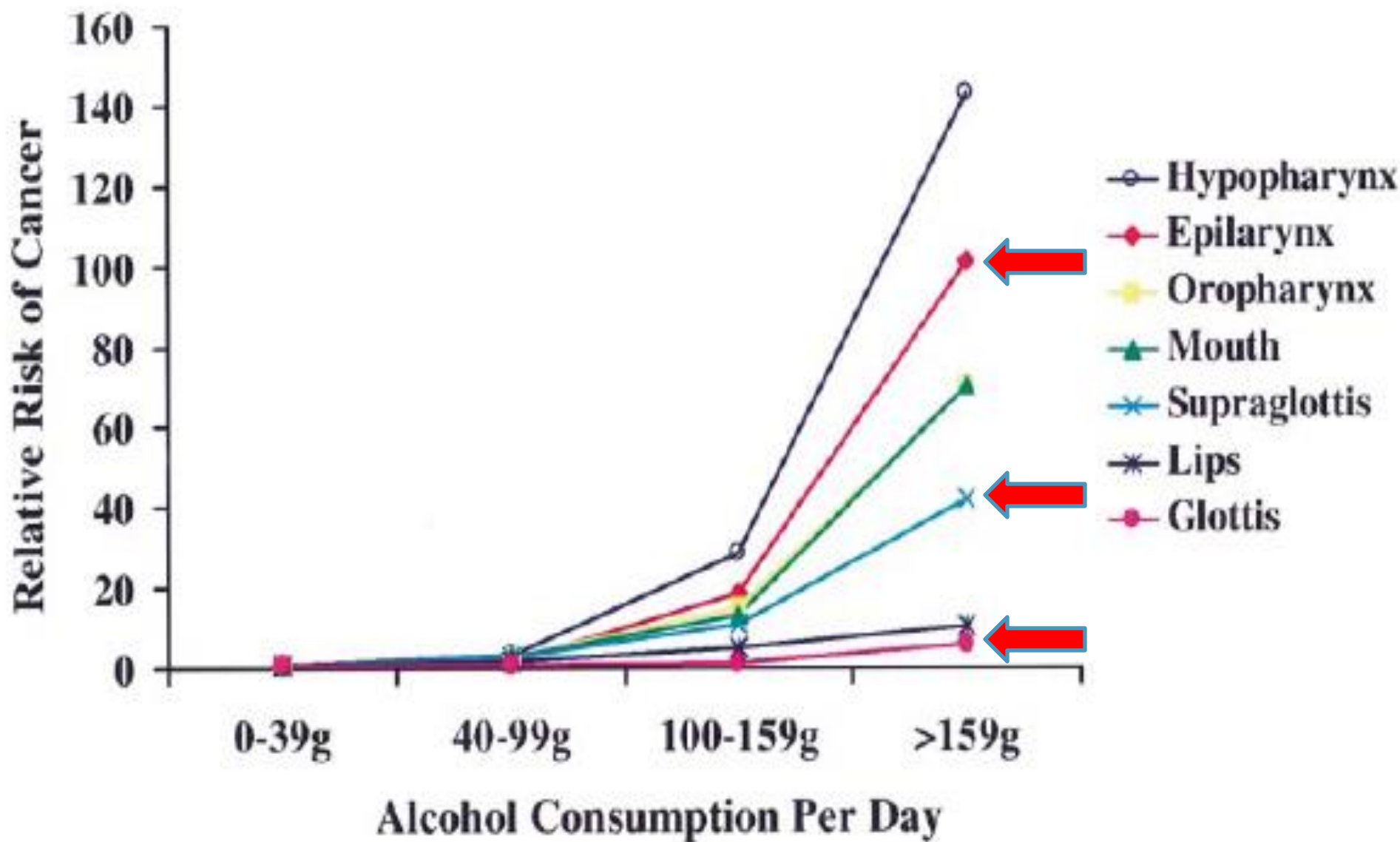


Figure 1-5. Relative risk of cancer for various head and neck sites relative to history of daily alcohol consumption adjusted for tobacco use. (Data from: Brugere J, Guenel P, Leclerc A, Rodriguez J. Differential effects of tobacco and alcohol in cancer of the larynx, pharynx and mouth. *Cancer* 1986;57:391-5.)

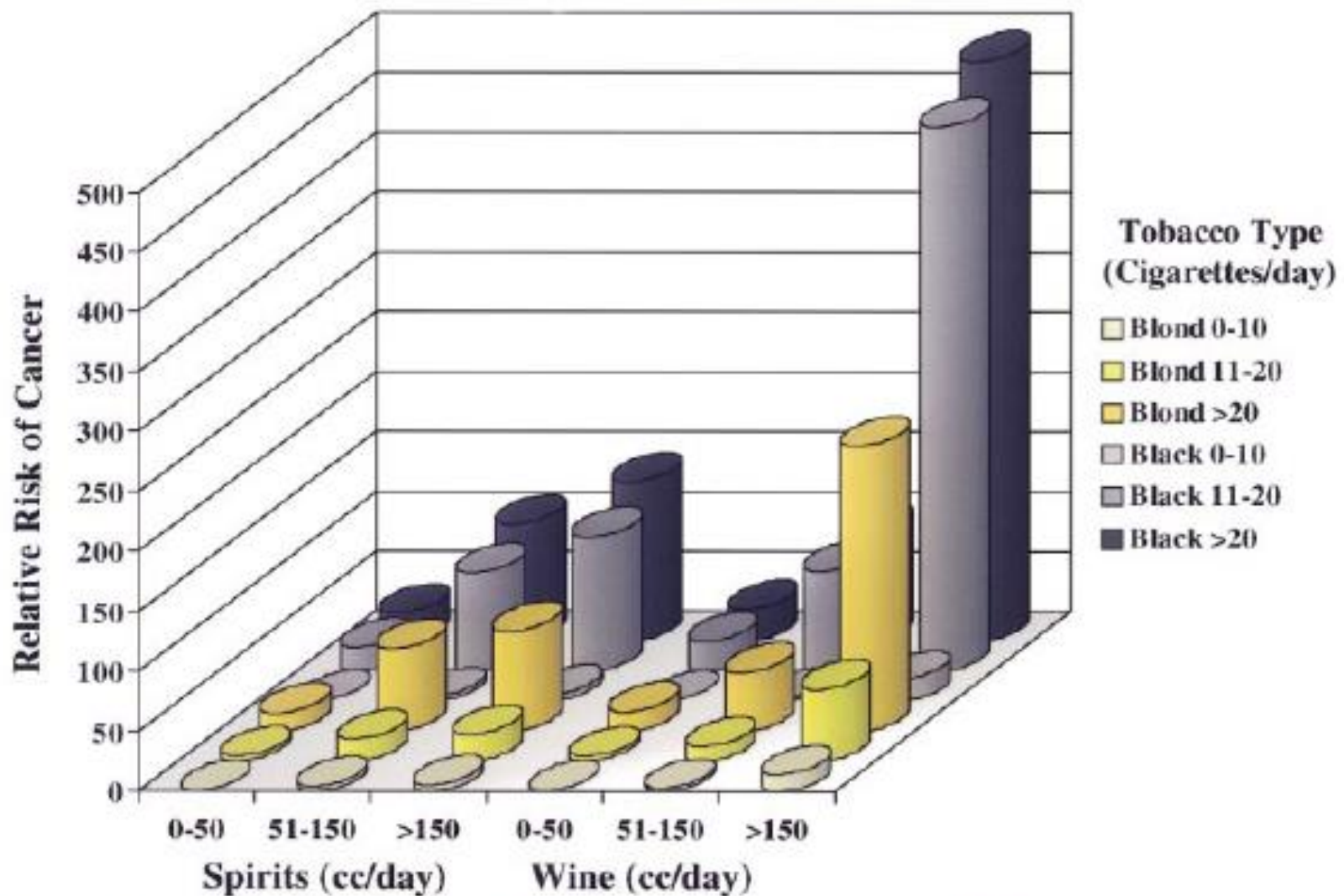


Figure 1-7. Graph demonstrating the odds ratio for exposure to alcohol and tobacco exposure in pharyngeal and laryngeal cancer patients. Odds ratio highest with heavy wine and black tobacco consumption. (Data from: Sancho-Garnier H, Theobald S. Black (air-cured) tobacco and blond (flue-cured) tobacco and cancer risk II: Pharynx and larynx cancer. Eur J Cancer 1993; 29A:273-6.).



# Tumour biology

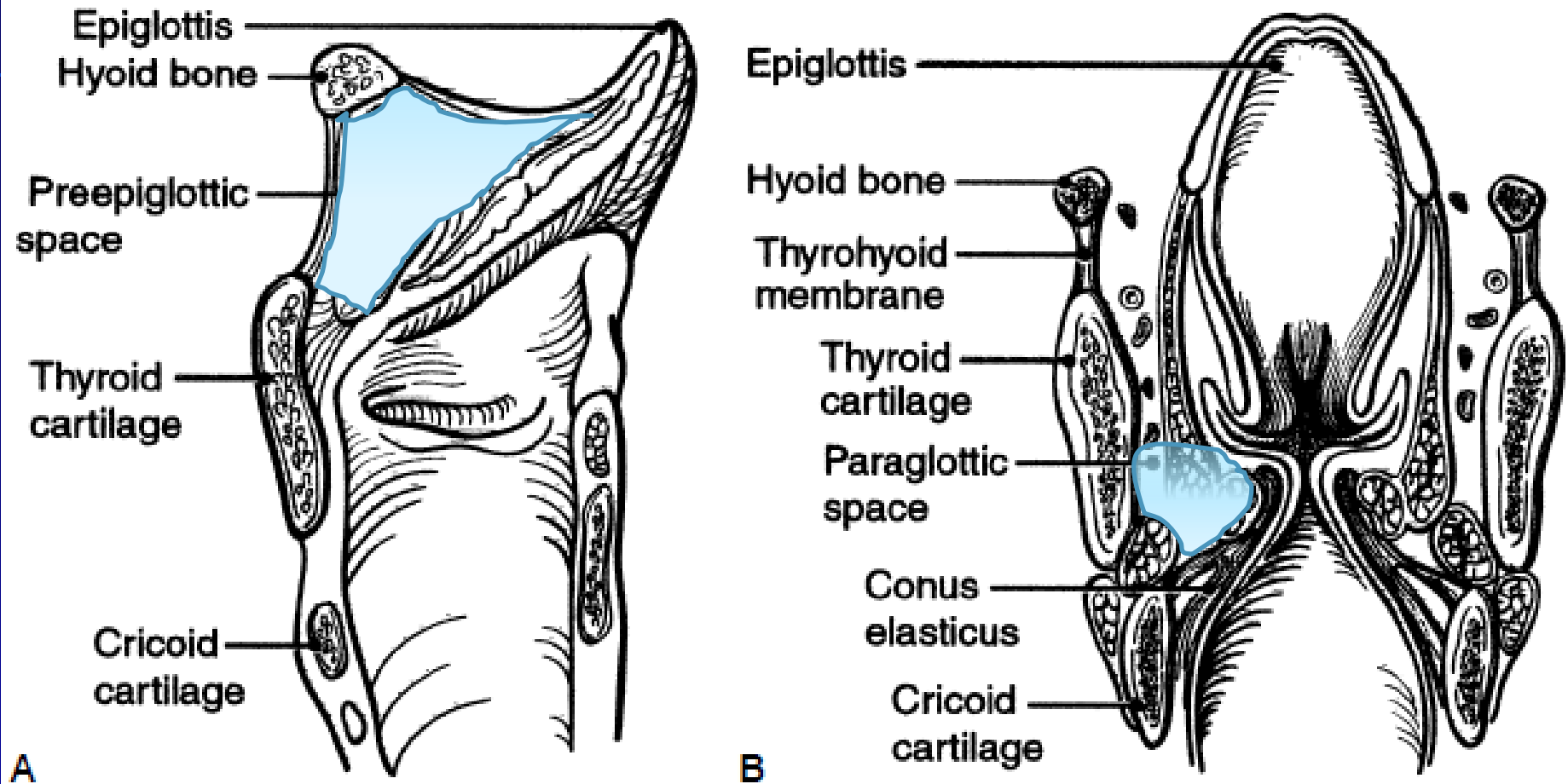
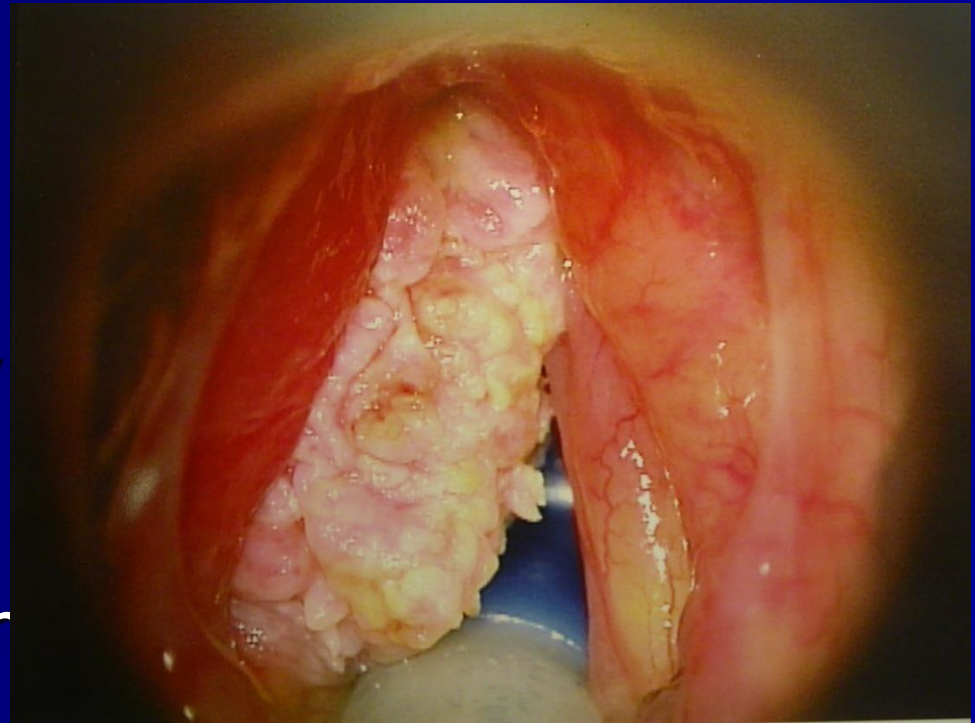


Figure 8-2. A, Sagittal section of larynx demonstrating the preepiglottic and B, coronal section of larynx demonstrating the paraglottic space.

# Assessment of the laryngeal cancer

- History, focus on symptoms of dysphonia, dyspnoea, stridor, dysphagia, aspiration, pain
- Office examination
  - Larynx / Pharynx
  - Neck
- Panendoscopy
- Imaging



# Regions of the larynx

- **Supraglottis**

- 5 parts: suprahyoid and infrahyoid epiglottis, aryepiglottic folds, arytenoids

- **Glottis**

- True vocal cords, floor of ventricle and region 5 mm below true vocal cords or 1 cm below lateral border of ventricle
- 3 parts: true cords, anterior commissure and ventricle

- **Subglottis**

- Region beyond 5 mm **below true vocal cords** or 1 cm below lateral border of ventricle to lower border of cricoid ring

# Transglottic carcinoma:

term to describe the growth pattern of tumours that cross the laryngeal ventricle to involve both true and false vocal cords.

Site of origin is uncertain

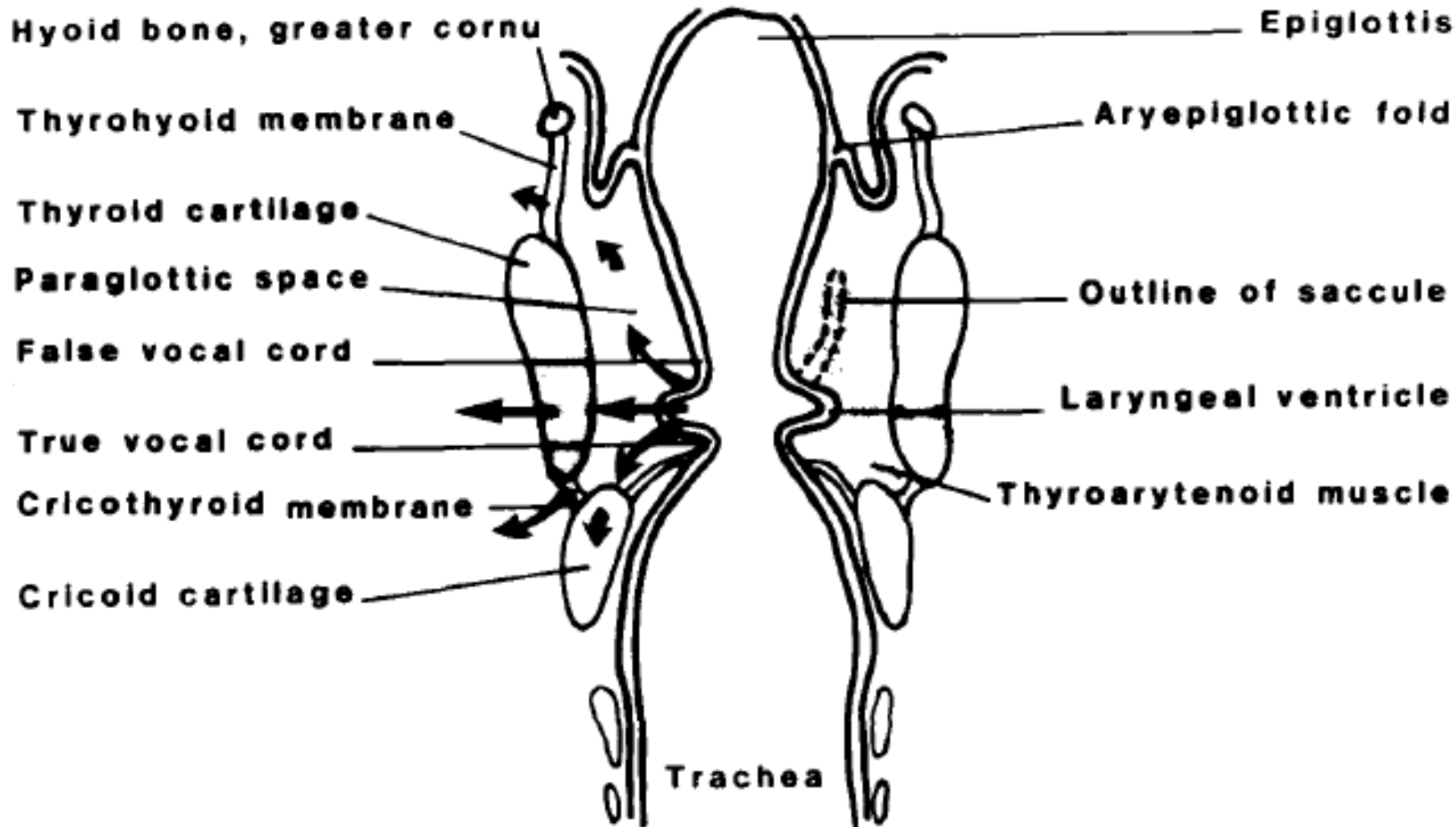


TABLE 5 T Staging for Tumors of the Larynx

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Supraglottis	
T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (eg, mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx
T3	Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex)
T4a	Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
Glottis	
T1	Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
T1a	Tumor limited to one vocal cord
T1b	Tumor involves both vocal cords
T2	Tumor extends to supraglottis and/or subglottis, or with impaired vocal cord mobility
T3	Tumor limited to larynx with vocal cord fixation
T4a	Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery or invades mediastinal structures
Subglottis	
T1	Tumor limited to the subglottis
T2	Tumor extends to vocal cord(s) with normal or impaired mobility
T3	Tumor limited to larynx with vocal cord fixation
T4a	Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery, or involves mediastinal structures

T2a / 2b

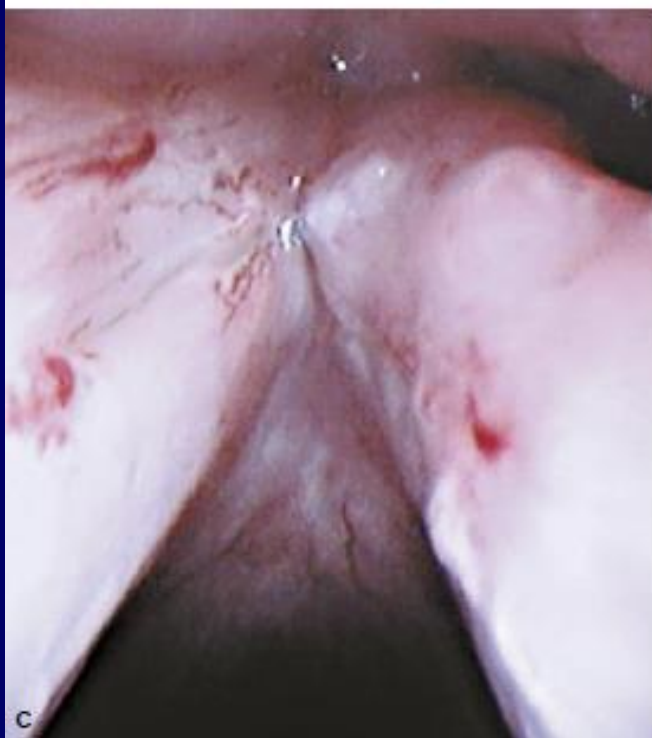
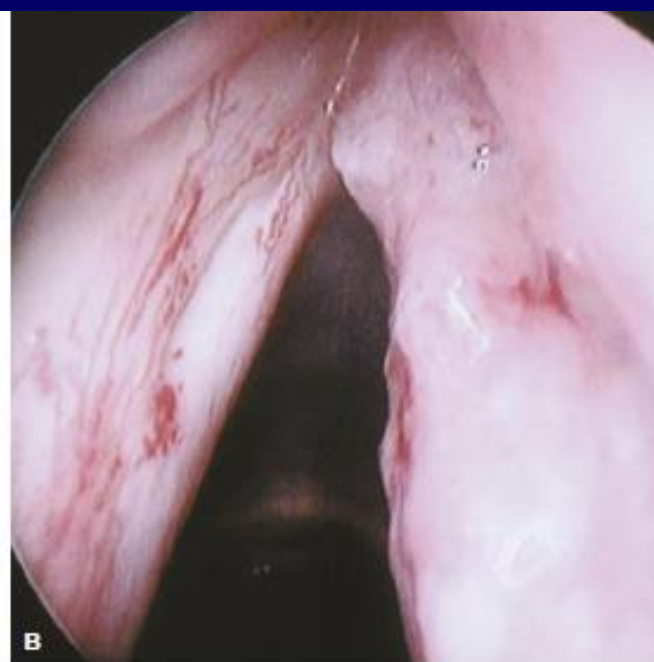


Figure 8-4. Endoscopic view and assessment of a laryngeal cancer using the A-0°; B-30°; C-70°; D-120° telescopes.



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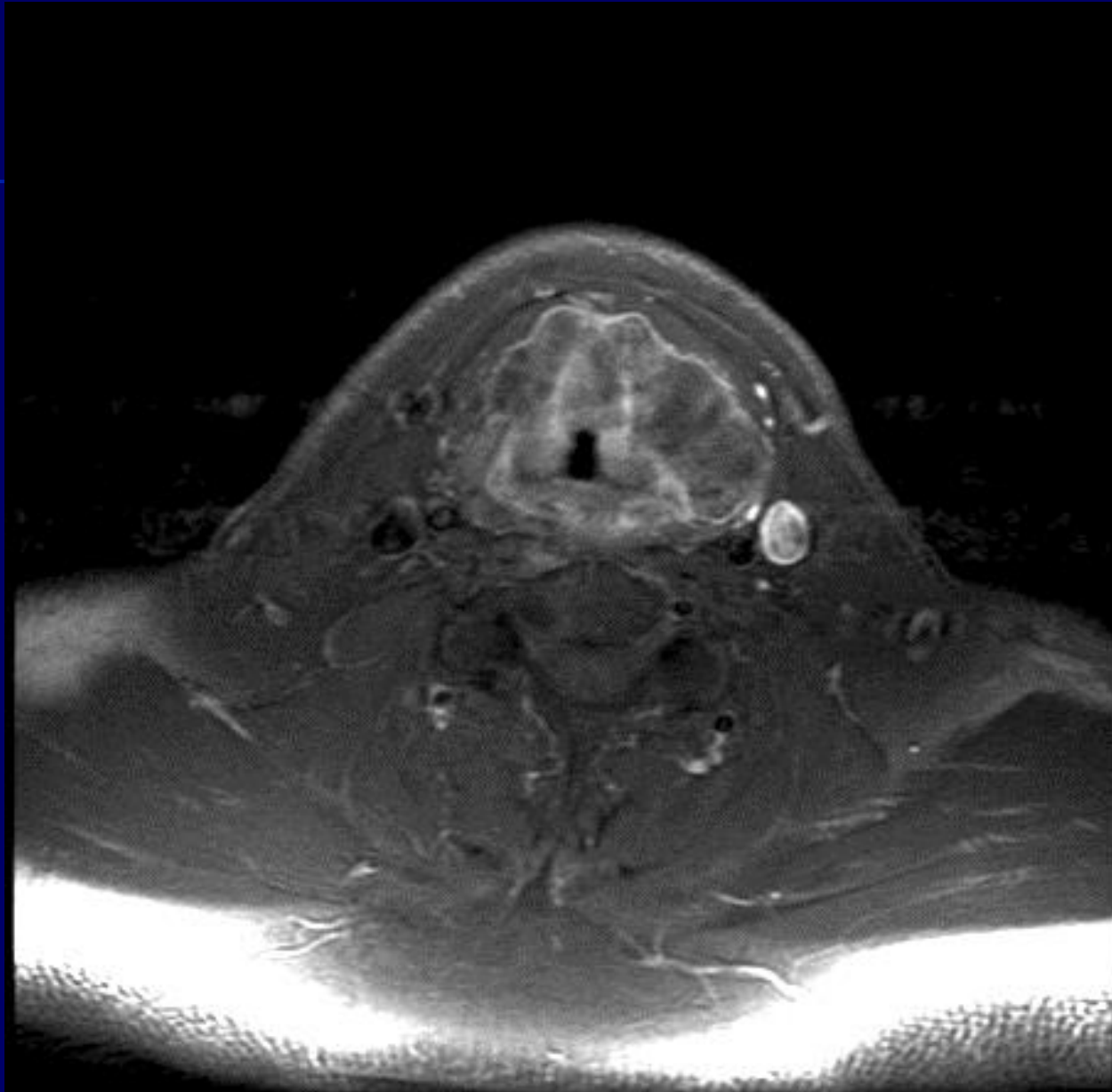


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COMMENT

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# Images





# Treatment

*In the last 2 decades, 5-year survival of patients with laryngeal cancer has not changed dramatically...due to the lack of improvement in survival, significant efforts have been made to improve the quality of life in these patients. Paramount to this is preservation of a functional larynx*

*Pioneering work on patient preferences showed that approximately 25% of healthy individuals interviewed were willing to trade a 20% absolute difference in survival for the opportunity to save their voice*

*Anatomic preservation is not functional preservation!*

# Pre-malignant disease

## Management of advanced premalignant laryngeal lesions

Felicia L. Johnson

### Purpose of review

Laryngeal carcinogenesis is a multistep process with premalignant lesions progressing to invasive carcinoma over a period of years. The approach to these advanced premalignant lesions has always been early diagnosis and treatment to prevent further progression. Unfortunately, with the current means of diagnosis and a lack of consensus regarding treatment of these lesions, the incidence of advanced laryngeal malignancies continues to rise. The purpose of this article is to review the most recent contributions to the literature regarding diagnosis and management of advanced laryngeal premalignant lesions.

### Recent findings

The current literature focuses on several new diagnostic

### Introduction

Laryngeal premalignant lesions include a wide spectrum of mucosal changes from simple hyperplasia or keratosis to carcinoma in situ (CIS). The World Health Organization classifies the various laryngeal precursor lesions into the following categories: hyperplasia, keratosis, mild, moderate or severe dysplasia, and CIS [1]. Unfortunately, there is no universally accepted histopathologic classification system and there is a lack of consensus regarding the diagnostic criteria for the various entities particularly in differentiating severe dysplasia from CIS. This results in poor reproducibility in the pathologic interpretation of these lesions and may have significant therapeutic implications.

# Early stage disease

There are no randomized studies in which radiation therapy was compared with conservation surgery with respect to

local control or survival for patients with limited-stage

- T1-T2 disease should be treated with either radiation or larynx preserving surgery
- Surgery should be with the aim of achieving clear margins
- Avoid combined modality therapy
- Selected stage III cases (e.g. T2 N+) are suitable for concurrent chemoradiotherapy
- Recurrence may be amenable to larynx-preserving surgery but majority of index T2 tumours will require laryngectomy

# Larynx-preserving surgery

- Transoral Laser
- Vertical Partial Hemilaryngectomy
- Fronto-lateral Partial Hemilaryngectomy
- Supraglottic Laryngectomy
- Supracricoid Laryngectomy + CHP / CHEP

# Transoral Laser Surgery

- Utilises Carbon Dioxide laser beam to resect tumour
- Offers a quick alternative to radiotherapy
- Is organ sparing
- Useful in managing laryngeal recurrence



Fig. 1

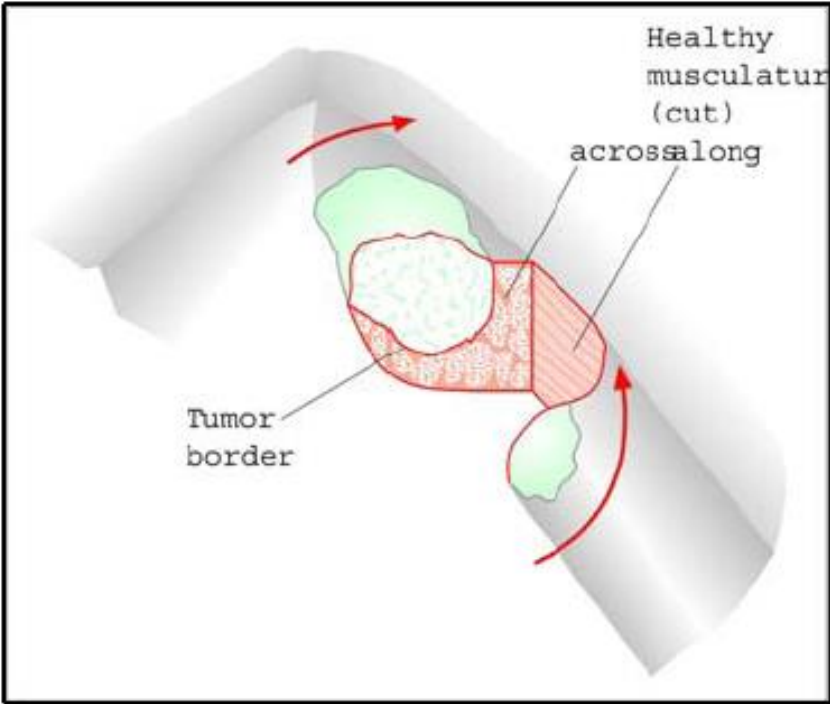
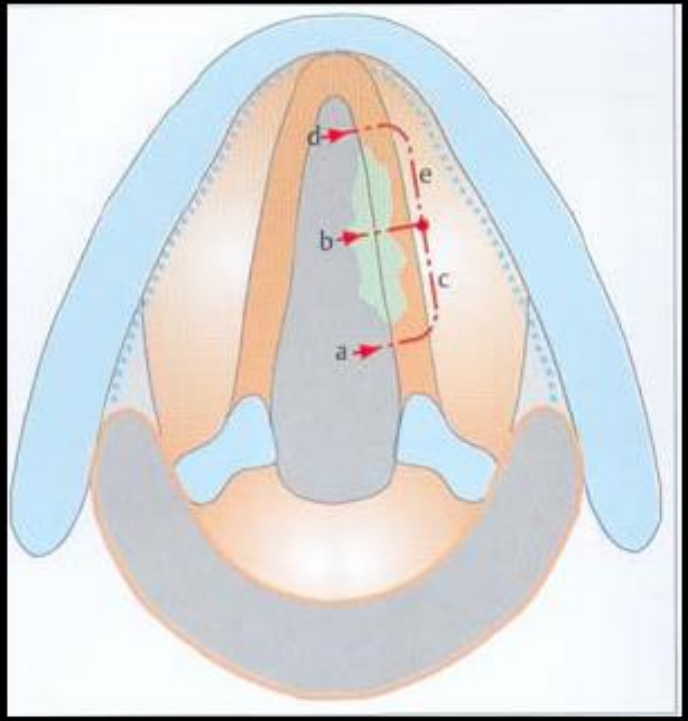


Fig. 2





## Results of 333 cases of vocal cord carcinomas pT1a (1979 - 2001)

Tumor extent: more than 1/3 of the vocal cord: 68%; anterior commissure involvement: 22%; only midcordal lesion: 14%.  
Complication rate: 1.2% (postoperative hemorrhage 2, edema 2; no tracheostomy, no feeding tube)  
Median follow-up: 72 months

Table 1: Oncologic Results of Laser Microsurgery for pT1a vocal cord carcinomas (n=333)

5 yrs Kaplan-Meier local control rate	96.2%
Larynx preservation rate	97.6%
5 yrs Kaplan-Meier disease-specific survival rate	100%
5 yrs Kaplan-Meier overall survival rate	86.8%

Fig. 4

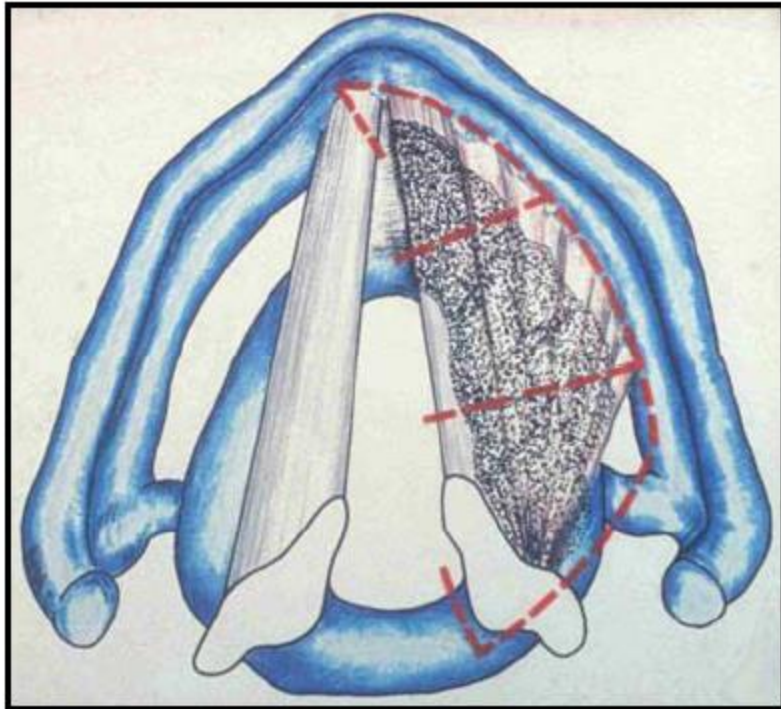
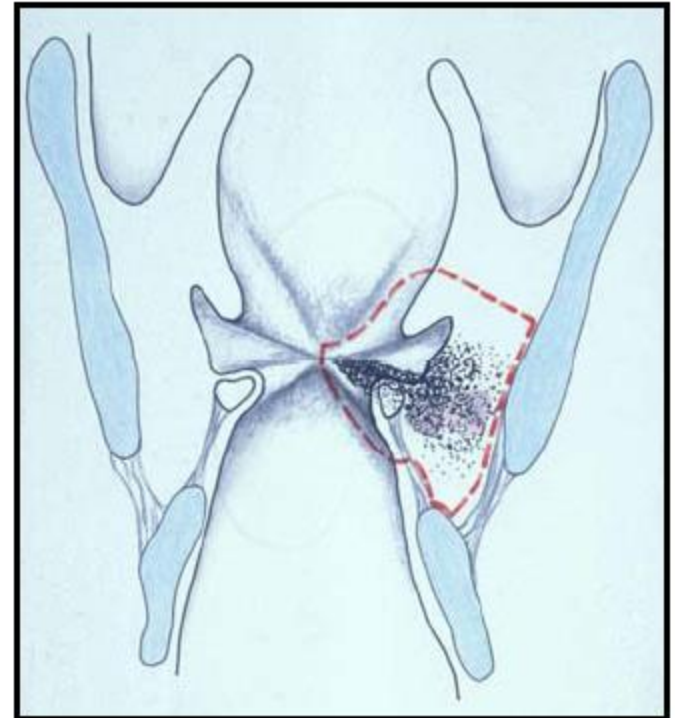


Fig. 5



## Results of 338 patients with pT2 and pT3 glottic cancer (1979 - 2001)

Stage Distribution: stage II 71%, stage III 27%, stage IV 2%

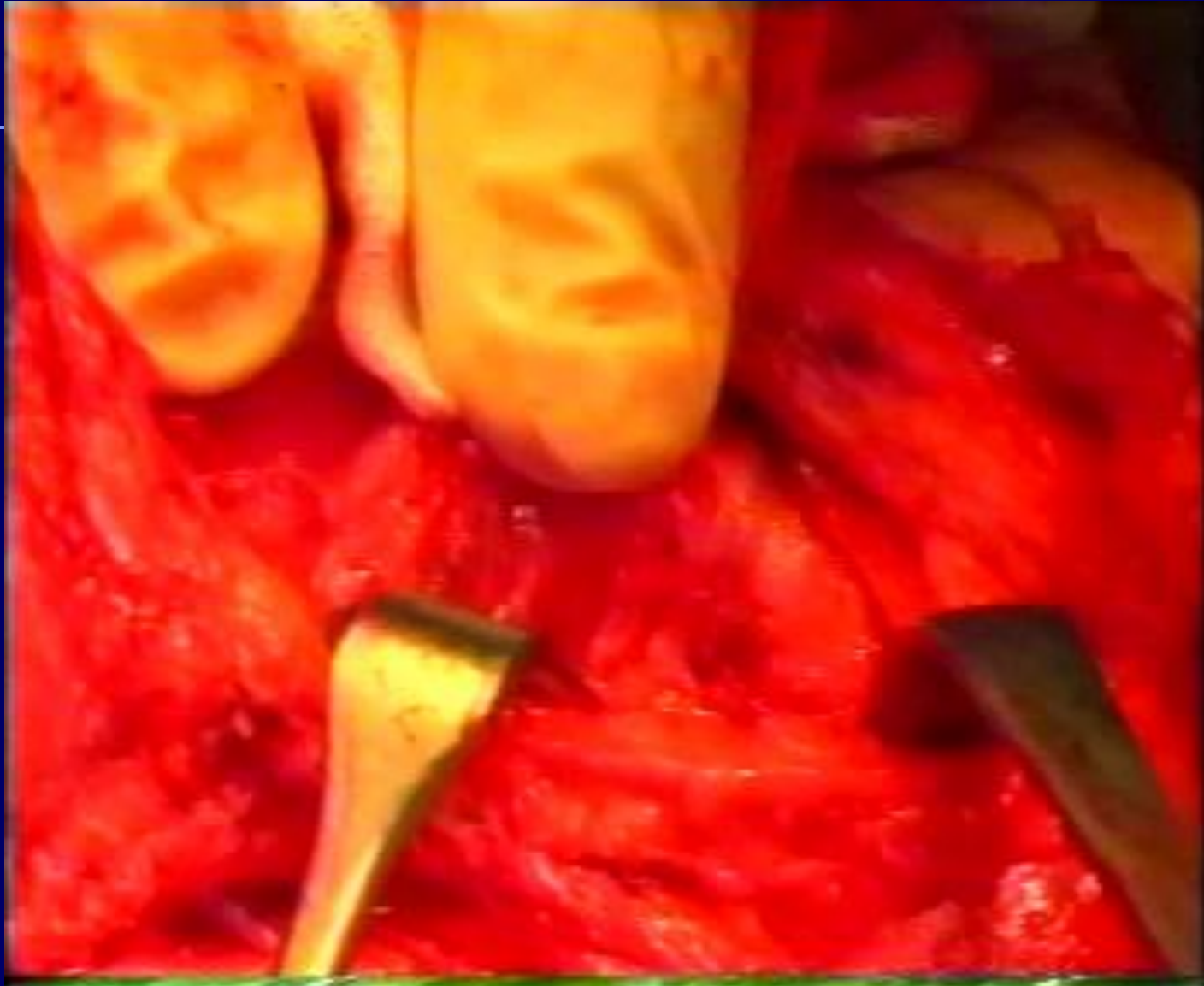
Median follow-up: 69 months

Table 3: Therapy of Glottic Carcinomas (n=338)

	<b>pT2a</b> (n=128)	<b>pT2b</b> (n=115)	<b>pT3</b> (n=95)
Laser	116 (91%)	87 (76%)	42 (44%)
Laser + ND	12	15	41
Laser + RT	-	11	3
Laser + ND + RT	-	2	9

	<b>pT2a</b> (n=128)	<b>pT2b</b> (n=115)	<b>pT3</b> (n=95)
5 yrs Kaplan-Meier local control rate	85%	65%	68%
5 yrs Kaplan-Meier larynx preservation rate	96%	84%	80%
5 yrs Kaplan-Meier recurrence-free survival rate	82%	61%	60%
5 yrs Kaplan-Meier overall survival rate	75%	65%	58%

# Supracricoid laryngectomy



# Advanced stage disease

- All patients should be considered for laryngeal preservation
- No organ-preserving strategy offers a survival advantage over laryngectomy and
- Selected T3 disease may be amenable to partial laryngeal surgery
- There is no role for induction chemotherapy prior to surgery outside a clinical trial

**Table 8–2. RESULTS OF CONVENTIONAL TREATMENT OF ADVANCED CARCINOMA OF THE LARYNX**

Author	Year	No.	Type of Therapy	Stage III/IV (%)	5 yr Survival (%)
Kirchner <sup>12</sup>	1977	308	S/RT	100	54–56*
Harwood <sup>13</sup>	1979	353	RT	54	70
Harwood <sup>43</sup>	1983	410	RT	66	57
Yuen <sup>41</sup>	1984	192	S	100	77
		50	S/RT	100	91
Mendenhall <sup>42</sup>	1992	100	RT	100	74
		65	S±RT	100	63
Nguyen <sup>11</sup>	1996	116	S/RT	100	68
Myers <sup>10</sup>	1996	65	S±RT	100	62†

Survival rates refer to disease-free survival when available, otherwise they refer to overall survival.

\* study included both laryngeal and non-laryngeal sites.

S = Surgery; RT = Radiation therapy; † 2-year survival.

**Table 2.** Phase III Studies of Induction Chemotherapy Followed by Radiation for Larynx Preservation

Study and Patient Characteristics	Study Arms	Treatment of Disease in the Neck	Indications for Salvage Surgery After Chemoradiation Therapy	Overall Survival		Rate of Larynx Preservation	
				%	Timeframe	%	Timeframe
<b>VA Laryngeal Cancer Study<sup>78</sup></b> (n = 332) Stage III/IV disease (%), 57/43 (2/3 primary lesions of the supraglottis); T3/T4 (%), 65/26; NO-N1 (%), 72	Chemoradiation Arm Induction chemotherapy (3 cycles standard cisplatin and fluorouracil) followed by radiation therapy (66-76 Gy to primary site 50-75 Gy to nodes)	Lymph node dissection if residual disease after radiation therapy	Less than partial response to chemotherapy after 2 cycles; residual disease at biopsy 12 weeks after completion of radiation therapy	68	2 years	66	2 years
	Surgery Arm Standard total laryngectomy followed by radiation therapy (50 Gy [no residual disease], up to 73 Gy [residual disease])	Lymph node dissection for all patients	—	68	2 years	—	—
<b>GETTEC Study<sup>82</sup></b> (n = 68) Stage III/IV (%), not provided; T3/T4 (%), 100/0; NO-N1 (%), 93	Chemoradiation Arm Induction chemotherapy (3 cycles standard cisplatin and fluorouracil) followed by radiation therapy (65-70 Gy to primary site 50-70 Gy to nodes)	Lymph node dissection if salvage surgery only	Less than 80% regression of tumor after chemotherapy, lack of return of laryngeal mobility	69	2 years	42	Median, 8 years
	Surgery Arm Standard total laryngectomy followed by radiation therapy (50 Gy [no residual disease], up to 70 Gy [residual disease])	Lymph node dissection for all patients	—	84	2 years	P = .006	

# Intergroup Head and Neck Trial (RTOG 9003)

(n 547) Stage III/IV (%), 65/35; T3/T4 (%), 79/10

**Table 3.** Phase III Studies of Concurrent Chemoradiation Therapy for Larynx Preservation

Study Arms	Treatment of Disease in the Neck	Indications for Salvage Surgery	Overall Survival		Larynx Preservation		Toxicity
			%	Timeframe	%	Timeframe	
<p>Primary radiation therapy: 70 Gy to primary site, 50-70 Gy to nodes</p> <p>Induction chemotherapy: cisplatin/fluorouracil (3 cycles) followed by radiation therapy for those who had a response (if salvage surgery, 50-70 Gy administered postoperatively)</p> <p>Concurrent chemoradiation: high-dose cisplatin (days 1, 22, 43) plus 70 Gy to primary site; 50-70 Gy to nodes</p>	Lymph node dissection after completion of radiation therapy for all patients with clinical involvement of nodes before beginning of treatment	Less than partial response to induction chemotherapy; residual disease found at biopsy after completion of radiation therapy	75	2 years	Radiation therapy alone		<p>Swallowing difficulties in 18% at 1 year and in 14% at 2 years</p> <p>Rate of grade 3 or 4 toxicity during radiation no different from that for radiation therapy-alone arm; swallowing difficulties in 9% at 1 year and 16% at 2 years</p> <p>Highest rate of grade 3 or 4 acute toxicity; no increase in late toxic effects; swallowing difficulties in 26% at 1 year and in 15% at 2 years</p>
			56	5 years	70	2 years	
			76	2 years	Induction chemotherapy		
			55	5 years	75	2 years	
			74	2 years	$P = .27$ v radiation therapy-alone arm		
54	5 years	Concurrent chemoradiation		88	2 years		
					$P < .001$ v radiation therapy-alone arm; $P = .005$ v induction-chemotherapy arm		



WORKUP<sup>a</sup>

- H&P
- Biopsy
- Chest x-ray or Chest CT<sup>b</sup>
- CT with contrast and thin cuts through larynx, or MRI of primary and neck recommended
- Examination under anesthesia with laryngoscopy
- Preanesthesia studies
- Dental evaluation

Multidisciplinary consultation as indicated

CLINICAL STAGING

Severe dysplasia/  
carcinoma in situ

- Total laryngectomy not required
- Most T1-2, any N

- Resectable
- Requiring total laryngectomy
- Most T3, any N

T4 disease

- Resectable
- Poor medical/surgical risk

TREATMENT OF PRIMARY AND NECK

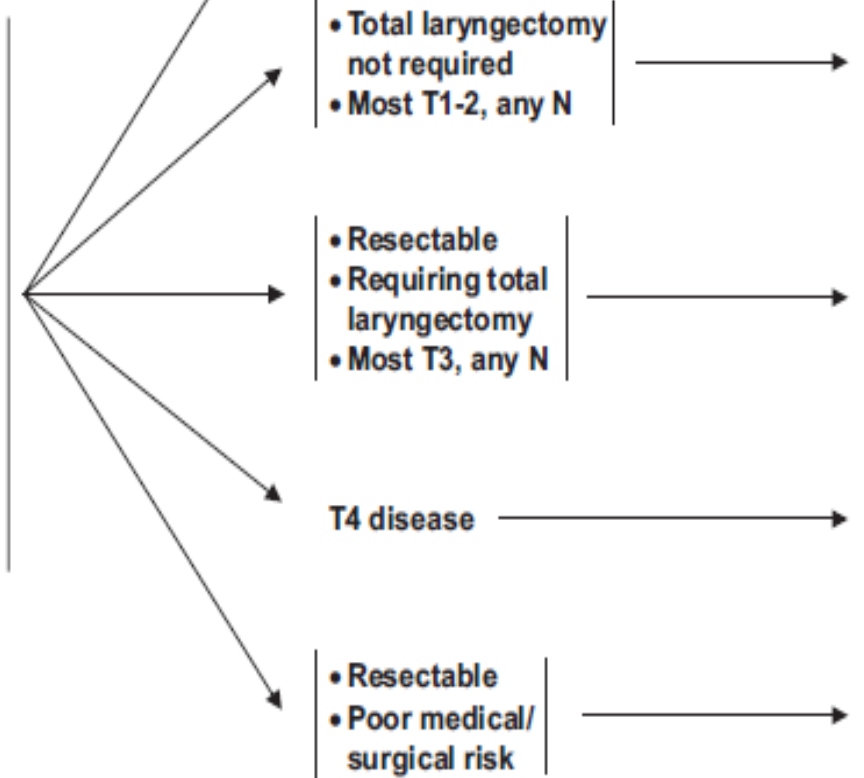
[See Treatment and Follow-up \(GLOT-2\)](#)

[See Treatment and Follow-up \(GLOT-2\)](#)

[See Treatment and Follow-up \(GLOT-3\)](#)

[See Treatment and Follow-up \(GLOT-4\)](#)

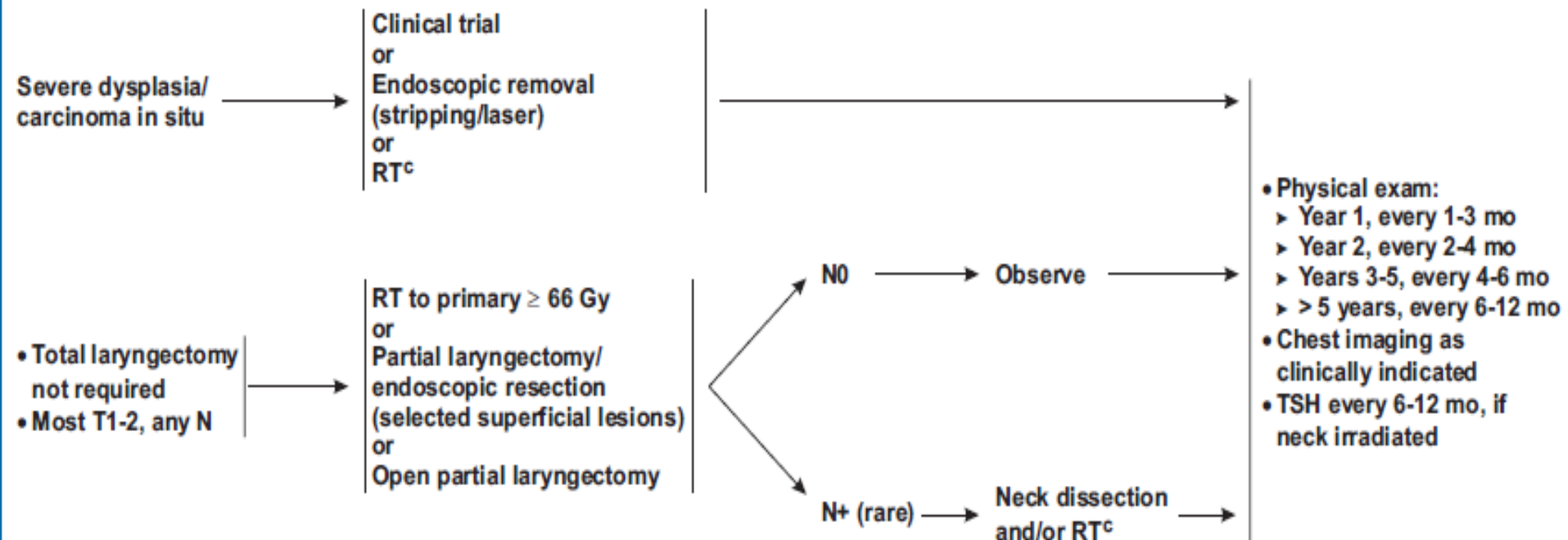
Definitive RT<sup>c</sup>



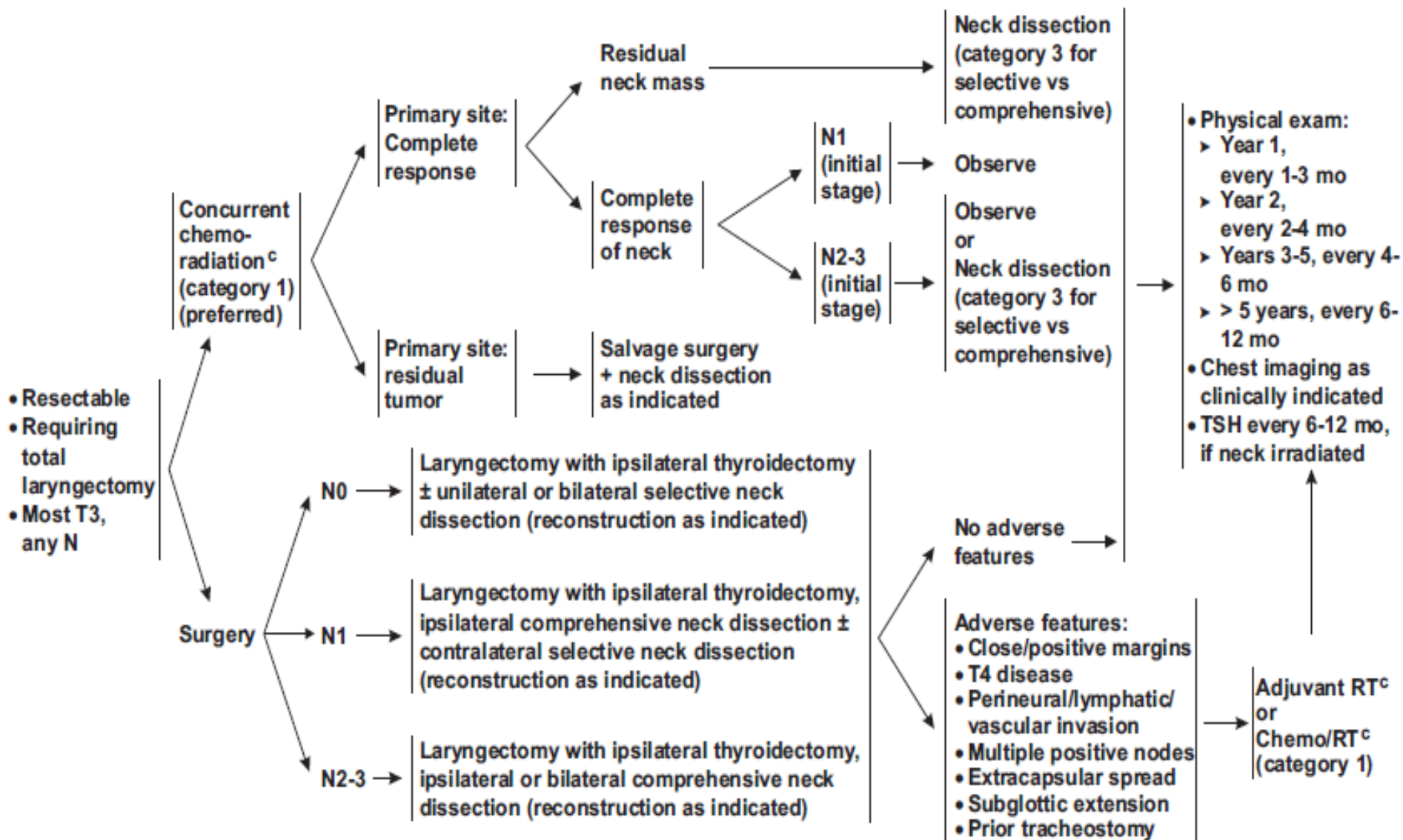
CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

FOLLOW-UP

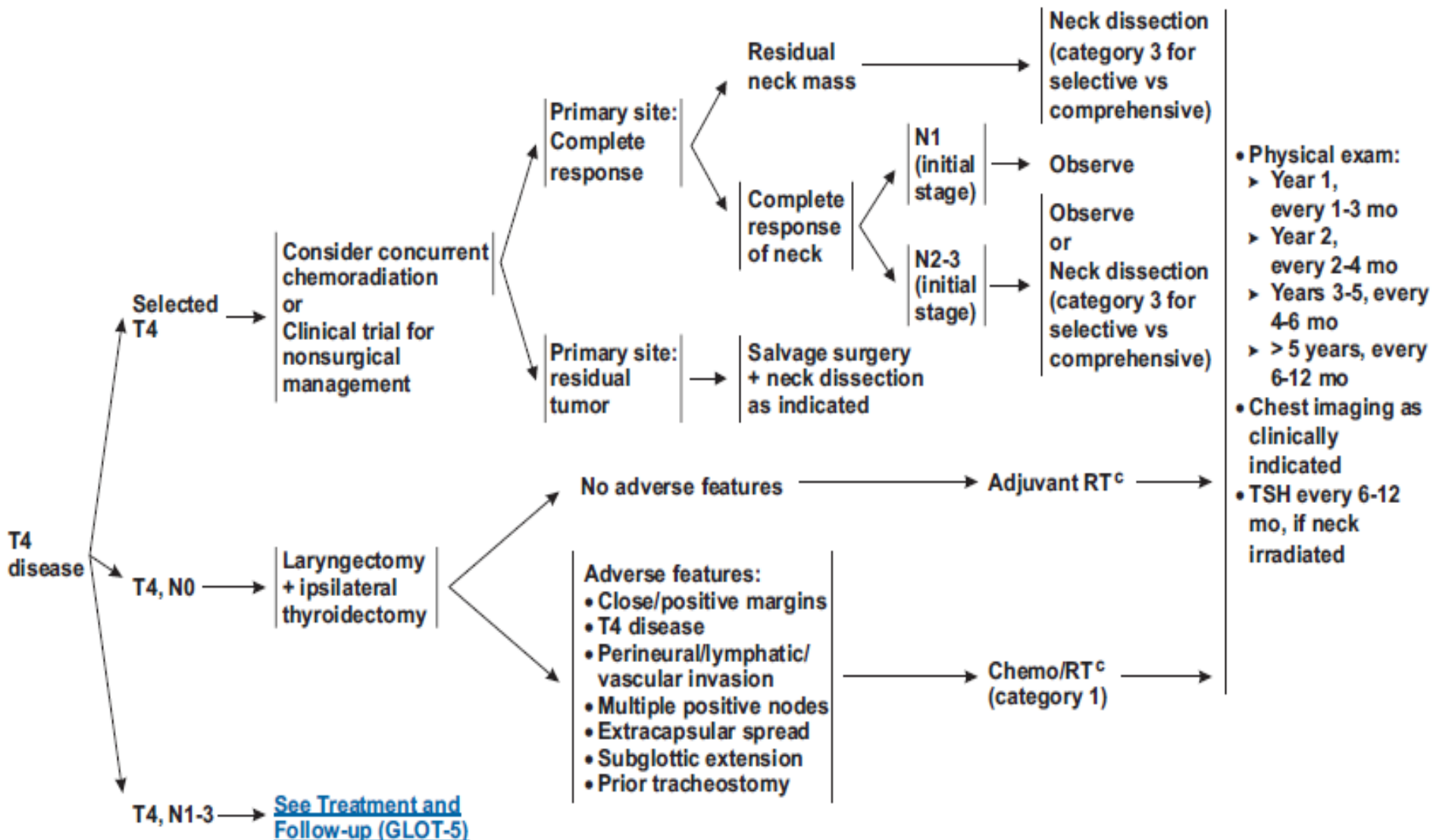


CLINICAL STAGING      TREATMENT OF PRIMARY AND NECK      FOLLOW-UP THERAPY



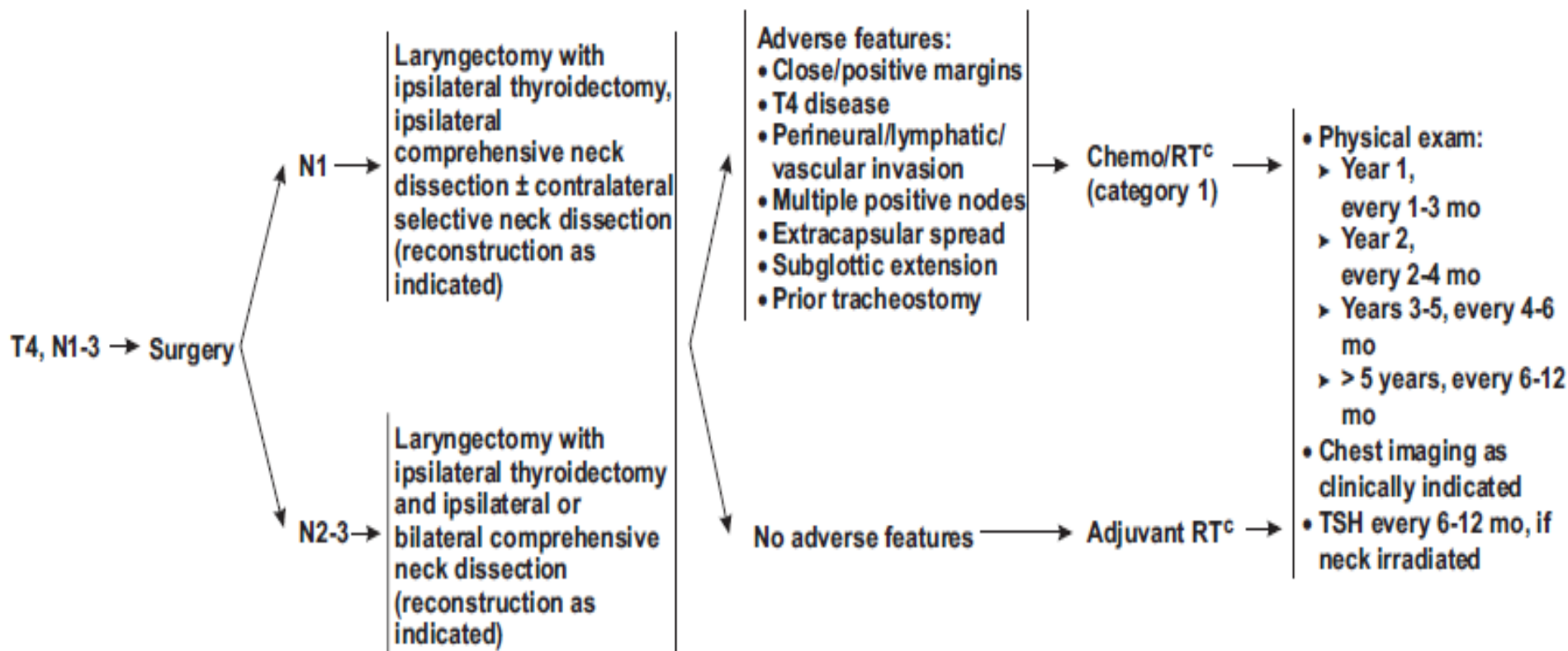
CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK



CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK



# RADIATION THERAPY GUIDELINES

## Definitive RT

- **Primary and gross adenopathy:**  
≥ 70 Gy (2.0 Gy/day)  
For early cancer of the glottic larynx,  
preferred dose is ≥ 2.0 Gy/day with  
total dose modification accordingly
- **Neck**
  - **Low-risk nodal stations:**  
≥ 50 Gy (2.0 Gy/day)

## Adjuvant RT

- **Primary:** ≥ 60 Gy (2.0 Gy/day)
- **Neck**
  - **High-risk nodal stations:**  
≥ 60 Gy (2.0 Gy/day)
  - **Low-risk nodal stations:**  
≥ 50 Gy (2.0 Gy/day)

WORKUP

- H&P
  - Biopsy
  - Chest x-ray or Chest CT<sup>a</sup>
  - CT with contrast and thin cuts through larynx or MRI of primary and neck recommended
  - Examination under anesthesia with laryngoscopy
  - Preanesthesia studies
  - Dental evaluation
- Multidisciplinary consultation as indicated

CLINICAL STAGING

- Resectable
- Not requiring total laryngectomy
- Most T1-2, N0

[See Treatment of Primary and Neck \(SUPRA-2\)](#)

- Resectable
- Requiring laryngectomy
- T3, N0
- T4, N0
- No cartilage destruction
- Low-volume base-of-tongue involvement

[See Treatment of Primary and Neck \(SUPRA-3\)](#)

- Resectable
- T4, N0
- Cartilage destruction
- Skin involvement
- Massive invasion of base of tongue

[See Treatment of Primary and Neck \(SUPRA-4\)](#)

Node positive disease

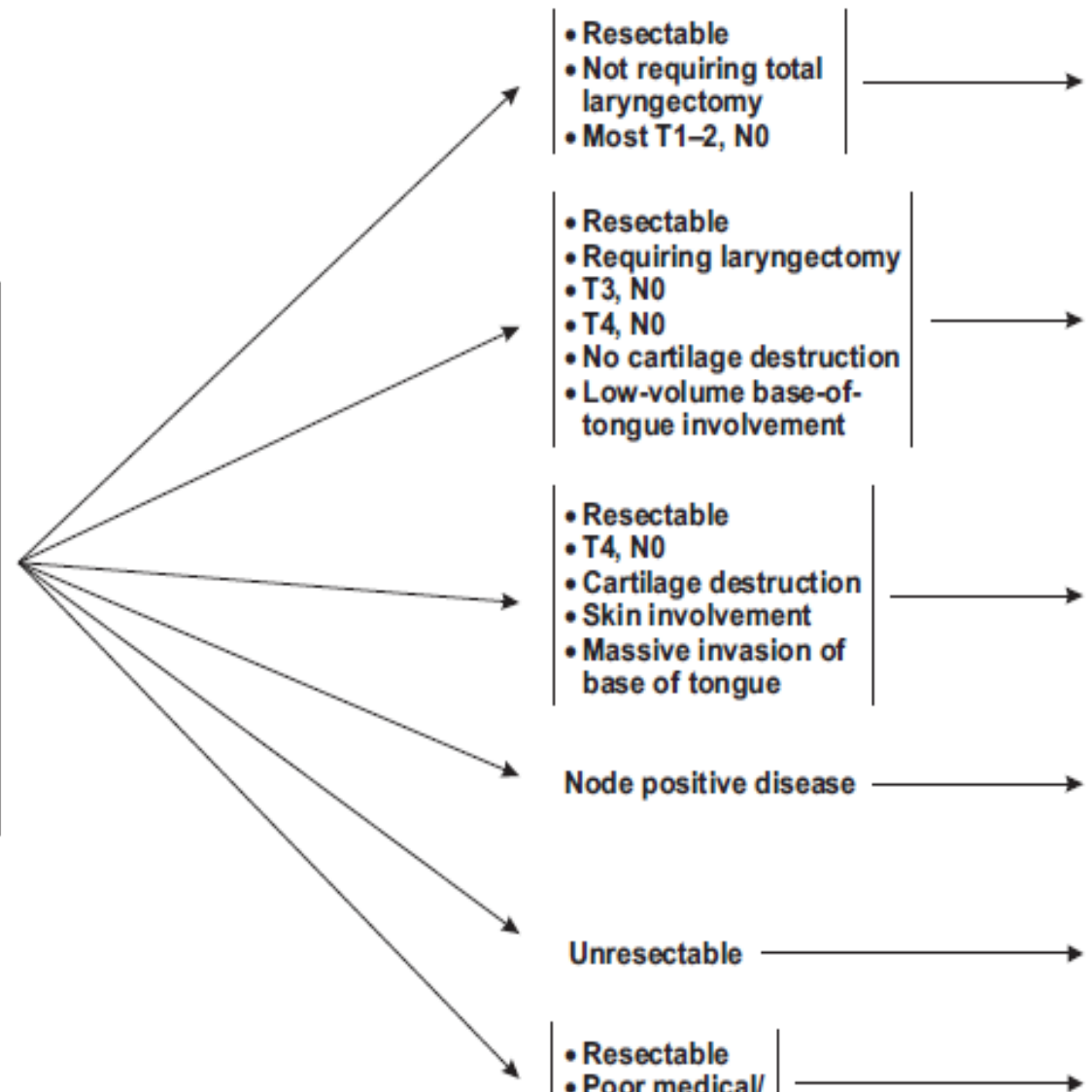
[See Workup and Clinical Staging \(SUPRA-5\)](#)

Unresectable

[See Treatment of Head and Neck Cancer \(ADV-1\)](#)

- Resectable
- Poor medical/surgical risk

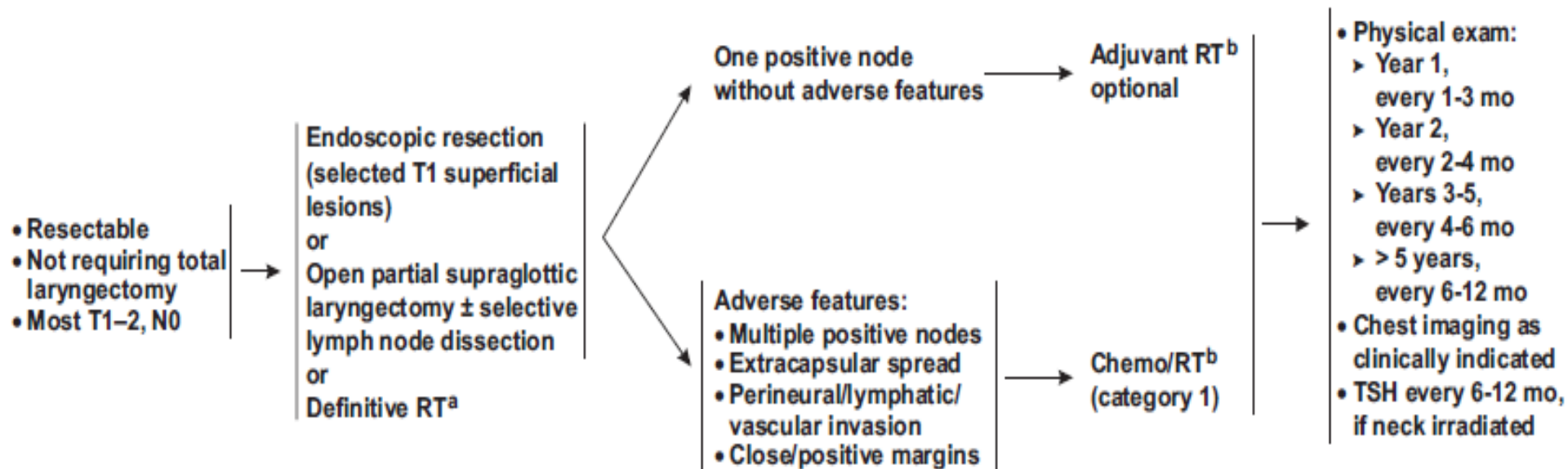
Definitive RT<sup>b</sup>



CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

FOLLOW-UP



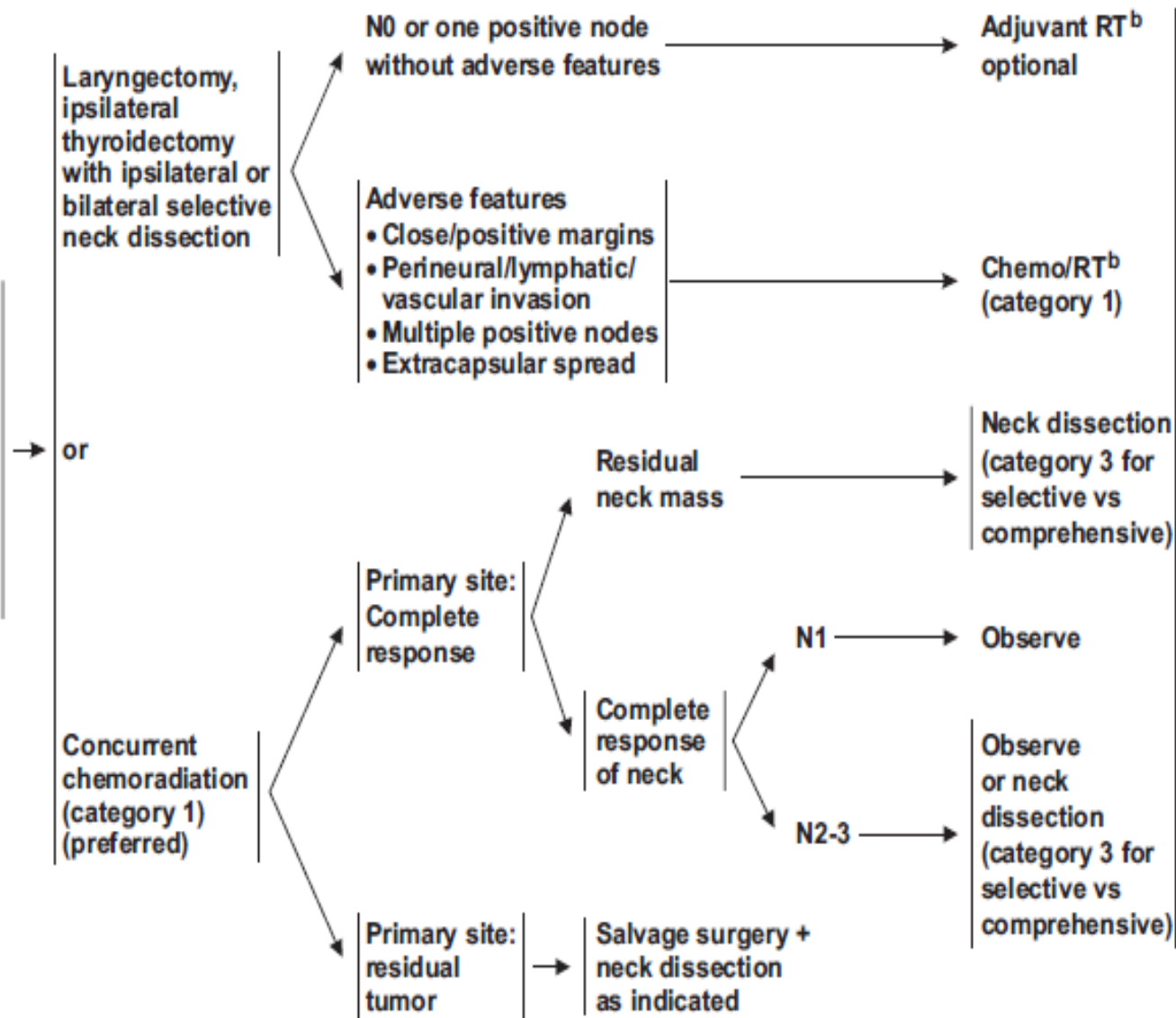


CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

FOLLOW-UP

- Resectable
- Requiring laryngectomy
- T3, N0
- T4, N0
- No cartilage destruction
- Low-volume base-of-tongue involvement



- Physical exam:
  - Year 1, every 1-3 mo
  - Year 2, every 2-4 mo
  - Years 3-5, every 4-6 mo
  - > 5 years, every 6-12 mo
- Chest imaging as clinically indicated
- TSH every 6-12 mo, if neck irradiated

CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

FOLLOW-UP

- Resectable
- T4, N0
- Cartilage destruction
- Skin involvement
- Massive invasion of base of tongue



Laryngectomy, ipsilateral thyroidectomy with ipsilateral or bilateral selective neck dissection or  
Clinical trial



Adjuvant RT<sup>b</sup>  
or  
Chemo/RT<sup>b</sup>  
(category 1)



- Physical exam:
  - Year 1, every 1-3 mo
  - Year 2, every 2-4 mo
  - Years 3-5, every 4-6 mo
  - > 5 years, every 6-12 mo
- Chest imaging as clinically indicated
- TSH every 6-12 mo, if neck irradiated

WORKUP

CLINICAL STAGING

Node positive disease →

- H&P
  - Biopsy
  - Chest x-ray or Chest CT<sup>a</sup>
  - CT with contrast and thin cuts through larynx/
  - MRI of primary and neck recommended
  - Examination under anesthesia with laryngoscopy
  - Preanesthesia studies
  - Dental evaluation
- Multidisciplinary consultation as indicated

- Resectable
- Not requiring total laryngectomy
- T1-2, N+ and selected T3-4

→ [See Treatment of Primary and Neck \(SUPRA-6\)](#)

- Resectable
- Requiring total laryngectomy
- Most T3-4, N+
- No cartilage destruction
- Low-volume base-of-tongue involvement

→ [See Treatment of Primary and Neck \(SUPRA-7\)](#)

- Massive T4, N+
- Cartilage destruction
- Skin involvement
- Massive invasion of base of tongue

→ [See Treatment of Primary and Neck \(SUPRA-8\)](#)

- Resectable
- Poor medical/surgical risk

→ [See Treatment of Primary and Neck \(SUPRA-8\)](#)

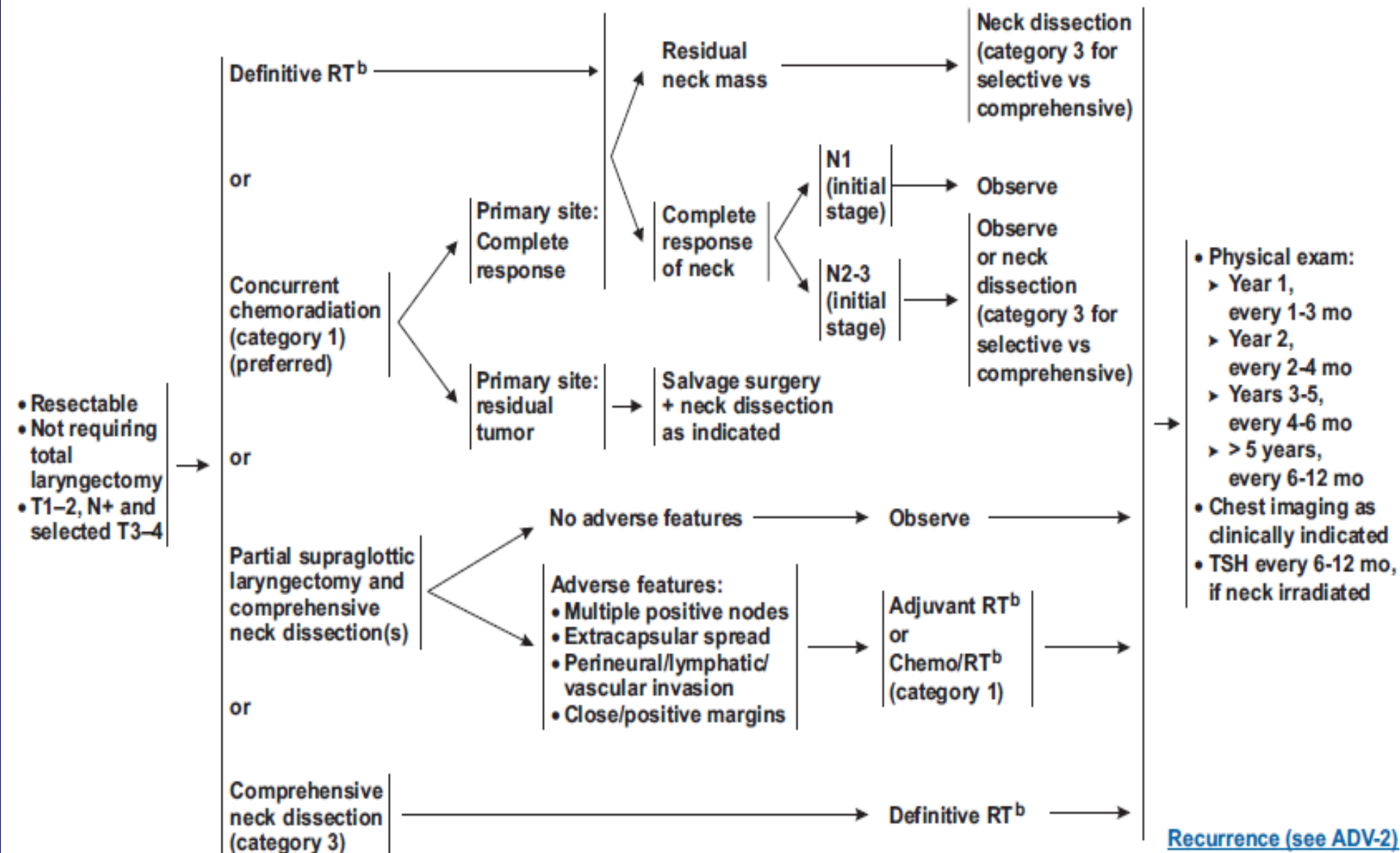
Unresectable →

→ [See Treatment of Head and Neck Cancer \(ADV-1\)](#)

CLINICAL STAGING

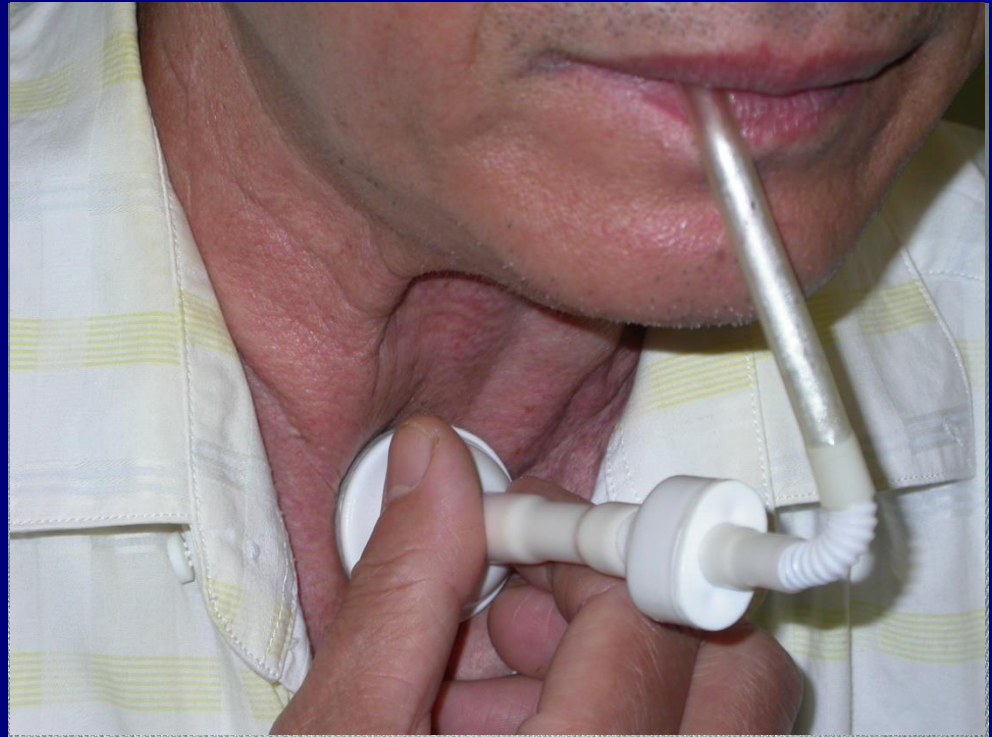
TREATMENT OF PRIMARY AND NECK

FOLLOW-UP



# Voice restoration in laryngectomees

- Electrolarynx
- Oesophageal speech
- Surgical voice restoration (TEP)



# Surgical Voice Restoration

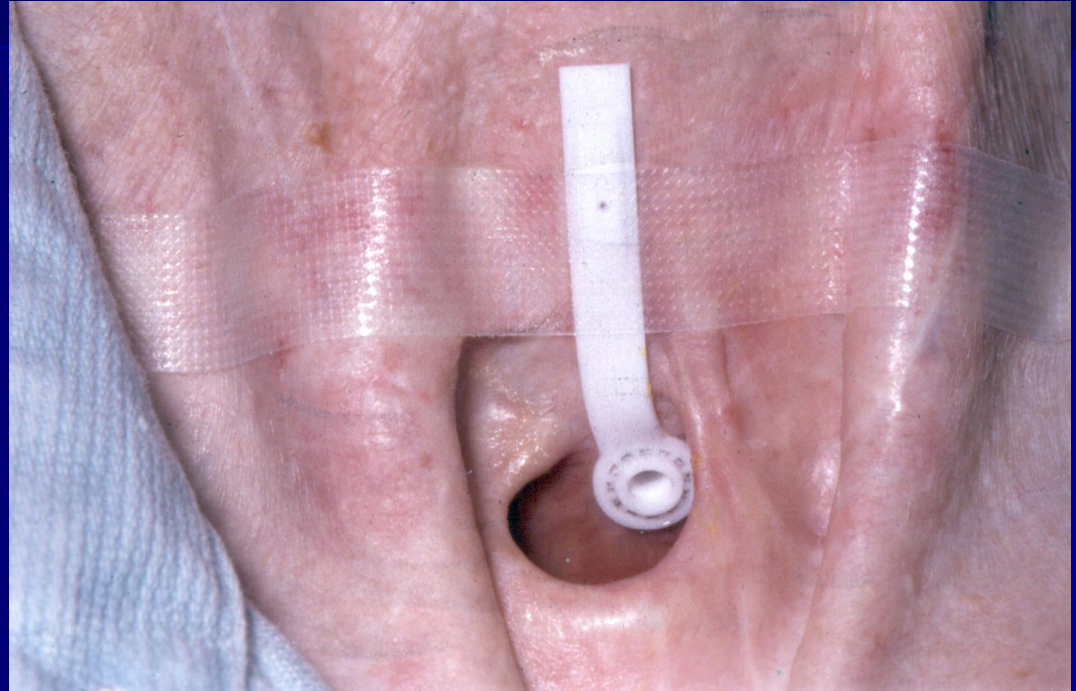
(Blom and Singer, 1978)

Following laryngectomy, voice is restored by creating a tracheo-oesophageal puncture

The pharyngo-oesophageal (P-E) segment vibrates as air passes through the fistula, into the upper oesophagus and up into the pharynx

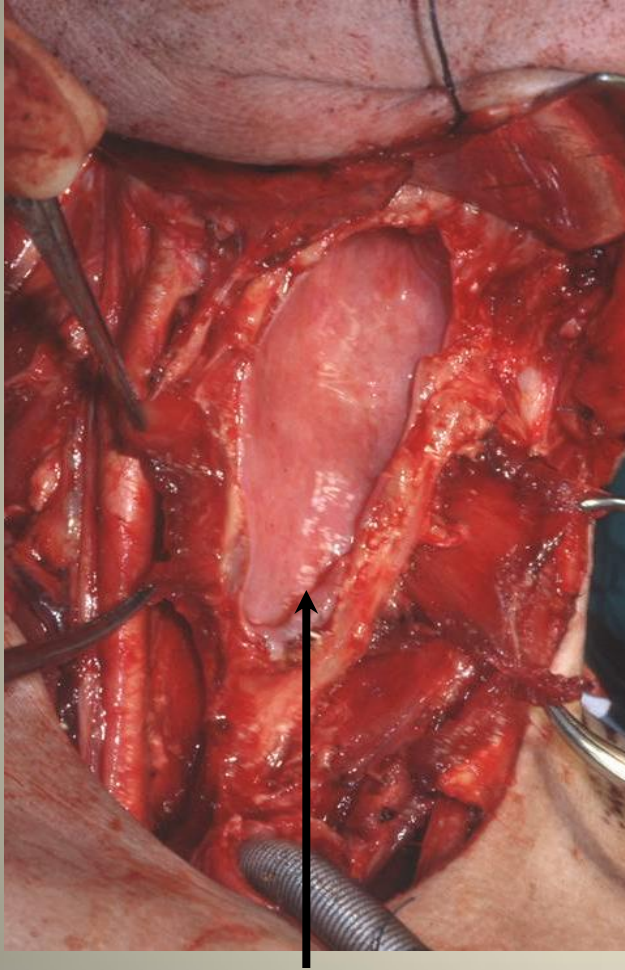


# A one-way valve is fitted

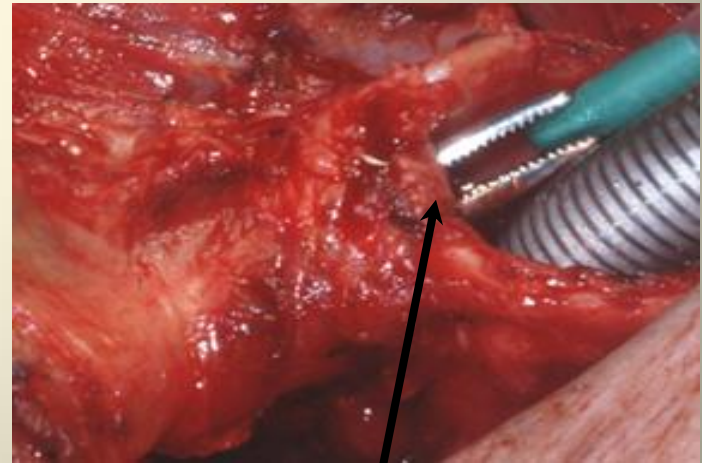
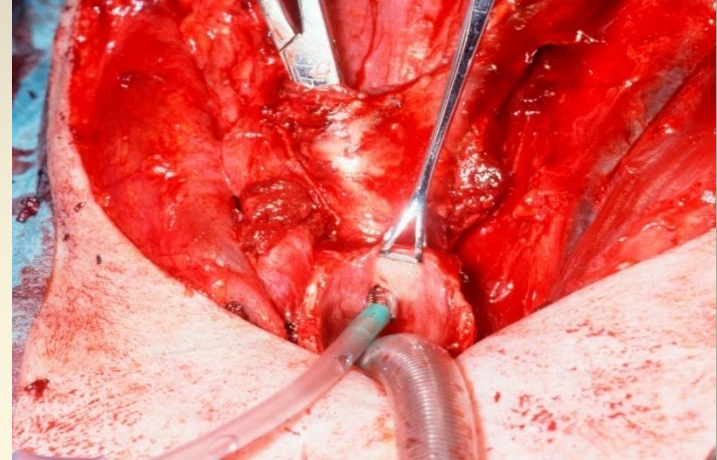


A one-way valve prevents leakage of saliva into the trachea

# Tracheo-oesophageal puncture (TEP)



**Pharyngeal defect following laryngectomy**



**Ryle's tube passed through the puncture**



# Cricopharyngeal myotomy

