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Surgery of Thyroid Cancer

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Occult and microscopic differentiated carcinoma of the thyroid is a clinically benign lesion, even when accompanied by lymph node metastases, and should be treated surgically by conservative procedures. Clinically detectable thyroid carcinomas may be of low-risk types in younger patients or high-risk types in older patients. Age is the primary determinant of risk. Low-risk patients should be treated conservatively since the risk of death is currently no higher than 1.5%. High-risk patients should be treated more aggressively since recurrence rates may be high and risk of death from disease may reach 15% to 20%. In all patients, total thyroidectomy should be avoided since it does not improve local control rates or cure rates and exposes the patient to considerable risk of iatrogenic hypoparathyroidism and recurrent nerve injury. This recommendation is particularly true for occult and microscopic disease as well as for low-risk disease, because risk of death from disease is so low.

The surgical treatment of thyroid carcinoma has been controversial for many years, with basic surgical philosophies ranging from the extremely radical [1] to the extremely conservative [2]. To these basic surgical philosophic differences are added the confounding factors of the biology of various types of thyroid cancer, ranging from almost totally and rapidly lethal [3] to nearly innocent [4]. Indeed, many conditions called cancer in some institutions [5] and treated aggressively are not clinically considered to be cancer by others [6]. Some authors [7] even deny that patients die of differentiated thyroid carcinoma. Thus, the development of a logical, consistent surgical approach is difficult or impossible without a clear appreciation of the biology of various clinical types of thyroid carcinoma.

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Data from the Lahey Clinic over the 40 years from 1931 to 1970 and previously published [8, 9] will be cited to illustrate some of the biologic features of the disease as we understand it. Results of our therapy will then be described to reemphasize these biologic assumptions.

Results of Surgical Treatment of Thyroid Cancer

The basic material on which our conclusions are based consists of records of 953 patients with various thyroid carcinomas first treated operatively by surgeons of the Lahey Clinic Foundation between the years 1931 and 1970. Of these, 792 had differentiated thyroid carcinoma of either pure follicular type or with papillary elements observed histologically and called papillary and mixed papillary and follicular carcinoma. All of the latter behave identically biologically [8], despite wide variations in the amount of papillary features, from pure papillary to follicular predominant forms. A total of 631 patients was available for a follow-up study of a minimum of 15 years, and in 98% of the patients we had actual knowledge of their exact status for at least that duration of time; 75% of patients had a minimum of 20 years of follow-up, and 27% had a 30-year period of observation. Of the 631 patients, 190 (30%) had follicular carcinoma and 441 (70%) had papillary and mixed papillary and follicular carcinoma.

Of these 631 patients, 31 had categorically "incurable" disease when first seen because of distant metastases or massive unresectable local extension of the primary cancer to other neck structures, such

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Table 1. Risk of tumor recurrence and death by age decade in 600 patients with thyroid cancer seen before 1961 who underwent curative operation and had a minimum of 15 years of follow-up.

	Age (years)	Total no. of patients	Recurrence rate		Death rate	
			No.	%	No.	%
Men*	< 30	28	5	18	3	11
	31-40	34	4	12	2	6
	41-50	31	10	32	5	16
	51-60	25	8	32	6	24
	> 61	14	6	43	4	29
Women†	< 30	115	17	15	3	3
	31-40	122	11	9	5	4
	41-50	85	5	6	2	2
	51-60	80	23	28	21	24
	> 61	66	24	36	22	33
Total		600	113		73	

*$P = 0.02$ recurrence; P = NS deaths.
†$P = 0.001$ recurrence; $P = 0.001$ deaths.

as esophagus, trachea, or larynx. They had biopsy only. Such patients were seen most commonly in the first 2 decades of the study but constituted only 0.6% of cases in the 1960's. Therefore, these cases were eliminated from our analysis because of the unfavorable bias they would contribute to consideration of the biology and therapy of thyroid carcinoma as it is encountered in the 1980's. Thus, 600 cases formed the basis for our intensive analysis.

Age

For many years it has been appreciated that age plays a major role in the behavior of differentiated thyroid cancer. In our studies [8, 9] as well as in reports of others [10-12], the magnitude of the impact of age has been described and quantified. In no other human cancer has such a clear-cut age-associated improvement in prognosis been related to younger age or been so apparent for cancers of similar histologic appearance. Indeed, histologically similar cancers of other organs in younger patients usually have a worse prognosis than in older patients.

In Table 1 it is apparent that the poorer prognosis with increasing age appears abruptly about the age of 40 years in men and about the age of 50 years in women. Men younger than 40 years have an 8% mortality rate compared to a 21% mortality rate for those older than 40 years. In women the difference is more striking, with a death rate of 3% for those less than 50 years of age and 30% for those more than 50 years of age. These differences between young and old patients are highly statistically significant for both recurrence and death. Some authors [11] have suggested that a continuum of worsening prognosis with age exists rather than a sharp change in prognosis as observed in our study. Many articles about treatment of differentiated thyroid cancer fail to mention this relationship of age to prognosis or to utilize this biologic variation in recommending therapeutic approaches [13-15].

Sex

Sex also has some relationship to prognosis (Table 1). It is interesting that at younger ages, the prognosis in men is slightly worse, but at older ages the prognosis in women is slightly worse, although neither difference is statistically significant.

Pathologic Type

In analyzing our data it became apparent that the effect of pathologic type of tumor on prognosis was of the same order of magnitude as sex (Table 2). The prognosis associated with pure follicular carcinoma was worse than that with papillary and mixed papillary and follicular types for similar ages, but

Table 2. Risk of death as a function of age and pathologic type in patients with thyroid cancer seen before 1961 who underwent curative operation and had a minimum of 15 years of follow-up.

Tumor type	< 40 years of age			> 50 years of age		
	No. of patients	Deaths		No. of patients	Deaths	
		No.	%		No.	%
Follicular*	74	4	5	81	34	42
Papillary and mixed papillary and follicular†	232	9	4	124	36	29

*$P < 0.00001$ ($P = 5 \times 10^{-7}$).
†$P < 0.00001$ ($P = 2 \times 10^{-9}$).

Table 3. Definition of risk group in patients with thyroid cancer seen before 1961 who underwent curative operation and had a minimum of 15 years of follow-up.*

Group	Total incidence		Recurrence		Death		% of recurrences that died of disease
	No.	%	No.	%	No.	%	
Highest risk group†							
Follicular	83	14	33	40	30	36	91
Men > 40 years							
Women > 50 years							
Intermediate risk group†							
Papillary	133	22	38	29	28	21	74
Men > 40 years							
Women > 50 years							
Low risk group†							
Follicular or papillary	384	64	42	11	15	4	36
Men < 40 years							
Women < 50 years							
Total	600	100	113	19	73	12	65

*From Cady, B., Sedgwick, C.E., Meissner, W.A., Wool, M.S., Salzman, F.A., Werber, J.: Risk factor analysis in differentiated thyroid cancer. Cancer *43*:810, 1979 [9].

†High vs. intermediate: NS recurrence; $P = 0.02$ death. High vs. low: $P = 0.001$ recurrence; $P = 0.001$ death. Intermediate vs. low: $P = 0.001$ recurrence; $P = 0.001$ death.

Table 4. Recurrence and death rates as a function of risk group and extent of local disease in patients with thyroid cancer seen before 1961 who underwent curative operation and had a minimum of 15 years of follow-up.

Extent of primary cancer	Low-risk group*					High-risk group†				
	No. of patients	Recurrence		Death		No. of patients	Recurrence		Death	
		No.	%	No.	%		No.	%	No.	%
Intraglandular	334	36	11	12	4	171	41	24	33	19
Extraglandular	50	6	12	2	4	45	30	67	25	56

*Intraglandular vs. extraglandular.

*Low risk group: NS.

†High risk group: $P < 0.001$ recurrence; $P < 0.001$ death.

this difference was not statistically significant and was also dependent on age.

Follicular carcinoma with major capsular invasion is well known to have a significantly worse prognosis than that with minor capsular invasion [16]. Other clinical factors were analyzed such as extent of primary cancer, nature of the surgical procedure on the thyroid gland, cervical lymph node involvement, size of tumor, and history of childhood irradiation. No factor or combination of factors had as much impact on prognosis as age, sex, and pathologic type.

Risk Groups

In Table 3 age, sex, and pathologic type were combined to obtain a categorization of risk groups. Further analysis of these data showed no statistically significant difference in rates of recurrence or death between the highest risk group of older men and women with follicular carcinoma and the older patients with papillary and mixed carcinomas. Also, no statistically significant difference was found between sexes or pathologic types in the younger age group. There were highly statistically significant differences, however, between the young patients (men 40 years and younger and women 50 years and younger) and the older patients. Thus, older patients had a 33% recurrence rate and a 27% death rate, and younger patients had an 11% recurrence rate and a 4% death rate. As is also apparent from Table 3, only 1/3 of young patients with recurrence or metastases died of disease, but 82% of older patients with recurrence died of disease. Nearly 2/3 of patients fall into the low-risk category.

Table 5. Changes in sex composition of risk groups by time period in 947 patients with thyroid cancer who underwent curative operation.

	1931–1950		1951–1960		1961–1970	
Group	No.	%	No.	%	No.	%
Low risk*						
Men	29	16	33	17	17	18
Women	157	84	165	83	77	82
High risk†						
Men	29	26	41	39	37	55
Women	82	74	64	61	30	45
Proportion of men in series	58	19	74	24	54	34

*Men vs. women: NS.
†Men vs. women: $P = 0.0005$.

The importance of age in prognosis was analyzed in a variety of ways, all indicating the preeminence of this simple feature. For instance in Table 4, for young age groups, no difference in prognosis existed between extraglandular primary thyroid cancer that could be resected and cancer confined within the thyroid capsule. In high-risk patients, however, more extensive but resectable local disease (extrathyroid) carried a far worse prognosis. A variety of other analyses were performed [9], and every factor studied indicated that the preeminent governing factor of prognosis is age rather than pathologic type of cancer, size or invasiveness of the primary cancer, involvement of lymph nodes by metastases, type of operative procedure performed, or use of external beam or radioactive iodine radiotherapy.

The data in Table 5 further emphasize the categorization into low-risk and high-risk groups. The ratio of men to women in low-risk thyroid carcinoma has been unchanged since 1930, whereas a highly statistically significant change has occurred in the ratio of men to women at high risk in recent years. Before 1950, only 1 of 4 patients with high-risk cancer was male, but by 1970 the majority of such patients were male. Such data indicate that 2 fundamentally distinct biologic varieties of differentiated thyroid carcinoma exist, and that perhaps these 2 basic types should be the principal determinant of therapy, with other features being of less importance generally but adding qualifiers to the overall approach.

During the 4 decades of the Lahey Clinic study, changes occurred in the extent of local disease as evaluated by the surgeon and pathologist and in the type of standard operation performed. Cancers that extended outside the thyroid gland decreased in frequency to 12%, and cancers that had a major penetration of the tumor capsule decreased in incidence from 80% to 45%. At the same time the percentage requiring bilateral resection of the thyroid gland to provide a reasonable margin of normal tissue beyond the primary cancer decreased from greater than 40% to only 23%. A higher proportion had only lobectomy for therapy of small cancers in recent years. In the 1960's, 60% of patients had the contralateral thyroid lobe subtotally excised to facilitate eventual use of radioactive iodine but not for actual surgical treatment of the primary cancer. In these patients, extreme care was taken to preserve the parathyroid glands, and total thyroidectomy was almost never performed. The general trend of surgery in the 1960's was more conservative in terms of removal of thyroid substance.

Local Recurrence

Table 6 shows the incidence of local recurrence in the thyroid gland and thyroid bed area (central neck). Patients with local recurrences were usually, but not always, operated on; whether this represented new disease in the opposite thyroid lobe or recurrent disease in the thyroid bed or adjacent lymph nodes was not always clear. For the sake of analyses, however, they are considered local recurrences. The overall local recurrence rate of 4% is

Table 6. Local recurrence of differentiated thyroid carcinoma as a cause of primary treatment failure in patients with thyroid cancer seen before 1961 who underwent curative operation and had a minimum of 15 years of follow-up.

		Local recurrence		Cured by retreatment of recurrence	
Risk group	No. of patients	No.	%	No.	%
High risk (older follicular)	83	3	4	1	33
Intermediate risk (older papillary)	133	12	9	3	25
Low risk (all young patients)	384	9	2	6	67
Total	600	24	4	10	42

Table 7. Prognosis related to lymph node metastases in 331 patients with thyroid cancer who underwent curative operation with neck dissection between 1941 and 1960.

	No node metastases			1-10 node metastases			> 10 node metastases		
	No. of patients	Deaths		No. of patients	Deaths		No. of patients	Deaths	
		No.	%		No.	%		No.	%
Intrathyroid cancer	131	17	13	91	6	7	11	0	0
Extrathyroid cancer	44	22	50	44	10	23	10	0	0

Table 8. Relationship of number of lymph node metastases and age in 331 patients with thyroid cancer who underwent curative operation with neck dissections between 1941 and 1960.

Sex	Lymph node metastases	Age (years)		
		< 40	40-50	> 50
Men	None	24	26	50
	1-10	63	26	11
	> 10	86	14	0
Women	None	43	22	35
	1-10	69	12	20
	> 10	78	22	0

similar to that reported by Tollefsen et al. [15], but this recurrence rate is considerably less in the young age group. Only 3 of 384 low-risk young patients eventually died of disease after local recurrence (0.8%). Thus, the operation performed at the Lahey Clinic has been very successful in the vast majority of patients and especially so in the low-risk group.

Neck Dissection

In keeping with this trend toward conservative surgical therapy, indications for neck dissection also changed during the 40 years of our study. Between 1951 and 1960, 47% of all patients had a neck dissection and more than 90% of these were formal radical neck dissections. Between 1961 and 1970 only 38% of patients had any standardized lymph node resection, and only 43% of these were radical neck dissections; 41% were limited resections of lymph nodes about the thyroid gland performed through the collar incision. We have not performed any radical neck dissections since 1970, and now limit ourselves to modified or limited dissections in differentiated thyroid carcinoma.

Lymph Node Metastases

There has always been confusion about the influence of lymph node metastases on survival of differentiated thyroid carcinoma. In our series it was found that lymph node metastases not only failed to worsen prognosis but also, strangely enough, were associated with a better prognosis (Table 7). In patients undergoing routine neck dissection between the years 1941 and 1960, the greater the number of lymph node metastases, the better the prognosis for resectable tumors that either were confined within the thyroid gland or had extended directly to the extrathyroidal tissues of the neck. However, examination of this unusual relationship shows that it is a function of age. As shown in Table 8, not a single patient with more than 10 metastatic lymph nodes

Table 9. Later node metastases of differentiated thyroid carcinoma as a cause of primary treatment failure in patients with thyroid cancer seen before 1961 who underwent curative operation and had a minimum of 15 years of follow-up.

Risk group	No. of patients	Recurrent node metastases		Cases cured by retreatment of node metastases	
		No.	%	No.	%
High risk (older follicular)	83	3	4	1	33
Intermediate risk (older papillary)	133	12	9	6	50
Low risk (all young patients)	384	17	4	15	88
Total	600	32	5	22	69

was over 50 years of age, and 86% of men and 78% of women with more than 10 node metastases were less than 40 years of age. The overriding influence of age in the biologic behavior of thyroid cancer is again demonstrated.

Lymph node metastases are a cause of failure of therapy in a small proportion of patients as shown in Table 9. In recent years with more conservative therapy of lymph nodes, we have found node metastases to be the primary cause of failure in a slightly larger number of low-risk patients, but, since nodal metastases have no adverse influence on survival, the cure rate has continued to improve in successive decades. Fifteen of 17 low-risk patients who were initial treatment failures as a result of cervical node metastases were still cured of disease by use of a modified or limited neck dissection. Older patients who were initial treatment failures because of cervical lymph node metastases had a far worse prognosis, yet nearly 50% (7 of 15) were cured by further therapy, usually a neck dissection.

Death Rate

Table 10 presents an overview of the results of surgical therapy of differentiated thyroid carcinoma by the decade in which the primary surgery was performed at the Lahey Clinic. In the 20 years before 1951, the death rate in low-risk younger patients was 7%. Since 1951, however, only 2 of 292 patients have died. Even though patients operated on in the 1960's had an average follow-up period of only 10 years rather than a minimum of 15 years, it can be projected that no more than an additional 1 or 2 deaths will occur [8] in these 292 patients for a maximum death rate of less than 1.5%. In the high-risk patients it can be predicted that the mortality rate of patients operated on in the 1960's will eventually become 10% to 15%, and the recurrence rate will range between 15% and 20%. These improvements in later years are highly significant statistically.

Change in Pathologic Types

Another change that has occurred in recent years is a marked reduction in incidence of undifferentiated forms of thyroid carcinoma from over 20% of all cases before 1951 to only 8% of cases seen in the 1960's. Currently, undifferentiated forms of thyroid carcinoma constitute less than 5% of all thyroid carcinomas seen at the Lahey Clinic. Thus, after 2 decades of increasingly conservative surgical therapy of differentiated thyroid carcinoma, fewer patients with undifferentiated disease are being seen.

Occult Disease

Among patients at the Lahey Clinic who had bilateral subtotal thyroidectomy for Graves's disease, 6% were found to have an associated unanticipated occult microinvasive papillary thyroid cancer. This 6% incidence of disease was discovered on histologic inspection of only a few sections of the thyroid specimen and corresponds to other reports in the American literature [1, 17]. The incidence and implication of such microscopic carcinoma have been the object of much debate since the reports of Sampson [6] and Fukunaga and Yatani [18]. In none of our young patients in whom microscopic thyroid cancer was discovered incidentally has a recurrence or death been observed, despite the fact that none underwent reoperation or had treatment directed at the thyroid cancer other than the initial operation for Graves's disease or other benign thyroid condition.

Table 10. Recurrence and death rates in patients who underwent primary surgery for differentiated thyroid cancer at the Lahey clinic.

Time period	Low-risk patients						High-risk patients					
	Incidence		Recurrence*		Death*		Incidence		Recurrence†		Death‡	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1931–1950	186	63	33	18	13	7	111	37	38	34	30	27
1951–1960	198	65	9	5	2	1	105	35	33	31	28	27
1961–1970§	94	58	6	6	0		67	42	8	12	5	8

Modified from Cady, B., Sedgwick, C.E., Meissner, W.A., Wool, M.S., Salzman, F.A., Werber, J.: Risk factor analysis in differentiated thyroid cancer. Cancer *43*:810, 1979 [9]

*$P < 0.001$.

†$P = 0.008$.

‡$P = 0.003$.

§Follow-up averages only 10 years.

Discussion

Occult Thyroid Carcinoma

In any discussion about surgical operations for differentiated thyroid carcinoma there must first be perspective about the occult microscopic papillary carcinomas that are seen so frequently [19]. The criterion for the diagnosis of occult cancer suggested by Woolner et al. [20] of lesions less than 1.5 cm in diameter has been accepted by many authors. However, in some studies [19] nearly all (84%) lesions discovered incidentally were less than 5 mm in diameter, and only 2% were more than 1.5 cm in diameter. The incidence of such occult carcinomas ranges as high as 28% of all thyroid glands inspected at autopsy in patients without known thyroid disease and is a function of the number of pathologic sections taken [19] and the geographic area [18]. In thyroid glands with clinical carcinoma already present, the incidence of other foci of microscopic papillary carcinomas has been reported to range as high as 58% [21], many with lymph node metastases.

No relationship seems to exist between countries with a high incidence of occult carcinoma of the thyroid found at autopsy and death rates or incidence rates of clinically detectable thyroid cancer [18]. Radiation to the thyroid area in children or even adults may increase the incidence of these microscopic cancers [19], but no published data suggest that the microcarcinomas associated with radiation behave biologically differently from lesions not associated with radiation.

Tollefsen and others [22, 23] feared that unresected papillary carcinoma left in patients over a long period would lead to undifferentiated carcinoma and, for that reason, advocated aggressive resection to eliminate all known foci of papillary carcinoma. However, the incidence of undifferentiated thyroid carcinoma has been decreasing sharply in our patients [8]. In addition, only 2 of 99 deaths from thyroid cancer in our series could be attributed to carcinoma that progressed from a differentiated to an undifferentiated form [8] despite careful pathologic review of all material including autopsies. Although many undifferentiated carcinomas may be accompanied by microscopic papillary carcinoma [24], it is by no means clear that the actual conversion from papillary forms to undifferentiated cancers occurs often enough to be of clinical concern.

In the Mayo Clinic experience with occult papillary carcinoma, not a single patient died of disease whether lymph node metastases were present or not [20]. At the Lahey Clinic we have also not recorded a death from disease in a patient in the low-risk age group with occult differentiated thyroid carcinoma. Thus, when confronted with a patient diagnosed as having thyroid carcinoma the surgeon must first ask how large the lesion is and how it was discovered. If the cancer is less than 1.5 cm in diameter, especially if it is less than 1.0 cm in diameter, is not evident clinically, and occurs in a young patient, the surgeon can assume that conservative therapy will suffice for cure, regardless of the presence of lymph node metastases [4] or whether lymph node metastases appear later [16]. This conservative therapy may consist of nodule excision only but should preferably be thyroid lobectomy; total thyroidectomy or even bilateral subtotal thyroidectomy seems excessive treatment and is accompanied by a higher chance of complications. Several surgeons advocate routine total thyroidectomy for such lesions [14, 25, 26], even when found incidentally, but such recommendations seem unreasonable considering the benign clinical behavior of these cancers.

These recommendations apply whether or not occult cancer occurs in the aftermath of childhood radiation. Favus et al. [5] screened a large number of adult patients who had had radiation during childhood and found palpable nodular abnormalities in 17% and thyroid scan abnormalities in an additional 11%. Of patients with abnormalities so discovered and operated on, 33% had thyroid carcinoma and, of these, only 11 of 60 (18%) had cancers larger than 1.5 cm in diameter. Nearly 1/2 of the cancers (47%) were not located in the nodule or scan abnormality that led to surgery but were found elsewhere in the thyroid specimen.

Even in screening programs for patients previously having radiation in childhood, almost 1/2 of the cancers discovered were clinically occult and 82% were less than 1.5 cm in diameter. These lesions would fulfill the criteria of Woolner et al. [20] for occult cancer and could be expected to be cured with conservative therapy.

If pathology reports returned after resection for Graves's disease, adenoma, thyroiditis, or multinodular goiter demonstrate clinically unsuspected "occult" cancer in young patients, reoperation need not be performed to provide the maximum chance of cure since adequate surgical therapy already has been performed.

When patients irradiated in childhood are followed up to detect thyroid cancer, thyroid scans should be avoided since they will pick up "cold" areas that might lead to surgical exploration and the discovery of incidental occult carcinoma. Such vigorous pursuit of thyroid cancer will create a population of cancer victims from normal subjects, in the absence of any threat to life. Physical examination of the thyroid gland at yearly intervals will suffice to detect clinical cancer that presents as a solitary nodule and will reduce iatrogenic problems. When

such patients are operated on for solitary or prominent nodules, a lobectomy, either total or near total, on the side of the nodule should be sufficient, since any other centers of multifocal disease will be very small and innocuous. Such clinical cancers should be handled according to the basic risk group.

Low-Risk Thyroid Carcinoma

Clinically detectable thyroid cancers are all larger than 1.0 cm in diameter and usually larger than 1.5 cm. By reference to the basic risk group described in Table 3, the surgeon may approach the problem with perspective as to prognosis and to the extent of operation required. Young patients (men less than 40 years of age and women less than 50 years) have an excellent prognosis, rarely, if ever, dying of disease following a limited resection of thyroid tissue around the tumor, generally a lobectomy [15]. If the primary cancer is large, invades extraglandular structures, or is follicular, contralateral subtotal thyroidectomy with precise attention to preservation of the parathyroid glands provides future opportunities for the use of radioactive iodine but does not by itself add to the curability of the cancer by surgery. In low-risk patients, less than 5% eventually need radioactive iodine for therapy of metastatic disease, unresectable lymph nodes, or local recurrences, since most patients with node involvement or local recurrence should first be treated by reoperation. Total thyroidectomy, while providing the theoretical benefits of eliminating multifocal microscopic cancer, is not necessary and increases substantially the complications of operation. Tollefsen et al. [15], reporting data from Memorial Hospital in New York, concur in this conservative approach.

The surgical treatment of lymph node metastases also must be based on an understanding of the biology. Considerable data indicate that the presence of lymph node metastases has no adverse effect on survival [24] or may even be associated with improved prognosis [8, 27, 28]. The entity of "lateral aberrant thyroid" described decades ago, while currently recognized as representing metastastic carcinoma of the thyroid [29], is noteworthy for its benign behavior [4]. In our experience, lymph node resections have been reduced in scope considerably over the decades without reducing the survival rate of low-risk patients. It is virtually impossible to resect all lymph nodes potentially involved with metastastic thyroid carcinoma because of the rich lymphatic pathways and the frequent involvement of mediastinal lymph nodes. Yet, failure to resect such nodes does not contribute to a worsened prognosis. Since 1970, we have not performed radical neck dissections; node resections consist of limited or modified neck dissection and many fewer neck dissections are performed.

Metastatic lymph nodes are a slightly more common cause of failure now than in earlier decades, yet overall survival and prognosis have improved. Thus, node resections should generally be conservative. If metastatic lymph nodes are palpable preoperatively, a modified node resection is performed after extending the collar incision up to the mastoid process; the spinal accessory nerve, submandibular space, jugular vein, and sternocleidomastoid muscle are preserved if possible. If lymph node metastases are not palpable preoperatively but are felt at the time of thyroidectomy, a limited node resection is performed through the thyroidectomy incision without extension, removing as much nodal tissue as possible, including that in the thoracic inlet. If no obviously involved lymph nodes are palpated at operation, no deliberate node resections are performed. In our series [9], 25% of patients in the low-risk group presented with clinically palpable lymph node metastases, frequently without a palpable primary carcinoma. After node dissections, 98% of these patients with macroscopic node metastases survived a minimum of 15 years without recurrence of disease. Therefore, lymph node metastases in low-risk patients do not carry the prognostic implications of node metastases in any other human cancer, and they may be treated conservatively without impairment of the excellent prognosis.

High-Risk Thyroid Carcinoma

In high-risk patients, the threat of recurrence and death is considerable, treatment of recurrences is less successful, and the basic surgical approach is justifiably more vigorous. Radioactive iodine is used more frequently, so contralateral thyroid lobectomy is more commonly required. Such cancers are larger, often involve adjacent structures, and generally are more aggressive. Total lobectomy of the ipsilateral thyroid should be performed. There is no evidence of an advantage of total thyroidectomy, and the advantages of preserving the posterior capsule of the contralateral side to reduce nerve injury and hypoparathyroidism have been described previously [30, 31]. The contralateral thyroid lobe should be removed subtotally. Local recurrence in high-risk papillary carcinoma in our series was 9% (Table 6), indicating the need to be more thorough surgically at the first operation in these patients than in low-risk patients.

Patients in the older, high-risk group have lymph node metastases much less commonly, and only 9% of such patients actually present with clinically palpable cervical lymph nodes. Therefore, they require

neck dissections less often but, when indicated, neck dissections should be more thorough, since the disease is far more threatening than in the younger patient [9]. Modified neck dissection should be the standard surgical approach for node metastases discovered at operation, but the jugular vein and sternocleidomastoid muscle should be sacrificed more often to ensure adequacy of node resection. If such patients have palpable or bulky mediastinal node metastases, we have performed mediastinotomy and dissection of all palpable and resectable disease.

In rare instances extension of the primary cancer or local recurrence requires tracheal resection or laryngectomy [32, 33] in high-risk patients, but these radical procedures are useful only in highly selected situations. Generally, these procedures are reserved for recurrent cancer, since radioactive iodine or external beam radiotherapy may control extensive local disease without sacrificing the larynx.

Etiology of Thyroid Carcinoma

The peculiarities of differentiated thyroid carcinoma have led me to speculate that thyroid carcinogenesis is at least a 2-step process. The first step, whether precipitated by external irradiation or other, as yet unknown, causes, produces the microscopic foci of carcinoma that are found so frequently and seem to be completely benign processes, since no geographic correlation exists between their incidence and the incidence or death rate of clinical thyroid carcinoma. In the second step, which occurs in an occasional patient, the occult microscopic foci of cancer develop progressive growth and the capacity to metastasize. The biologic behavior of the clinical cancer that results from this second step is dependent on age and other factors as yet not understood. In younger patients a relatively innocuous cancer develops, whereas in older patients, particularly in women, the resultant clinical cancer is fairly aggressive in biologic behavior. Yet another type of neoplasm is seen in the giant cell undifferentiated cancer that is almost universally fatal, yet arises from the same follicular cell, and is accompanied by a high incidence of associated microscopic papillary thyroid cancer. This probably results from another distinctive carcinogenic step after the formation of microscopic differentiated lesions, of a nature that is distinct from the process seen in differentiated cancers.

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Invited Commentary

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Papillary carcinoma of the thyroid is a tumor that frequently has regional lymph node metastases. However, it has a better prognosis than almost any other human malignant tumor. Due to the discrepancy between early dissemination of the carcinoma and the good prognosis, there are considerable differences in opinion about treatment. Cady recommends rather conservative operations for the treatment of papillary and follicular carcinomas. His recommendations are based on a large follow-up study from the Lahey Clinic.

I have performed the same kind of study on all cases of thyroid cancer diagnosed in Finland during a 5-year period [1, 2]. The results were similar in many respects. Cady regards age as the most important determinant of risk in differentiated carcinoma (papillary and follicular), even more important than the histologic type. I can agree with him only partly in this respect. If we take all thyroid carcinomas, the correlation of age with prognosis is clear. In my series the relative 10-year survival rates for patients under and over 50 years of age were 72% and 42% [2]. A similar correlation with age was seen within each histologic type (papillary, follicular, and anaplastic carcinoma) but the differences were smaller than in the whole series. The relative 10-year survival rates for patients under and over 50 years were 90% and 69% for papillary carcinoma, and 49% and 36% for follicular carcinoma, including inoperable cases.

In papillary carcinoma the differences in survival rate seem mainly to be due to the fact that age is linked to the extent of disease; old patients have more extensive primary tumors than young patients. In my series the mean age of patients with extraglandular tumors was 53 years, but the mean age of patients with intraglandular or occult tumors was 42 years [1]. However, as Cady reported, within different degrees of extension of the primary tumor, age seems to correlate with prognosis. The mean age of patients with extraglandular tumors was 46 years for those who survived and 64 years for those who died from cancer [3]. So, in papillary carcinoma age seems to be an important determinant of risk.

In follicular carcinoma the different survival rates