# Thyroid Cancer: The Case for Total Thyroidectomy

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Abstract—Since there are no prospective studies concerning the treatment of thyroid cancer, there continues to be a considerable disagreement about the 'best' or most appropriate form of surgical treatment for patients with papillary or follicular thyroid cancer. Some surgeons recommend selective treatment depending upon the type of thyroid tumor and stage of the disease. Some advocate thyroid lobectomy and isthmusectomy, some near total thyroidectomy, and some total thyroidectomy for patients with papillary and follicular thyroid cancer.

Total thyroidectomy for thyroid cancer would be the treatment of choice for virtually all patients with thyroid cancers if it could be done without complications. We therefore reviewed 160 consecutive patients who had total thyroidectomy for suspected or proven thyroid cancer to determine the complication rate of total thyroidectomy. One hundred and three patients had primary operations, 57 had reoperations with completion of total thyroidectomy and 124 had thyroid cancer. Serious complications (i.e. vocal cord paralysis or hypoparathyroidism) included two cases of transient bilateral recurrent nerve palsy, two patients with presumed transient unilateral vocal cord paralysis, three recurrent laryngeal nerves that were purposely sacrificed because of invasion of the nerve, and one case of permanent hypoparathyroidism. Two other patients developed postoperative wound infections. Only one of the permanent complications, the case of permanent hypoparathyroidism, could have been avoided by a lesser procedure.

The experienced surgeon can perform a total thyroidectomy with minimal morbidity, and this procedure has certain theoretical and practical advantages. It should not be done, however, if it will result in a significant complication rate and, in selected patients, it may be preferable to leave a small amount of thyroid tissue to protect the blood supply to the parathyroid glands or recurrent laryngeal nerve.

#### INTRODUCTION

THERE continues to be considerably controversy concerning how much thyroid tissue should be removed in patients with thyroid cancer. Some surgeons such as Cady [1], Carcangiu [2], Crile [3], Farrar [4], Schroeder [5], Wanebo [6] and their colleagues advocate thyroid lobectomy including isthmusectomy; some such as Beahrs [7] and Buckwalter and Thomas [8], recommend near total thyroidectomy; and others such as Attie [9], Beierwaltes [10], Clark [11], Harness and Thompson [12], Heitz [13], Lennquist [14], Massin [15], Samaan [16], Schlumberger [17] and their associates advocate total thyroidectomy

The arguments in favor of lobectomy are that this

operation has a lower morbidity (only one recurrent nerve at risk and only two parathyroid glands at risk) and the prognosis following this operation is comparable in some studies to that occurring after more aggressive operations. The remaining thyroid tissue can subsequently be ablated by radioactive iodine. The arguments for near total thyroidectomy are that it has a greater chance of removing all thyroid tumor from within the thyroid gland, but it is less likely than total thyroidectomy to result in complications. A smaller dose of radioactive iodine would subsequently be required, after near total thyroidectomy than after lobectomy, to ablate the remnant thyroid tissue. Most supporters of the above two approaches admit that in patients with bilateral tumors, metastatic disease or recurrent cancer total thyroidectomy is often necessary. Total thyroidectomy has the advantage of removing all thyroid tissue and thus intrathyroidal tumor, and total thyroidectomy also allows the use of radio-

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active iodine for scanning and ablating possible residual local tumor or metastases.

There is little question that lobectomy exposes the patient to less risk of surgically induced complications including injury to the recurrent laryngeal nerves or hypoparathyroidism than does total thyroidectomy. There is also nearly unanimous agreement that any thyroid operation less than lobectomy, except for lesions in the isthmus, is contraindicated because of a higher recurrence and death rate, and because it makes reoperation more difficult [18]. Total thyroidectomy has certain theoretical and practical advantages in contrast to less extensive operations. Several major questions, however, remain: (1) can a total thyroidectomy be done? (2) can it be done safely? (3) is it worth doing? that is, does it lower the recurrence rate and/or improve survival?

This report concerns the senior surgeon's experience with 160 consecutive patients having total thyroidectomy at the University of California Medical Center and the Veterans Administration Medical Center from January 1977 to January 1987. The age of the patients ranged from 21 to 78 years. There were 93 women (mean age 41 years) and 67 men (mean age 44 years). Fifty-seven of these operations are completion total thyroidectomy after one or more previous operations and 124 patients had thyroid cancer. Twenty-four patients had concomitant modified radical neck dissections and 16 had the regionally involved nodes removed. Twelve of these patients also had coexistent parathyroid tumors removed and two patients had a median sternotomy.

Virtually all of the patients who had total thyroidectomy for benign thyroid nodules had a history of receiving low-dose therapeutic radiation. All thyroid cancers were considered papillary if there were any papillary elements as designated by the American Thyroid Association [19]. Follicular thyroid cancers therefore had only follicular elements. Several patients had more than one tumor (one papillary and separate follicular in opposite lobe, one papillary and mucin positive adenocarcinoma, one Hurthle cell and papillary carcinoma, and one papillary carcinoma and C cell hyperplasia). Total thyroidectomy is defined as the surgeon's attempt to perform an extra-capular removal of the entire thyroid gland, preserving the parathyroid glands, recurrent laryngeal nerves and external laryngeal nerves. The technique used is comparable with that previously reported [20-22] and operating telescopes (2.5 power magnification with wide angle viewing by Designs for Vision) were used by the operating surgeon. Briefly, the technique of total thyroidectomy consists of ligating the branches of the inferior thyroid artery proximally, and by carefully dissecting the parathyroid glands from the

thyroid gland. As the tissues are dissected from the thyroid gland, the recurrent laryngeal nerve is identified low in the neck, or high in the neck at the level of the ligament of Berry just before it enters the cricothyroid muscle. The nerve is usually not initially identified on the lateral side of the thyroid gland because this technique makes devascularization of the parathyroid glands more likely. Only small amounts of tissue are divided at any one time so that the recurrent nerves are not damaged. Occasionally it is necessary to transplant a parathyroid gland. This usually occurs when the parathyroid glands are situated anteriorly on the thyroid gland and therefore must be swept from the thyroid gland on a long vascular pedicle (Figs 1A and 1B). The nature of the presumed normal parathyroid gland is confirmed by biopsy and frozen section examination before transplantation to avoid mistakenly transplanting thyroid cancer.

In a previous study we have reported that total thyroidectomy results in no iodine uptake, above background levels, in 26% of our patients, whereas 74% of our patients had some uptake (generally less than 1%) either in the thyroid bed or elsewhere [11]. Serum calcium levels were measured on the evening of thyroidectomy and on the subsequent two mornings prior to discharge in patients who remained in the hospital more than one day postoperatively. In patients who were discharged on the first postoperative day, the serum calcium level was determined as an outpatient. A patient was judged to have hypoparathyroidism if he required both calcium and vitamin D to sustain a normal serum calcium level. Examination of the vocal cords was only done if the patient was noted to have, or volunteered to have, a change in voice or difficulty swallowing.

# **RESULTS**

During a 10 year period, 124 patients had a total thyroidectomy for thyroid cancer (papillary 95, follicular 15, medullary 9, Hurthle cell 4, undifferentiated 1) (Table 1), and 36 patients had a total thyroidectomy for benign thyroid disorders, almost all having a history of receiving low dose therapeutic radiation.

Complications occurred in 10 patients (5.6%) and permanent complications in three patients (1.9%). As we have reported previously [11], two patients in the first 82 consecutive patients treated by total thyroidectomy had transient bilateral recurrent laryngeal nerve palsy and one patient had permanent hypoparathyroidism. The patient with hypoparathyroidism required bilateral modified radical neck dissections for extensive lymph node metastases. No other patients took calcium for more than 6 weeks. In the subsequent 66 patients we have had two presumed unilateral recurrent nerve

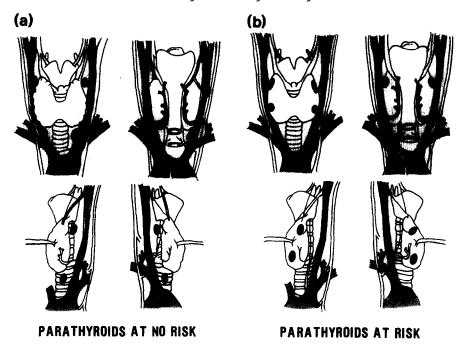


Fig. 1a and b. Illustration of thyroid and parathyroid glands. When parathyroid glands are situated anteriorly on the thyroid gland (Fig. 1a), there is more risk of injury because they can be devascularized when dissecting them free from the thyroid. When the parathyroid glands are situated off the thyroid gland (Fig. 1b) it is much easier to preserve them.

Table 1. Histology of malignant thyroid neoplasms

Type	No.	(Percentage)
Papillary*	95	(77)
Follicular	15	(12)
Medullary	9	(7)
Hurthle	4	(3)
Undifferentiated	1	(1)
Total	124	(100)

<sup>\*</sup>Several patients had more than one malignant tumor type and 36 patients had benign thyroid neoplasms.

palsies and three permanent unilateral nerve palsies. The two patients with probable transient palsies of the recurrent laryngeal nerve were hoarse for approx. 1 month and their normal voices returned spontaneously. In three patients with a permanent palsy, the left recurrent largyngeal nerve was purposely sacrificed. One occurred in a 32 year old man from Germany who had an invasive left sided papillary thyroid cancer with regional node metastases. He had a total thyroidectomy and left modified neck dissection and the left recurrent laryngeal nerve was preserved by fracturing the tumor from the nerve. At the completion of the operation, however, the nerve was encased in tumor and it was therefore purposely sacrificed (Fig. 2). A primary nerve anastomosis was performed, but at 6 months his nerve was not functioning. The second patient was a 33 year old woman with a papillary thyroid carcinoma that invaded the esophagus and recurrent nerve (Fig. 3). She also had tumor fractured

off the recurrent laryngeal nerve but because all the tumor could not be removed the nerve was sacrificed. The third patient was a 69 year old women with an invasive papillary thyroid cancer that invaded the trachea and the left recurrent laryngeal nerve. She was treated by a total thyroid-ectomy, a left modified radical neck dissection, stripping of tumor from the esophagus and left recurrent laryngeal nerve as well as resection of the left posterior wall of the trachea. Because all tumor could not be removed from the left recurrent laryngeal nerve it was sacrificed.

Other complications included streptococcal wound infections in two patients; one in a 33 year old woman after a total thyroidectomy for Hashimoto's thyroiditis and papillary thyroid cancer, and one after a completion total thyroidectomy in a 62 year old man who had two previous thyroidectomies at another hospital. He had also previously received 100 millicuries of radioactive iodine for a recurrent follicular thyroid carcinoma. This patient required a median sternotomy for removal of his invasive recurrent follicular carcinoma that extended into the mediastinum and also involved the regional cervical nodes (Fig. 4). There were no cases of postoperative bleeding requiring reoperation or other complications.

The duration of hospitalization is illustrated in Fig. 5. All but 12 patients (7.5%) were discharged within 3 days of operation and 120 patients (75%) were discharged within 2 days. None of these patients required rehospitalization.

The reasons why the 12 patients required hospitalization for more than 3 days after total thyroidec-

tomy are listed in Table 2. Five patients had modified radical neck dissections as well as total thyroidectomy and two patients had median sternotomy as well as a regional or modified neck dissection. Bilateral transient vocal cord paralysis occurred in two patients and resolved spontaneously within 5 days [11]. One patient had papillary thyroid cancer, Hashimoto's thyroiditis and involvement of mediastinal lymph nodes, and one patient with a rapidly enlarging (approx. 200 g) goiter was diagnosed as having an undifferentiated thyroid carcinoma by frozen section examination of a lymph node. On permanent section, he was found to have only thyroiditis. Four patients were hospitalized for more than 3 days for initiation of chemotherapy or external radiation therapy and one patient remained hospitalized for further evaluation of amyloidosis.

Table 2. Reasons for prolonged hospitalization in 12 patients (total thyroidectomy)

Associated procedures or conditions	No.	(Percentage)
Modified radical neck		
dissection (MRND)	3	(25)
MRND plus median		, ,
sternotomy	2	(17)
Bilateral transient nerve		
palsy	2	(17)
Further medical treatment		
of tumor	4	(33)
Further evaluation of		
amyloidosis	1	(8)
Total	12	(100)

## **DISCUSSION**

Some surgeons argue against total thyroidectomy because they feel that the risk of this operation is too high to warrant this procedure, and the prognosis in some retrospective studies is no better after total thyroidectomy than after lesser procedures [1, 4-6]. Total thyroidectomy obviously should not be done in a patient who is mentally deficient and will not take thyroid hormone and should not be done by a surgeon not trained in this procedure. It is also unnecessary for papillary thyroid cancers less than 1.5 cm in size since the prognosis is so good [23, 24]. Total thyroidectomy should also not be done in patients when it will make them hypoparathyroid, because the parathyroid glands are situated anteriorly on the thyroid gland. In these patients a near total thyroidectomy is preferable and a small amount of thyroid tissue is left to protect the parathyroid glands, or the parathyroid glands should be autotransplanted. When a small amount of thyroid tissue is left to protect parathyroid glands this tissue can subsequently be ablated with radioactive iodine.

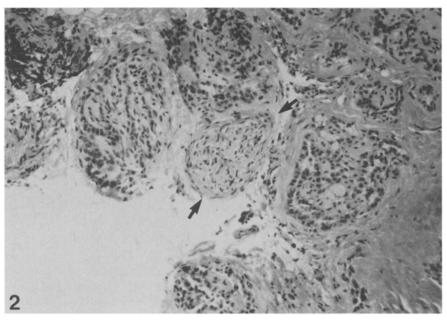
When one plans to autotransplant parathyroid tissue, the presumed normal parathyroid gland always should be biopsied first to make sure one does not transplant metastatic thyroid cancer. Using magnification at the time of thyroidectomy appears to be helpful in avoiding both hypoparathyroidism as well as injury to the recurrent laryngeal nerves.

When should a recurrent laryngeal nerve be purposely sacrificed? In most patients if the vocal cords are functioning normally the recurrent laryngeal nerve can be dissected free from the tumor whereas if the nerve is not functioning, it should be sacrificed. In some patients, however, the nerve is directly invaded and still functioning. Resection appears indicated if in these patients, there is no other evidence of metastatic disease.

This study, as have other studies [9-12, 14], demonstrates that total thyroidectomy can be performed safely with a minimal complication rate. A surgeon does not perform total thyroidectomy unless he can perform this operation with safety because one will not be referred patients if there is an appreciable complication rate. A procedure less than total thyroidectomy in these 160 patients would have avoided only one permanent and possibly four transient complications.

The primary reason some surgeons advocate lesser procedures than total thyroidectomy is because of fear of complications [40]. They justify this approach by stating that most patients do well with less extensive operations. They add that the results in some retrospective studies suggest that the survival rate does not differ when total thyroidectomy is compared to leser procedures [4, 6]. We would agree that most patients (approx. 80%) with papillary and follicular thyroid cancer do well almost regardless of how they are treated, and about 5% do poorly regardless of how they are treated. This leaves about 15% who appear to benefit from total thyroidectomy and subsequent scanning and treatment with radioactive iodine and TSH suppressive therapy [23, 26]. Because most patients do well, large numbers of patients are required to demonstrate significant differences in survival rate in response to treatment [23]. We feel that the lives of approx. 15% of patients with thyroid cancer may be lost because of less than complete treatment.

One might suggest that it is possible to select patients who will benefit from more aggressive treatment. We know that certain factors influence survival in patients with papillary and follicular thyroid cancer including: (1) age of the patient (older patients do worse), (2) sex (men do worse than women) and (3) stage of the tumor (large tumors, invasive tumors, regional node involvement and distant metastases are detrimental to survival). Recent studies also suggest that DNA analysis [27] and adenylate cyclase response to TSH or EGF



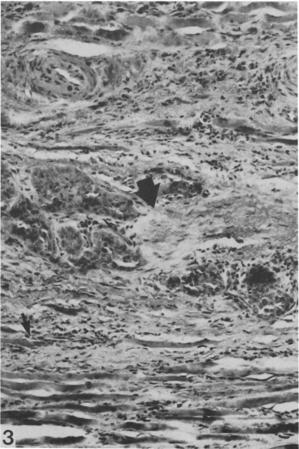


Fig. 2. Photomicrograph demonstrating left recurrent laryngeal nerve (arrow) completely surrounded by papillary thyroid carcinoma (magnification  $200 \times$  — photographed by Timothy Whitney).

Fig. 3. Photomicrograph of invasion of a papillary thyroid carcinoma into the esophageal musculature (small arrow) and left recurrent laryngeal nerve (larger arrow) (magnification 200×—photographed by Timothy Whitney).

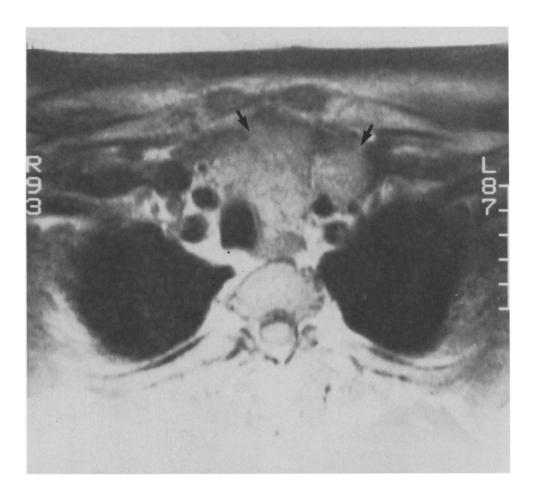


Fig. 4 Magnetic resonance imaging (MRI) scan of a 62 year old man with recurrent follicular thyroid carcinoma with extension substernally despite two previous partial thyroid resections and 100 millicuries of radioactive iodine (arrows delineate anterior extension of tumor).

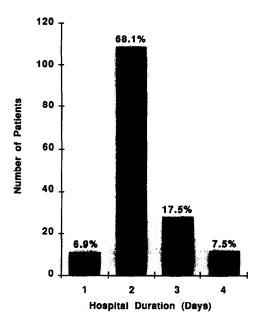


Fig. 5. Duration of hospitalization in patients treated by total thyroidectomy.

binding may be helpful for predicting survival [28, 29]. Perhaps some day we will be able to determine preoperatively who will require total thyroidectomy and who can receive minimal treatment.

What is the rationale for total thyroidectomy? Most patients with differentiated thyroid cancer have at least microscopic involvement of the regional lymph nodes [30]. Most clinicians, however, do not recommend prophylactic node dissection because former studies suggest that despite the presence of microscopic disease in the nodes of 80% of these patients, only 10% of patients develop recurrent disease [31]. Several studies have demonstrated that patients who receive an ablative dose of radioactive iodine after total thyroidectomy have the lowest rate of local recurrence [23] or distant metastases [15, 17]. This is probably because it destroys the micrometastases. Rossi et al. [32] reported that 73% of their patients who received ablative therapy with radioactive iodine appeared to benefit from this procedure. Obviously, one must ablate any residual normal thyroid tissue before one can use radioactive iodine to ablate any residual thyroid cancer. This wastes the radioactive iodine

that might be required later to treat further persistent or recurrent disease. We would agree with the recent conclusion by Schlumberger et al. [17] who reported that 'It is much easier to cure micrometastases (with radioactive iodine) than it is to palliate macronodules. Hence, the aim of the management should be to detect and treat metastases as soon as possible.' By doing a total thyroidectomy one can subsequently administer radioactive iodine to be sure that there are no functioning metastases and treat metastases that are evident by scanning.

Total thyroidectomy also eliminates micro- or macrometastaes in the contralateral thyroid lobe that occurs in 30-87.5% of persons with papillary thyroid carcioma [11, 33-35] and also decreases the risk of recurrent central neck disease [22, 33, 35]. This is important because about half of the patients who develop recurrent differentiated thyroid cancer die of central neck disease [36, 37]. Total thyroidectomy also decreases the small chance of a differentiated thyroid cancer becoming an undifferentiated thyroid cancer, and allows one to use serum thyroglobulin levels to follow patients for recurrent disease. Overall the complication rate of total thyroidectomy when used selectively by surgeons experienced in this procedure [9, 11, 12, 28, 39] compares favorably to lesser operations [4, 6, 24]. In some reports, however, the complication rate of total thyroidectomy is appreciably higher [4, 23, 27, 40].

In conclusion, total thyroidectomy can be done with minimal morbidity by a surgeon trained in this technique. It allows the earliest possible treatment of micrometastases by radioactive iodine and residual microscopic cancer is present in most of these patients. It also appears to be the best operation for obtaining long term survival [15, 23, 28]. Despite these compelling reasons for total thyroidectomy, the main goal in treating patients with thyroid cancer is to do what is best for a specific patient. Thyroid lobectomy with isthmusectomy is an acceptable operation for unilateral papillary and follicular thyroid cancers but lumpectomy and subtotal thyroidectomy are unacceptable forms of treatment with higher recurrence rates and death rates. Total thyroidectomy is the preferred form of treatment when, and only when, it can safely be performed.

### REFERENCES

- 1. Cady B, Rossi R, Silverman M, Wool M. Further evidence of the validity of risk group definition in differentiated thyroid carcinoma. Surgery 1985, 98, 1171-1178.
- Crcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. Papillary carcinoma of the thyroid: a clinicopathologic study of 241 cases treated at the University of Florence, Italy. Cancer 1985, 55, 805-828.
- 3. Crile G Jr, Antunez AR, Esselstyn CB, Hawk WA, Skillern PG. The advantages of subtotal thyroidectomy and suppression of TSH in the primary treatment of papillary carcinoma of the thyroid. *Cancer* 1985, 55, 2691–2697.

- Farrar WB, Cooperman M, James AG. Surgical management of papillary and follicular carcinoma of the thyroid. Ann Surg 1980, 192, 701-704.
- 5. Schroeder DM, Chambors A, France DL. Operative strategy for thyroid cancer: is total thyroidectomy worth the price? *Cancer* 1985, **58**, 2320-2328.
- Wanebo HJ, Andrews W, Kaiser DL. Thyroid cancer: some basic considerations. Am J Surg 1981, 142, 474-479.
- 7. Beahrs OH. Surgical treatment for thyroid cancer. Br J Surg 1984, 71, 976-979.
- 8. Buckwalter JA, Thomas CG Jr. Selection of surgical treatment for well differentiated thyroid carcinomas. *Ann Surg* 1972, **176**, 565-578.
- 9. Attie JM, Moskowitz GS, Marqouleff D, Levy LM. Feasibility of total thyroidectomy in the treatment of thyroid carcinoma: postoperative radioactive iodine evaluation of 140 cases. Am J Surg 1979, 138, 555-562.
- 10. Beierwaltes WH, Nishiyama RH, Thompson NW, Copp JE, Kubo A. Survival time and 'cure' in papillary and follicular thyroid cancer with distant metastasis: statistics following University of Michigan therapy. *J Nucl Med* 1982, **23**, 561-568.
- 11. Clark OH. Total thyroidectomy. The treatment of choice for patients with differentiated thyroid cancer. Ann Surg 1982, 196, 361-370.
- 12. Harness JK, Fung L, Thompson NW, Burney RE, McLeod M. Total thyroidectomy: complications and technique. World J Surg 1986, 10, 781-786.
- 13. Heitz P, Moser H, Staub JJ. Thyroid cancer: a study of 573 thyroid tumors and 161 autopsy cases observed over a 30-year period. Cancer 1976, 37, 2329-2337.
- Lennquist S. Surgical strategy in thyroid carcinoma: a clinical review. Acta Chir Scand 1986, 152, 321–338.
- 15. Massin JP, Savoie JC, Garnier H, Guiraudon G, Leger FA, Bacourt F. Pulmonary metastasis in differentiated thyroid carcinoma: study of 58 cases with implications for the primary tumor treatment. *Cancer* 1984, 53, 982–992.
- 16. Samaan NA, Maheshwari YK, Nader S et al. Impact of therapy for differentiated carcinoma of the thyroid on analysis of 706 cases. J Clin Endocrinol Metab 1983, 56, 1131-1138.
- 17. Schlumberger M, Tubiana M, DeVathaire F et al. Long term results of treatment of 283 patients with lung and bone metastases from differentiated thyroid carcinomas. J Clin Endocrinol Metab 1986, 63, 960-970.
- 18. France CJ, Kouchy C, Hergt K, Brines DA. Relationship of histology to prognosis in thyroid carcinoma. *Arch Surg* 1963, **8**, 588-592.
- 19. Beierwaltes W, DeGroot LJ, Feind CR, Kriss JP, Meissner WA, Werner SC. Classification of thyroid disease: report of the committee on nomenclature of the American Thyroid Association. *J Clin Endocrinol Metab* 1969, **28**, 860-862.
- 20. Attie JN, Khafif RA. Preservation of parathyroid glands during total thyroidectomy. Improved technique utilizing microsurgery. Am J Surg 1975, 130, 399-403.
- 21. Perzik SL. The place of total thyroidectomy in the management of 909 patients with thyroid disease. Am J Surg 1976, 132, 480-483.
- 22. Thompson NW, Nishiyama RH, Harness JK. Thyroid carcinoma: current controversies. Curr Probl Surg 1978, 15, 1-67.
- 23. Mazzaferri EL, Young RL. Papillary thyroid carcinoma: a ten year follow-up report of the impact of therapy in 576 patients. Am J Med 1981, 70, 511-518.
- 24. McConachey WM, Hay ID, Wollner LB, van Heerden JA, Taylor WF. Papillary thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy and outcome. *Mayo Clin Proc* 1986, **61**, 978–996.
- 25. Wells SA Jr, Ross AJ III, Dale JK, Gray RS. Transplantation of the parathyroid glands: current status. Surg Clin North Am 1979, 59, 167-177.
- Clark OH. TSH suppression in the management of thyroid nodules and thyroid cancers. World J Surg 1981, 5, 39.
- 27. Cohn K, Backdahl M, Forslund G et al. Prognostic value of nuclear DNA content in papillary thyroid carcinoma. World J Surg 1984, 8, 474-480.
- 28. Duh QY, Gum ET, Gerend PL, Raper SE, Clark OH. Epidermal growth factor receptors in normal and neoplastic thyroid tissue. Surgery 1985, 90, 1000-1006.
- Siperstein A, Zeng QH, Levin KE, Clark OH, Adenylate cyclase activity as a predictor of thyroid tumor aggressiveness, International Association of Endocrine Surgeons Meeting, Abstract C<sub>2</sub>6, 1987.
- 30. Noguchi S. Endocrine surgery issue. Surg Clin N Am 1987, 67, 251-261.
- 31. Hutter RVP, Frazell EL, Foote FW Jr. Elective radical neck dissection: an assessment of its uses in the management of papillary thyroid cancer. Cancer 1970, 20, 87.
- 32. Rossi RL, Cady B, Silverman ML, Wool MS, Horner TA. Current results of conservative surgery for differentiated thyroid carcinoma. World J Surg 1986, 10, 612-622.
- 33. Clark OH. Thyroid nodules and thyroid cancer. In Clark OH, ed.: Endocrine Surgery of the Thyroid and Parathyroid Glands. St. Louis, C. V. Mosby, 1985.
- 34. Hirabayashi RN, Lindsey S. Carcinoma of the thyroid gland: a statistical study of 390 patients. J Clin Endocrinol Metab 1961, 21, 1596-1610.
- 35. Russell WO, Ibanez ML, Clark RL, White EC. Thyroid carcinoma: classification, intraglandular dissemination, and clinicopathological study based upon whole organ

- sections of 80 glands. Cancer 1963, 11, 1425-1460.
- 36. Mazzaferri EL, Young RL, Oertel JE et al. Papillary thyroid carcinoma: the impact of therapy in 576 patients. Medicine 1977, 56, 176-196.
- 37. Silverberg SG, Hutter RVP, Foote FW Jr. Fatal carcinoma of the thyroid: histology,
- metastases, and causes of death. Cancer 1970, 25, 792–802.

  38. Jacobs JK, Aland JW Jr, Ballinger JF. Total thyroidectomy: a review of 213 patients. Ann Surg 1983, 197, 542–549.
- 39. Lennquist S. In: Endocrine Surgery issue. Surg Clin Am 1987, 67, 213-232.
- 40. Foster RS Jr. Morbidity and mortality after thyroidectomy. Surg Gynecol Obstet 1978, 146,