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EDITORIAL – ENDOCRINE TUMORS

American Joint Committee on Cancer: Endocrine Surgery

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Changes in the 8th edition of the American Joint Committee on Cancer Staging Manual represent a departure from previous editions. The charge of the new committees was to identify key prognostic indicators and incorporate these factors into the staging schemata. As a result, the 8th edition manual represents a stronger and more clinically relevant staging and sets a backdrop for comprehensive, personalized, precision medicine. This version creates a lattice for future expansions while maintaining traditional parameters of anatomic extent of disease. The hours of discussion, intense analysis to resolve controversies, data-seeking methods, and expertise cannot be quantified. We are hopeful that this paradigm will prescribe better care for cancer patients.

The 8th edition has made specific advances forward with respect to endocrine diseases. Endocrine tumors are represented together in a distinct endocrine section, which is different from previous clustering based on anatomic region. The endocrine unit encompasses three categorical disease sites—thyroid, parathyroid, and adrenal. Within these three categories, there has been molecular individualization and precision by cell origin and behavior. Medullary thyroid carcinoma (MTC) is now a stand-alone chapter, separate from well-differentiated or anaplastic thyroid tumors. Neuroendocrine adrenal tumors (which also include paragangliomas) are now included in a stand-alone chapter distinct from adrenal cortical tumors. A parathyroid carcinoma chapter has been added and includes atypical parathyroid neoplasms (Tis).

Clinicians will recognize several obvious prognostic factor changes, including the age cutoff for well-differentiated thyroid cancer staging being increased from 45 to 55 years. In addition, there has been clarification that minor extrathyroidal extension does not affect T category or stage, and gross extrathyroidal extension has been assigned specific designated categories depending on whether the invasion is into strap muscles or into surrounding organs. Regional lymph node classification is more anatomically clear with regard to location relative to midline. All mid-nodal compartments, including paratracheal and anterior superior mediastinum, are central and are categorized together, separate from lateral neck disease present in a non-midline location. The declaration of the absence of regional metastasis has become more precise. The categories now communicate cytologic confirmation of the absence of locoregional nodal involvement from clinical suggestion of no nodal disease. While analysis of molecular mutation status is being increasingly utilized when information is available, genetic data were not included because they are not routinely recommended for initial risk stratification. The staging of adrenal cortical carcinoma is now congruent to reflect level I data of the European ACC Network, a robust international community. T4 disease incorporates invasion into surrounding organs or large vessels, and stage IV disease is reserved for any tumor with distant metastases.

For the first time, registry variables now actively encourage the collection of preoperative tumor markers specific for endocrine tumors: calcitonin and carcinoembryonic antigen (CEA) for MTC; highest serum calcium and parathyroid hormone level for parathyroid carcinoma; and fractionated metanephrines, chromogranin A levels and plasma methoxytyramine for pheochromocytoma and paraganglioma. Registry collection will include recording genetic mutation information and hereditary or sporadic onset (germline mutation status) for MTC and neuroendocrine adrenal tumors. Important details such as number, diameter of the largest positive lymph node, and size of metastatic focus have been introduced for all thyroid carcinoma metastases. Necessary details of precise primary and

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metastatic tumor location will be collected for neuroendocrine tumors.

Significant emphasis was placed on the clinical relevance of establishing the collection so that future editions will have robust information to perform large-scale models for the endocrine domain. Our approach was to set up provisions that would be useful and usable for tumor- and patient-related prognostic factors in addition to anatomic stage. Collection of information on these rare tumors is complex, but consistency is paramount for developing and validating outcome modeling. This registry collection will facilitate the ability to create better personalized probabilistic predictions, particularly through the use of accurate risk models or calculators.