COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Neuroendocrine Tumors (Carcinoid Tumors) of the Stomach

Version: StomachNET 4.0.0.1   **Protocol Posting Date:** June 2017
Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Gastrectomy (Partial or Complete)	
Tumor Type	**Description**
Well-differentiated neuroendocrine tumors of the stomach	

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy
Excisional biopsy (includes endoscopic resection and polypectomy)
Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)
Recurrent tumor
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Poorly differentiated neuroendocrine carcinoma including small cell and large cell neuroendocrine carcinoma (consider Stomach protocol)
Other epithelial tumors including mixed adenoneuroendocrine carcinoma (consider Stomach protocol
Lymphoma (consider Hodgkin or non-Hodgkin Lymphoma protocols)
Gastrointestinal stromal tumor (GIST) (consider GIST protocol)
Non-GIST sarcoma (consider Soft Tissue protocol)

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

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Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting
All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired "Data element: Response" format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    o Anatomic site or specimen, laterality, and procedure
    o Pathologic Stage Classification (pTNM) elements
    o Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e. all required elements must be in the synoptic portion of the report in the format defined above.

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2018*

* Beginning January 1, 2018, the 8th edition AJCC Staging Manual should be used for reporting pTNM.

CAP Stomach NET Protocol Summary of Changes

Version 4.0.0.1
Corrected Notes for area on table to 2mm^2

Version 4.0.0.0
The following data elements were modified:
Pathologic Stage Classification (pTNM, AJCC 8th Edition)
Histologic Type and Grade
Mitotic Rate
Microscopic Tumor Extension
Margins

The following data elements were deleted:
Specimen
Specimen Size

Surgical Pathology Cancer Case Summary

Protocol posting date: June 2017

STOMACH:

Select a single response unless otherwise indicated.

Procedure (Note A)
___ Endoscopic resection
___ Partial gastrectomy, proximal
___ Partial gastrectomy, distal
___ Partial gastrectomy, other (specify): _____
___ Total gastrectomy
___ Other (specify): _____
___ Not specified

Tumor Site (select all that apply) (Note B)
___ Gastric cardia/fundus
___ Gastric body
___ Gastric antrum
___ Gastric pylorus
___ Stomach, not otherwise specified
___ Other (specify): _____

Tumor Size (Note C)
Greatest dimension (centimeters): ___ cm (specify size of largest tumor if multiple tumors are present)
+ Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined (explain): _____

Tumor Focality
___ Unifocal
___ Multifocal (specify number of tumors): _____
___ Cannot be determined

Histologic Type and Grade (Notes D and E)[#]
___ G1: Well-differentiated neuroendocrine tumor
___ G2: Well-differentiated neuroendocrine tumor
___ G3: Well-differentiated neuroendocrine tumor
___ Other (specify): _____
___ GX: Well-differentiated neuroendocrine tumor, grade cannot be assessed
___ Not applicable

Note: For poorly differentiated (high-grade) neuroendocrine carcinomas, the College of American Pathologists (CAP) protocol for carcinoma of the stomach[1] should be used.

Mitotic rate and/or Ki67 labeling index is required to determine histologic grade

Mitotic Rate (Note E)[#]
___ <2 mitoses/2mm^2
___ 2-20 mitoses/2mm^2
      + Specify mitoses per 2mm^2: _____
___ >20 mitoses per 2mm^2
      + Specify mitoses per 2mm^2: _____
___ Cannot be determined (explain): _____
___ Not applicable

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be
clinically important but are not yet validated or regularly used in patient management.

*Mitotic rate should be reported as number of mitoses per 2 mm^2, by evaluating at least 10 mm^2 in the most mitotically active part of the tumor (eg, if using a microscope with a field diameter of 0.55 mm, count 42 high power fields [10 mm^2] and divide the resulting number of mitoses by 5 to determine the number of mitoses per 2 mm^2 needed to assign tumor grade).*

Ki-67 Labeling Index (Note E)
___ <3%
___ 3% to 20%
         + Specify Ki-67 percentage: ____%
___ >20%
         + Specify Ki-67 percentage: ____%
___ Cannot be determined (explain): _____
___ Not applicable

Tumor Extension
___ No evidence of primary tumor
___ Tumor invades the lamina propria
___ Tumor invades the submucosa
___ Tumor invades the muscularis propria
___ Tumor invades through the muscularis propria into subserosal tissue without penetration of overlying serosa
___ Tumor penetrates visceral peritoneum (serosa)
___ Tumor invades other organs or adjacent structures (specify): _____
___ Cannot be assessed

Margins (Note F)
Note: Use this section only if all margins are uninvolved and all margins can be assessed.
___ All margins are uninvolved by tumor
         Margins examined: _____
         Note: Margins may include proximal, distal, omental (radial), deep, mucosal, and others.
         + Distance of tumor from closest margin (millimeters *or* centimeters): ___ mm *or* ___ cm
         + Specify closest margin: _____

Individual margin reporting required if any margins are involved or margin involvement cannot be assessed

For gastrectomy specimens only

Proximal Margin
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

Distal Margin
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

Omental (Radial) Margin (Note F)
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

Other Margin(s) (required only if applicable)
Specify margin(s): _____
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be
   clinically important but are not yet validated or regularly used in patient management.

For endoscopic resections only

<u>Deep Margin</u>
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

<u>Mucosal Margin</u>
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

<u>Other Margin(s) (required only if applicable)</u>
Specify margin(s): _____
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

Lymphovascular Invasion
___ Not identified
___ Present
___ Cannot be determined

+ Perineural Invasion
+ ___ Not identified
+ ___ Present
+ ___ Cannot be determined

Regional Lymph Nodes

___ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes are present in the specimen)

Number of Lymph Nodes Involved: ____
___ Number cannot be determined (explain): _____

Number of Lymph Nodes Examined: ____
___ Number cannot be determined (explain): _____

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note G)

Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.

<u>TNM Descriptors (required only if applicable) (select all that apply)</u>
___ m (multiple primary tumors)
___ r (recurrent)
___ y (posttreatment)

+   Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be
    clinically important but are not yet validated or regularly used in patient management.

<u>Primary Tumor (pT)</u>
___ pTX: Primary tumor cannot be assessed
___ pT0:   No evidence of primary tumor
___ pT1#: Invades the lamina propria or submucosa and less than or equal to 1 cm in size
___ pT2#: Invades the muscularis propria or greater than 1 cm in size
___ pT3#: Invades through the muscularis propria into subserosal tissue without penetration of overlying serosa
___ pT4#: Invades visceral peritoneum (serosa) or other organs or adjacent structures

Note: For any T, add (m) for multiple tumors [TX(#) or TX(m), where X = 1–4 and # = number of primary tumors identified##]; for multiple tumors with different Ts, use the highest.

Example: If there are 2 primary tumors, 1 of which penetrates only the subserosa, we define the primary tumor as either T3(2) or T3(m).

<u>Regional Lymph Nodes (pN)</u>
___ pNX: Regional lymph nodes cannot be assessed
___ pN0:   No regional lymph node metastasis
___ pN1:   Regional lymph node metastasis

<u>Distant Metastasis (pM) (required only if confirmed pathologically in this case)</u>
___ pM1:   Distant metastasis
___ pM1a: Metastasis confined to liver
___ pM1b: Metastasis in at least one extrahepatic site (eg, lung, ovary, nonregional lymph node, peritoneum,
              bone)
              Specify site(s), if known: _____
___ pM1c: Both hepatic and extrahepatic metastases
              Specify site(s), if known: _____

+ Additional Pathologic Findings (select all that apply) (Note H)
+ ___ None identified
+ ___ Atrophic gastritis
+ ___ Intestinal metaplasia of gastric mucosa
+ ___ Glandular dysplasia of gastric mucosa
+ ___ Endocrine cell hyperplasia
+ ___ Absence of parietal cells
+ ___ Tumor necrosis
+ ___ Other (specify): _____

+ Comment(s)

Explanatory Notes

A. Application and Tumor Location

This protocol applies to well-differentiated neuroendocrine tumors (carcinoid tumors) of the stomach. Poorly differentiated neuroendocrine carcinomas (small cell and large cell neuroendocrine carcinoma) and tumors with mixed glandular/neuroendocrine differentiation are not included[1].

Because of site-specific similarities in histology, immunohistochemistry, and histochemistry, neuroendocrine tumors of the digestive tract have traditionally been subdivided into those of foregut, midgut, and hindgut origin (Table 1). In general, the distribution pattern along the gastrointestinal (GI) tract parallels that of the progenitor cell type, and the anatomic site of origin of GI neuroendocrine tumors is an important predictor of clinical behavior.[2]

Table 1. Site of Origin of Gastrointestinal Neuroendocrine Tumors

	Foregut Tumors	**Midgut Tumors**	**Hindgut Tumors**
Site	*Stomach, Proximal Duodenum*	*Jejunum, Ileum, Appendix, Proximal Colon*	*Distal Colon, Rectum*

Immunohistochemistry
  Chromogranin A
  Synaptophysin
  Serotonin
	86%-100% +
	50% +
	33% + [16]
		82%-92% +
		95%-100% +
		86% + [16]
			40%-58% +
			94%-100% +
			45%-83% + [3-5,16]

Other Immunohistochemical Markers	Rarely, + for pancreatic polypeptide, histamine, gastrin, somatostatin, vasoactive intestinal peptide (VIP), or adrenocorticotropic hormone (ACTH)	Prostatic acid phosphatase + in 20%-40% [16,17]	Prostatic acid phosphatase + in 20%-82% [3-5,17]
Carcinoid Syndrome	Rare	5%-39% [6,7]	Rare

B. Site-Specific Features

Well-differentiated gastric neuroendocrine tumors are divided into 3 types (Table 2).[3] Type 1 tumors arising in the setting of autoimmune atrophic gastritis with associated hypergastrinemia are the most common. These lesions are composed of enterochromaffin-like (ECL) cells and are usually found as multiple small nodules/polyps in the body of the stomach and limited to the mucosa and submucosa. Type 1 lesions are generally indolent and may regress; lymph node metastases are very rare and occur only when the tumors are large (greater than 2 cm) and infiltrate the muscularis propria.

Type 2 gastric neuroendocrine tumors are rare. These multifocal small tumors, which are associated with multiple endocrine neoplasia (MEN) type 1 with Zollinger-Ellison syndrome, develop in the body of the stomach, are usually smaller than 1.5 cm, and are confined to the mucosa or submucosa. However, in contrast to type 1 tumors, 10% to 30% metastasize. Tumors greater than 2 cm and invading the muscularis propria and exhibiting vascular invasion are more likely to metastasize.

Type 3 gastric neuroendocrine tumors, the second most common neuroendocrine tumor in the stomach, are sporadic solitary tumors that are unassociated with atrophic gastritis, hypergastrinemia, or endocrine cell hyperplasia. These tumors may occur anywhere in the stomach. Metastasis is common and is associated with larger mean size, angioinvasion, and invasion of muscularis propria. Surgical resection is usually advised for solitary gastric neuroendocrine tumors, particularly those larger than 2.0 cm, but tumors smaller than 1.0 cm have been rarely reported to metastasize.[4]

C. Tumor Size

For well-differentiated neuroendocrine tumors in any part of the gastrointestinal tract, size greater than 2.0 cm is associated with a higher risk of lymph node metastasis. In the stomach, types 3 neuroendocrine tumors are significantly larger than type 1 tumors,[3] which usually measure 1 cm or less[5,6] (Table 2). Tumor size correlates

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with depth of invasion for gastric neuroendocrine tumors, with larger tumors more likely to be deeply infiltrative and thus at higher risk for metastases. Regardless of size, any nodules with invasion are defined as neuroendocrine tumors; lesions without invasion can be regarded as neuroendocrine cell dysplasia or hyperplasia.

Table 2. Types of Well-Differentiated Gastric Neuroendocrine Tumors

	Type 1	**Type 2**	**Type 3**
Frequency	70-80% of cases	Rare	10-15% of cases
Multiplicity	Multifocal	Multifocal	Solitary
Size	0.5-1.0 cm	~1.5 cm or less	Variable; one-third are larger than 2 cm
Location	Corpus	Corpus	Anywhere in stomach
Hypergastrinemia	Present	Present	Absent
Association	Chronic atrophic gastritis	Multiple endocrine type 1 (MEN-1)	Sporadic
Background gastric mucosa	Enterochromaffin-like (ECL) cell hyperplasia, partial or complete loss of parietal cells, intestinal metaplasia	ECL cell hyperplasia, no loss of parietal cells	Usually normal
Clinical Behavior	Usually indolent	10-30% metastasize	71% of tumors >2 cm with muscularis propria and vascular invasion have lymph node metastases
Demographic Profile	70-80% are females in their 50s and 60s	Equally in males and females, mean age 50 y	More common in males, mean age 55 y

D. Histologic Type

The World Health Organization (WHO) classifies neuroendocrine neoplasms as well-differentiated neuroendocrine tumors (either the primary tumor or metastasis) and poorly differentiated neuroendocrine carcinomas.[5-8] Historically, well-differentiated neuroendocrine tumors have been referred to as "carcinoid" tumors, a term which may cause confusion because clinically a carcinoid tumor is a serotonin-producing tumor associated with functional manifestations of carcinoid syndrome. The use of the term "carcinoid" for neuroendocrine tumor reporting is therefore discouraged for these reasons.

Classification of neuroendocrine tumors (NETs) is based upon size, functionality, site, and invasion. Functioning tumors are those associated with clinical manifestations of hormone production or secretion of measurable amounts of active hormone; immunohistochemical demonstration of hormone production is not equivalent to clinically apparent functionality.

Although specific histologic patterns in well-differentiated neuroendocrine tumors, such as trabecular, insular, and glandular, roughly correlate with tumor location, these patterns have not been clearly shown independently to predict response to therapy or risk of nodal metastasis and are rarely reported in clinical practice. Immunohistochemistry and other ancillary techniques are generally not required to diagnose well-differentiated neuroendocrine tumors. Specific markers that may be used to establish neuroendocrine differentiation include chromogranin A, synaptophysin, and CD56.[6] Because of their relative sensitivity and specificity, chromogranin A and synaptophysin are recommended. Immunohistochemistry for specific hormone products, such as gastrin, may be of interest in some cases. However, immunohistochemical demonstration of hormone production does not equate with clinical functionality of the tumor.

E. Histologic Grade

Cytologic atypia in well-differentiated neuroendocrine tumors has no impact on clinical behavior of these tumors. The WHO classification[8] and others[9] use mitotic rate and/or Ki-67 index as one of the criteria for potential for aggressive behavior. Mitotic rate should be reported as number of mitoses per 2 mm^2, by evaluating at least 10 mm^2 in the most mitotically active part of the tumor. Only clearly identifiable mitotic figures should be counted; hyperchromatic, karyorrhectic, or apoptotic nuclei are excluded. Because of variations in field size, the number of high-power fields (HPF) (at 40X magnification) for 10 mm^2 (thereby 2 mm^2) must be determined for each microscope (Table 3). For example, if using a microscope with a field diameter of 0.55 mm, count 42 HPF and divide the resulting number of mitoses by 5 to determine the number of mitoses per 2 mm^2 needed to assign tumor grade.

Table 3. Number of HPF Required for 10 mm^2 Using Microscopes With Different Field Diameter

Field Diameter (mm)	Area (mm^2)	Number of HPF for 10mm^2
0.40	0.125	80
0.41	0.132	75
0.42	0.139	70
0.43	0.145	69
0.44	0.152	65
0.45	0.159	63
0.46	0.166	60
0.47	0.173	58
0.48	0.181	55
0.49	0.189	53
0.50	0.196	50
0.51	0.204	49
0.52	0.212	47
0.53	0.221	45
0.54	0.229	44
0.55	0.238	42
0.56	0.246	41
0.57	0.255	39
0.58	0.264	38
0.59	0.273	37
0.60	0.283	35
0.61	0.292	34
0.62	0.302	33
0.63	0.312	32
0.64	0.322	31
0.65	0.332	30
0.66	0.342	29
0.67	0.353	28
0.68	0.363	28
0.69	0.374	28

Ki-67 index is reported as percent positive tumor cells in area of highest nuclear labeling ("hot spot"), although the precise method of assessment has not been standardized. A number of methods have used to assess Ki-67 index, including automatic counting and "eyeballing."[10,11] Automated counting is not widely available and requires careful modification of the software to circumvent the inaccuracies.[10] Eye-balling can be used for most tumors; however, for tumors with Ki-67 index close to grade cut-offs, it is recommended to perform the manual count on the print of camera-captured image of the hot spot. It has been recommended that a minimum of 500 tumor cells be counted to determine the Ki-67 index, and a notation is made if less cells are available. Grade assigned based on Ki-67 index is typically higher than that based on mitotic count, and the case is assigned to the higher of the 2 if both methods are performed.[8]

It is important to note that there are a small group of well-differentiated neuroendocrine tumors with a Ki-67 index >20% and a mitotic rate usually <20 per 10 HPF. In WHO-2010, these tumors were considered as G3 poorly differentiated neuroendocrine carcinomas. However, they have typical morphology of well-differentiated tumors. Previous studies (most on pancreatic neuroendocrine tumors) have demonstrated that these tumors have a worse prognosis than grade 2 (Ki-67=3-20 % and mitosis <20/10 HPF) neuroendocrine tumors, but they are not as aggressive as poorly differentiated neuroendocrine carcinomas.[12] In addition, these tumors do not have the genetic abnormalities seen in poorly differentiated neuroendocrine carcinomas.[13] Furthermore, unlike poorly differentiated neuroendocrine carcinomas, they are less responsive to platinum-based chemotherapy.[14] In the WHO-2017 blue book of endocrine tumors and AJCC 8th edition,[15] those with typical morphology of well-differentiated tumors are classified as "well differentiated neuroendocrine tumor" but as grade 3. Here, the updated classification for "endocrine" tumors is adapted, and following grading scheme is recommended to grade well-differentiated gastroenteropancreatic neuroendocrine tumors (Table 4).

Table 4

Recommended Grading System for Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumors

Grade	Mitotic Rate (per 2mm^2)	Ki-67 index (%)
Well-differentiated neuroendocrine tumor, G1	<2	<3
Well-differentiated neuroendocrine tumor, G2	2-20	3-20
Well-differentiated neuroendocrine tumor, G3	>20	>20

F. Circumferential (Radial) Margin
For surgical resection specimens, margins include the proximal, distal, and radial margins. The radial margins represent the nonperitonealized soft tissue margins closest to the deepest penetration of tumor. In the stomach, the lesser omental (hepatoduodenal and hepatogastric ligaments) and greater omental resection margins are the only radial margins. For endoscopic resection specimens, margins include mucosal margins and the deep margin of resection. It may be helpful to mark the margin(s) closest to the tumor with ink. Margins marked by ink should be designated in the macroscopic description.

G. Pathologic Stage Classification
The TNM staging system for gastric neuroendocrine tumors of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended.[15]

By AJCC/UICC convention, the designation "T" refers to a primary tumor that has not been previously treated. The symbol "p" refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

TNM Descriptors
For identification of special cases of TNM or pTNM classifications, the "m" suffix and "y," "r," and "a" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "m" suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The "y" prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The "r" prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the "r" prefix: rTNM.

The "a" prefix designates the stage determined at autopsy: aTNM.

N Category Considerations
The specific nodal areas of the stomach are listed below.[13]

Greater curvature of stomach: Greater curvature, greater omental, gastroduodenal, gastroepiploic, pyloric, and
        pancreaticoduodenal
Pancreatic and splenic areas: Pancreaticolienal, peripancreatic, splenic
Lesser curvature of stomach: Lesser curvature, lesser omental, left gastric, cardioesophageal, common hepatic,
        celiac, and hepatoduodenal

Involvement of other intra-abdominal lymph nodes, such as retropancreatic, mesenteric, and para-aortic, is classified as distant metastasis.[13]

M Category Considerations
The liver is the most common metastatic site. Metastases to extrahepatic sites, such as lung, ovary, peritoneum and bone, are rare. Involvement of the celiac, para-aortic, and other nonregional lymph nodes is also considered M1 disease. In the AJCC 8th edition, M is subcategorized into M1a (hepatic only), M1b (extrahepatic only), and M1c (both hepatic and extrahepatic).

H. Additional Pathologic Findings
Most gastric neuroendocrine tumors (type-I) arise in the setting of hypergastrinemia secondary to atrophic gastritis such as autoimmune gastritis (see Note B). Autoimmune gastritis may be also associated with glandular dysplasia and, in rare cases, gastric adenocarcinoma. Coagulative tumor necrosis, usually punctate, may indicate more aggressive behavior,[9] which is more commonly seen in type-III gastric neuroendocrine tumors, and should be reported.

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