Gastrointestinal Stromal Tumors (GIST)

What are GISTs?

- Rare type of soft tissue sarcoma
  - 4500-6000 adults (2009) – all sites
- Different from carcinomas
  - Develop in muscle layer of gut rather than mucosa
  - Grow outward (exophytic)
- Described as a distinct entity in 1998
  - Umbrella term for most mesenchymal tumors of stomach and intestine
  - Most tumors historically called leiomyosarcoma are now classified as GISTs
Proposed Cell of Origin

- Interstitial cells of Cajal
  - "Pacemaker cells of gut"
  - Send signals to muscles of GI tract to move food and liquid through system (peristalsis)

GIST Primaries

<table>
<thead>
<tr>
<th>% GISTs</th>
<th>% Prim Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>5%</td>
</tr>
<tr>
<td>Stomach</td>
<td>55%</td>
</tr>
<tr>
<td>Small intestine</td>
<td>30%</td>
</tr>
<tr>
<td>Large intestine</td>
<td>2%</td>
</tr>
<tr>
<td>Rectum</td>
<td>5%</td>
</tr>
<tr>
<td>Other (very rare)</td>
<td></td>
</tr>
</tbody>
</table>
  - Peritoneum, mesentery, omentum, liver, pancreas, ovaries, uterus, prostate

GIST Histologies

- Codes added to ICD-O-3 (2001)
  - 8935/3 Stromal sarcoma, NOS
  - 8936/0 Gastrointestinal stromal tumor, benign
  - 8936/1 Gastrointestinal stromal tumor, NOS
  - 8936/3 Gastrointestinal stromal sarcoma
- 30-50% malignant
  - Criteria for malignancy vary by primary site
- AJCC 7th Edition GIST chapter includes all behaviors
  - Separate reportability rules apply
Making the Diagnosis

- Microscopic examination of resected tissue
  - Tumor size cut points: 2, 5, 10 cm
  - Mitotic activity cut point: 5 mitoses/50 HPFs
- AJCC Anatomic Stage/Prognostic Groups use mitotic rate (low/high) in determining Stages I and II

GIST Schemas

- Esophagus
- Stomach
- Small Intestine
- Appendix
- Colon
- Rectum
- Peritoneum
  - Omentum and mesentery

- T, N, M definitions common to all GIST sites
- T category cutpoints: 2, 5, 10 cm
- Stage groupings different

GIST Common Tables

- Tumor Size
  - Slight wording differences from solid tumors
- TS/Ext Eval
- LN Eval
- Nodes Pos
- Nodes Exam
- Mets Eval
### GIST Tumor Size

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>No mass/tumor found</td>
</tr>
<tr>
<td>001-998</td>
<td>001 - 988 millimeters (code exact size in millimeters)</td>
</tr>
<tr>
<td>989</td>
<td>999 millimeters or larger</td>
</tr>
<tr>
<td>990</td>
<td>Microscopic focus or foci only, no size of focus given</td>
</tr>
<tr>
<td>991 &lt; 1 cm</td>
<td></td>
</tr>
<tr>
<td>992</td>
<td>&lt; 2 cm, or &gt; 1 cm, or &quot;between 1 cm and 2 cm&quot; Stated as T1, NOS</td>
</tr>
<tr>
<td>993</td>
<td>&lt; 3 cm, or &gt; 2 cm, or &quot;between 2 cm and 3 cm&quot;</td>
</tr>
<tr>
<td>994</td>
<td>&lt; 4 cm, or &gt;= 3 cm, or &quot;between 3 cm and 4 cm&quot;</td>
</tr>
<tr>
<td>995</td>
<td>&lt; 5 cm, or &gt; 4 cm, or &quot;between 4 cm and 5 cm&quot; Stated as T2, NOS</td>
</tr>
<tr>
<td>996</td>
<td>Stated as T3, NOS</td>
</tr>
<tr>
<td>997</td>
<td>Stated as T4, NOS</td>
</tr>
<tr>
<td>999</td>
<td>Unknown; size not stated Not documented in patient record</td>
</tr>
</tbody>
</table>

### GIST CS Extension

- Varies by primary site
- Very similar to carcinoma schema for same site (depth of invasion)
  - Slight differences in wording
  - Elimination of T subcategories (T1a, T1b, …)
  - Carcinoma polyp codes generate error in TNM7
- TNM7 mapping driven by tumor size, not depth of invasion

### GIST CS Lymph Nodes

- Nodal metastases rare in GISTs
  - If no information on nodes, assume negative and code as 00
- Schemas vary by primary site
- Similar to carcinoma schema for same site
  - No N2, N3 codes
  - No tumor deposit codes
  - Slight differences in wording
GIST CS Mets at Dx

- Distant metastases relatively rare for GISTs
- Schemas vary by primary site
  - Esophagus, stomach, small intestine, peritoneum—same as carcinoma schema for same site
  - Appendix, colon, rectum—substantial differences from carcinoma schema for same site
    - Carcinomas split mets into M1a, M1b

Mets at Dx-Metastatic Sites

- 4 new fields
  - Bone excluding marrow
  - Lung excluding pleura and pleural fluid
  - Brain excluding spinal cord and other CNS
  - Liver
- Code 0 when CS Mets at Dx is 00
- Code structure
  0 – No
  1 – Yes
  8 – Not applicable
  9 – Unknown

MX Eliminated

- MX has been eliminated from 7th Edition
  - Clinical M0
  - Unless clinical or pathologic evidence of mets
- cM only requires history and physical
- Infer cM0 unless known cM1
GIST Site-Specific Factors

- Mitotic count
- Kit immunohistochemistry
- Kit gene mutation
- PDGFRA gene mutation
- Tumor multiplicity
- Location (SSF #) varies by primary site

Mitotic Count

- Mitotic count: number of cells actively dividing
  - <5 mitoses/high power field – low mitotic rate
  - >5 mitoses/high power field – high mitotic rate
- Source: pathology report/protocol
  - Pathologist instructions: scan slide for area of greatest mitotic activity

- Usually documented as mitoses per 50 high power fields (HPF)
  - Standard magnification is 40X
  - Also described as ‘per 5 mm²’ (square millimeters)
- Site-specific factor code
  - Implied decimal between 2nd and 3rd digit
  - .8 mitoses/50HPF 008
  - 5 mitoses/50HPF 050
### Mitotic Count (1)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>0 mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>0 mitoses per 5 square millimeters (mm²)</td>
</tr>
<tr>
<td></td>
<td>Mitoses absent</td>
</tr>
<tr>
<td></td>
<td>No mitoses present</td>
</tr>
<tr>
<td>001-008</td>
<td>1-8 mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>1-8 mitoses per 5 mm²</td>
</tr>
<tr>
<td>009</td>
<td>0.9 mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>0.9 mitoses per 5 mm²</td>
</tr>
<tr>
<td></td>
<td>Stated as &lt; 1 mitosis per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>Stated as &lt; 1 mitosis per 5 mm²</td>
</tr>
<tr>
<td>010-100</td>
<td>1-10 mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>1-10 mitoses per 5 mm²</td>
</tr>
<tr>
<td>110</td>
<td>11 or more mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>11 or more mitoses per 5 mm²</td>
</tr>
</tbody>
</table>

### Mitotic Count (2)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>988</td>
<td>Not applicable: information not collected for this case</td>
</tr>
<tr>
<td>990</td>
<td>Specific number not stated, described as ≤ 5 mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>Specific number not stated, described as ≤ 5 mitoses per 5 mm²</td>
</tr>
<tr>
<td>995</td>
<td>Specific number not stated, described as &gt; 5 mitoses per 50 HPF</td>
</tr>
<tr>
<td></td>
<td>Specific number not stated, described as &gt; 5 mitoses per 5 mm²</td>
</tr>
<tr>
<td>999</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Not stated</td>
</tr>
<tr>
<td></td>
<td>Not documented in patient record</td>
</tr>
</tbody>
</table>

### KIT Immunohistochemistry (IHC)

- **Source:** pathology report (special immunofluorescent stain)
  - Mutated cells stain brown
  - Confirms diagnosis of GIST
- **Also known as** CD117, c-kit receptor, SCFR (stem cell factor receptor)
**KIT IHC**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>010</td>
<td>Positive</td>
</tr>
<tr>
<td>020</td>
<td>Negative/normal; within normal limits</td>
</tr>
<tr>
<td>030</td>
<td>Borderline; undetermined whether positive or negative</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable; information not collected for this case</td>
</tr>
<tr>
<td>997</td>
<td>Test ordered, results not in chart</td>
</tr>
<tr>
<td>998</td>
<td>Test not done (test was not ordered and was not performed)</td>
</tr>
<tr>
<td>999</td>
<td>Unknown or no information Not documented in patient record</td>
</tr>
</tbody>
</table>

**KIT Gene Mutation**

- Source: specialty/reference lab report
- C-kit gene regulates cell growth and differentiation
- 85-90% of GISTs contain oncogenic mutations of KIT receptor tyrosine kinase gene
  - Mutations primarily of exon 11 and 9, and rarely of exons 13 and 17
  - Exon: A segment of a gene that contains instructions for making a protein
- Specific exon mutation may indicate potential response to targeted therapy drugs
  - Imatinib mesylate (Gleevec) and Sutent

**KIT Gene Mutation**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>KIT gene test performed, negative for mutations</td>
</tr>
<tr>
<td>010</td>
<td>KIT gene test performed, positive for mutation of exon 9</td>
</tr>
<tr>
<td>020</td>
<td>KIT gene test performed, positive for mutation of exon 11</td>
</tr>
<tr>
<td>030</td>
<td>KIT gene test performed, positive for mutation of exon 13</td>
</tr>
<tr>
<td>040</td>
<td>KIT gene test performed, positive for mutation of exon 17</td>
</tr>
<tr>
<td>800</td>
<td>KIT gene test performed, positive for other specified mutation</td>
</tr>
<tr>
<td>810</td>
<td>KIT gene test performed, positive for more than one mutation</td>
</tr>
<tr>
<td>850</td>
<td>KIT gene test performed, positive NOS; specific mutation(s) not stated</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable; information not collected for this case</td>
</tr>
<tr>
<td>997</td>
<td>KIT gene test ordered, results not in chart</td>
</tr>
<tr>
<td>998</td>
<td>KIT gene not done (test not ordered and not performed)</td>
</tr>
<tr>
<td>999</td>
<td>Unknown; Not documented in patient record</td>
</tr>
</tbody>
</table>
PDGFRA Gene Mutation

- **Source**: specialty/reference lab report
- **Platelet-Derived Growth Factor Receptor, Alpha polypeptide type**
  - A.k.a. CD140A; MGC74795; PDGFR2; Rhe-PDGFR
  - Gene encodes a cell surface tyrosine kinase receptor
  - Found in mesenchymal cells
  - Mutually exclusive with KIT
- **PDGFR** regulates cell proliferation, cellular differentiation, cell growth and development
  - 30-40% of KIT-negative GISTs contain mutations of PDGFRA

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>010</td>
<td>PDGFRA gene test performed, positive for mutations</td>
</tr>
<tr>
<td>020</td>
<td>PDGFRA gene test performed, negative for mutations</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable: information not collected for this case</td>
</tr>
<tr>
<td>997</td>
<td>PDGFRA gene test ordered, results not in chart</td>
</tr>
<tr>
<td>998</td>
<td>PDGFRA gene test not done (test was not ordered and not performed)</td>
</tr>
<tr>
<td>999</td>
<td>Unknown Not documented in patient record</td>
</tr>
</tbody>
</table>

Tumor Multiplicity

- **Source**: pathology report
- **Record presence of anatomically separate, multiple GISTs**
  - Various sizes
  - May occur in the setting of neurofibromatosis type 1 or familial GIST syndrome
Tumor Multiplicity

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>Multiple GIST primaries are not present</td>
</tr>
<tr>
<td>010</td>
<td>Multiple GIST primaries are present</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable: information not collected for this case</td>
</tr>
<tr>
<td>999</td>
<td>Unknown Not documented in patient record</td>
</tr>
</tbody>
</table>

GIST Peritoneum SSF 10
Location of Primary Tumor

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Stage Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>010</td>
<td>Mesentery</td>
<td>GISTSmallIntestine</td>
</tr>
<tr>
<td>020</td>
<td>Omentum</td>
<td>GISTStomach</td>
</tr>
<tr>
<td>030</td>
<td>Pelvic Peritoneum</td>
<td>GISTSmallIntestine</td>
</tr>
<tr>
<td>040</td>
<td>Rectouterine pouch</td>
<td>GISTSmallIntestine</td>
</tr>
<tr>
<td>040</td>
<td>Cul de sac</td>
<td>GISTSmallIntestine</td>
</tr>
<tr>
<td>040</td>
<td>Pouch of Douglas</td>
<td>GISTSmallIntestine</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable for this schema (may be used when AJCC staging is not derived)</td>
<td></td>
</tr>
<tr>
<td>998</td>
<td>Other specified peritoneal site</td>
<td>GISTSmallIntestine</td>
</tr>
</tbody>
</table>

GIST Treatment

- **Surgical resection**
  - Based on primary site and extent of disease
  - Complete surgical resection possible in 80+% of patients

- **Chemotherapy**
  - Gleevec (imatinib)
    - Neoadjuvant, adjuvant, or for metastases
  - Sutent (sunitinib) for Gleevec-refractory or intolerant cases

- **For distant metastases**
  - Liver: wedge resections, RFA, cryosurgery, chemoembolization
GIST Resources

- GIST Support International
  - Gistsupport.org
- AJCC Cancer Staging Manual, 7th Edition
  - Chapter 16, Gastrointestinal Stromal Tumor
- Cancer.gov
  - Adult soft tissue sarcoma article includes GIST

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Neuroendocrine Tumors (NET)

What are Neuroendocrine Tumors?

- Derived from neuroendocrine cells
  - Release a hormone in response to a signal from the nervous system
- Found in almost every organ
- Examples
  - Carcinoids, islet cell tumors, small cell lung carcinoma, Merkel cell carcinoma and others
- Often secrete hormones in excess, causing a variety of symptoms
Neuroendocrine Cells

- Originate from diffuse neuroendocrine system
  - Embryologically derived from neuroectoderm and endoderm (gut)
- Cells do not form organ
  - Single cells or small clusters scattered throughout other organs
    - Lungs, stomach, and intestines
  - Occur in aggregates or sheets within other organs
    - Islets in pancreas or medullary portion of adrenal
      - Form small collections of cells called “bodies”
    - Carotid body or glomus jugulare

What Do Neuroendocrine Cells Do?

- Dual roles in both endocrine system and nervous system
- Functions
  - Produce large variety of biologically active substances
  - Regulate neighboring cells (paracrine regulation) by excreting biologically active amines and hormones
  - Regulate numerous processes in body

Where Do Neuroendocrine Cells Go?

- Lung
- Gastrointestinal tract
  - Stomach, small intestine, colon, appendix
- Pancreas
- Thyroid gland
- Adrenal gland
- Thymus
- Skin
- Nasal cavity, paranasal sinuses
- Heart
- Other sites that develop carcinoids and small cell carcinomas
Why Are NETs Different From Carcinomas?

- Rare, so not well understood
- Defined by secretory products and cytoplasmic proteins rather than location or embryologic derivation
- Malignant NETs tend to be more aggressive
- Metastasize earlier
  - Liver most common
- Cause unusual symptoms

Useful Definitions

- NETs defined by location
  - Different locations have different characteristics
- Foregut
  - Pharynx, esophagus, stomach, duodenum, liver, pancreas, gallbladder, respiratory system
- Midgut
  - Jejunum, ileum, pancreas, right colon, 2/3 transverse colon
- Hindgut
  - Distal 1/3 transverse colon, left colon, rectum, upper anal canal

Carcinoids and NETs in AJCC 7th Ed. and CSv2

Staging/Coding

- GI tract
  - Carcinoid: separate staging by site: stomach, small intestine, colon, rectum, ampulla of Vater
  - Need size and/or depth of invasion
  - Small cell/large cell NET: stage with carcinoma
- Pancreas: stage with carcinoma
- Lung: stage with carcinoma
- Skin: separate classification for Merkel cell carcinoma
Gastrointestinal Carcinoids

- Preferred terminology for carcinoid
  - Well-differentiated neuroendocrine tumor
- Grow slowly for many years
- Metastasize to regional nodes, liver, bone
- Likelihood of metastases relates to tumor size
  - < 1 cm – 15% develop mets
  - > 2 cm – 95% develop mets
- Separate staging from carcinomas in
  AJCC 7th Ed, CSv2

GI Carcinoids (NET)
Mapping to T Category in AJCC 7th Ed.

Appendix
Tumor size and location (organ)
Small Intestine
Depth of invasion, tumor size, and segment involved
Stomach
Depth of invasion, tumor size
Large Intestine
Tumor size, depth of invasion

Distribution of GEP Carcinoids

Liver > 1%
Pancreas 2-3%
Small intestine 39%
Appendix 26%
Stomach 2-4%
Colon 5-7%
Rectum 15%
Carcinoid Histologies

- Neuroendocrine carcinoma, NOS (8246)
  - Umbrella term covering carcinoids and some adenocarcinomas
- Carcinoid, NOS (8240)
  - Also called typical carcinoid or low grade or well-differentiated neuroendocrine carcinoma; code to 8240
  - Most common sites: rectum, appendix; uncommon in colon
  - Locally invasive, rarely metastasizes
  - Good prognosis if size is < 2 cm

- Enterochromaffin (EC) cell carcinoid (8241)
  - Produces serotonin (associated with carcinoid syndrome)
  - Most common in appendix
- ECL cell tumor (Entero-Chromaffin-Like) (8242)
  - Non-peptide secreting tumor of gastric fundus/body mucosa
  - Multiple, polypoid presentation
- Atypical carcinoid tumor (8249)
  - A.k.a. moderately differentiated NET
  - More aggressive than a typical carcinoid
  - Uncommon in gastrointestinal tract

Other NETs

- Gastrinoma, malignant (8153/3)
  - NET of G cells
  - Duodenal/ileal, gastric
  - Causes hypersecretion of gastric acid and peptic ulceration
Other Carcinoids

- Goblet cell carcinoid (8243)
  - More aggressive than usual carcinoid
  - Staged/coded with carcinoma of appendix
- Composite carcinoid (8244)
  - Single tumor containing both carcinoid and adenocarcinoma
- Adenocarcinoid (8245)
  - Specific type usually found in appendix
  - Also called mucinous carcinoid/goblet cell carcinoid (8243) in other organs
  - Less common than typical carcinoid in appendix
  - Patients are older

CS Common Tables for NETs

- Tumor Size
  - Slight wording differences from solid tumors
- TS/Ext Eval
- LN Eval
- Nodes Pos
- Nodes Exam
- Mets Eval

General Notes for NET Schemas

- Note 1: Only well-differentiated neuroendocrine tumors staged.
  - Grade code not needed to select the correct schema (code in 6th digit of morphology code)
- Note 2: NET schemas used for carcinoid tumors and malignant gastrinomas
- Note 3: NET histologies not staged in AJCC 6th Ed.
  - CSv2 algorithm will not derive 6th Ed T, N, M or stage group
### CS Tumor Size

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>No mass/tumor found</td>
</tr>
<tr>
<td>001-988</td>
<td>001 - 988 millimeters (code exact size in millimeters)</td>
</tr>
<tr>
<td>989</td>
<td>989 millimeters or larger</td>
</tr>
<tr>
<td>990</td>
<td>Microscopic focus or foci only, no size of focus given</td>
</tr>
<tr>
<td>991</td>
<td>Described as “less than or equal to 1 cm”</td>
</tr>
<tr>
<td>992</td>
<td>Described as “greater than 1 cm”</td>
</tr>
<tr>
<td>993</td>
<td>Stated as T1, NOS with no other information on size</td>
</tr>
<tr>
<td>994</td>
<td>Stated as T2, NOS with no other information on size</td>
</tr>
<tr>
<td>999</td>
<td>Unknown; size not stated</td>
</tr>
<tr>
<td></td>
<td>Not documented in patient record</td>
</tr>
</tbody>
</table>

### CS Extension – NET

- **Ampulla of Vater**
  - Similar to carcinoma schema for site
  - No code 000
  - Separate codes for “Stated as T_, NOS”

- **Appendix**
  - Substantial differences from new carcinoma schema for appendix
  - No code 000, 050
  - No polyp codes
  - New T1 subcategories
  - No T4 subcategories

- **Stomach**
  - Similar to carcinoma schema for site
  - No subcategories for T1, T4

- **Small Intestine**
  - Similar to carcinoma schema for site
  - No code 000, 050
  - Code 450 split to 460 and 470
  - No subcategories for T1, T4
  - Separate codes for “Stated as T_, NOS”
CS Extension - NET

- Colon
  - Similar to carcinoma schema for site
  - No 000, 050
  - No T4 subcategories

- Rectum
  - Similar to carcinoma schema for site
  - No 000, 050
  - No T4 subcategories

CS Lymph Nodes – NET

- Small Intestine – Appendix – Colon – Rectum
  - Similar to carcinoma schema for site
  - No tumor deposits code
  - No N2

- Stomach
  - Similar to carcinoma schema for site
  - No N2, N3

- Ampulla of Vater
  - No differences from carcinoma schema for site

CS Mets at Dx – NET

- Ampulla of Vater – Stomach – Small Intestine
  - No differences from carcinoma schema for site

- Colon – Rectum
  - NET schema not subdivided into M1a and M1b codes
  - Similar to colon schema in CS version 1

- Appendix
  - Subdivided into mucinous and non-mucinous criteria
  - Subdivided into M1a and M1b codes
Mets at Dx-Metastatic Sites

- 4 new fields
  - Bone excluding marrow
  - Lung excluding pleura and pleural fluid
  - Brain excluding spinal cord and other CNS
  - Liver

- Code 0 when CS Mets at Dx is 00

- Code structure
  - 0 – No
  - 1 – Yes
  - 8 – Not applicable
  - 9 – Unknown

MX Eliminated

- MX has been eliminated from 7th Edition
  - Clinical M0
  - Unless clinical or pathologic evidence of mets

- cM only requires history and physical

- Infer cM0 unless known cM1

NETS Mapping

- T – combination of tumor size and location/level of invasion

- N – all involved regional lymph nodes map to N1 (no N2, N3)

- M – all distant mets map to M1 (no M1a or M1b subcategories)

- Stage Grouping – different from carcinoma schema for site
CSv2 SSFs for GI/Biliary Carcinoids

<table>
<thead>
<tr>
<th>Clin Assess Reg LN</th>
<th>CEA</th>
<th>Serum Chromogranin</th>
<th>Urine 5-HIAA</th>
<th>Mitotic Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>x</td>
<td>Not used</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Sm Intest</td>
<td>Not used</td>
<td>Obsolete</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Colon</td>
<td>x</td>
<td>Obsolete</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Appendix</td>
<td>x</td>
<td>Obsolete</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Rectum</td>
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<td>Obsolete</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Ampulla</td>
<td>Not used</td>
<td>Not used</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Clinical Assessment of Regional LN

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Stomach</th>
<th>Colon/Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>Nodes not clinically evident</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>Mets in LN determined clinically</td>
<td>1 to 6</td>
<td>1 to 3</td>
</tr>
<tr>
<td>200</td>
<td>Mets in LN determined clinically</td>
<td>7 to 15</td>
<td>4 or more</td>
</tr>
<tr>
<td>300</td>
<td>Mets in LN determined clinically</td>
<td>15 or more</td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>Clinically positive regional nodes, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>988</td>
<td>Not applicable: Information not collected for this case</td>
<td></td>
<td></td>
</tr>
<tr>
<td>999</td>
<td>Unknown if nodes are clinically evident</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mitotic Count

- Source: pathology report
- Mitotic count: number of cells actively dividing
- Usually documented as mitoses per 10 high power fields (HPF)
  - Usual high power is 40x magnification
  - Also described as `per 2 mm²` (square millimeters)
- Implied decimal between 2nd and 3rd digit in SSF code
  - 0.5 mitoses/10HPF 005
  - 12 mitoses/10HPF 120
### Mitotic Count (1)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>0 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>0 mitoses per 2 square millimeters (mm²)</td>
</tr>
<tr>
<td></td>
<td>Mitoses absent</td>
</tr>
<tr>
<td></td>
<td>No mitoses present</td>
</tr>
<tr>
<td>001-008</td>
<td>1-8 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>1-8 mitoses per 2 mm²</td>
</tr>
<tr>
<td>009</td>
<td>0.9 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>0.9 mitoses per 2 mm²</td>
</tr>
<tr>
<td></td>
<td>Stated as &lt; 1 mitosis per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>Stated as &lt; 1 mitosis per 2 mm²</td>
</tr>
<tr>
<td>010-500</td>
<td>1-50 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>1-50 mitoses per 2 mm²</td>
</tr>
<tr>
<td>510</td>
<td>51 or more mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>51 or more mitoses per 2 mm²</td>
</tr>
</tbody>
</table>

### Mitotic Count (2)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>988</td>
<td>Not applicable: information not collected for this case</td>
</tr>
<tr>
<td>990</td>
<td>Specific number not stated, described as &lt; 2 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>Specific number not stated, described as &lt; 2 mitoses per 2 mm²</td>
</tr>
<tr>
<td>995</td>
<td>Specific number not stated, described as 2 – 20 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>Specific number not stated, described as 2 – 20 mitoses per 2 mm²</td>
</tr>
<tr>
<td>997</td>
<td>Specific number not stated, described as &gt; 20 mitoses per 10 HPF (40x field)</td>
</tr>
<tr>
<td></td>
<td>Specific number not stated, described as &gt; 20 mitoses per 2 mm²</td>
</tr>
<tr>
<td>999</td>
<td>Unknown; not stated</td>
</tr>
<tr>
<td></td>
<td>Not documented in patient record</td>
</tr>
</tbody>
</table>

### Chromogranin A

- **Source**: pathology report (immunohistochemistry stain) or clinical lab report
- **Other names**
  - Serum chromogranin A, CGA, chromogranin
- **Marker for neuroendocrine tumors**
  - Family of proteins in secretory granules found throughout neuroendocrine system
- **Reference range**
  - Path report: Positive/negative
  - Lab: 6.0 – 40.0 ng/mL
Chromogranin A

Notes
- Specific but not sensitive immunostain for neuroendocrine cells. Positive more often for well-differentiated NET (carcinoid) than poorly-differentiated NET (neuroendocrine carcinoma).

Site-specific Factor note
- Record the highest CgA lab value recorded in the medical record prior to treatment.
- Example: pretreatment CgA of 400 nanograms per milliliter (ng/ml)
  - Record as 400

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>0 ng/ml</td>
</tr>
<tr>
<td>001</td>
<td>1 or less ng/ml</td>
</tr>
<tr>
<td>002-979</td>
<td>002-979 ng/ml</td>
</tr>
<tr>
<td>980</td>
<td>980 or greater ng/ml</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable: information not collected for this case</td>
</tr>
<tr>
<td>997</td>
<td>Test ordered, results not in chart</td>
</tr>
<tr>
<td>998</td>
<td>Test not done (test was not ordered and was not performed)</td>
</tr>
<tr>
<td>999</td>
<td>Unknown or no information Not documented in patient record</td>
</tr>
</tbody>
</table>

Urinary 5-HIAA Lab Value Level

Source: clinical laboratory report (urine test)
Other names
- 5-hydroxyindoleacetic acid (5-HIAA); quantitative 5-HIAA urine
Carcinoids release excessive serotonin (a vasoconstrictor)
- Metabolized to 5-HIAA and excreted in urine
Reference range: 2-8 mg/24 hours
- Results > 25/24 hours indicate carcinoid
- Many drugs can also affect 5-HIAA results
Urinary 5-HIAA Lab Value Level

- Site-specific Factor Note
  - Record the highest urinary 5-HIAA lab value recorded in the medical record prior to treatment.
  - Example: pre-treatment 5-HIAA of 550 nanograms/milliliter (ng/ml)
  - Record as 550

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>0 ng/ml</td>
</tr>
<tr>
<td>001</td>
<td>1 or less mg/24hours</td>
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<tr>
<td>002-979</td>
<td>002-979 mg/24hours</td>
</tr>
<tr>
<td>980</td>
<td>980 or greater mg/24hours</td>
</tr>
<tr>
<td>988</td>
<td>Not applicable: information not collected for this case</td>
</tr>
<tr>
<td>997</td>
<td>Test ordered, results not in chart</td>
</tr>
<tr>
<td>998</td>
<td>Test not done (test was not ordered and was not performed)</td>
</tr>
<tr>
<td>999</td>
<td>Unknown or no information Not documented in patient record</td>
</tr>
</tbody>
</table>

NET/Carcinoid Treatment

- Surgical resection
  - If primary is localized and resectable, 70-90% 5 year survival
  - If metastatic at diagnosis, 2 year median survival
- No known effective adjuvant therapy for positive nodes
- For distant metastases
  - Liver: wedge resections, RFA, cryosurgery, chemoembolization
  - Palliation: combination chemotherapy or radiation
**NET Resources**

- AJCC Cancer Staging Manual, 7th Edition
  - Chapter 17, Neuroendocrine Tumors
- Cancer.gov
  - Carcinoid tumor, gastrointestinal
- Endotext.org
- Caringforcarcinoid.org

**Reading Lab Results**

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<thead>
<tr>
<th>Number</th>
<th>Prefix</th>
<th>Written</th>
<th>Unit</th>
<th>Abbrev.</th>
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</thead>
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<td>Mega-</td>
<td>M</td>
<td>Liter</td>
<td>L, l</td>
</tr>
<tr>
<td>1000</td>
<td>Kilo-</td>
<td>k</td>
<td>Unit</td>
<td>U</td>
</tr>
<tr>
<td>10</td>
<td>Deka-</td>
<td>da</td>
<td>Meter</td>
<td>m</td>
</tr>
<tr>
<td>1 (baseline)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/10</td>
<td>Deci-</td>
<td>d</td>
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<td></td>
</tr>
<tr>
<td>1/100</td>
<td>Centi-</td>
<td>c</td>
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<tr>
<td>1/10000</td>
<td>Milli-</td>
<td>m</td>
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</tr>
<tr>
<td>One millionth</td>
<td>Micro-</td>
<td>µ, u, or mc</td>
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<td></td>
</tr>
<tr>
<td>One billionth</td>
<td>Nano-</td>
<td>n</td>
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</tr>
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<td>One trillionth</td>
<td>Pico-</td>
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<td></td>
</tr>
<tr>
<td>One quadrillionth</td>
<td>Femto</td>
<td>f</td>
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<td></td>
</tr>
</tbody>
</table>

**Inquiry & Response System**

- Submit questions to Inquiry & Response System
  - Allows tracking for educational purposes
  - Provides information for all

- http://web.facs.org/coc/default.htm
American Joint Committee on Cancer
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AJCC@facs.org

AJCC Web Site
www.cancerstaging.org