Gastric Tumors

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Benign Tumors

- **Neoplastic**:
  - Epithelial adenomas*
  - Fundic gland polyps*
  - GISTs = benign gastrointestinal stromal tumors
  - Lipomas
  - Leiomyomas
  - Neural tumors (e.g. Schwannomas)

- As any lesion you can find, in any organ of the GI tract, the tumors can be benign or malignant.
- Benign tumors can also have neoplastic changes (they are not normal cells) or non-neoplastic.
- They are considered benign because the risk of aggressive growth or metastasis is very low.
- *Polyps and adenomas are areas of the mucosa that grow into polypoid shape (called لحميه in Arabic). Can be in any part of the GI: the colon, stomach or anywhere else. They are benign but they do increase the risk of malignancy slightly

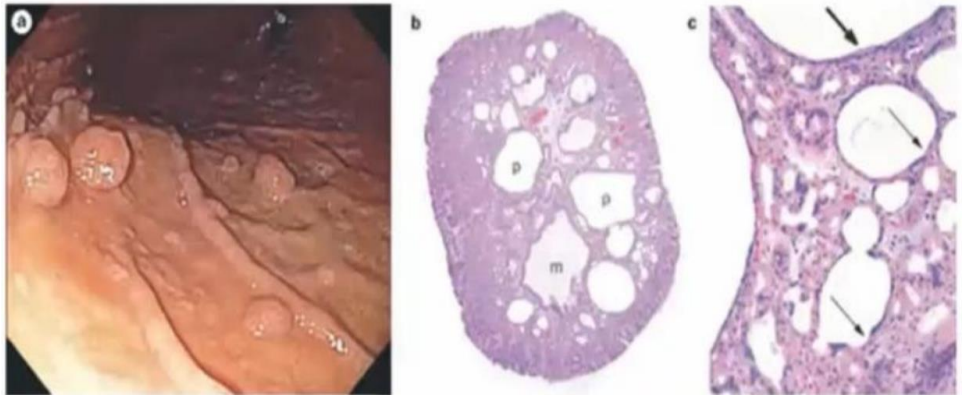
Benign Tumors

- **Non-Neoplastic**:
  - Hyperplastic polyps
  - Inflammatory fibroid polyps
  - Hamartomatous polyps
- These are benign lesions comprised of non-neoplastic normal tissue, do not have high risk of malignancy.

Malignant Tumors

- Adenocarcinoma (when someone says there is a pt with gastric cancer they usually mean adenocarcinoma)
- Primary gastric lymphoma**
- GISTs = **g**astro**i**ntestinal **s**tromal **t**umors which are of mesenchymal origin.
- Metastatic deposits from other organs
- Carcinoids (neuroendocrine tumors)
- Rare tumor (there is a long list of rare tumors but they are beyond the scope of this lecture)
- **We have not covered **primary gastric lymphoma** in this lecture, you will learn about it when you start to discuss Hodgkin and Non-Hodgkin lymphoma of body. This is considered **non Hodgkin** and can be of different types, the most common one is **MALT** tumor. Treatment is vastly shifting to **nonsurgical** treatment and surgery is reserved for complications or unresponsive lesions
- My advise for you is to read the primary malignant tumors, ignore the metastasis.
- Also read about the types of gastric polyps and how they evolve into malignant tumors.

Mucosal polyps

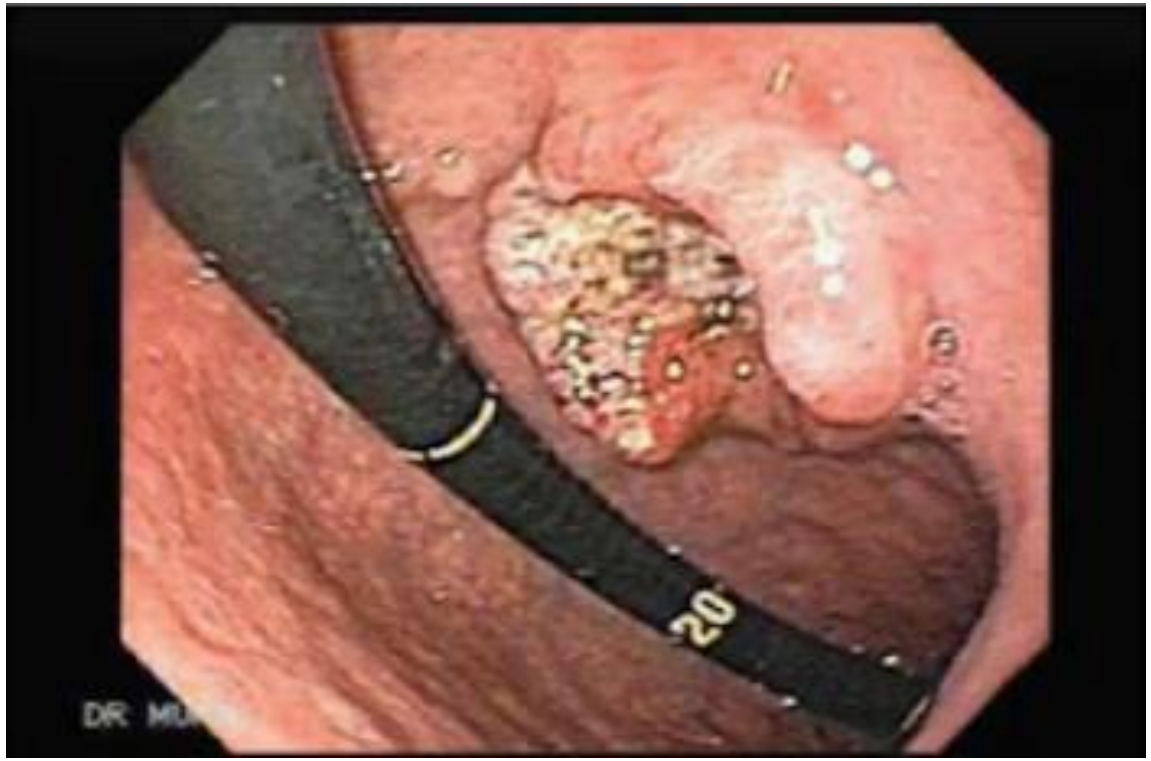


- Benign lesions.
- Epithelial polyps are rare.
- **Types**:
  - Hyperplastic polyps; 80% to 85%
  - Fundic gland polyps (~10%)
  - Adenomatous polyps (~5%)
  - Their frequency are one to one three so is their risk of transmission to malignancy.
- They increase the risk of developing gastric cancer, with **adenomatous polyps** having the highest risk of transforming into malignancy, however the risk overall seems to be on the lower side.

Gastric Adenocarcinoma (Gastric Cancer)

- Any patient with any type of gastric tumor is usually asymptomatic unless the tumor grows into a big enough size to cause symptoms.
- Then they present with anorexia, nausea, vague abdominal pain, early satiety, and/or dysphagia.
- 50% present beyond locoregional confine. Because they are rarely symptomatic until the tumor is big enough, that makes the majority of the pts presenting with disease beyond the locoregional confine. So when gastric tumor patients present symptomatic usually the cancer is beyond the stomach and has invaded surrounding structures and is beyond surgical therapy at least.
- Most common sites of metastatic disease (of gastric cancer) are the liver, the peritoneal surfaces, and lymph nodes. Other organs include ovaries, or other distant. It can also penetrate the stomach wall and invade surrounding structures.

This is how a gastric cancer looks on endoscopy. And as you learned from the peptic ulcer lecture any ulcer that does not heal should be biopsied because it might be cancer.



Gastric Cancer

- **Lauren classification**: histological classification that divides gastric cancer into diffuse and intestinal as they have different histological appearance and different way of presenting.
  - Diffuse
  - Intestinal
  - Both types are very aggressive although diffuse is more aggressive, and they both comprise the second most common cause for mortality of a cancer of bowel and lung cancer.

INTESTINAL	DIFFUSE
Environmental	Familial
Gastric atrophy, intestinal metaplasia	Blood type A
Men >women	Women >men
Increasing incidence with age	Younger age group
Gland formation	Poorly differentiated, signet ring cells
Hematogenous spread	Transmural/lymphatic spread
Microsatellite instability *APC* gene mutations	Decreased E-cadherin
p53, p16 inactivation	*p53, p16* inactivation

Gastric Cancer

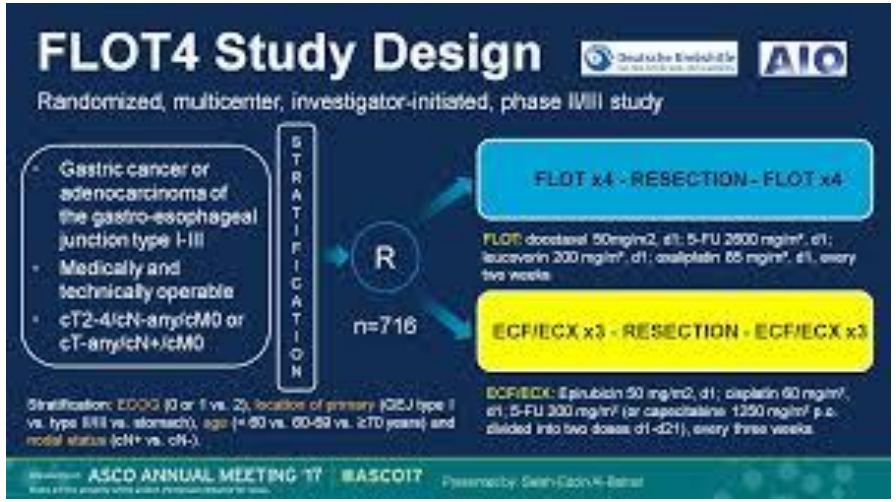
- **Risk factors** (anything that causes inflammation of the stomach):
  - Helicobacter pylori – reported in around 85% of all gastric cancer pts. This prevalence can be seen in any case series reposting gastric cancer histology.
  - Diet – can influence gastric cancer occurrence, it is a known risk factor. Back in the old days when there was no refrigeration (تبريد), people used to conserve food with high salt preparation and this was found to be correlated with stomach cancer. But since refrigeration was introduced the percentage of gastric cancer reduced in certain societies.
  - Obesity
  - Smoking
  - Long-term stomach inflammation (gastritis)
  - GERD
  - Family history and genetics – can play a strong role, there are certain genetic conditions that can predispose you to developing gastric cancer (see next slide).

Gastric cancer

- Known hereditary conditions that cause a genetic predisposition to developing stomach cancer (the common ones are):
  - Hereditary diffuse gastric cancer (CHD1)
  - Hereditary nonpolyposis colorectal cancer (also called HNPCC, or Lynch syndrome) – can give you not only colon cancer but also gastric cancer.
  - Li-Fraumeni syndrome
  - Familial adenomatous polyposis
  - Peutz-Jeghers syndrome

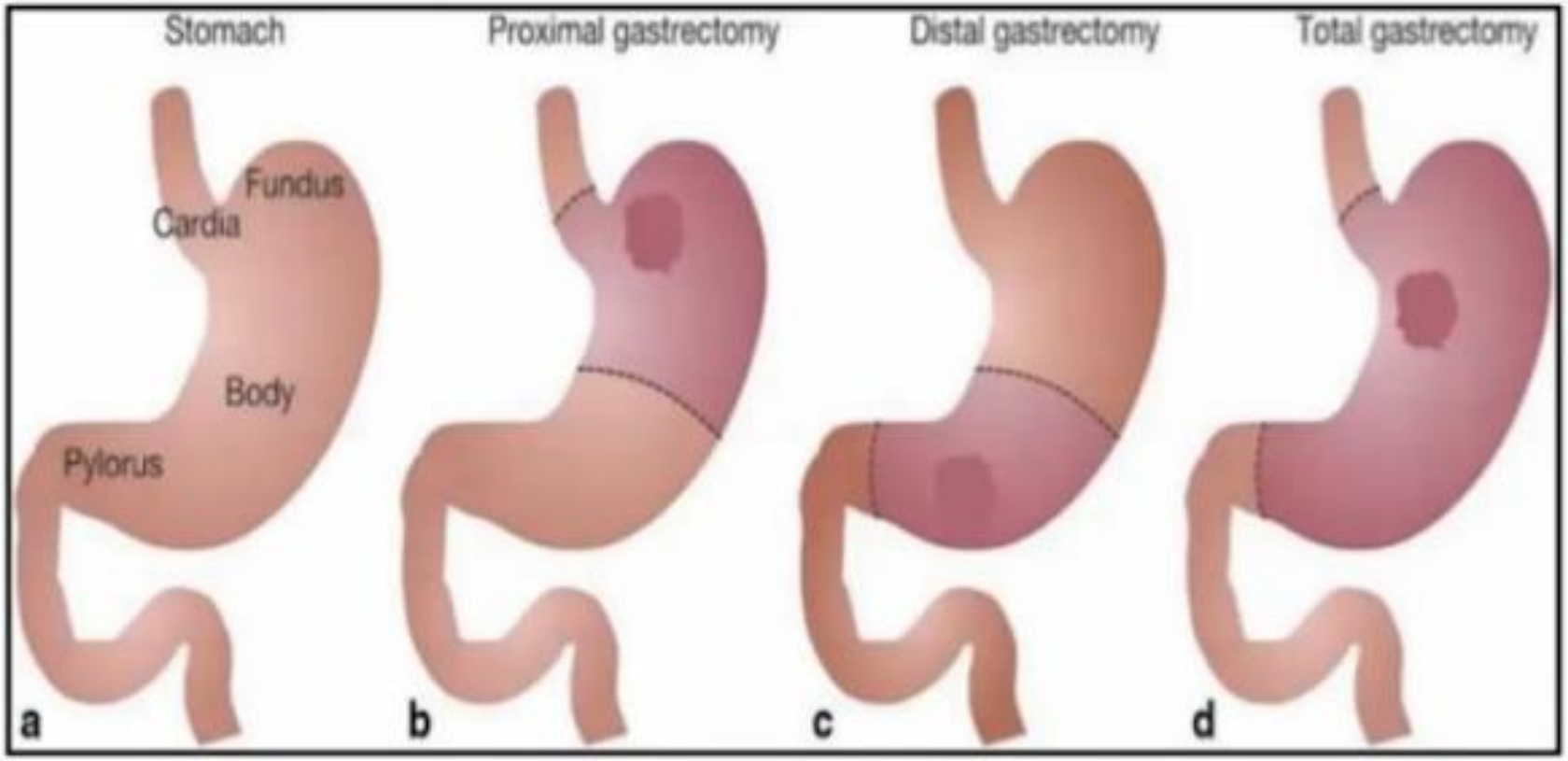
  - Certain populations can have genetic risk factor of inheriting gastric cancer but from all the pool of gastric cancer these comprise a small proportion.

Gastric cancer

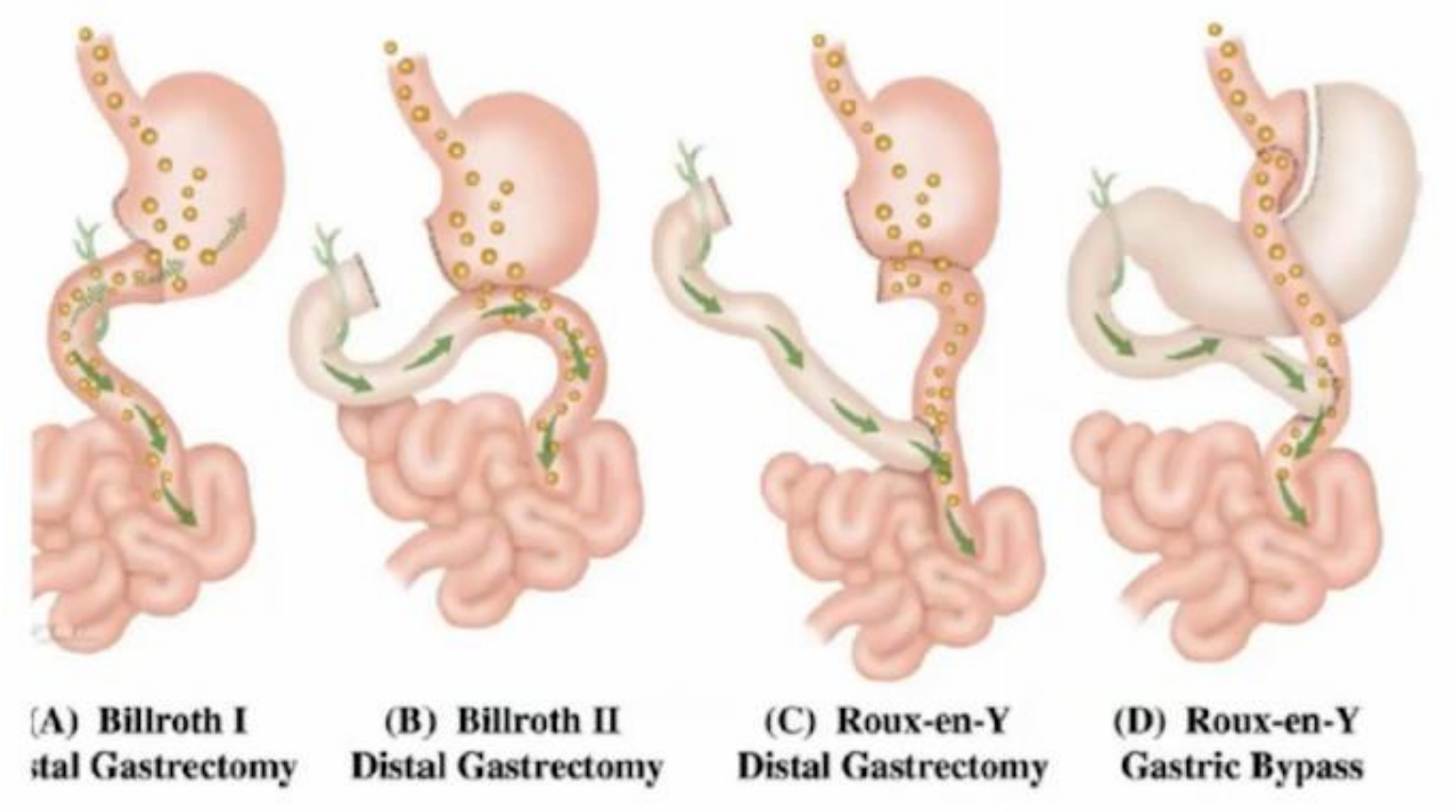


- **Diagnosis**:
  - CT Scan
  - Endoscopy
  - Biopsy
  - We do CT scan and endoscopy but the only way to confirm is with **tissue biopsy** and after confirming the diagnosis we need to stage the pt: we want to see if this is an early cancer that can be treated and resected or if it is advanced.

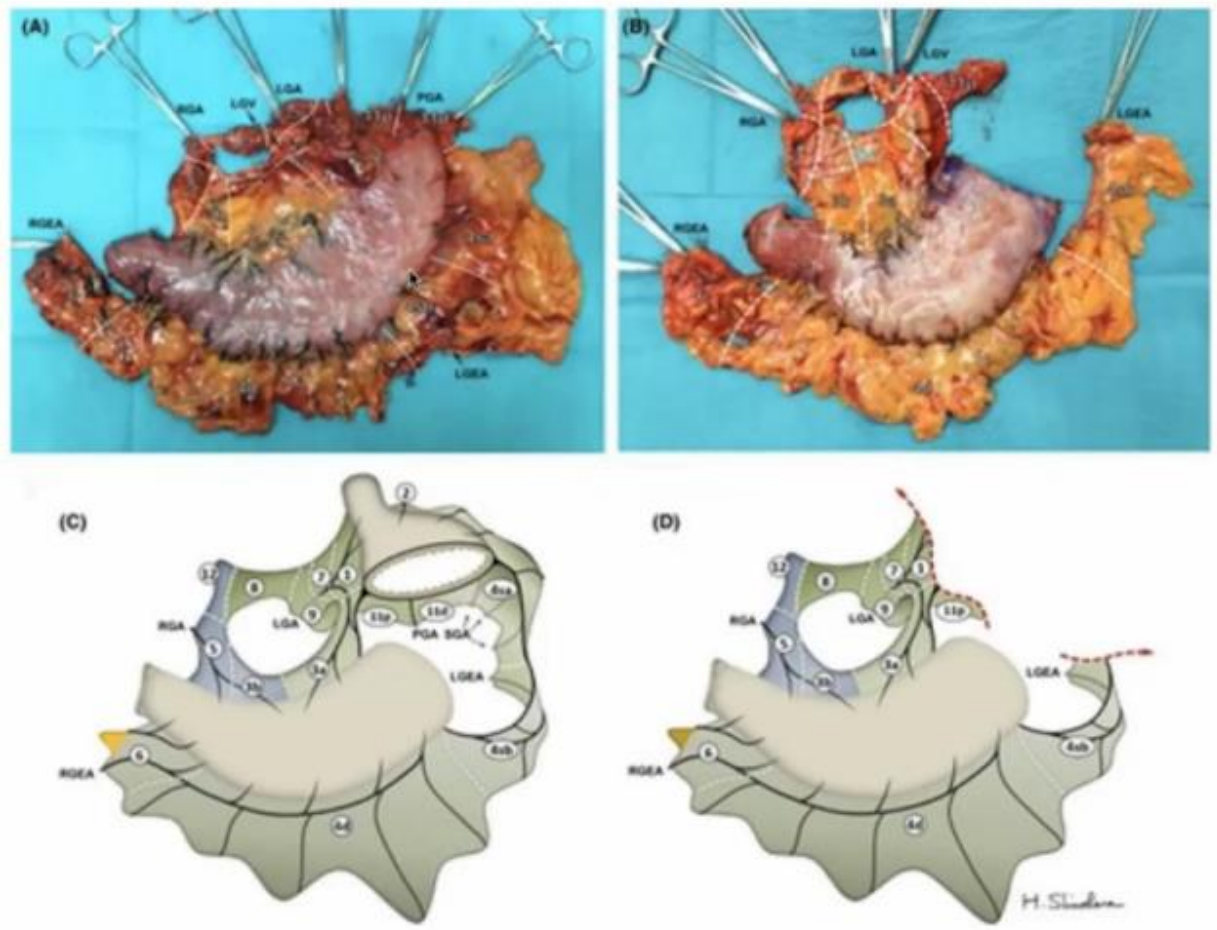
- **Treatment**
  - Perioperative Chemotherapy
  - Surgery
  - If the cancer is resectable, nowadays, the standard of care is to give perioperative chemotherapy (before and after surgery) and this perioperative ”or neoadjuvant” treatment is followed by **staging laparoscopy** to stage the cancer and make sure there are no peritoneal metastasis followed by surgery. We resect the **stomach** and the surrounding **lymph nodes** which drain the stomach to prevent recurrence through lymphatic spread.



In general the resection of gastric cancer can be done based on the location of the mass.
The proximal gastrectomy (second picture “B”) is pretty much abandoned these days and we only perform either distal gastrectomy or total gastrectomy.



After performing gastrectomy we have to reconstruct the stomach. The way we reconstruct the GI tract is either through Billroth 1 (A), Billroth 2 (B) or Roux-en-Y reconstruction (C). (D) is an obesity related surgery. So only A, B, and C reconstruction are related to gastric cancer



As we said, when you resect gastric cancer, It is not enough to resect the stomach only we also include the regional lymph nodes. You see here 2 pathological specimens showing all the lymph nodes surrounding the stomach that are included with the resection and this is done to decrease the risk of recurrence and it is done following pre operative chemotherapy.

Gastrointestinal Stromal Tumors (GISTs)

- Stromal or mesenchymal neoplasms typically present as **subepithelial** neoplasms (**submucosal**).
- Originates from the interstitial cells of Cajal (ICCs), sometime referred to as the gastrointestinal pacemaker cells – they are the ones that manage the peristalsis.
- Histologically can be Spindle cell type (70 percent), Epithelioid type or mixed.
- GISTs are identified mainly by expression of the **KIT protein** and frequently harbor activating mutations in the KIT or platelet-derived growth factor receptor alpha **(PDGFRA) genes**.

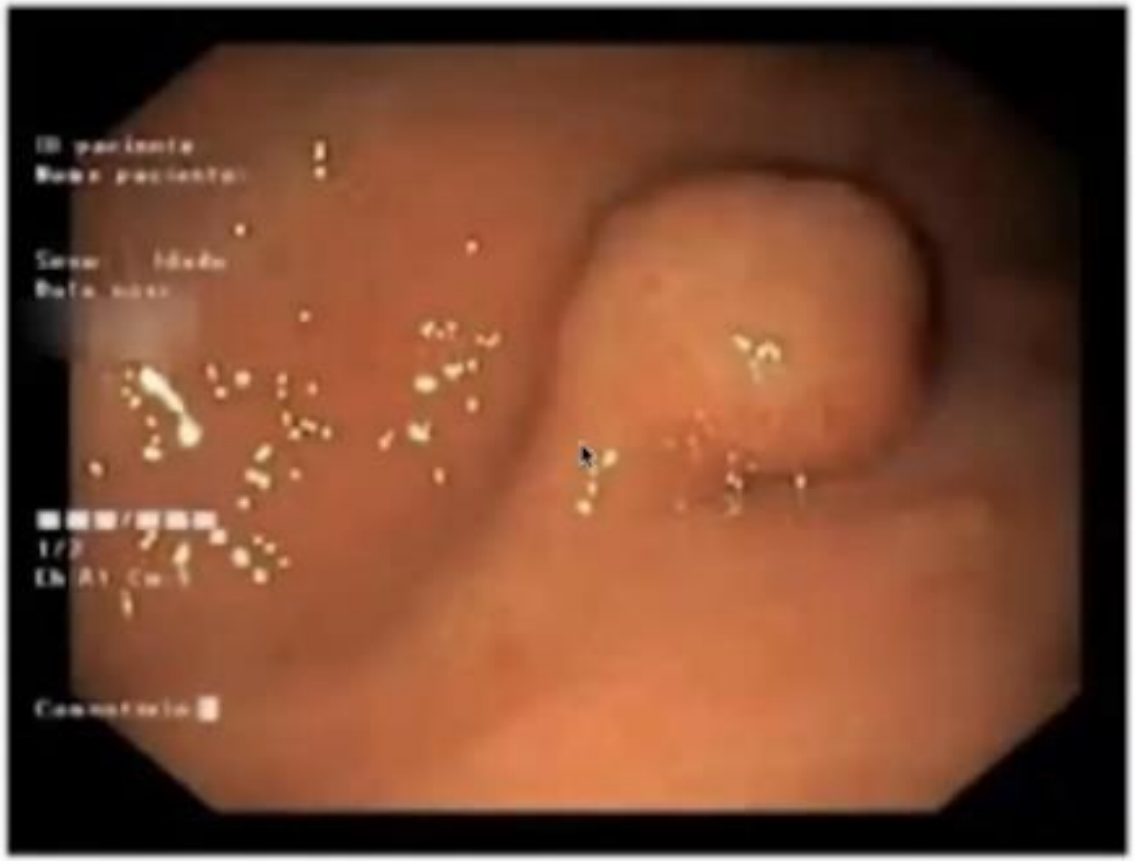
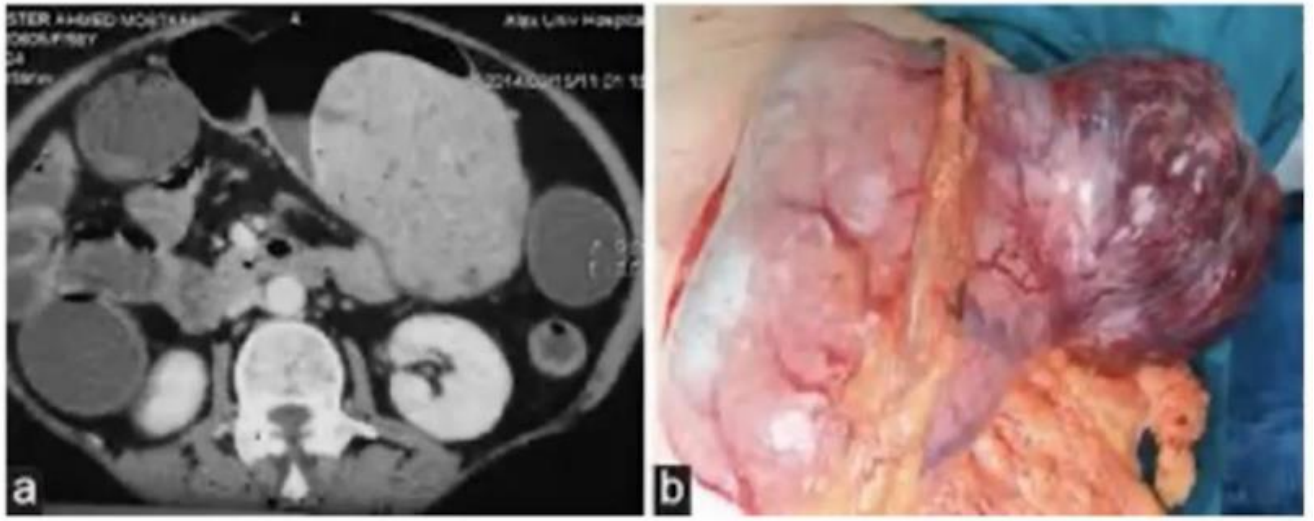


Fig. 1. Fifteen-millimeter SET located in the gastric fundus.

This is how they look on endoscopy, and as you can see the mucosa is intact and the tumor is submucosal, because they originate in the submucosa or subepithelial layer where the neural plexus is present.

Gastric GISTs

- **Presentation** (same as any gastric tumor):
  - Overt or ocular gastrointestinal bleeding – so the pt develop anemia and etiology is unknown so you work up the pt see an ulcer, take biopsy and comes back GIST.
  - Incidental finding on imaging (asymptomatic) - **most** of the time.
  - Abdominal pain/discomfort – very rarely when they are very big they can cause discomfort or early satiety.
  - Acute abdomen
  - Asymptomatic abdominal mass



Gastric GIST

- **DDx** (of all submucosal lesions includes mesenchymal lesions):
  - Lipomas
  - Schwannomas
  - Hemangiomas
  - Leiomyomas
  - Leiomyosarcomas (malignant variant of leiomyomas)
  - This is a classic **exam question** asking you to mention the differential diagnosis for this tumor.

Histological staining

Type	CD117	DOG-1	PKC-theta	CD34	SMA	S100 protein	Desmin
GISTs	+ (>95%)	+ (97%)	+ (72%)	+ (60 to 70%)	+/– (30 to 40%)	– (5% +)	Very rare
Leiomyoma	–	–		+ (10 to 15%)	+	–	+
Leiomyosarcoma	–	–	+ (10%)	–	+	–	+
Schwannoma	–	–	+ (10%)	–	–	+	–

- The way we differentiate between these different submucosal lesions on pathology depends on a group of immuno-histo-chemistry staining for different receptors.
- If you follow this table you can see how we can differentiate between them.

Gastric GIST

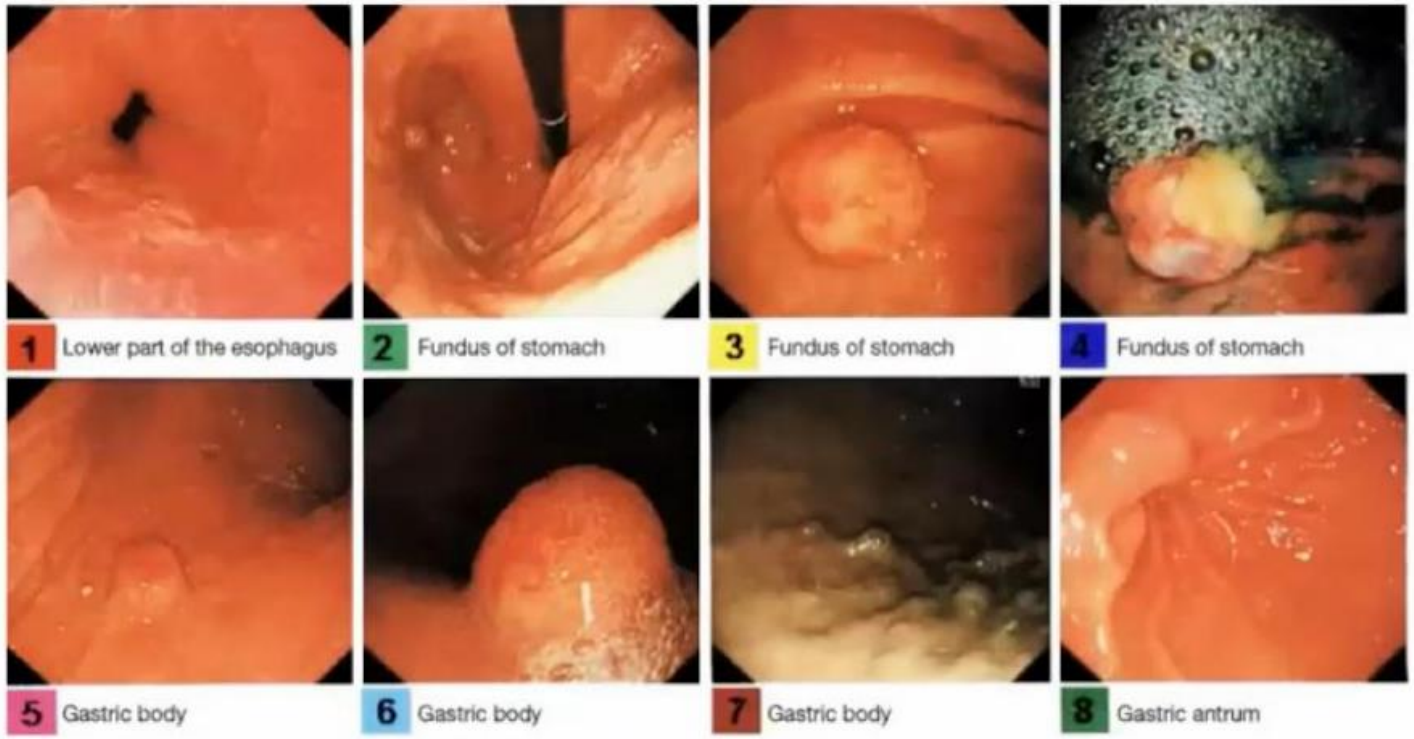
- **Diagnosis**:
  - CT scan
  - Endoscopy (EUS) – b/c these lesions are submucosal we utilize a special type of endoscopy which combines endoscopy with US guided biopsy so we can evaluate the lesion beyond the mucosa and then biopsy it through US.
  - Biopsy.
  - Initially we start with CT and endoscopy but we need biopsy to confirm the diagnosis.
- **Treatment:**
  - Once the diagnosis is confirmed and the mass is resectable, with minimal morbidity to the pt, surgery is usually the primary treatment.
  - Surgery
  - Imatinib (tyrosine kinase inhibitor) – used as an adjuvant or neoadjuvant utilized in treating GIST – considered one of the prime examples of targeted therapy in medicine.

Gastric GIST

- So treatment of GIST is either imatinib followed by surgery OR by surgery right away OR performing surgery then giving imatinib as an adjuvant.
- This is usually based on **3 factors**: mitotic count of the tumor on pathology, the size of the tumor, and the location.
- Certain GIST are more aggressive than others. For example duodenal GIST is considered more aggressive than gastric GIST and a mitotic count that is high with a large tumor has a higher risk of recurrence than small tumor with low mitosis, so in conditions with intermediate or high risk imatinib is advisable.

Gastric neuroendocrine tumors (gastric NETs)

- Cancers that begin in specialized cells called neuroendocrine cells. Neuroendocrine cells have traits similar to those of nerve cells and hormone producing cells.
- Neuroendocrine tumors, like GIST, can happen throughout the GI tract not only in the stomach.



Gastric NETs

- Types:
  - Type **1** gastric NETs, which represent 70 to 80 percent of all gastric NETs, are associated with chronic atrophic gastritis.
  - Type **2** gastric NETs (~5%), the underlying cause of type 2 gastric NETs is a pancreatic or duodenal (or somewhere in the upper GI tract) **gastrinoma** (Zollinger-Ellison syndrome).
  - The first 2 types are characterised by **elevated gastrin** levels. To differentiate between type 1 and 2 we measure the **pH of the stomach** the presence of high gastrin levels
  - Type **3** (**sporadic**) gastric NETs occur in the absence of atrophic gastritis or the Zollinger-Ellison syndrome (~**20%**).
- Management based on type:
  - Type 1 – when small we do endoscopic resection and surveillance, surgery is not indicated except in very rare cases where enterectomy is advised if the lesions are too many and cannot be managed endoscopically.
  - Type 3 – treated as adenocarcinoma of the stomach by radical resection with lymph node dissection.