**Carcinoma of the stomach**

**Introduction**
- Carcinoma of the stomach is still the second most common cause of cancer death worldwide, although the incidence and mortality have fallen dramatically over the last 50 years in many regions.
- The incidence of gastric cancer varies in different parts of the world and among various ethnic groups.
- Despite advances in diagnosis and treatment, the 5-year survival rate of stomach cancer is only 20 per cent.

**Definition**
- Malignant lesion of the stomach

**Epidemiology**
- Can occur at any age
- But Peak incidence is 50-70 years old.
- It is more aggressive in younger ages.
- Studies have confirmed that incidence declines in Japanese immigrant to America.
- Japan has the world highest rate of gastric cancer.
- Twice more common in male than in female
- Dust ingestion from a variety of industrial processes may be a risk.

**Risk factors**
<table>
<thead>
<tr>
<th>Predisposing</th>
<th>Environmental</th>
<th>Genetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pernicious anemia &amp; atrophic gastritis (achlorhydra)</td>
<td>1. H.pylori infection → Sero(+)patients have 6-9 folds risk</td>
<td>Blood group A</td>
</tr>
<tr>
<td>2. Previous gastric resection</td>
<td>2. Low socioeconomic Status</td>
<td>HNPCC: Hereditary non-polyposis</td>
</tr>
<tr>
<td>3. Chronic peptic ulcer (give rise to 1%)</td>
<td>3. Nationality (JAPAN)</td>
<td></td>
</tr>
<tr>
<td>4. Smoking</td>
<td>4. Diet (prevention)</td>
<td></td>
</tr>
<tr>
<td>5. Alcohol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Site**
- Proximal tumors are more common in developed countries, among whites, and in higher socio-economic classes.
- Distal tumors continue to predominate in Japan in contrast to the increasing prevalence of proximal tumors in the rest of the world.

**Classiﬁcation (acc to tumor behavior)**
- Intestinal forms gland-like tubular structures that frequently ulcerate
- Diffuse type represents the major histological type in endemic areas,
  - is more frequent in women and younger patients, and
  - is associated with blood group A, indicating genetic susceptibility.
- Mixed gastric carcinomas composed of intestinal and diffuse components have also been identified.
- The poorly differentiated diffuse-type is characterized by infiltration and thickening of the stomach wall (“leather bottle appearance”) without the formation of a discrete mass.

**Types (acc to microscopic appearance)**
- **Adenocarcinoma**
  - About 90% to 95% of cancers of the stomach.
  - These cancers develop from the cells that form the innermost lining of the stomach (the mucosa).
  - 4% of stomach cancers are lymphomas.
- **Lymphoma**
  - These are cancers of the immune system tissue that are sometimes found in the wall of the stomach.
- **Gastrointestinal stromal tumor (GIST)**
  - These are rare tumors that start in very early forms of cells in the wall of the stomach called interstitial cells of Cajal.
  - Some of these tumors are non-cancerous (benign); others are cancerous.
  - Although GISTs can be found anywhere in the digestive tract, most are found in the stomach.
- **Carcinoid tumor**
  - These are tumors that start in hormone-making cells of the stomach.
  - Most of these tumors do not spread to other organs.
  - About 3% of stomach cancers are carcinoid tumors.
- **Other types**
  - Such as squamous cell carcinoma, small cell carcinoma, and adeno-squamous, these cancers are very rare.

**Inherited cancer syndromes**
- Hereditary diffuse gastric cancer (defects in the CDH1 gene)
- Hereditary non-polyposis colorectal cancer (HNPCC)
- FAP, mutations in the APC gene.
- BRCA1 and BRCA2
- Peutz-Jeghers syndrome (PJS)
- A family history of stomach cancer

**nb**
- Approximately 95 per cent of stomach tumours are epithelial in origin and designated as adenocarcinomas. Adenosquamous, squamous, and undifferentiated carcinomas are rare

**Morphology by naked eye**
- **Polypoid**
- **Ulcerative**
- **Superficial spreading**
- **Linitis plastica**

**Clinical presentation**
- **Common**
  - Loss of appetite
  - Weight loss
- **General GI complains**
  - Epigastric pain
  - bloating , Early satiety
  - Nausea & vomiting*, Dysphagia*
- **Others**
  - Anemia
  - Epigastric mass, Hepatomegaly, Ascitis
  - Jaundice.
  - Blumers shelf
- **Sister mary joseph node**
- **Krukenberg tumor**
- **Irish node**
- **Virchows node**

**Diet (prevention)**
- Low socioeconomic Status
- Alcohol.
- Chronic peptic ulcer (achlorhydra)
- Dust ingestion
- H. pylori infection, obesity, and dietary factors.

**Studies**
- In African Americans, is of the epidemic type
- Inherited cancer syndromes
  - BRCA1 and BRCA2
  - FAP,
  - HNPCC:
  - Peutz-Jeghers syndrome (PJS)

**Other**
- APPROXIMATELY 95 PER CENT OF STOMACH TUMOURS ARE EPITHELIAL IN ORIGIN AND DESIGNATED AS ADENOCARCINOMAS. ADENOSQUAMOUS, SQUAMOUS, AND UNDIFFERENTIATED CARCINOMAS ARE RARE
Spread

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>lamina propria &amp; submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>muscularis &amp; subserosa</td>
</tr>
<tr>
<td>T3</td>
<td>serosa</td>
</tr>
<tr>
<td>T4</td>
<td>Adjacent organs</td>
</tr>
<tr>
<td>N0</td>
<td>no lymph node</td>
</tr>
<tr>
<td>N1</td>
<td>Epigastric node</td>
</tr>
<tr>
<td>N2</td>
<td>main arterial trunk</td>
</tr>
<tr>
<td>M0</td>
<td>No distal metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>distal metastasis</td>
</tr>
</tbody>
</table>

**Direct spread**
- Tumor penetrates the muscularis, serosa & adjacent organs (Pancreas, colon, liver)

**Lymphatic spread**
- Usually with extensive disease
- Liver 1st involved then lung & bone

**Blood – borne metastasis**
- This is common anywhere in peritoneal cavity
- (Ascites)
- Kruekenberg tumor (ovaries)
- Sister Joseph nodule (umbilicus)

**Transperitoneal spread**
- Intrahepatic jaundice by hepatomegaly

Complication

1. Peritoneal and pleural effusion
2. Obstruction of gastric outlet or small bowel
3. Bleeding
4. Intrahepatic jaundice by hepatomegaly

**Investigations**

**Upper GI endoscopy**
- Exournals dyspepsia >45 years
- Dyspepsia with alarm symptoms (weight loss, anaemia, recurrent vomiting, bleeding)
- Dyspepsia & family h/o gastric carcinoma

**Abdominal / pelvic CT scanning**

**Endoscopic ultrasound (EUS)**
- Depth of the tumour
- Enlarged perigastric/coeliac lymph nodes

**Upper GI series**
- Less invasive than endoscopy, and it might be useful in some situations
- A double-contrast technique may be used to look for early stomach cancer

**PET scan**
- In this test, radioactive substance (usually a type of sugar related to glucose, known as FDG) is injected into a vein.
- The amount of radioactivity used is very low and will pass out of the body over the next day or so.
- Because cancer cells are growing faster than normal cells, they use sugar much faster, so they take up the radioactive material.
- PET is sometimes useful if the doctor thinks the cancer might have spread but doesn’t know where

**Biopsy**
- Endoscopic
- CT guided
- EUS guided

**Others**
- Magnetic resonance imaging (MRI) scan
- Chest x-ray
- Laparoscopy
- Lab tests
  - CBC
  - A fecal occult blood test
  - Liver and kidney functions
  - ECG and Echo

**Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumour invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour invades muscularis propria or subserosa</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour penetrates serosa without invasion of adjacent structure</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour invades adjacent structures</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastases</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1 to 6 regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 7 to 15 regional lymph nodes</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in more than 15 regional lymph nodes</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

**Treatment**

**Surgical Resection & Adequate Lymphadenectomy is the only curative treatment except if there are metastases or co – morbid**

- Resection of tumour
- Grossly negative margin of at least 5 cms
- Partial gastrectomy
- Confirmed on frozen section
- block resection of adjacent involved organs

**Lymphadenectomy**
- D1: stations 3-6
- D2: stations 1, 2, 7, 8 and 11
- D3: stations 9, 10 and 12

**Extent of gastrectomy**
- Radical subtotal gastrectomy → (Distal tumour)
- Total gastrectomy → (Proximal tumour)
Endoscopic resection → Endoscopic mucosal resection and endoscopic submucosal resection can be used only to treat some very early-stage cancers, where the chance of spread to the lymph nodes is very low.

Survival benefit to adjuvant radio-chemotherapy is marginal in patients who have undergone adequate resection.

<table>
<thead>
<tr>
<th>Palliative surgery</th>
<th>For people with unresectable stomach cancer, surgery can often still be used to help control the cancer or to help prevent or relieve symptoms or complications.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Subtotal gastrectomy:</td>
</tr>
<tr>
<td></td>
<td>- Gastric bypass (gastrojejunostomy):</td>
</tr>
<tr>
<td></td>
<td>- Endoscopic tumor ablation:</td>
</tr>
<tr>
<td></td>
<td>- Stent placement:</td>
</tr>
<tr>
<td></td>
<td>- Feeding tube placement:</td>
</tr>
</tbody>
</table>

Chemo can be used in different ways to help treat stomach cancer:
- Chemo can be given before surgery for stomach cancer. This, known as neoadjuvant treatment.
- Chemo may be given after surgery to remove the cancer. This is called adjuvant treatment.
- Chemo may be given as the primary (main) treatment for stomach cancer that has spread (metastasized) to distant organs.

<table>
<thead>
<tr>
<th>Target therapy</th>
<th>Trastuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- About 1 out of 5 of stomach cancers has too much of a growth-promoting protein called HER2/neu (or just HER2) on the surface of the cancer cells.</td>
</tr>
<tr>
<td></td>
<td>- Tumors with increased levels of HER2 are called HER2-positive.</td>
</tr>
<tr>
<td></td>
<td>- Trastuzumab (Herceptin) is a monoclonal antibody, a man-made version of a very specific immune system protein, which targets the HER2 protein.</td>
</tr>
<tr>
<td></td>
<td>- Giving trastuzumab with chemo can help some patients with advanced, HER2-positive stomach cancer live longer than giving chemo alone.</td>
</tr>
</tbody>
</table>

Ramucirumab (Cyramza®)
- In order for cancers to grow and spread, they need to create new blood vessels so that the tumors get blood and nutrients.
- One of the proteins that tells the body to make new blood vessels is called VEGF.
- VEGF binds to cell surface proteins called receptors to act.
- Ramucirumab (Cyramza®) is a monoclonal antibody that binds to a receptor for VEGF.
- This keeps VEGF from binding to the receptor and signaling the body to make more blood vessels.
- This can help slow or stop the growth and spread of cancer.