GASTRIC TUMOURS

BENIGN EPITHELIAL GASTRIC POLYPS

Fundic Gland (50%): (HP/PPI/polyposis syndromes)
Sporadic(B-catenin) <1% dysplasia → *biopsy or excise (>1cm/dysplastic) → rpt OGD 12 mths*
Polyposis syndrome (FAP/MYH1 etc) → *biopsy or excise (>1cm/dysplastic) → rpt OGD 12 mths + polyposis assessment*

Hyperplastic (75%):
Hyperproliferative response to injury (**gastritis)**; 20% dysplastic
Bx polyp + intervening mucosa (excise dysplastic) → treat HP → OGD 12mths

Adenoma (10%):
Intestinal = associated with CAG (men>50/lesser curve/increase risk w/ size **50%>2cm cancerous**)
Non-intestinal
Excise + Bx intervening mucosa →OGD 12mths (6mths if incomplete excision of dysplastic polyp)

Hamartomas (xx%):
P-J/JP/Cronkite-Canada → *excise >1cm → OGD 12mths*

Inflammatory: Bx → *excise if dysplastic → no follow-up if non-dysplastic*

GASTRIC CANCER

Epidemiology: M/Japan /declining incidence (?cardia rising)

Aetiology: (a)Inflammation: Type A= P. anaemia/Type B= H. Pylori/Erosive (NSAIDS,smoking,EtOH etc)/Reflux (bile, esp after resection)
(b)Polyps
(c)Ulcers (typically border of atrophic mucosa)
Atrophic gastritis →intestinal metaplasia → dysplasia → cancer (Correa hypothesis)

Macro: Polyp/Ulcer/Infiltrative/Unclassificable lesions (Borrman)
Morphological subtypes **Lauren**: intestinal/diffuse||**Ming**: expanding vs infiltrative **WHO:** tubular/papillary/mucinous/poorly diff

Micro: **adenocarcinoma**

Spread: local=
nodes= 16 stations(10%T1s, 80% T4s) **extent (number) of nodal spread most important prognostic factor**
mets= liver

Genetics: FGF4, p53, APC, DCC, k-ras, B-catenin, p27, bci-2, c-MYC, cMET, SIP-1, DNA MMR, E-Cad, nm23
Hereditary Diffuse Gastric Cancer: autodom w/ 70% lifetime risk; 1/3 have CDH1 germline mutation (TSG)
Syndromes: Lynch/FAP/P-J/JP/Li Fraumeni
Other: Polymorphisms in H. pylori response

MESENCHYMAL

GIST
Lymphoma:
MALT: 50+/ESI; PUD symptoms/neoplastic B cells slowly spread to nodes; 77% regress with H. pylori Tx
Diffuse Large B-Cell: 50% MALT foci so treat H. pylori; EBV confers resistance to CRT
Rare: glomus/myofibroblast tumour/leiomyoma/schwannoma/Kaposi's sarcoma/synovial sarcoma

STAGING GASTRIC CANCER (ESMO)

1. **OGD + Bx**
2. **CTTAP:** TNM staging (T: 90% accurate)(N: miss perigastrics)(M: miss peritoneal seeds)
3. **EUS:** prox+distal extent of tumour → resection margins (T+N accurate)
4. **Laparoscopy:** all resectables for hepatic mets/peritoneal mets/cytology (*SAGES*)

PET: nodes + mets less FDG avid ||Sentinel Node: multiple LN stations involved at same time; concept defunct

T	N	M
T0	N0	M0 No mets
Tis	N1 1-2	M1 Distant mets
T1a Mucosa	N2 3-6	+ive cytology
T1b Submucosa	N3a 7-15	Peritoneal seeding
T2 Muscularis Propria	N3b >15	
T3 Subserosa (not visceral perit)		
T4a Visceral peritoneum		
T4b Adjacent structures		

EARLY GASTRIC CANCER

Tumour confined to muscosa (T1a)/submucosa (T1b) without muscularis propria invasion (irresepective of nodal mets)

Site: fundus commonest

(a)Endoscopic appearances: *IIc ulcerating commonest; true III is rare*

Paris classification predicts submucosal invasion

-57% Protruding type O-$I_{p/s}$

-40% Non-protruding/non-elevated 0-II a(elevated) ||b(flat)|| c(depressed)

-100% Excavated O-III

(b)Revised Vienna Classification:

Negative/indeterminate → repeat OGD

Mucosal (T1a) low-grade dysplasia → EMR/ESD || Mucosal (T1a) High grade → EMR/ESD or surgery (D1+/D2 if unfavourable)

Submucosal (T1b) → surgery (D2 lymphadenectomy)

SIZE >30mm || ULCERATION$_{(III)}$/DEPRESSED$_{(IIc)}$ || POOR DIFFERENTIATION → 45% node positive in T1 EGCs

1(a)ENDOSCOPIC RESECTION: *T1a low-grades/some high grades*

EMR vs ESD: equivalent LR up to 10mm; EMR up to 20mm lesions en block; ESD >20mm reduces LR risk

6mthly surveillance for 5 yrs (metachronous in 14%/residual disease)

1(b)SURGERY: *T1a high grades/T1a unfavourable characteristics/ T1b*

(i)Total gastrectomy in mid/upper third

Prox gastrectomy with D1+ lymphadenectomy in upper third: distal nodes uninvolved in 1/3 of upper tumours; mostly 7/8a

(ii)Distal gastrectomy in mid/distal third

PPG in mid third: suprapyloric nodes uninvolved in 90% T1s; involved in 10% (T1a 3%, T1b 18%)

Need 5cm margin between tumour and GOJ if intestinal/expanding (8cm if diffuse/infiltrative) *(JGCA: 3/5)*

2. NODES: (i)T1a = D1/D1 (ii)T1b= D2 (also T1a unfavourables)

3. CHEMO: PERIOPERATIVE epirubicin/Cisplatin/5FU *(MAGIC trial)*

ESMO GUIDELINES

EMR/ESD: T1a/<20mm/non-ulcerated or depressed ?differentiation

SURGICAL RESECTION: stage IB-III ie T1N1/T2N0 onwards until M1

INDUCTION THERAPY: perioperative chemo (adjuvant if missed) in T1N1/T2 stage IB; not Tis/T1N0 stage 0/1A

EXTENT OF LN DISSECTION: Taiwan RCT = increased 5yr survival in D3 vs D1 (59.5 v 53.6%)

Indication: submucosal/unfavourable mucosal (>30mm/undiff/depressed or ulcerated)

OUTCOMES: 5yr survival 90%+ (both West and Japan)

RADICAL SURGICAL MANAGEMENT OF GASTRIC CANCER

Resection Margins

Proximal margin main determinant of type of resection 5cm intestinal, 8cm diffuse (JGCA say 3+5)

Types

1. Total Gastrectomy: whole stomach (proximal tumours)
2. Proximal Gastrectomy: proximal stomach with pylorus preserved (proximal tumours if >50% preservable
3. Distal Gastrectomy: preserves cardia (mid/lower third tumours) *RCTs: DG non-inferior to TG in distals*
4. Pylorus-preserving Gastrectomy: TG preserving pylorus (EGC w/o nodal potential)
5. Segmental Gastrectomy: circumferential resection
6. Local Resection: non-circumferential resection

Recon

TOTAL: **Roux-en-Y** is standard/**jejeunal interposition** equivalent/**pouch:** 13 supportive RCTs
Ideal length of Roux loop: 50cm (short= dumping, long= malabsorption)

PROXIMAL: (i)**Jejeunal transposition** + pyloroplasty/myotomy (isoperistaltic vs reflux) *dumping*
(ii)**Oesophagogastrostomy** *reflux*

DISTAL:

(i)Roux-en-Y: locally advanced with high recurrence risk/small remnant/reflux pre-op/cannot tolerate leak
Pro: low leak rate/no bile reflux/won't obstruct if recurs
Con: internal hernia/lose access to biliary tree/nutritional deficits
Avoid if need access to biliary tree

(ii)Billroth I: EGC with low recurrence risk/need access to biliary tree
Pro: no internal hernia/keep access to biliary tree/physiological food passage
Con: higher leak rate/bile reflux/obstruct if recurs
Avoid if cannot tolerate leak/small remnant/locally advanced with high recurrence rate/reflux pre-op

LYMPHADENECTOMY

50% of T4s and 10% T1s (3% T1a, 18% T1b) nodal positive→ JGCA recommends: early D1/1+ and locally advanced D2
Evidence: Taipei RCT and Dutch D1/2 showed survival benefit/mortality reduction respectively with D2

D1: 1-7 (perigastrics) D2: 1-11 D4+: para-aortic
D1+: 1-9 + 11 D3: 12-15

N1 (perigastrics)	**N2**	**N3**	**N4: (para-aortic)**
1: Right cardia	7: Left gastric artery	12: Hepatoduodenal	16: para-aortic
2: Left cardia	8: Common hepatic artery	13: Posterior to head of pancreas	
3: Lesser omentum	9: Coeliac trunk	14: SMA	
4: Greater omentum	10: Splenic hilum	15: Middle colic artery	
5: Suprapyloric	11: Splenic artery		
6: Infrapyloric			

SPLENECTOMY

Spleen/pancreas body in dorsal mesogastrium share vessels/lymphatics with stomach(via GS ligament)s
JGCA → splenectomy if (i)**T2-4 greater curve tumours** (ii)**invasion of splenic hilum/pancreatic tail**

DISTAL PANCREATECTOMY

Aim: complete nodal dissection along splenic artery and hilum (but can dissect No11 nodes without pancreatectomy!)
Dutch/British D1/2 studies: DP+S high M&M so **only if directly invades pancreas and could still get R0 resection**

CHEMO

PERIOPERATIVE: downstaging and overall survival increase *(MAGIC trial)*

Early Complications

1. LEAK: (i)Anastomotic (Billroth I>R-en-Y)
   (ii)Duodenal stump if aff limb obst/ischaemia (catheter -> fistula/duodenal decompression/keep eating)
2. BLEEDING: (i)Immediate= haemostasis (ii)Delayed: pseudo-aneurysms esp GDA

Late Complications

1(a)EARLY DUMPING SYNDROME: within 30 mins of meal, SI fills rapidly with hyperosmotic load → ECF drawn into gut
Symptoms: bloat/cramp/palpitations/nausea
Management: small meals, less osmotic load (low sugar/salt), guar gum or pectin
1(b)LATE DUMPING SYNDROME: rapid carb dump into jejeunum → insulinaemia → hypoglycaemia
Symptoms: neuroglycopaenia
Management: low carb, regular meals
1153 gastrectomies: 68% early vs 38% late dumping
OGTT= 75g oral glucose → (i) HCt rises, early dumping (ii)BM drops, late dumping

2. NUTRITIONAL: Vit B_{12} no parietal cells → macrocystic anaemia (1mg hydroxycobalamin 3mthly for life)
   Iron: (i)need acid to reduce Fe^{3+} to Fe^{2+} and (ii)duo-jejeunal absorption bypassed
   Fat/ADEK malabsorption: less mixing time as shorter jejeunum/BP limb bypasses jej section

4. BILE REFLUX (Billroth I) – give cholestyramine/sucralfate to bind bile; surgically recon

5. INTERNAL HERNIA (Roux-en-Y)

6. SMALL STOMACH SYNDROME

PALLIATIVE CARE

Median survival 8 mths
Aims: (i)relieve dysphagia/GOO (ii)extend survival with good QoL

Features:

Epigastric pain/bloating/early satiety
Vomiting/haematemesis
Reflux
Dysphagia (pseudoachalasia or true cardia obstruction)
Constitutionals
OE: supraclav LNs, jaundice, ascites, pleural effusion

Treatment

1. Chemo: (i)cisplatin/5FU/epirubicin combo therapy (ii)test for HER-2 → add trastuzumab
2. Gastric outlet obstruction: (i)stent if short prognosis (ii) anterior gastrojej if longer
3. Bleeding: laser/APC

GIST

Soft tissue sarcomas of mesenchymal origin arising in GI tract (3% of all GI tumours)
Arise from interstitial cells of Cajal (pacemakers in myenteric plexus)

Epidemiology:
A:58yrs median G: ESI I: 900/yr

Pathology:
Micro: smooth muscle/neural/undifferentiated→ 70% spindle cell, 20% giant epitheloid, 10% mixed
Macro: submucosal
Site: 70% stomach, 20% SB, 10% elsewhere (60% submucosal)
Spread: nodal spread rare || mets= liver/peritoneum
Genetics: (i)CD117 c-KIT1 in 90% (ii)DOG1 (iii) CD34 *Kit proto-ongcogene → Kit TKr activates → cell growth

Clinical features
Symptoms: pain/bleeding/early satiety/constitutionals(fever, night sweats, weight loss)
Signs: mass

Investigations
Diagnostic 1. **OGD:** submucosal 2. **EUS + FNA:** hypoechoic, homogenous lesion (FNA for diagnosis + mutanalysis guides drug tx)
Staging: **CTTAP**
Other: MRI treatment response by Choi criteria; FDG-PET for tumour response on imatinib

Management of locoregional disease
1. RESECTION (large >3cm, symptomatic)
Stomach: local resection ||Oesophagus: oesophagectomy + jej interposition/prox gastrectomy|| Small bowel: resection
No role for endoscopic resection
Nodes: no role for lymphadenectomy

2. SURVEILLANCE: small (<3cm) and asymptomatic

Management of unresectable/metastatic disease
Imatinib 400mg/d → 5yr survival 50% (otherwise dead in 12mths)
SE's= tumour **haemorrhage**
Resistance (c-KIT exon 9 mutation) in 20%
Treatment response by **Choi criteria**= 10% size reduction + 15% density reduction

Outcomes
Untreated: 12mth survival
Locoregional disease: 90% 5yr survival if R0 resection
Imatinib: 50% 5 yr survival in unresectables

LEIOMYOMA: Submucosal || Management: (i) surveillance with EUS every 1-2yrs if asymptomatic (ii)excise symptomatic or growing
LEIOMYOSARCOMA Treat as malignant if >2cm on EUS
GASTRIC LYMPHOMA
Epidemiology: M/60yo median
Investigations: OGD-Bx/EUS-FNA/CTTAP/BM aspirate
Staging: Blackledge 1: GI tract 2:abdo nodes(local=pergastric, distant= paraaortic) 3:serosal breach 4: disseminated extranodal disease

Low-grade MALT:
(i)associated with H. pylori; regress with HP treatment in stage 1; 6mth OGD for 2yrs afterwards
(ii) R-CHOP Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone if fails to regress

High-grade MALT:
Treatment: CHOP (with surgery for bleeding, emergency or if CHOP fails)

MENETRIER's DISEASE: acquired gastropathy with 10% malignancy risk→ giant rugae 1>cm in body + foveolar hyperplasia ||Sx= abdo pain/peripheral oedema
Ix: OGD + deep Bx (pit"gland ratio) || Mx= (i)cetuximab (ii)gastretomy