# SMALL INTESTINAL NETs/MIDGUT CARCINOIDS

30% of GEP-NETS; 25% of all small bowel neoplasms
Commonest cause of carcinoid syndrome
Late middle-age (mean age 65); slight male preponderance

## PATHOLOGY

Originate from **Enterochromaffin cells (EC)** in intestinal crypts (secrete serotonin and substance P)
Site: terminal ileum; submucosal  Size: 1cm or less
Macro: flat, fibrotic submucosal tumour +/_central navelling; tiny area or circumferential ring of fibrosis

## PATHOGENESIS

**1. Primary tumour** only cause obstruction if advanced
**2. Fibrosis:** serotonin, growth factors etc from neuroendocrine mets →reaction in mesentery → obstruct mes vessels/bowel
(a)distal ileal mesentery contracts→tethers mes. root to retroperitoneum (b)fibrotic bands attach to serosa
**3. Mesenteric mets**: (a)grow→obstruction (b)encase and occlude mesenteric vessels
**4. Vascular Elastosis**: specific angiopathy in advanced SI NETs (elastin prolif in adventitia → thickening of mes. vessel walls)

Thus:
**(1)Bowel obstruction:** mass; fibrotic bands; mesenteric mets
**(2)Bowel ischaemia**: mets encase mesenteric vessels; fibrotic contraction in mesentery; vascular elastosis

## SPREAD

Mets: Mesentery/liver/brain/ovary/breast/skin/bone/muscle  ***carcinoid syndrome implies liver mets***
Nodes: 70-90% mesenteric mets (mistaken for primaries when close to bowel wall)/neck/mediastinum/peripheral

## CLINICAL FEATURES

*Slow growth →* ***long prodrome*** *before diagnosis*
(a)**Borborygmi/pain**; intermittent attacks getting more frequent until…
(b)**Subacute/acute obstruction** (30-45% discovered at emergency op)
(c)**Bleeding** in later disease (small, submucosal)
(d)**Carcinoid syndrome** (i)due to liver mets (ii)without mets if retroperitoneal invasion, bypassing liver
*Flush/Sweating/Palpitations/Diarrhoea/chocolate or alcohol intolerance*

## Carcinoid syndrome (5% of carcinoids)

Vasoactive substances escape hepatic degradation due to (i)liver mets (ii)extraportal carcinoid eg bronchial
Flushing and diarrhoea commonest symptoms (chocolate and alcohol typical precipitants)

INVESTIGATIONS

*A. BLOODS and URINE*

**Plasma Chromogranin A** – more sensitive than urinary 5-HIAA

-non-specific (false +itives: liver/renal failure/IBD/atrophic gastritis/chronic PPI use)

Useful for: (a)early diagnosis (b)reflects tumour load → treatment response/recurrence (c)prognostic value

**Pentagastrin provocation test**

**Urinary 5-HIAA** (serotonin metabolite specific for SI NETs): occurs late, implies liver mets

*B. IMAGING:*

**CT** (first investigation): primaries too small/mesenteric nodes and their retroperitoneal extension/liver mets

**OctreoScan:** 90% of small intestinal NETs have type 2 & 5 somatostatin receptors

**MRI:** better than CT for liver mets

**US:** visualise and biopsy liver mets

**PET:** [$^{18}$F]deoxyglucose (FDG) is rarely positive in lower proliferation rates so positivity means aggressive lesions

*Serotonin precursor 5-HTP labelled w/ $^{11}$C or gallium-68 identifies small NETs sensitively → monitor treatment response*

*C. BIOPSIES:*

-Immunoreactivity to **serotonin**

-85% of small intestinal NETs stain with **chromogranin A** and **synaptophysin**

-Proliferation rate by **Ki67 antibody** (high proliferation rate and undifferentiated pattern has poor prognosis)

-Micro: **mixed insular and glandular growth pattern**; if purely insular and trabecular = less favourable prognosis)

SURGICAL MANAGEMENT

1. **Somatostatin** to prevent carcinoid crisis
2. Small bowel and mesenteric **resection**

LIVER METASTASES

Surgery

RF ablation

Liver embolization

Liver transplantation

MEDICAL MANAGEMENT

RADIOTHERAPY

OUTCOMES

5 year survival 67% from 40 year Swedish follow-up study

Better survival in younger patients (<50years)

Worse: nodal or distant mets, perit. Disease, high 5-HIAA, age, emergency, significant wt loss, high prolif/poor differentiation

RECTAL NETs

15% of GEP-NETs; 2% of rectal tumours
Rare in Blacks/Asians
Pathology: neuroendocrine EC-cell tumour
Spread: risk of dissemination appreciable at 1cm+
Features: (i)As per rectal tumour (ii)Carcinoid syndrome if liver mets
Investigations: classical TMs absent; histology, KI67 * CgA/urine 5HIAA not useful*
Management: (i)Small <1cm= local excision (ii)2cm+ as for CRC 1-1.9= assess for invasion
Outcomes: 90% 5yr survival if localised (30% if mets); 4-5 mth median survival if recurrent

COLON NETs

10% OF GEP-NETS; 5% of colonic tumours
Sites: proximal colon mainly
Spread: liver spread common
Features: as for CRC + carcinoid in proximal lesions
Investigations: as for CRC
Management: as for CRC
Outcomes 37% 5yr survival

APPENDICEAL NETs

6% of GEP-NETs
Path: serotonin-producing Ec cells
Sites: 75% tip (so rarely cause appendicitis) T1a <1cm T1b 1-2cm T2 2-4cm/caecal T3 >4cm/ileal ||N1=nodes ||M1=mets
Size: 90% <1cm
Spread:
Management
(i) appendicetomy if <1cm or 1-2cm localised at tip
(ii) right hemi if >2cm/near base/involved resection margins/mesoappendix spread/angioinvasion/nodal spread/high proif rate

Follow-up
None if curative appendicectomy
If needed right hemi → 5HIAA + CgA at 3 mths + CT/MRI/OctreoScan