Pathological mimics of malignancy in the GI tract

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How do we become aware of the problems and the errors?

- in house: double reporting, casual second opinion, etc
- review at multidisciplinary meetings and network reviews
- second 'expert' opinion practice
- medicolegal practice
- duty of care and GMC reviews
- the literature – brave papers, 'Lesson of the Month'

Mimics of neoplasia in the GI tract

- problems with reactive v dysplasia just as common if not more so than benign v malignant
- implications of an erroneous diagnosis often just as severe (cf HGD and oesophageal resection)
- we will stick with just five important "mimics'

Basil C Morson, doyen of GI pathologists

"It's your job to control surgeons"

Peter G Isaacson, doyen of lymphoma pathologists

Biopsy appearances easily mistaken for malignancy in gastrointestinal endoscopy

P. ISAACSON

Mimics numbers 1 & 2

- Type 1 lesions: only in the stomach.

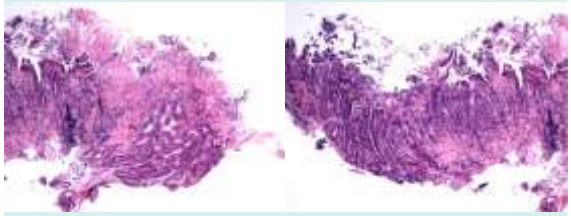
  Superficial ulceration with irregular and atypical acinar structures fading into regular regenerative glands

- Type 2 lesions: oesophagus, stomach and rectum

  Abnormal stromal cells associated with ulceration

Isaacson PG. Histopathology 1982; 6: 377-389.

Mimic number 1 - Reactive gastritis with erosions

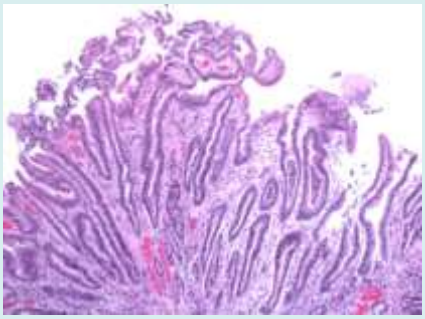


Overdiagnosis of cancer

Reactive gastritis with erosions is the commonest cause of misdiagnosis of gastric cancer

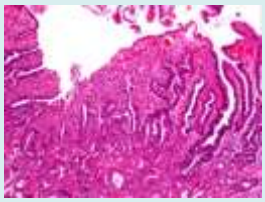
Isaacson et al, 1982

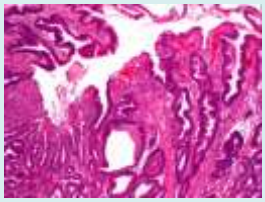
Reactive gastritis mimicking dysplasia – it's all 'dysplastic'!!



Overdiagnosis of dysplasia

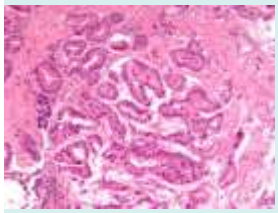
Reactive gastritis with intestinal metaplasia

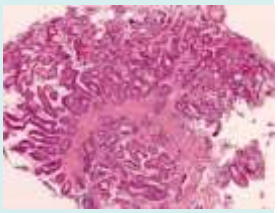




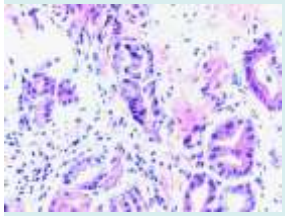
Overdiagnosis of cancer

Reactive gastritis with malorientation/ tangential sectioning





Isaacson type 1 – this week's case



Mimic number 1 - Reactive gastritis with erosions

- never diagnose dysplasia or cancer when the dodgy cells are in fibrinous material
- context – are the clinical and endoscopic features suggestive of cancer?
- what helps? – histochemistry and immunohistochemistry do not help much
- what to do – second opinion, expert opinion, ASK FOR ANOTHER BIOPSY (especially after treatment)

Mimic number 2

- Type 2 lesions: oesophagus, stomach and rectum

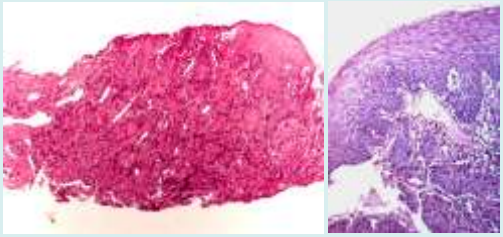
  Abnormal stromal cells associated with ulceration

  Isaacson PG. Histopathology 1982; 6: 377-389

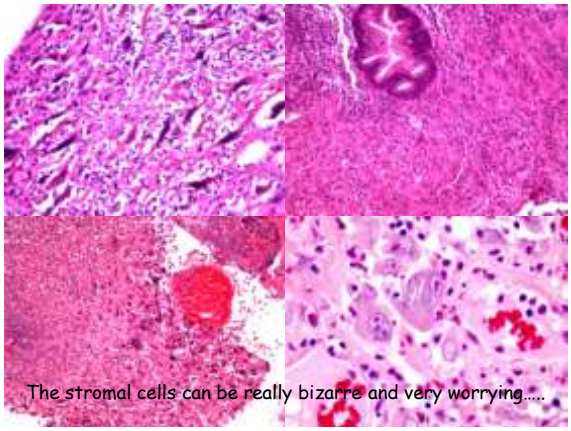
- especially in association with proliferative epithelium (usually squamous but sometimes glandular)

'Inflammatory polyp at the OGJ'

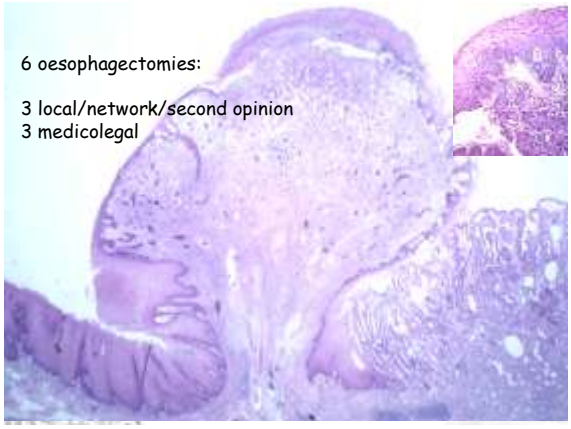
It is both proliferative squamous (sometimes glandular) epithelium and the bizarre stromal cells that cause the trouble



Isaacson et al, 1982
Al-Sam, Lakhani & Davies, 1998
Gill, Piris & Warren, 2003



The stromal cells can be really bizarre and very worrying.....

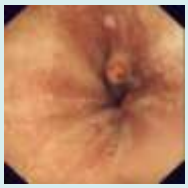


6 oesophagectomies:

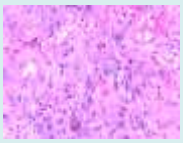
3 local/network/second opinion
3 medicolegal

Mimic number 2 – bizarre stromal cells with/without proliferative epithelium

- context – are the clinical and endoscopic features suggestive of cancer?
- what helps? – immunohistochemistry
- what to do – discuss in MDTM, second opinion, expert opinion, ASK FOR ANOTHER BIOPSY (especially after treatment)



This week's OGJ polyp……

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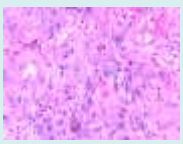
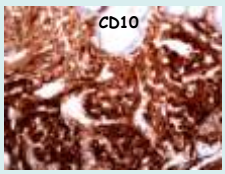


'Inflammatory polyp at the OGJ'

- immunos helpful: cytokeratin versus ASMA, vimentin, CD10
- if in doubt, ask for a second biopsy/EMR



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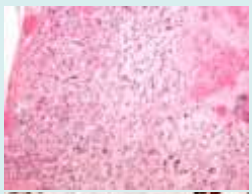
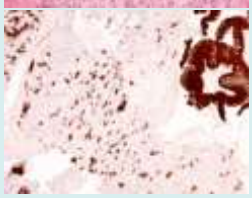


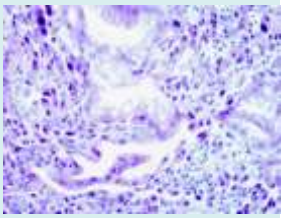


Mimic number 2 – bizarre stromal cells with/without proliferative epithelium

- context – are the clinical and endoscopic features suggestive of cancer?
- what helps? – immunohistochemistry
- what to do – discuss in MDTM, second opinion, expert opinion, ASK FOR ANOTHER BIOPSY (especially after treatment)
- but don't get too hung up on mimics because occasionally the mimic is the real thing…..

Mimic number 3

- 64 F. Polyp with superficial ulcer in stomach.

not Gloucestershire slides!

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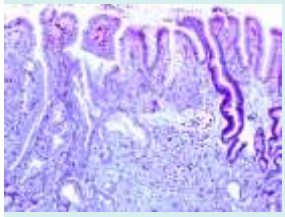
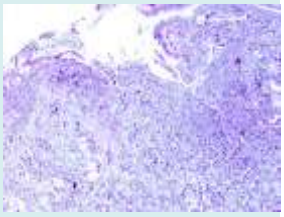

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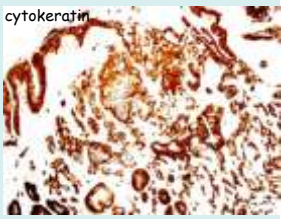
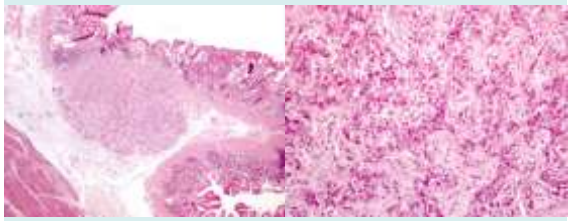


Mimic number 3

- 64 F. Polyp with superficial ulcer in stomach.
- Here comes the total gastrectomy……..



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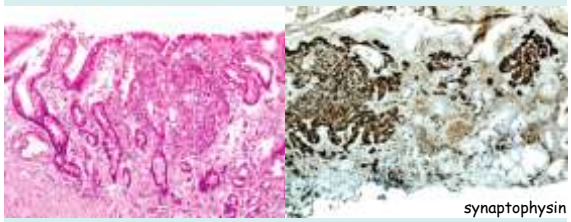

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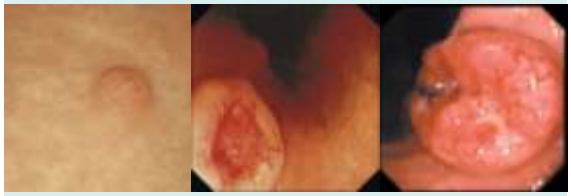
ET/NET/carcinoid v carcinoma

Four types of gastric ET:

- @ chronic atrophic gastritis
- @ Zollinger-Ellison syndrome
- sporadic ET
- @ intrinsic abnormality of parietal cells

The first is the commonest, is benign (unless..) and treated very conservatively (EMR/nothing)

Context in gastric ETs



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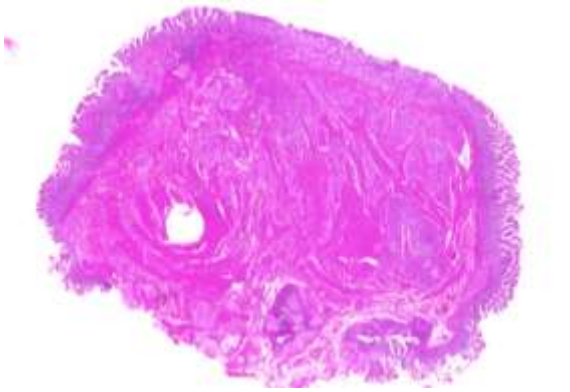
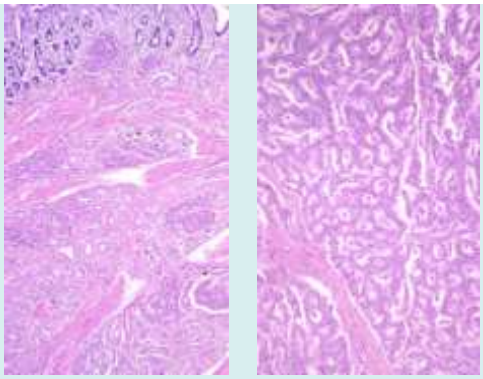
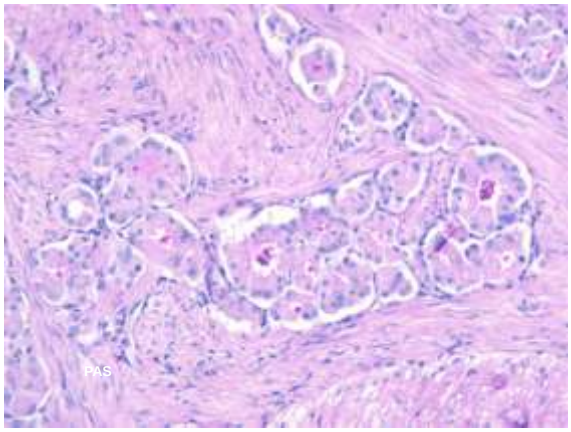
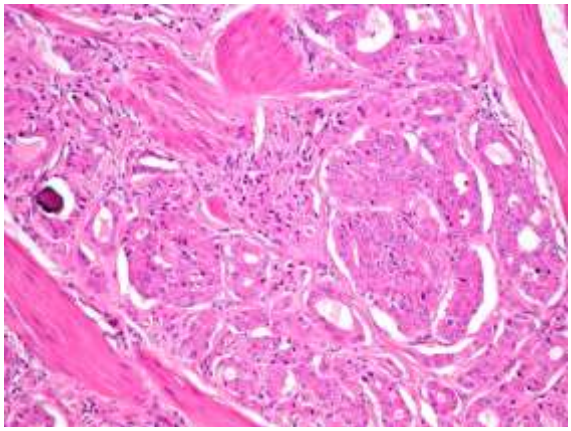
46M. Mass in D2. EMR resection.

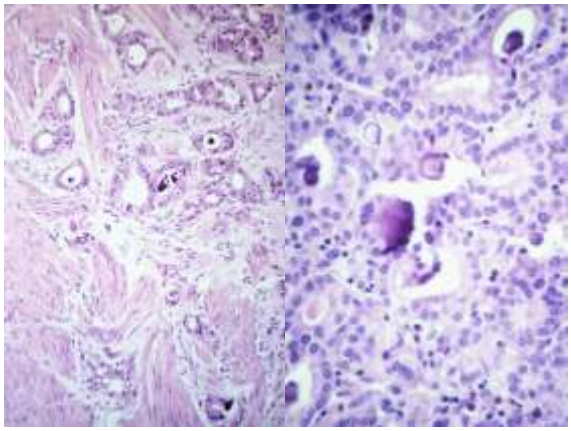


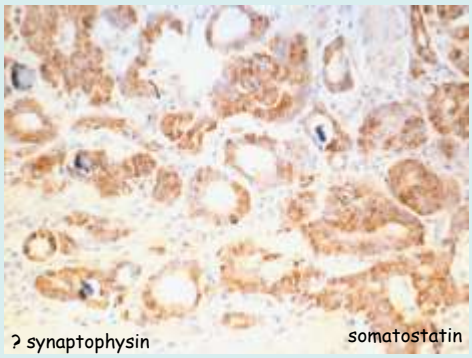


Is this pancreatic adenocarcinoma or metastatic prostatic carcinoma?


PAS







Duodenal D-cell ETs

- glandular architecture
- PAS-positive luminal cell borders
- psammoma bodies

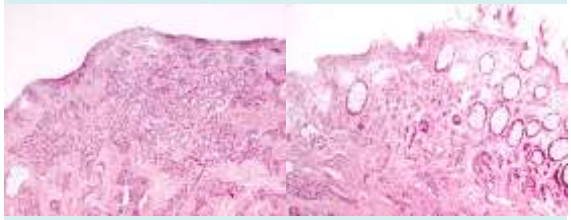
- non-argentaffin
- non-argyrophil by Grimelius
- synaptophysin positive
- usually chromogranin A positive
- somatostatin positive

Duodenal D-cell ETs

- tumours of low grade malignancy
- lymph node metastasis in ~25%
  (usually >2 cm)
- distant metastasis very uncommon
- very good prognosis after local excision

Mimic number 3

- 62M. Polyp in the rectum.



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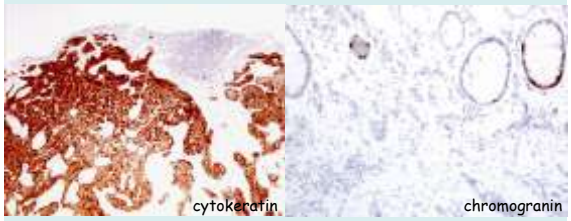

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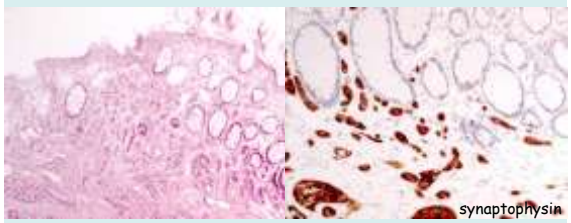
Mimic number 3

- 62M. Polyp in the rectum.
- Here comes the anterior resection



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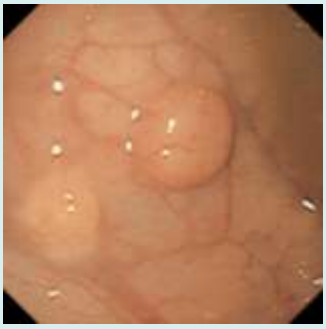
Context in rectal carcinoids



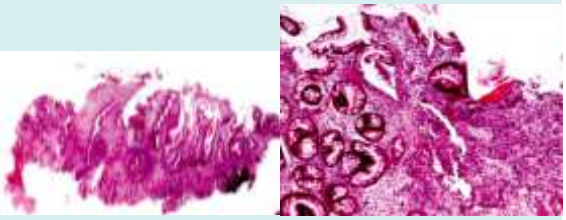
Mimic number 3 – Endocrine tumours of the GI tract

- context – are the clinical and endoscopic features suggestive of cancer?
- context – what does the adjacent gastric mucosa show? What is the serum gastrin? Does the patient have pernicious anaemia?
- what helps? – immunohistochemistry, certainly, but understand the results…..
- what to do – discuss in MDTM, second opinion, expert opinion, ASK FOR ANOTHER BIOPSY

Mimic number 3 – ETs of the GI tract

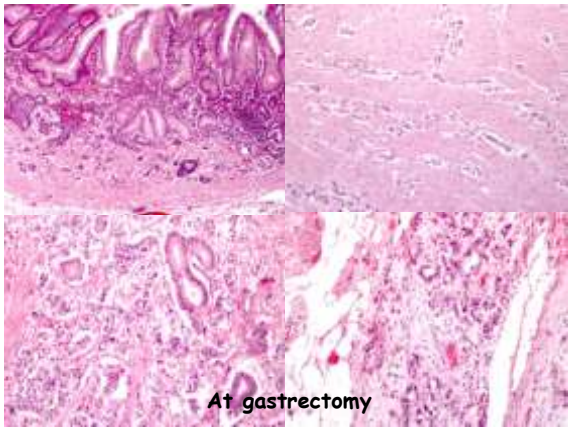
- BUT ……
- don't forget that the occasional 'mimic' is the real thing……

63M. Polyp in stomach. Biopsies.



- called 'carcinoid', possibly arising in CAG
- BUT obstructed picture
- and CT showed large mass in proximal stomach
- total gastrectomy

63M. Total gastrectomy.



Mimic number 3 – ETs of the GI tract

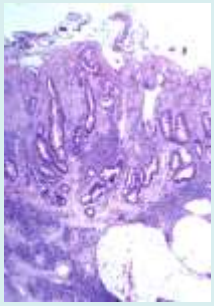
- don't forget that the occasional 'mimic' is the real thing……
- chronic atrophic gastritis predisposes to carcinoma of the stomach….
- you can get composite tumours and neuro-endocrine carcinomas
- be careful, context is all important but don't overcall 'benign' gastric and rectal endocrine tumours

Mimic number 4 – mucosal prolapse

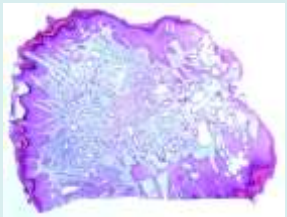
- all encompassing pathological concept
  du Boulay, Fairbrother & Isaacson, 1983
- fibro-muscular proliferation in the lamina propria, epithelial hyperplasia, superficial ulceration with secondary inflammation and relative paucity of inflammation
- solitary ulcer (mucosal prolapse) syndrome, inflammatory cloacogenic polyps, at stomata, in the sigmoid colon associated with diverticular disease & elsewhere
  Lobert & Appelman, 1981; du Boulay et al, 1983; Saul, 1987; Chetty et al, 1993
- epithelial hyperplasia & villiform architecture – mimics villous adenoma in the colorectum, especially in inflammatory cloacogenic polyp
- mucosal prolapse often accompanied by misplaced epithelium, in the colon and rectum (so-called colitis cystica profunda) and at stomata – mimics carcinoma

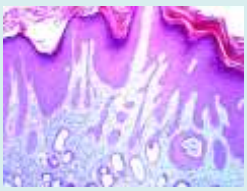
Ileostomy nodule

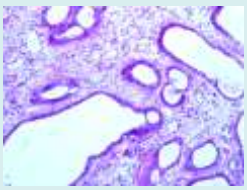
Beware the inflamed ileostomy with mucosal prolapse



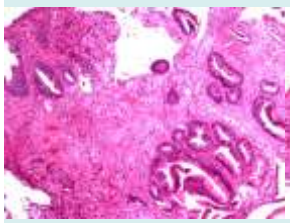
Nodule on colostomy







Solitary ulcer (mucosal prolapse) syndrome



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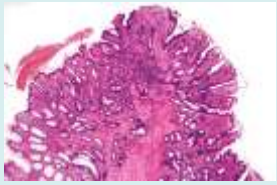
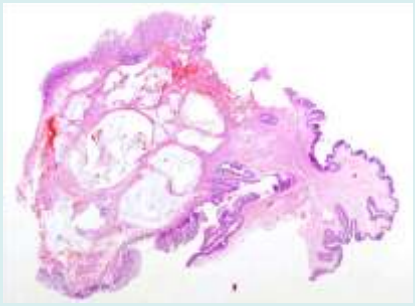
Polypoid mucosal prolapse

- lower rectal/anal most common: inflammatory cloacogenic polyp
- epithelial (villous) hyperplasia traps the unwary into calling them large villous adenomas
- may be seen in association with diverticulosis, at stomas, in SUMPS, etc



PITFALL

Inflammatory cloacogenic polyp (polypoid mucosal prolapse at the anorectal junction) with florid proctitis cystica profunda



PITFALL

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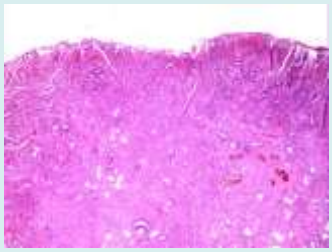
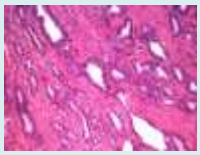




Mimic number 4 – mucosal prolapse

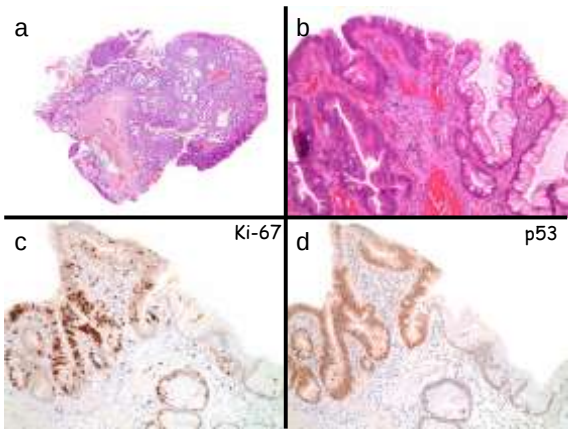
- BUT ……
- don't forget that the occasional 'mimic' is the real thing……
- the changes of classical solitary ulcer (mucosal prolapse) syndrome may occur as a complication of associated carcinoma

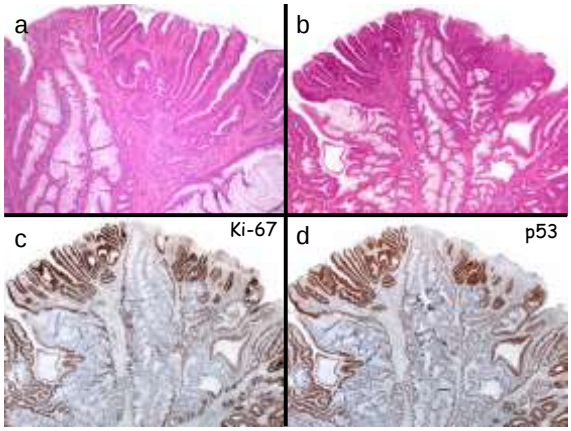
Li & Hamilton, 1998

Polypoid mucosal prolapse at the anorectal junction

- a word of warning with inflammatory cloacogenic polyp
- 4 cases of adenomas of the lower rectum causing secondary polypoid mucosal prolapse

Parfitt & Shepherd, 2008

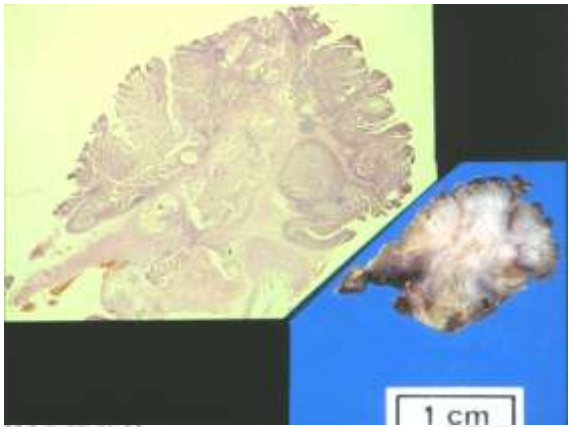


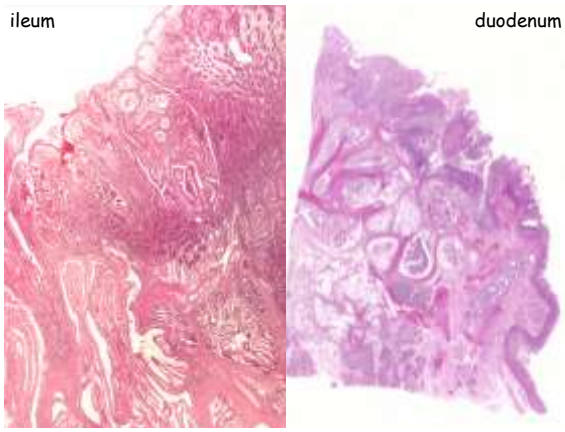


Mimic number 5 – epithelial misplacement in intestinal polyps

- misplacement of epithelium into the submucosa and beyond is a potent mimic of malignancy
- there are clues to the appropriate diagnosis
- Peutz-Jeghers polyps in the small intestine
- small hyperplastic polyps in the left colon and rectum
- larger serrated polyps in the right colon (especially into lympho-glandular complexes)
- adenomas, ESPECIALLY LARGE ONES IN THE SIGMOID COLON

Peutz-Jeghers syndrome



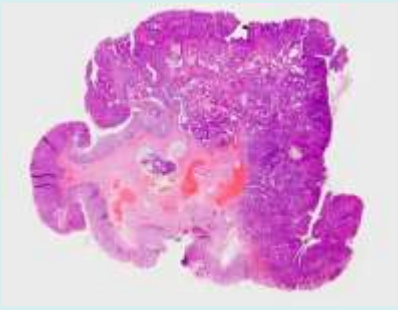


Epithelial misplacement in adenomas

- 85% in sigmoid colon
- unusual in rectum (unless there has been previous meddling)
- same epithelium as surface, accompanied by lamina propria, haemosiderin deposition
- what about misplaced epithelium at the diathermy margin?
- this is the biggest difficult diagnostic issue in BCSP

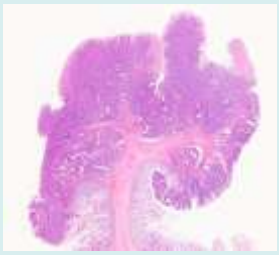
Epithelial misplacement vs invasive carcinoma

There is a very important adage in pathology:
why make two diagnoses when one will do?

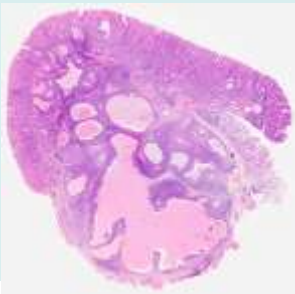


BSCP case

- sigmoid colonic polyp in 62M
- superficial ulceration and inflammation
- with epithelial misplacement

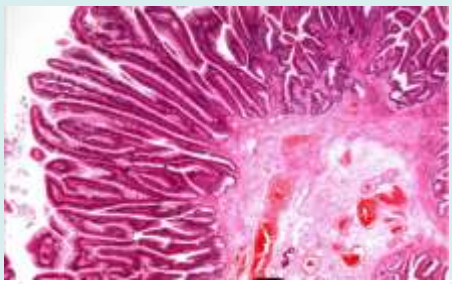


64M. BCSP. Descending colonic polyp



- epithelial misplacement in a lympho-glandular complex
- just like in inverted hyperplastic polyps…

Artefactual epithelial misplacement



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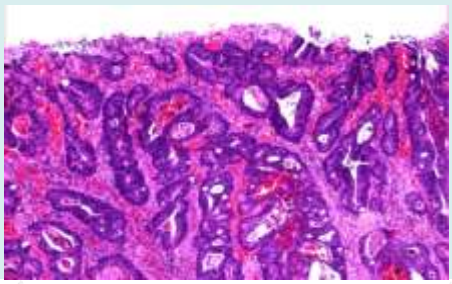
'Enhancement' of dysplastic change with inflammation and superficial ulceration



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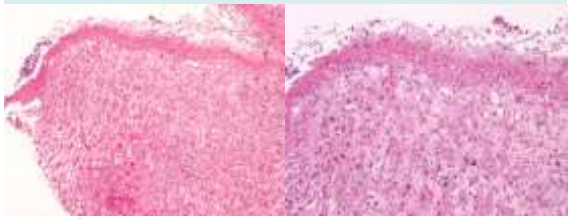
Mimic number 5 – epithelial misplacement in intestinal polyps

- misplacement of epithelium into the submucosa and beyond is a potent mimic of malignancy
- there are clues to the appropriate diagnosis, especially in adenomas:
  - site and size
  - haemosiderin and accompaniment by lamina propria
  - cytology similar to surface neoplasm
- but don't get too hooked up on mimics – it may be the real thing.....
- sigmoid colonic polyps with such changes are selected into BCSP (they bleed)
- national 'expert' panel has been established, funded by BCSP, to deal with the very difficult cases we are seeing in BCSP

Overdiagnosis of cancer

"Large craggy gastric ulcer. ? malignant." Gastric biopsies.



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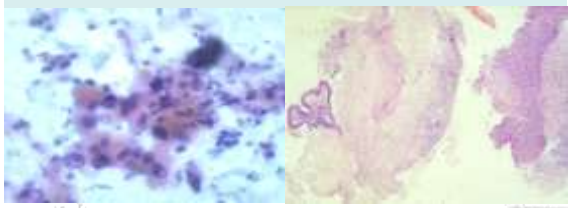
Overdiagnosis of cancer

"Large craggy duodenal ulcer". Duodenal cytology and biopsies.



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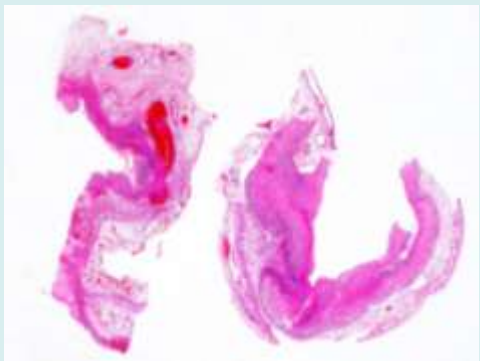
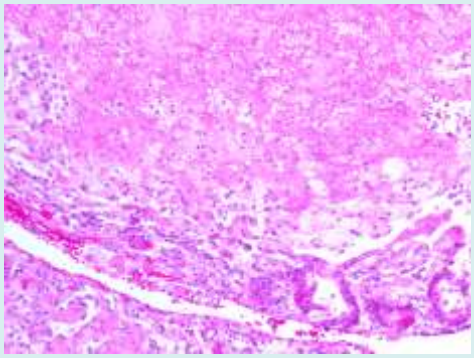
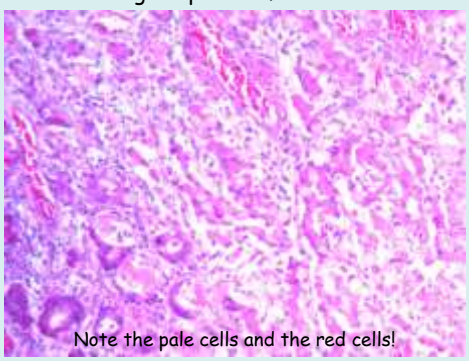
38 F. Appendicectomy for acute appendicitis. Six months later small bowel resection for obstruction.



Low power of mucosa and overlying fibrinous exudate

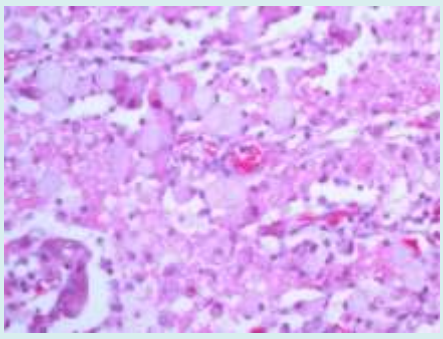


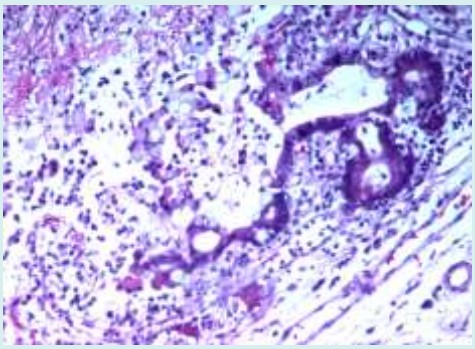
Higher power of mucosa

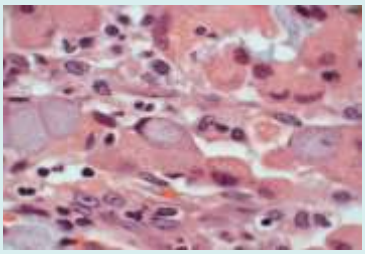


Note the pale cells and the red cells!

Higher power of mucosa







- these are goblet cells
- other surviving cells are endocrine cells and Paneth cells
- they are selectively preserved, presumably because of their less need for oxygen
- but become strikingly dissociated

35F. Small bowel resection.

CK7

This is subacute ischaemia with necrosis of most epithelial cells and survival and dispersal of goblet cells

Survival and dispersal of goblet cells in small and large intestinal ischaemia, mimicking signet ring cell carcinoma

- *Biedrzycki et al. Lesson of the Month: Isolated intramucosal goblet cells in subacute ischaemic enteritis: mimicry of signet ring cell carcinoma. Histopathology 2005; 46: 460-462.*
- also seen in pseudomembranous colitis:
  Abdulkader et al. Signet-ring cells associated with pseudomembranous colitis. Virchows Arch 2003; 442: 412-4.

Avoiding the pitfalls

- know of them and recognise them
- correlate with clinical data
- think of the context
- do levels, do special stains: routine (AB)PAS
- immunohistochemistry – cytokeratin, synaptophysin, stromal markers, etc
- molecular biology, especially for malignant lymphoma in stomach

Avoiding the pitfalls

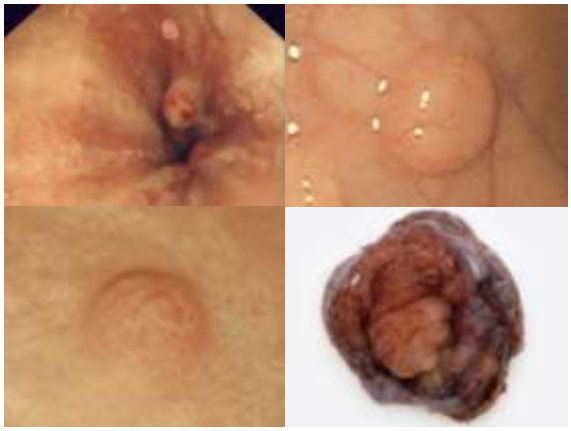
- be honest and use clinically useful categories: "indefinite for dysplasia", "please repeat!"
- ask for a bigger biopsy such as EMR – much easier interpretation…..
- MDTM discussion
- double reporting
- ask a friend (or an expert if he/she ain't a friend)
- subspecialisation (my friend Bryan Warren has seen hundreds of these and he doesn't get them wrong….)

The three most important factors when assessing problematic GI biopsies:

CONTEXT

CONTEXT

CONTEXT



Take home messages

- there are any number of conditions that mimic malignancy in the GI tract
- reactive conditions mimicking dysplasia are as common and cause as many problems as those that mimic malignancy & the implications of an erroneous diagnosis may be just as severe
- all pathologists must be aware of the implications of their diagnoses: if the implication of a diagnosis is major surgery, then pathologists need to ensure that they recognise all mimics of malignancy
- don't get too fixated with 'mimics: occasionally the 'mimic' is the real thing!!