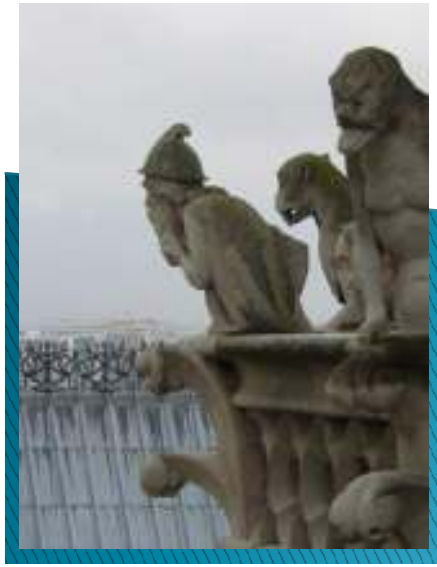
Bile duct neoplasms: current concepts and controversies 2010 Gnomes meeting

Alastair Burt
Newcastle University



WHO classification 2010: Bile duct neoplasms

- *Benign*
- Bile duct adenoma (peribiliary gland hamartoma
- and others) 8160/0
- Microcystic adenoma 8202/0
- Biliary adenofibroma 9013/0

- *Premalignant lesions*
- Biliary intraepithelial neoplasia, grade 3 (BilIN-3) 8148/2*
- Intraductal papillary neoplasm with low- *or*
- intermediate-grade intraepithelial neoplasia 8503/0
- Intraductal papillary neoplasm with high-grade
- intraepithelial neoplasia 8503/2*
- Mucinous cystic neoplasm with low- *or*
- intermediate-grade intraepithelial neoplasia 8470/0
- Mucinous cystic neoplasm with high-grade
- intraepithelial neoplasia 8470/2

- *Malignant*
- Intrahepatic cholangiocarcinoma 8160/3
- Intraductal papillary neoplasm with an associated
- invasive carcinoma 8503/3*
- Mucinous cystic neoplasm with an associated
- invasive carcinoma 8470/3

Aims of presentation

- Briefly review benign biliary lesions and mimics
- Update classification of mucinous cystic neoplasms
- Review advances in precursor lesions in the bilary tract (intrahepatic) with particular reference to papillary lesions
- Consider cholangiocarcinoma outliers/variants

Bile duct adenomas and related lesions

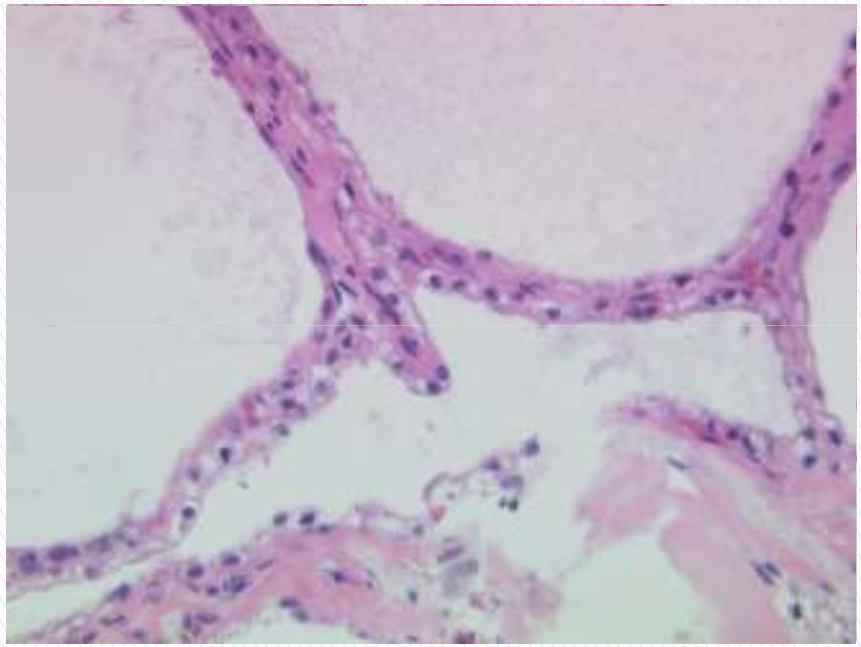
- BDA: classically subcapsular <1cm
- ? Peribiliary gland hamartoma
- Possibly non-neoplastic
- Seen in areas of parenchymal extinction

- Biliary adenofibroma: distinguished by stroma – similar lesions in animal models
- May be within spectrum of DPM

Varnholt et al (2003)

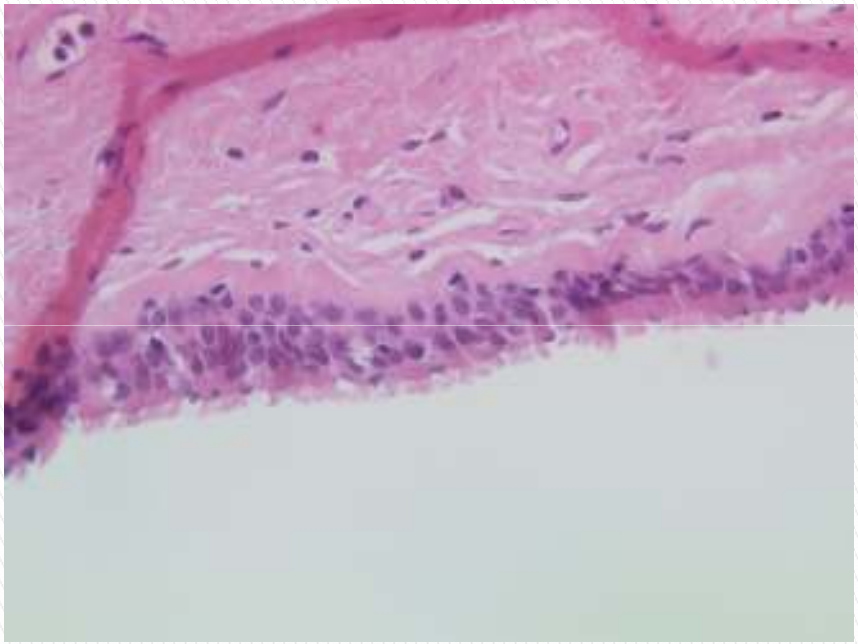
Microcystic adenoma

- Rare neoplasm: often large
- Analogous to pancreatic lesions
- K 7/19 positive
- MUC 1 positive
- NSE and inhibin
- Malignant potential defined by metastasis!
- Devaney et al (1994)



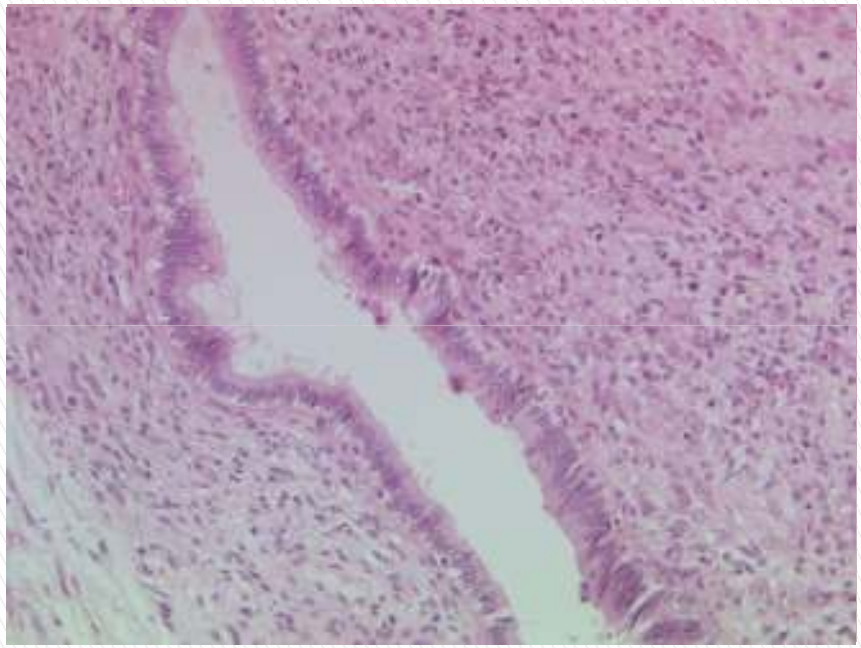
Ciliated foregut cyst

- Normally incidental finding
- Classically lined by mature respiratory epithelium
- May have other elements incl. thyroid
- Increased reporting of these during last decade (Jakowski et al (2004)
- St Louis case: focal pyloric gland metaplasia



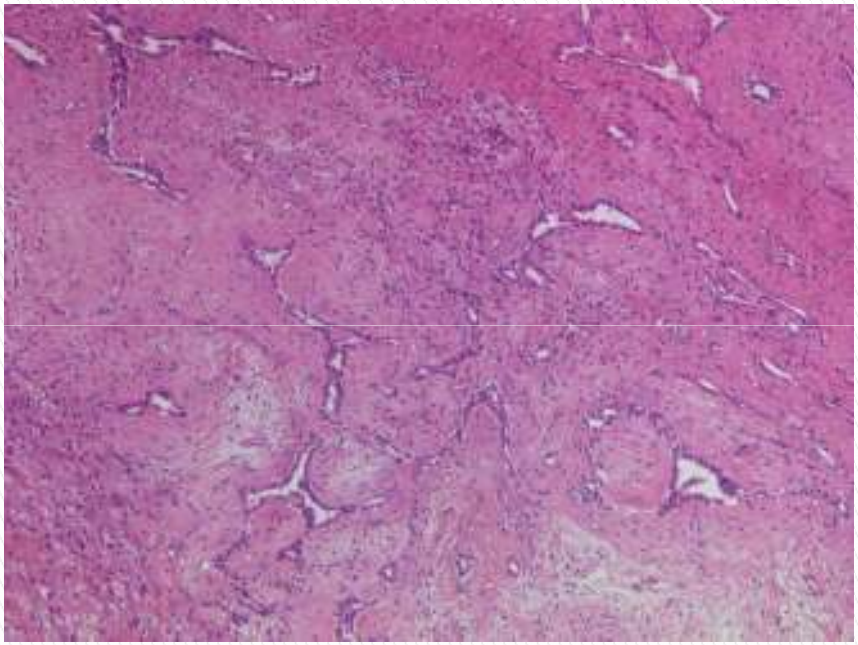
Inflammatory pseudotumour of bile ducts

- 5 month old
- Bile duct stricture with intrahepatic mass (2.5cm)
- Left hepatectomy
- Form of myofibroblastic tumour
- Hata et al; J Ped Surg 1992; 12: 1549



Mesenchymal hamartoma

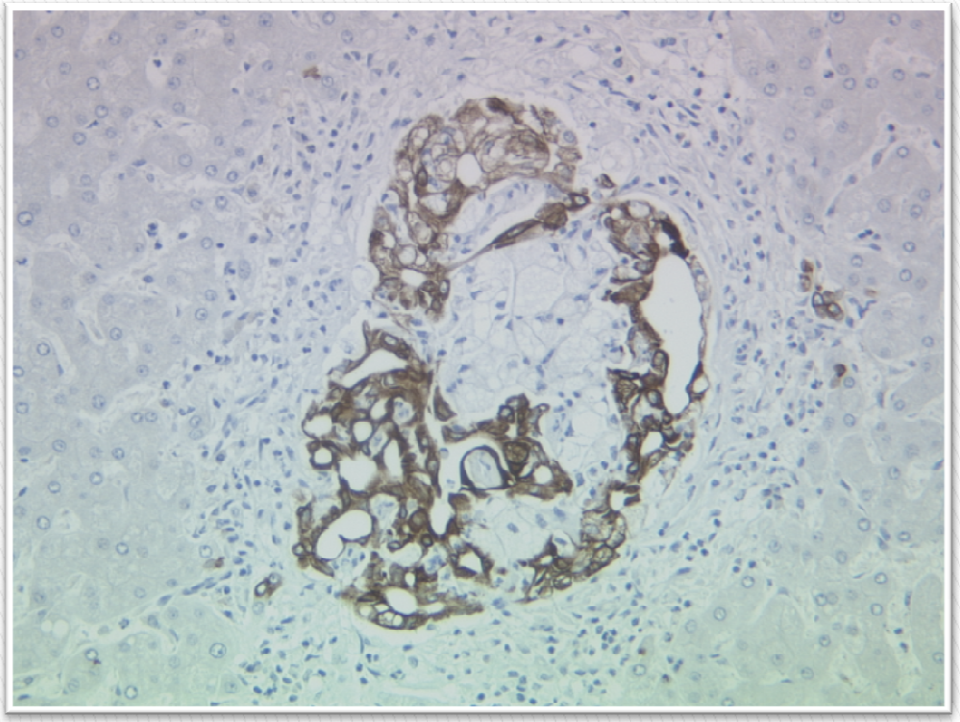
- 25 year old female with lesion identified as probable FNH
- MH: 50% diagnosed in first year of life but can present in adulthood
- Presents with abdominal pain
- May be more ‘mature’ than infantile version with fibrosis and paucity of ducts
- Within spectrum of DP



Cook et al (2002)

Newcastle B

- 39 year old woman with liver masses identified on US
- Left lateral sectionectomy and non-anatomical resection of segment VI and IVB
- Segment II/III and segment VI: telangiectatic adenoma
- Lesion from IVB circulated: ill defined lesion approx 20 mm in diameter; 5 mm from resection margin

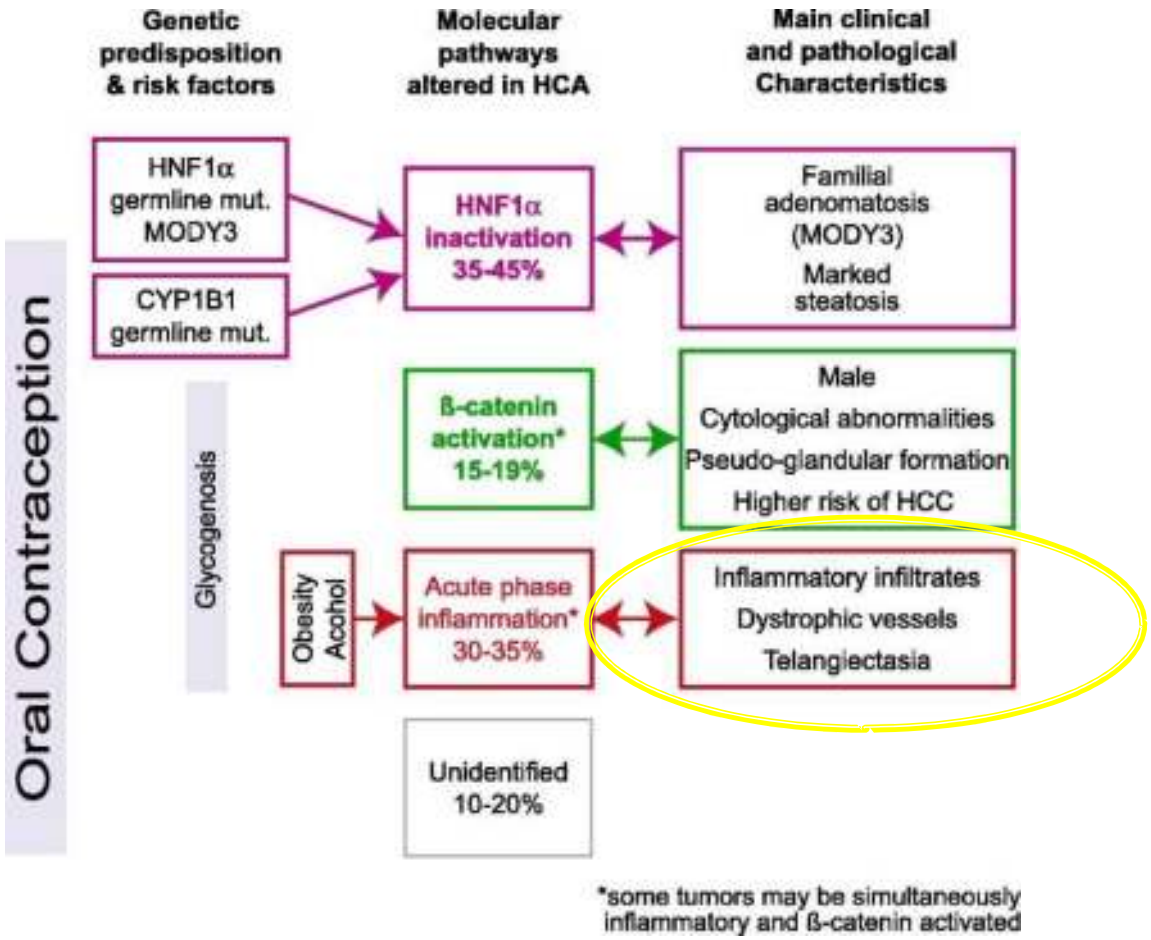


Newcastle B

- Beta catenin negative
- Strong diffuse staining for serum amyloid A of lesional hepatocytes *(courtesy BP)*
- Negative for L-FABP
- Patchy staining of ductular structures by glutamine synthetase *(courtesy BP)*
- Diagnosis: telangiectatic adenoma with exuberant and atypical 'ductular reaction'

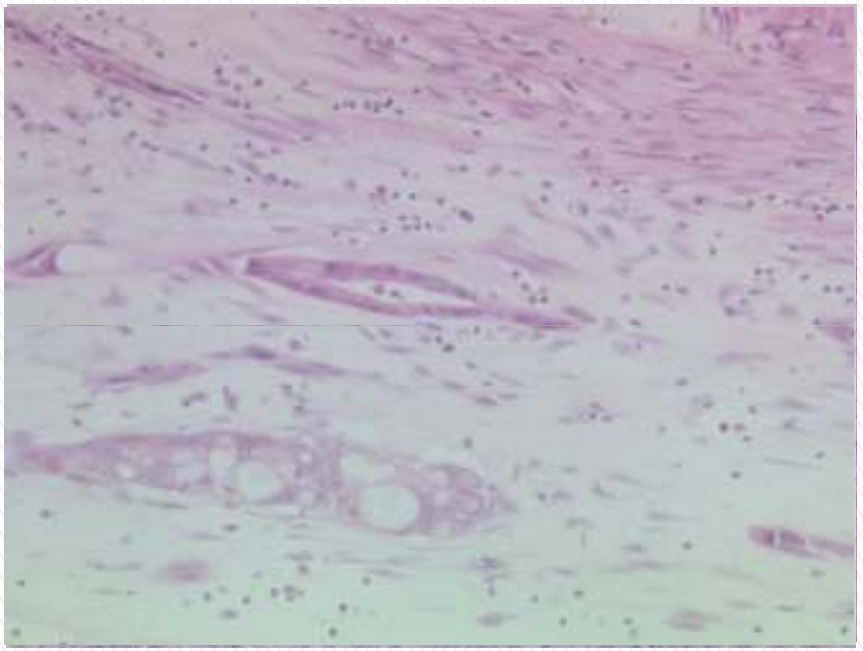
Newcastle B

Group 3: Inflammatory features: associated with IL6ST gene mutations and involvement of gp130 co-receptor signalling



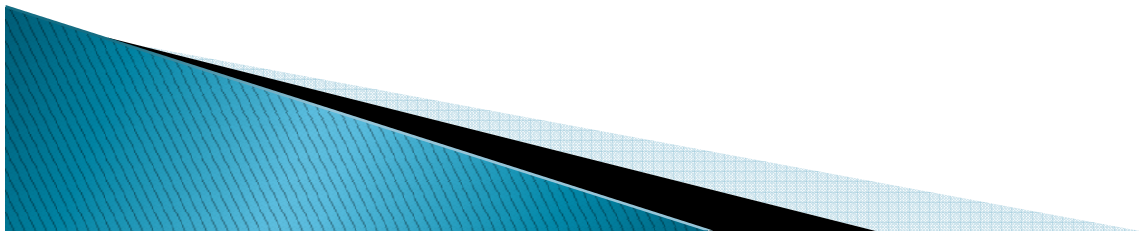
Mucinous cystic neoplasms

- Now akin to nomenclature elsewhere!
- ? Gonadal rests or embryonic gallbladder
- Almost exclusively female tumour
- Stroma ER and PgR positive: expression hormonally regulated?
- Ballooned cells: inhibin positive
- No continuity with gallbladder or BDs
- Multilocular; up to 30cm



Other precursor lesions in the biliary tract

- Biliary intraepithelial neoplasia
  - BiliN 1
  - BiliN 2
  - BiliN3
- Intraduct papillary neoplasm of the bile duct (IPN-B):
  - Mucinous variants (cyst forming)
    - IPN main duct type
    - IPN branch duct equivalent

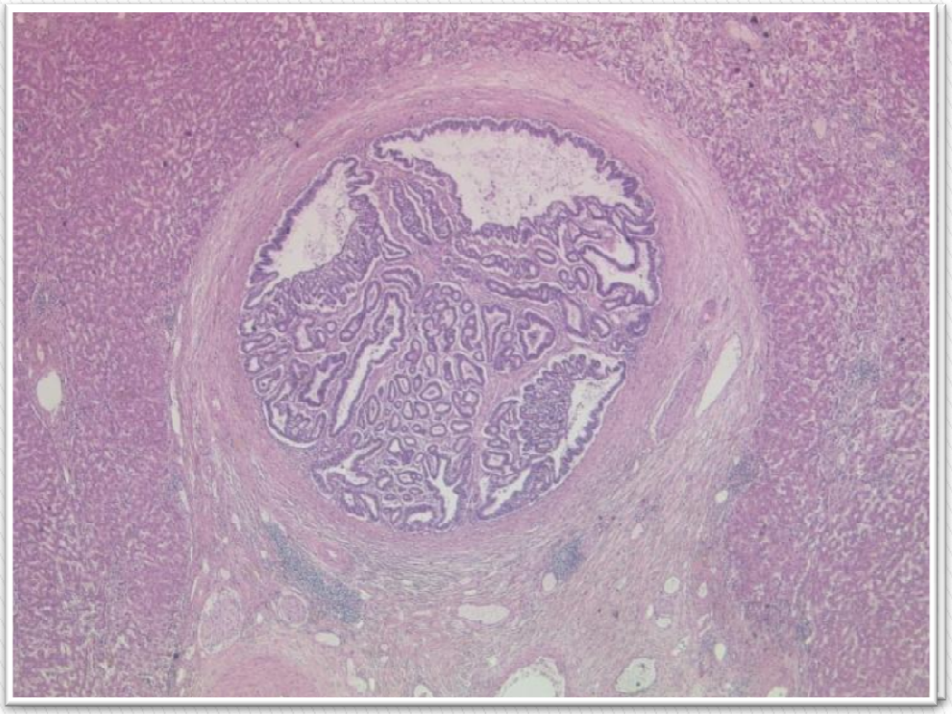


BilIN: flat precursor lesions

- Described in hepatolithiasis
- May have micropapillary projections but lack a stalk
- Increased nuclear: cytoplasmic ratio
- Loss of polarity
- BilIN 1-3: good kappa values in some hands!
- Note distinction between BilIN 1 and reactive atypia may be difficult
- May involve peribiliary glands

Newcastle C

- 63 year old female with obstructive jaundice
- CBD lesion noted on ERCP and MR
- No known past medical history other than ? irritable bowel syndrome
- Left hemi-hepatectomy performed
- CBL/hepatic duct dilated to 13 mm by cystic/solid mass
- Extended along duct for 25 mm
- On sectioning pale tumour mass abutting onto posterior capsular surface



Intraductal papillary neoplasms

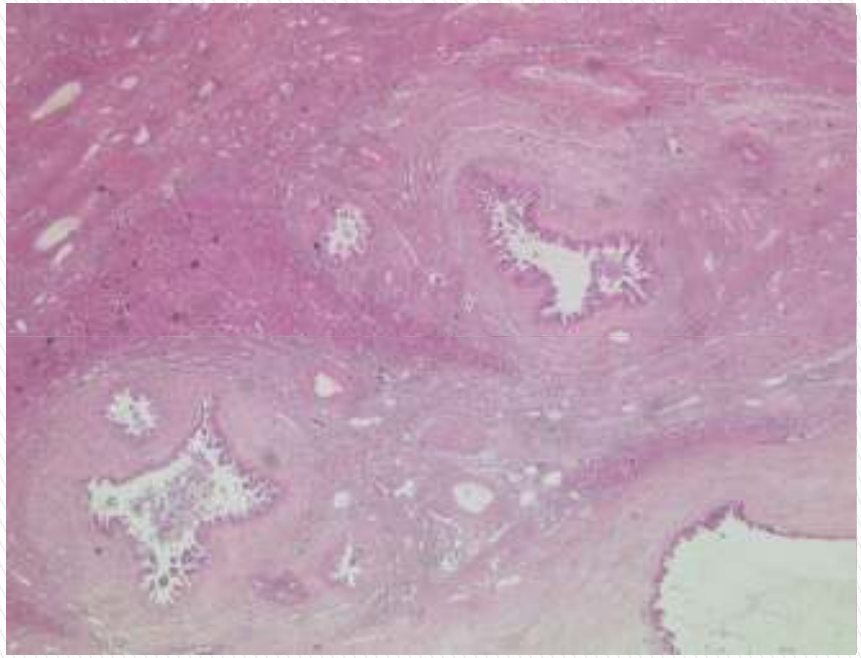
- Classical papillomas/papillomatosis
- Fibrovascular stalks
- Some cystic with mucin production: differential diagnosis with biliary mucinous cystic neoplasms
- Classified on basis of cytological features
- BiliN terminology not used: restricted to flat lesions
- IPN-B: low, intermediate or high grade
- Molecular events less well characterised than for progression in hepatocytic neoplasms

Intraductal papillary neoplasms: IPN-B

- Dilated bile ducts filled by noninvasive papillary/villous structures
- Can occur within extrahepatic and intrahepatic ducts
- May be field change with several lesions present
- Several phenotypes: pancreaticobiliary; intestinal; oncocytic and gastric
- Pattern of invasive malignancy evolving from these similar to that seen in pancreas

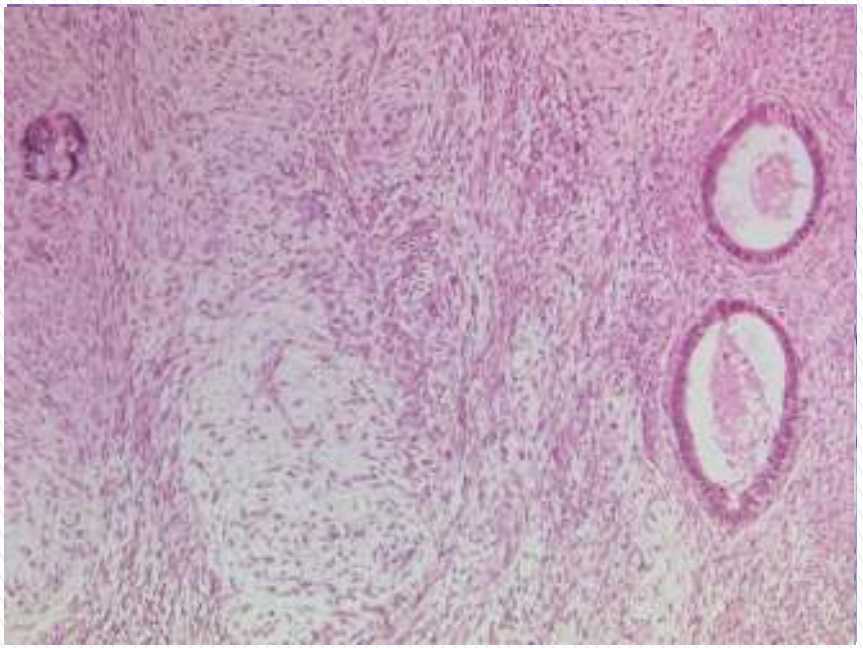
IPN-B

- MUC5ac and MUC1 positive
- Claudin 18 positive
- May have goblet cell areas
- Pattern of invasive malignancy evolving from these similar to that seen in pancreas



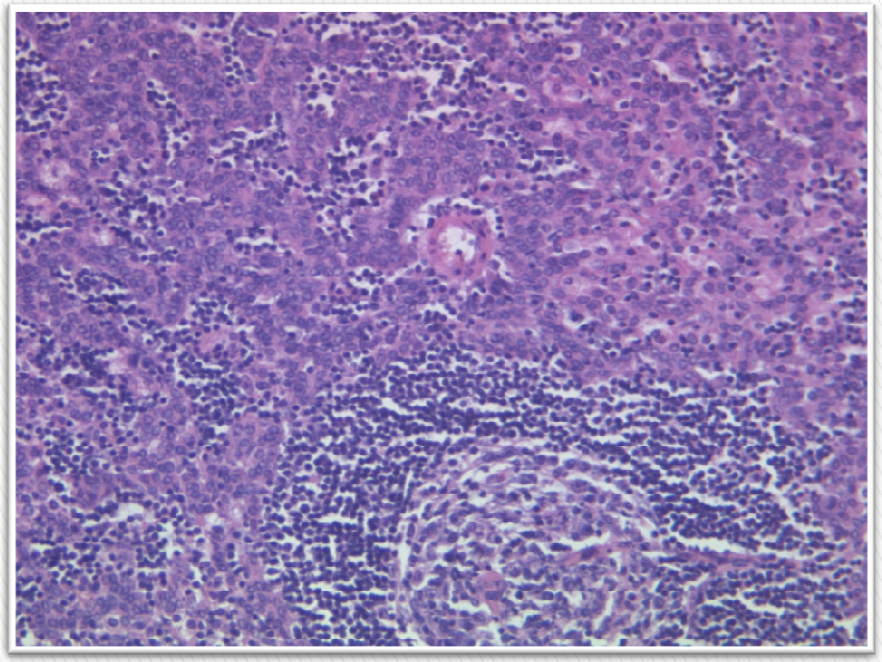
Cholangiocarcinoma: outliers

- Some CCC are p62 positive
- Others: evidence of syncytial formation
- Carcinoma with osteoclast-like giant cells; Akatsu et al (2006)
- Extrahepatic equivalent: Albores-Savadra et al (2000)
- May also have apocrine differentiation
- Adenosquamous
- Mucoepidermoid
- Signet ring CC
- Clear cell carcinoma
- Sarcomatous CC and carcinosarcoma



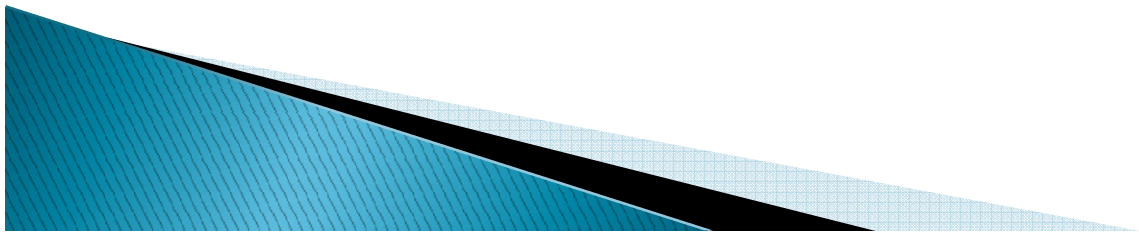
Newcastle A

- 62 year old female: cholecystectomy for pain
- Nodule in segment V noted and excised
- Measured 15x13x12 mm
- No evidence of extrahepatic tumour
- Referred case: adenoca of unknown origin?



Lymphoepithelioma-like cholangiocarcinoma (LELC)

- First LELC in liver described by *Hsu et al* in 1996
- 13 cases in literature: reviewed by *Adachi et al (Pathol International 2008; 58:69-74)*
- 9/13 EBV +ve: no other known associations; all but two in Asia
- Mean age 53; M=F; mean size 4cm
- Prognosis thought to be better than CC but note small number of cases and relatively short follow up (only one death reported)

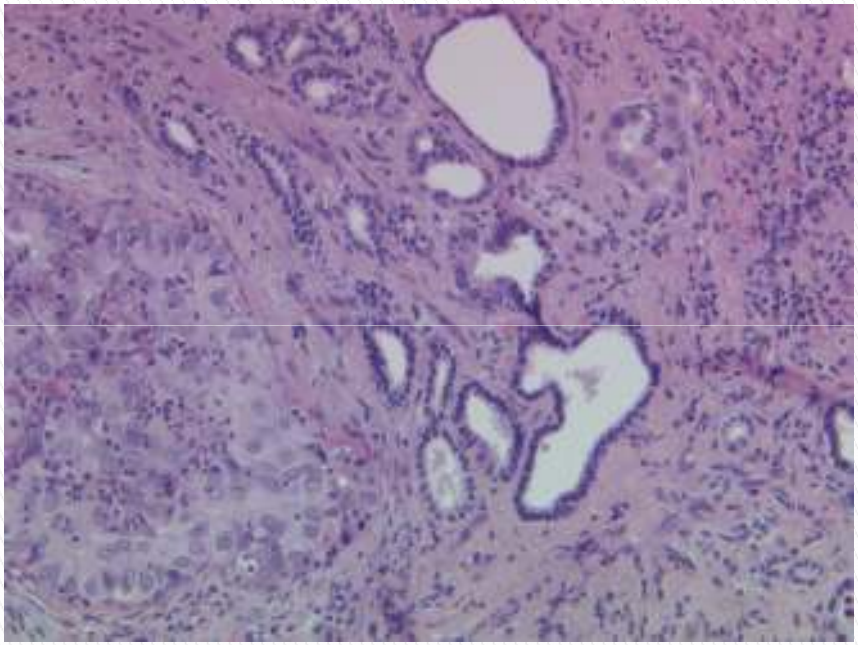


Lymphoepithelioma-like cholangiocarcinoma (LELC)

- Lymphoepithelioma classically described in nasopharynx; ++ Far East
- Lymphoepithelioma-like carcinoma described in a variety of sites including salivary gland, stomach, lung, cervix, bladder
- Some associated with EBV but not all
- Lymphocyte-rich GCA: some EBV associated; others associated with microsatellite instability (*Leung et al, 1999; Grogg et al, 2003; Herath & Chetty, 2008*)

Adenocarcinoma ex DPM

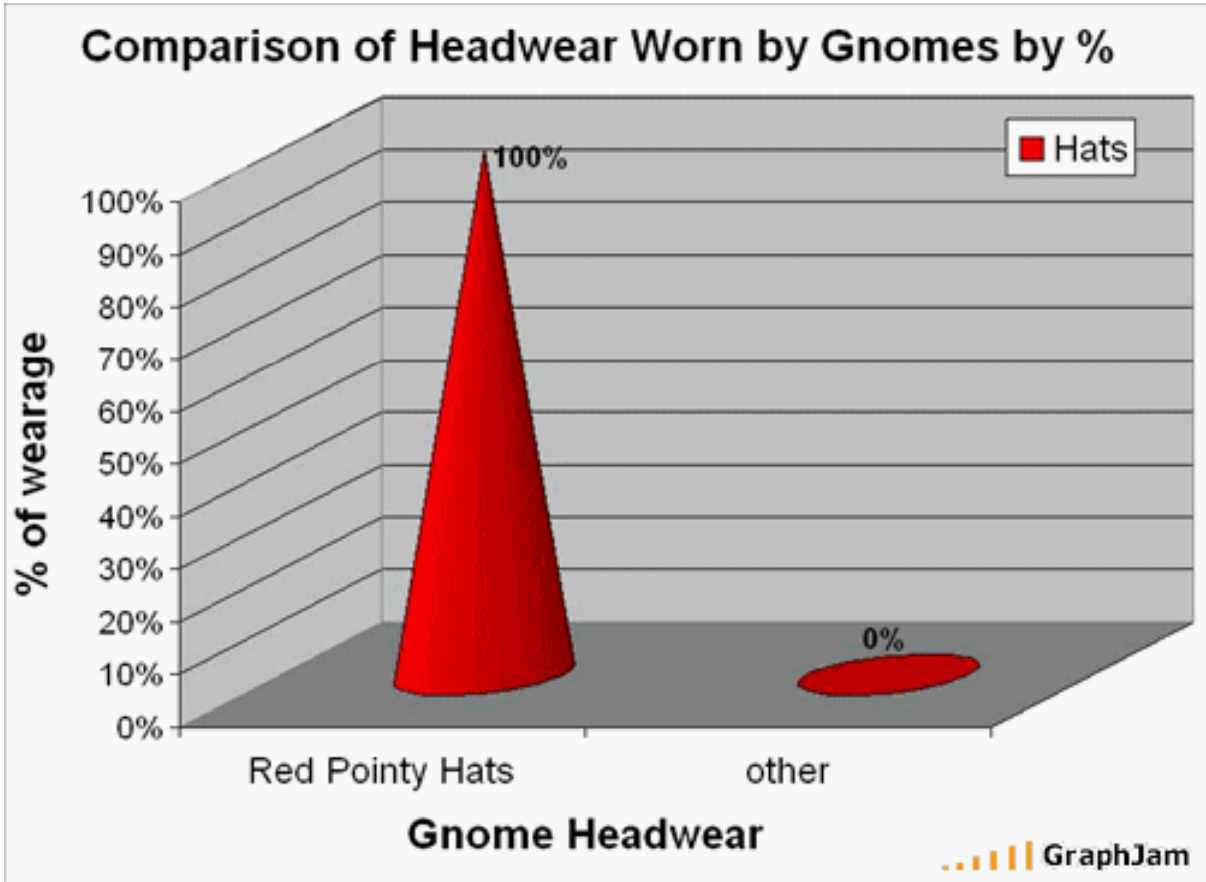
- Cholangiocarcinoma may arise in VMCs
- Rare in CHF
- Some may represent collision lesions
- Carcinoma also seen arising from peribiliary glands



A year in the life of Gnomes

The recession takes its troll

Important data from recent study



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