NHS
Birmingham Women's and Children's
NHS Foundation Trust

Gynaecological Pathology Reporting

Peritoneal cytology

Tony Williams

Birmingham

- Ascites
- Abdominopelvic peritoneal washings in gynaecological procedures
- Ovarian cyst aspirates

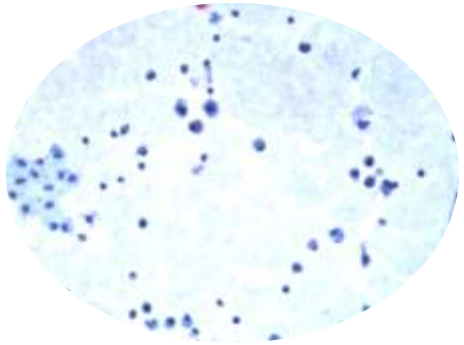
- Clinical guidance; RCOG & European
- RCPath Tissue Pathway and Datasets
- Consider areas of low clinical utility

Logistics

- Nature of cytology specimen not always clear
- Pot containing fluid; ascites, washings, cyst aspirate, cyst drainage
- Resection/Cytology specimen requests may not refer to each other

- Histology and cytology specimens go in separate directions
- May be reported by different pathologists / different departments without knowledge of each other

Q: Can specimens be stored in the ‘fridge over the weekend?
- Yes if necessary; increasingly degenerate, care in interpretation



Tissue pathways for serous fluids & peritoneal washings

- 20 ml required, sterile container
- Direct smear, cytocentrifugation and LBC methods are acceptable (split LBC to allow air dried)
- At least one air dried (Papanicolaou) and one fixed preparation (Romanowsky) required.
- Any clot in the specimen should be prepared histologically as a cell block and reported
- Save an aliquot for cell block (stained by H&E and additional if required)

Tissue Pathways for exfoliative cytology and fine needle aspiration RCPath (Jan 2010)

Ascites: Avoid duplication

Greater number of malignant cells and groups cf washings with higher rates of detection

- In resection for advanced tubo-ovarian cancer or drainage with image guided biopsy:
- Correlate with resection/biopsy specimen before considering immunohistochemistry to avoid duplication
- ? Circumstances to retain cell block as archival tissue

Ovarian cancer: recognition and initial management

- **Methods of tissue diagnosis other than laparotomy**

- If surgery has not been performed, use histology rather than cytology to obtain a tissue diagnosis.
- To obtain tissue for histology use percutaneous image-guided biopsy if this is feasible
- Consider laparoscopic biopsy if percutaneous image-guided biopsy is not feasible or has not produced an adequate sample.

- Use cytology if histology is not appropriate.

NICE Clinical guideline [CG122] Published date: April 2011/Rev March 2016

Test performance of cytology vs histology

- Cytologic testing has lower diagnostic accuracy
- In women with peritioneal carcinomatosis of unknown origin or presumed advanced ovarian cancer
  - Cytomorphology with immunocytochemistry rates of definitive diagnosis 57% to 87%
  - Histopathology plus immunohistochemistry rates of definitive diagnosis between 87% and 97%

Abdominopelvic washings

'It went well but I also ended up with a positive pelvic wash.
My Gyn/Onc is pretty sure that it happened during the D & C/ Hysteroscopy'

'I find it confusing you can be stage one with positive washings'

'Endometrial cancer cells in my peritoneal wash. My doc suggested to treat it aggressively'

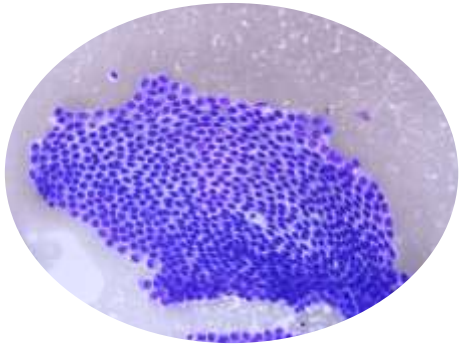
'Everything was good except for the washings'

Abdominopelvic washings

- Easily taken at time of laparoscopy
- Intraperitoneal fluid aspirated first
- 50-100 ml warm physiological saline instilled and aspirated usually as a single specimen
- Initial step in examination before disruption however uterus already manipulated

- Routine testing in benign disease generally discouraged
- Influences postoperative staging of ovary and fallopian tube cancer
- Historically used, still sometimes performed in endometrial cancer and sarcoma – guidance on reporting

Peritoneal wash cytology



- Adequacy: Not well defined
- Should expect to see a few mesothelial cells

- Sensitivity a significant issue
  - Gross residual disease false negative rate up to 66 %
  - Microscopic disease false negative rate up to 86 %

- Limiting factors
  - Biology of disease: Minimal exfoliation, fibrosis, adhesions
  - Specimen collection technique,
  - Transport, cytopreparation, scant cellularity, blood, interpretation error

Strategies to increase sensitivity / ease of reporting

LBC: Small increase in sensitivity

Flow cytometry

Cell block with immuno: No evidence for increase in sensitivity - may increase specificity with elimination of false positives

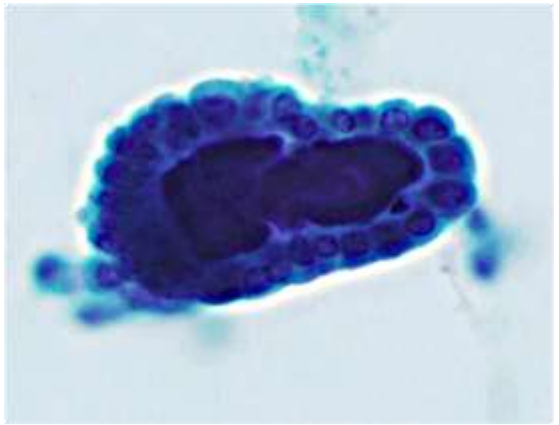
All small studies

Benign findings

Inflammation/peritonitis
Collagen balls
Reactive mesothelium / hyperplasia
Peritoneal inclusion cysts
Endosalpingiosis
Endometriosis
Vascular tangles (vessels, fibrinoid material, adherent mesothelial cells)

False positive (up to 9%)

- Reactive mesothelial cells
- Endometriosis
- Endosalpingiosis
- Psammoma bodies
- Ectopic pancreas &c



- Get a second opinion

My Gyn/Onc is pretty sure that it happened during the D & C/ Hysteroscopy'

- Increased positive PW in Stage I endometrial ca in after hysteroscopic (12.8 %) versus D&C (3.4%) sampling
- 12.5% in lapararoscopic procedure with uterine manipulator
- 2.5% in non manipulated hysterectomy

Dovnik & al Radiol Oncol 2017 Mar 1; 51(1): 88–93

Krizova & al Am J Surg Path 2011 35 (1) 115-26

AP washing cytology / ascites in staging gynaecological malignancy

- Endometrium
- Uterine Sarcoma
- Ovary, fallopian tube & peritoneum

Dataset for histological reporting of **endometrial cancers**

- Peritoneal cytology moved to non-core items on the basis of 2009 staging
- Significance of positive peritoneal cytology as an independent prognostic factor is controversial … 2009 FIGO staging does not take account of the results of peritoneal cytology.
- If peritoneal fluid is submitted the results should be recorded in the pathology report (without altering stage).
- Evidence still accumulates; may be prognostic factor in some tumours; some oncologists will consider in direction of management

- Advanced stage (III or IV) disease is associated with positive peritoneal cytology in c 25% of cases.

Standards and datasets for reporting cancers RCPath Feb 2014

Dataset for histological reporting of **uterine sarcomas**

- Identification of malignant cells in peritoneal washings does not influence the FIGO staging of uterine sarcomas
- Presence of absence of tumour cells should be documented if washings have been performed
- Significance of washings in an individual case should be discussed at gynae onc MDTM.

- One study found negative peritoneal cytology associated with better survival in uterine sarcoma

Standards and datasets for reporting cancers RCPath Dec 2016

FIGO staging criteria for cancer of the ovary, fallopian tube, and peritoneum

Stage IA Tumor limited to one ovary (capsule intact) or fallopian tube No tumor on the external surface of the ovary or fallopian tube No malignant cells in ascites or peritoneal washings

Stage IB Tumor limited to both ovaries (capsules intact) or fallopian tubes No tumor on the external surface of the ovaries or fallopian tubes No malignant cells in ascites or peritoneal washings

Stage IC includes tumor limited to one or both ovaries or fallopian tubes, with any of the following:

Stage IC1: Surgical spill

Stage IC2: Capsule ruptured before surgery, or tumor on ovarian or fallopian tube surface

Stage IC3: Malignant cells in the ascites or peritoneal washings

Stage IIA: Extension and/or implants on the uterus and/or ovaries and/or fallopian tubes

Stage IIB: Extension to other pelvic intraperitoneal tissues

Stage III, tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes

Stage IIIA1: Positive (cytologically or histologically proven) retroperitoneal lymph nodes only

Stage IIIA1(i) Metastasis up to 10 mm in greatest dimension

Stage IIIA1(ii) Metastasis more than 10 mm in greatest dimension

Stage IIIA2: Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes

Stage IIIB Iinvolves macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes.

Stage IIIC iinvolves macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes.

Stage IVA: Pleural effusion with positive cytology

Stage IVB: Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

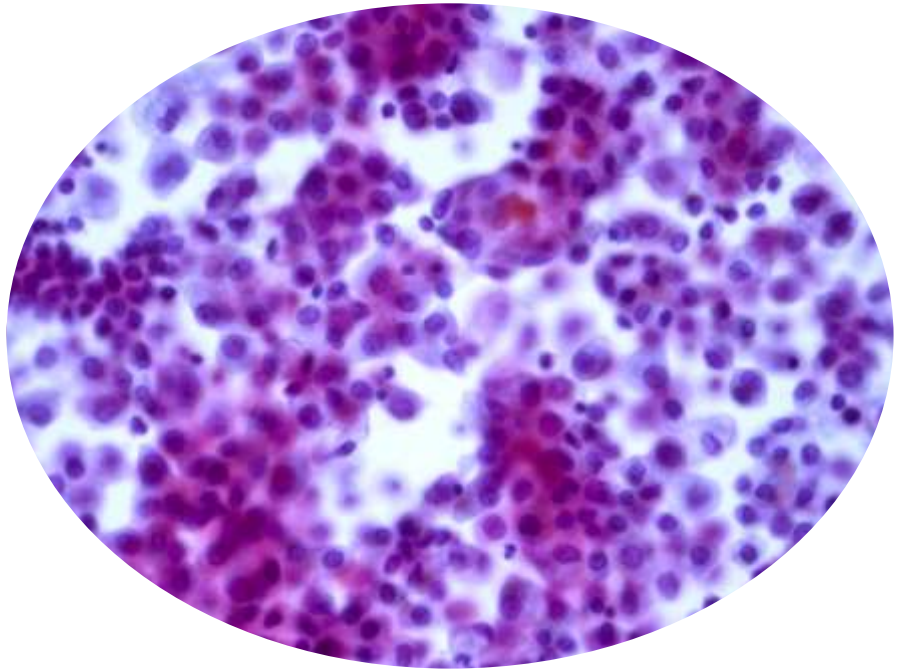
Datasets for the histopathological reporting of neoplasms of the **ovaries and fallopian tubes** and primary carcinomas of the **peritoneum**

- Cytological assessment of peritoneal fluid forms part of the staging system
- Results should be integrated into histology report
- Note difficulty with serous epithelial cells with serous borderline tumours; ..close correlation between the histology and cytology specimens since if the cytology is reported in isolation this may be diagnosed as malignant
- Pleural fluid may also be sent for examination

- Histological subtype of tumours affects the

rate of detection in pelvic washings;

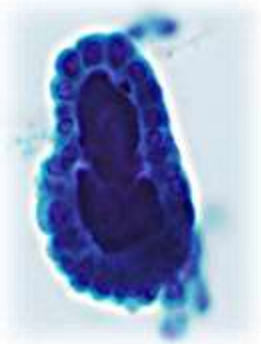
Serous > mucinous / endometrioid > clear cell

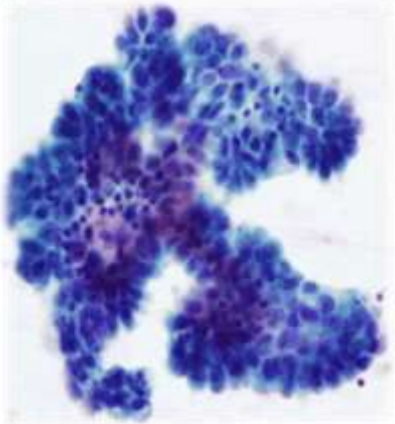


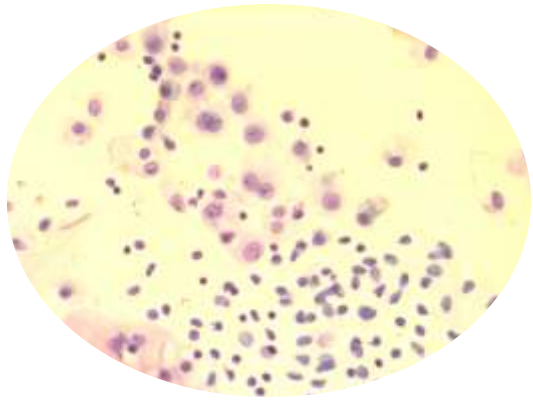
Standards and datasets for reporting cancers RCPath Dec 2010

Serous cellular groups

	Endosalpingiosis	Borderline Tumour	Adenocarcinoma
Architecture	Few simple smooth contoured papillae	Large branching papillae	Smaller irregular papillae
Cells	Orderly and cohesive	Crowded, some single	More frequent single cells
Nuclear atypia	Minimal, fine granular chromatin	Mild to moderate	Notable







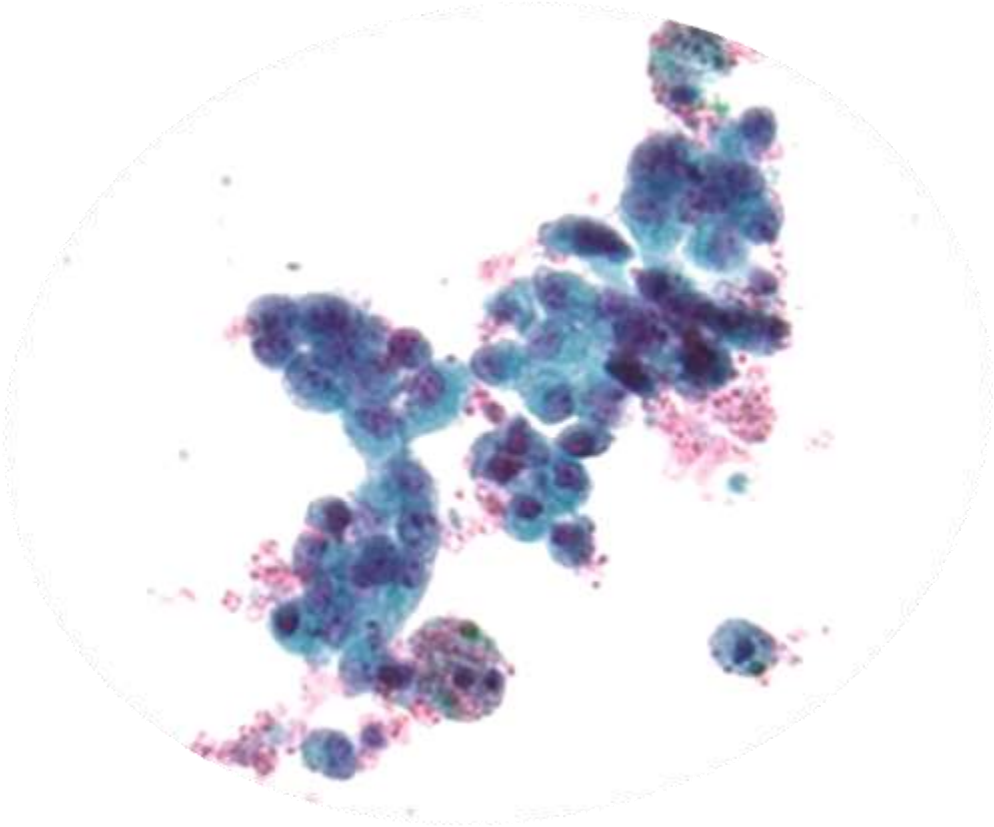
Distinction between papillary clusters from serous borderline tumours and low grade serous carcinoma in cytological specimens is not robust: This distinction should be made on histology
Report 'serous neoplasm' or explain
Weir & Bell 2001. Cancer. 2001 93(5):309–318

Abdominopelvic washings cytology to diagnose endometriosis

- Recommendation for laparoscopy with confirmatory histology (evidence for laparoscopy alone lacking; negative histology does not exclude endometriosis)
- Not AP washing cytology
- Exclude malignancy by biopsy of ovarian and deep infiltrating disease

European Society of Human Reproduction and Embryology Guideline on the management of women with endometriosis Sept 13 replacing RCOG Green-top Guideline 24

Endometriosis



- Most frequently reactive mesothelial cells
- Small columnar cells with bland nuclei
- Sheets, balls, occasional tubules
- Inconspicuous clinging stromal cells
- Macrophages, haemosiderin
- Generally lack atypia or mitoses
- Decidua, eosinophilic and mucinous metaplasia described and mislead

Abdominopelvic washings cytology in investigation of chronic pelvic pain

- Diagnostic laparoscopy has been regarded in the past as the ‘gold standard’ in the diagnosis of chronic pelvic pain. It may be better seen as a second-line investigation if other therapeutic interventions fail
- Some recommend that all suspicious areas should be biopsied.
- No recommendation for PW cytology (case reports, reviews)

RCOG Green-top Guideline 41 (May 2012)

Risk Reducing Salpingo-oophorectomy

- No clear role for washings in detecting occult malignancy but staging investigation if identified.

Retrospective observational cohort of 70 women with RRSO with high risk BRCA1/2 mutation or deletion:

No increase in detection of occult malignancy with pelvic washings

Miller H &al., J Minim Invasive Gynecol 2017 24(5): 772-776

Eitan &al., Gynecol Oncol 2006 102(2):315-8

Paediatric uterine adnexal biopsy/resection

- Test performance in pediatric age group not well defined
- 350/656 episodes included cytology
- Low rate of malignancy (8%); 3 positive cytology
- 1 upstaged tumour, not relevant to therapy

Vadva Z & al., Pediatr Dev Pathol 2016 19(5) 401-8

Ovarian aspirate cytology: Management of ovarian cysts in **post**menopausal women

- Aspiration is **not** recommended for the management of ovarian cysts in postmenopausal women

(except for the purposes of symptom control in women with advanced malignancy who are unfit to undergo surgery or further intervention).

- Aspiration again often not therapeutic: c 25% of cysts in postmenopausal women recur within 1 year of the procedure.
- Poor at distinguishing between benign and malignant tumours - sensitivities c 25%.
- Spillage and seeding of cancer cells with negative impact on overall and disease-free survival of stage I cancer patients
- Risk of needle track recurrence

RCOG Green-top guideline 34 (July 2016) RCOG

Ovarian aspirate cytology: Suspected ovarian masses in **pre**menopausal women

- Resolution rates of simple ovarian cysts similar with expectant management or ultrasound guided needle aspirations used (46% vs 44.6% respectively).
- Recurrence rates after laparoscopic needle aspiration of simple cysts are high (from 53% to as high as 84%).
- For highly selected cases, following discussion between the woman and her clinician, transvaginal or laparoscopic aspiration may be an appropriate intervention.

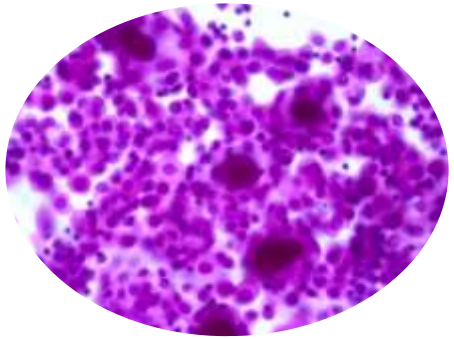
Green-top Guideline 62 (2011) RCOG

Strategy for ovarian cyst aspirates

- Cyst drained to facilitate delivery with separate cytological and histological specimen
- Unlikely to make cytological preps if cyst received intact
- Correlate the cytology with the histology specimen (confusion of worrisome atypia in reactive/degenerate ‘WARD’ cells)

- Difficulties with abundant follicular cells or abundant mucinous cells

- H/E on a fixed cytospin



Test performance of immunostains on cytological specimens

- Control material often histological so variablility in fixation and preparation
- Only 65 pc report good results
- Problems with eg cytokeratin, ER, CD3, CD20, TTF1 – then some variab
- Optimise for frequent limited panels with adjustments in retrieval and antibody titre

Q: CytoLyt

- Variability with some antibodies (CD138, WT1, calretinin)
- Different in different cell types – eg WT1 in serous carcinoma ok, in mesothelial cells may need higher concentration of antibody
- ER weaker staining cf FFPE
- Unexpected S100 positivity
- Discordance in cytology vs histology immunopanels c 15%

Q: Include immunostains for mesothelial cells in panel

- Yes: IQC for antigenicity, recognizing different populations in cell block

Fisher & al (2014) Immunohistochemistry Practices of Cytopathology Laboratories Arch Pathol Lab Med 138 1167-1172

Unnecessary specimens

? Discard: Full circumstances often unclear

? Retain and don’t process: Traumatic specimens w rapid decay

? Process and don’t look

? Cytology alone: Few degenerate cells of uncertain significance

? Cytology with cell block: Care interpreting immunochemistry on cell blocks with scant groups