Classification of Fallopian Tube Lesions
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High Grade Serous Carcinoma:
Heterogeneous group of tumours characterized by:

- Varied architectural patterns
- Nuclear pleomorphism
- High proliferation rate (> 12 MF/10 HPF)
- p53 mutations 96%, and by immunohistochemistry:
  - Nuclear p53 overexpression 70%
  - Negative staining 30%
- Loss of BRCA1 or BRCA2 function 33%:
  - Germline mutations 15%
  - Somatic tumour mutations 6%
  - DNA methylation 12%

Currently:
- Cannot reliably distinguish between hereditary and sporadic High Grade Serous Carcinoma based on morphology and immunohistochemistry
- Cannot distinguish between BRCA1 and BRCA2 mutation associated tumours

Risk Reducing Salpingo-oophorectomy:

- About 70% of high risk women undergo prophylactic salpingo-oophorectomy
- Risk Reducing Salpingo-oophorectomy (RRSO) decreases rate of death before age 70 by 77%
- RRSO is recommended in:
  - BRCA1 mutation carriers – after 35 yr
  - BRCA2 mutation carriers – after 40 yr.
- Guidelines for surgery in BRCA1/2 mutation carriers (JOGC 2007):
  - Complete removal of both ovaries and fallopian tubes. Hysterectomy is not routinely recommended.
  - Peritoneal surfaces should be inspected and fluid collected for cytological analysis.
  - *Ovaries and fallopian tubes should be examined in their entirety by a pathologist who is aware of the high risk status of the patient.*

Protocol for Handling Prophylactic Salpingo-Oophorectomy Specimens:

These instructions apply to all salpingo-oophorectomy specimens with a clinical history: Prophylactic or RRSO or FOC or family history or BRCA or mutation carrier.

**Note:**
Surface epithelium - The external surface of the ovary and fallopian tube should be handled as gently as possible; rubbing or scraping it or allowing it to dry should be avoided. Please do not place on absorbent material like paper towels.

Sampling for Microscopic Examination

1. Ovaries
   - Fix for 24-48 hours
   - Handling surface carefully, the ovaries should be serially sectioned perpendicular to the long axis, and submitted in toto.
   - If lesion is present, submit 1 representative section/cm, or in toto if small lesion.

2. Fallopian tubes
• Fix for 24-48 hours
• Submit in toto, cross sectioned except fimbriae, which are longitudinally sectioned following the Sectioning and Extensively Examining the FIMbriated End (SEE-FIMS) protocol.
• Bisect the tubes near the fimbriated end
• Section the fimbriated end longitudinally
• Serial section the remaining tube at 2-3 mm intervals
• Sections of tube should be submitted in cassettes separate from ovarian sections

PROPHYLACTIC SALPINGO-OOPHORECTOMY – SECTIONS:
• Fimbriae and distal tube sections:
  o 1 H&E and p53 and MIB1
    • Or
  o 1 H&E and 2 unstained for IHC
• Proximal and mid tube sections:
  o 1 H&E
• Ovaries:
  o 1 H&E

PROPHYLACTIC SALPINGECTOMY-OOPORECTOMY – REPORTING:

High Grade Serous Carcinoma, Occult:
• Invasive carcinoma not detected clinically (normal serum CA125, TVUS)
• No minimum size
• Invasive component may involve tube and/or ovary
• 159 consecutive RRSO specimens (Finch et al 2006):
  o BRCA1 5% occult ca
  o Stage Ia to IIb
  o BRCA2 2% occult ca
• HGSC of any size is treated with adjuvant chemotherapy, possibly laparotomy and staging

Note: In Ontario, all new diagnoses of HGSC should include the following comment:

“In the province of Ontario, all women with invasive serous ovarian carcinoma (including fallopian tube and peritoneal) are eligible for genetic testing for mutations in the BRCA1 and BRCA2 genes. A referral for genetic counselling to discuss genetic testing is indicated.

For genetics clinics in your area, visit:
https://cagc-accg.ca/component/option,com_sobi2/Itemid,30/"

Serous Tubal Intraepithelial Carcinoma (STIC)
• Earliest recognizable form of tubal High Grade Serous Carcinoma
• Is the immediate precursor of invasive carcinoma of the fallopian tube
• Shares genetic abnormalities with invasive HGSC
• STIC is diagnosed in 8% RRSO in BRCA1/2 mutation carriers
• STIC is uncommon but does occur in women at low genetic risk
• Present in up to 60% of sporadic HGSC
• Accurate diagnosis is very important:
  o Extra-tubal spread may occur in the absence of invasion of the tube stroma
  o Clinicians may perform staging
  o Clinicians may recommend adjuvant chemotherapy
• STIC has a wide morphological spectrum
• For improved reproducibility of diagnosis, use validated diagnostic algorithm (Vang et al 2012):
  • Morphology + p53 + Ki67
Diagnosis of STIC requires:

1. Abnormal morphology (either unequivocal or suspicious for STIC)
   AND
2. P53 – abnormal pattern by IHC:
   a. Diffuse nuclear moderate to strong expression in >75% of cells within lesion
   or
   b. Complete absence of expression within lesion
   AND
3. Ki67 – high nuclear expression by IHC:
   a. >10% positive cells within lesion

**Serous Tubal Intraepithelial Lesion (STIL)**

- Less common and the clinical significance is uncertain but STIL is presumed to be a cancer precursor with abnormalities not sufficient for a diagnosis of STIC
- Wide range of morphological and immunohistochemical features
- Diagnosis requires application of the diagnostic algorithm (Vang et al 2012)
- Other terminologies in the literature: proliferative p53 signature, atypical hyperplasia, tubal intraepithelial neoplasia, tubal dysplasia, tubal epithelial atypia
- A diagnosis of STIL should be accompanied by a description of the abnormal features and a comment indicating that the features are insufficient for a diagnosis of STIC

**P53 Signature:**

- Benign appearing non-ciliated tubal epithelium with overexpression of p53 but no increased proliferation
- Most frequent in distal tube
- May be bilateral, multifocal
- Are common in women at high and low genetic risk of serous carcinoma
- May represent a latent cancer precursor, but is of no known clinical significance, and is usually not reported when found

**SCOUT:**

- Discrete expansion of secretory cells (secretory cell outgrowth) with wild type p53 expression and no increased proliferation
- Not limited to the distal tube
- May express bcl2, β-catenin
- May be PAX2 negative
- Are seen more frequently in association with HGSC
- SCOUT is of no known clinical significance and is not reported

**Other:**

- Metaplasia:
  - Mucinous
  - Transitional
  - Endometrioid
- Reactive:
  - Inflammatory
  - Pregnancy-related changes
- Papillary tubal hyperplasia
- Serous adenofibroma
- Metastatic carcinoma
References: