- **WHO 5th edition: Updates in the Classification of Ovarian Tumors**

- **C. Blake Gilks**

- **University of British Columbia, Vancouver Canada**

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WHAT’S NEW FOR OVARY?

Ovarian Carcinoma Classification (1)

- Largely unchanged from the 4th edition
- The five main ovarian carcinoma histotypes (High-grade serous, Low-grade serous, Endometrioid, Clear cell and Mucinous) differ with respect to precursor lesions, risk factors, genetic events during oncogenesis, immunophenotype, patterns of spread, response to chemotherapy, and patient outcomes i.e. they are different diseases

Ovarian Carcinoma Classification (2)

- Mixed carcinoma has re-appeared, after being removed from the 4th edition.
- Mixed carcinomas are rare (<1%) and usually consist of admixtures of tumour types that are seen in association with endometriosis (e.g. endometrioid, clear cell)
- Mixed carcinoma should only be diagnosed when the two histotypes are unequivocally present; preferably there should also be demonstration that the immunophenotype is different in the two components
- “Most carcinomas which look “mixed” from a morphological viewpoint represent a single neoplastic-type with areas morphologically mimicking another tumour type”

Ovarian Carcinoma Classification (3)

- Rare ovarian carcinoma variants now include Mesonephric-like carcinoma and dedifferentiated carcinoma, for the first time. These ovarian carcinomas are morphologically indistinguishable from their more common endometrial counterparts.
- Carcinosarcoma is considered a carcinoma variant rather than a true mixed epithelial and mesenchymal tumour
- Seromucinous carcinoma is mentioned but only to indicate that it probably does not exist as a distinct entity and most carcinomas arising from seromucinous borderline tumor are of endometrioid type

Ovarian Carcinoma Classification (4)

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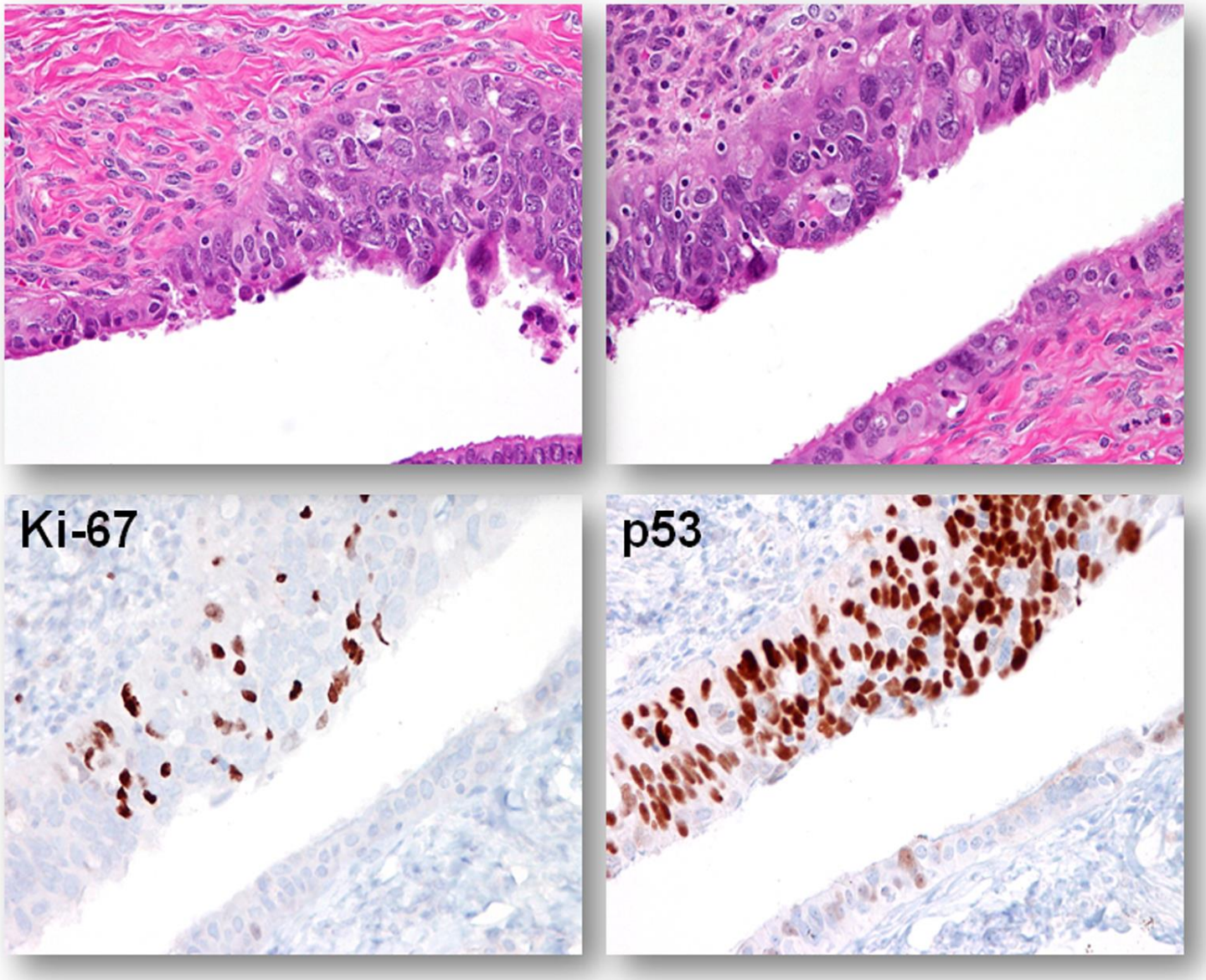
- Mixed carcinomas are rare (<1%) and usually consist of admixtures of tumour types that are seen in association with endometriosis (e.g. endometrioid and clear cell)
- Mixed carcinoma should only be diagnosed when the two histotypes are unequivocally present; preferably there should also be demonstration that the immunophenotype is different in the two components



It is now accepted that most high-grade serous carcinomas arise from the fallopian tube (STIC illustrated, above)

New Criteria for High-grade Serous Carcinoma Primary Site Assignment

Primary site	Criteria for diagnosis
Fallopian tube	STIC present *or* Mucosal HGSC present *or* Part or entire length of tube inseparable from tubo-ovarian mass
Ovary	Both fallopian tubes separate from ovarian mass *and* No STIC or mucosal HGSC in either tube
Tubo-ovarian	Fallopian tubes and ovaries not available for complete examination *and* Pathological findings consistent with extrauterine HGSC
Peritoneal	Both tubes and both ovaries fully examined *and* No gross or microscopic evidence of STIC or HGSC in tubes or ovaries

Genetic Variation in Sertoli-Leydig Cell Tumors

There are three molecular subtypes of SLCT:

1. *DICER1*-mutant (younger patient age, moderately/poorly differentiated tumour, retiform or heterologous elements),

2. *FOXL2* c.402C>G (p.Cys134Trp)-mutant (postmenopausal patients, moderately/poorly differentiated tumour, no retiform or heterologous elements)

3. *DICER1*/*FOXL2*-wildtype (intermediate patient age, no retiform or heterologous elements, including all well-differentiated tumours).

Summary of changes in Ovary section of WHO 5th edition

- Mostly minor refinements with no major changes, as occurred for cervical and vulvar neoplasia
- Recent advances in the understanding of the origin of high-grade serous carcinoma are reflected in the guidelines for primary site assignment for this tumor type
- New data on molecular pathology of sex cord-stromal tumors is included