TECHNOLOGY TRANSFER IN DIAGNOSTIC PATHOLOGY
10TH CENTRAL EUROPEAN REGIONAL MEETING

Gynecological Pathology

ORGANIZED BY THE HUNGARIAN DIVISION OF THE INTERNATIONAL ACADEMY OF PATHOLOGY

CO-SPONSORED BY ISGyP

Visegrád, June 27-29, 2019

Dear Participants, dear Colleagues,

This is our great pleasure to welcome you this year again in Visegrád, at the Technology Transfer in Diagnostic Pathology, 10th Central European Regional Meeting - Gynecological Pathology event.

We have an outstanding Faculty which will ensure the high quality of the lectures and slide seminars. Our many thanks go to members of the Faculty who accepted our invitation to Visegrád for this last weekend of June. We also hope you will enjoy the natural beauty of this place and the view from the terrace as well as the company of your fellow colleagues from different countries. We hope this event will bring together pathologists and will be an initial step toward fruitful collaborations as well.

Being the 10th jubilee of the conferences organized by the IAP Hungarian Division, we would like to make this occasion a bit more special. We hope those colleagues who were lucky enough to be one of every 10th registered participants enjoy already the small present they got at the registration desk on arrival.

We invite all participants to partake in a photo contest: BEST MOMENTS OF THE 10TH CENTRAL EUROPEAN REGIONAL MEETING, TECHNOLOGY TRANSFER IN DIAGNOSTIC PATHOLOGY.

We wish you a very good conference and an unforgettable weekend in Visegrád.

Janina Kulka and Lilla Madaras
President and Secretary
of IAP HD

Cover picture: Eszter Mattioni (1902 – 1993): Danube Bend.
Courtesy of Kieselbach Gallery

from-till	Thursday, 27 June	from-till	Friday, 28 June	from-till	Saturday, 29 June
9.00-12.00	**Registration**	9.00-11.00	**Epithelial neoplasia - Slide seminar 8 cases** C. Simon Herrington – Case 1 and 2 Xavier Matias-Guiu – Case 3 and 4 Sigurd F. Lax – Case 5 Naveena Singh – Case 6 and 7 Pavel Dundr – Case 8 and 9	9.00-9.30	**New concepts in gyneco-oncological surgery** Zoltán Novák
				9.30-10.00	**New concepts in cervical screening** C. Simon Herrington
				10.00-10.30	**Cervical adenocarcinoma and precursors** Simona Stolnicu
				10.30-11.00	**Gynecological tumours in familial syndromes** Pavel Dundr
		11.00-11.30	**Coffee break**	11.00-11.30	**Coffee break**
		11.30-12.00	**Endometriosis and associated neoplasia** Xavier Matias-Guiu	11.30-13.30	**Pitfalls in selected areas of gynecopathology - Slide seminar** Thomas Krausz
12.00-13.00	**Lunch**	12.00-12.30	**Ovarian serous borderline tumours and prognosis (micropapillary/cribriform SBT, microinvasion, implants)** Naveena Singh		
		12.30-13.00	**Ovarian carcinoma: The most common mistakes in diagnosis** Pavel Dundr		
13.00-13.30	**Opening ceremony**	13.00-14.00	**Lunch**	13.30-14.00	**Closing remarks**
13.30-14.00	**Benign lesions of the cervix** C. Simon Herrington				
14.00-14.30	**HPV and HPV associated lesions of the cervix** C. Simon Herrington	14.00-14.30	**Difficulties in staging of gynecological neoplasms (cervical squamous-, adenocarcinoma, endometrial carcinoma etc.)** Naveena Singh	14.00-15-00	**Lunch**
14.30-15.00	**Precursor lesions of endometrial cancer** Sigurd F. Lax	14.30-15.00	**Molecular pathology and biomarker testing in endometrial carcinoma** Xavier Matias-Guiu		
15.00-15.30	**Precursors of and site of origin assessment in high grade serous carcinoma** Naveena Singh	15.00-15.30	**Molecular pathology and biomarker testing in different types of ovarian carcinoma** Xavier Matias-Guiu	15.00-	**Departure**
15.30-16.00	**Coffee break**	15.30-16.00	**Coffee break**		
16.00-18.00	**Precursor lesions - Slide seminar 8 cases** C. Simon Herrington – Case 1 and 2 Sigurd F. Lax – Case 3 and 4 Naveena Singh - Case 5 Lilla Madaras - Case 6 and 7 Pavel Dundr- Case 8	16.00-17.00	**E-poster**		
		17.00-17.30	**Precision oncotherapy of gynecological malignancies** István Peták		
		17.30-18.00	**Ovary - mucinous tumours and metastases** Sigurd F. Lax		

Pavel Dundr
Professor of Pathology

C. Simon Herrington
Professor of Molecular Cancer Pathology

Thomas Krausz
Professor and Vice Chair of Pathology

Sigurd F. Lax
Professor of Pathology

Xavier Matias-Guiu
Professor of Pathology

Zoltán Novák
Head of Department of Gynecology

Naveena Singh
Professor of Pathology

Simona Stolnicu
Professor of Pathology

CHAIRPERSONS

Thursday		Friday		Saturday	
		09:00-11:00	Thomas Krausz, Xavier Matias-Guiu	09:00-11:00	Zsuzsa Schaff, Simona Stolnicu
		11:30-13:00	Naveena Singh, Pavel Dundr	11:30-13:30	László Vass, C. Simon Herrington
13:30-15:30	Zsuzsa Schaff, Sigurd F. Lax	14:00-15:30	Gábor Méhes, Pavel Dundr		
16:00-18:00	C. Simon Herrington, Lilla Madaras	16:00-17:00	Thomas Krausz, Janina Kulka		
		17:00-18:00	Xavier Matias-Guiu, Sigurd F. Lax		

Benign Cervical Lesions

C Simon Herrington, Professor of Pathology, University of Edinburgh, UK

The importance of benign lesions of the cervix lies largely in their distinction from neoplastic intraepithelial lesions and invasive tumours. The main benign squamous lesions are squamous metaplasia, atrophic changes (arguably both normal processes rather than a lesion) and condyloma, the latter a manifestation of HPV infection. Metaplastic and atrophic squamous epithelium can mimic intraepithelial neoplasia; and condyloma can on occasion mimic invasive carcinoma, particularly colposcopically. A wider range of benign lesions affects the cervical glandular epithelium, including those that mimic microscopic intraepithelial and invasive disease, such as microglandular hyperplasia, mesonephric remnants and tuboendometrioid metaplasia; and those that can mimic a tumour, such as endocervical polyps and Müllerian papilloma. Mesenchymal lesions, such as leiomyoma, can also involve the cervix and present as cervical masses. A wide range of infections and other inflammatory disorders can involve the cervix. These can represent local cervical pathology or be a manifestation of systemic disease, for example vasculitis.

Benign lesions of the cervix

Benign squamous lesions
- Squamous metaplasia
- Condyloma acuminatum (including squamous papilloma)
- Atrophic changes (including 'transitional metaplasia')

Benign glandular lesions
- Endocervical polyp
- Müllerian papilloma
- Nabothian cysts
- Tunnel clusters
- Lobular endocervical glandular hyperplasia (LEGH)
- Diffuse laminar endocervical hyperplasia
- Mesonephric remnants and hyperplasia
- Arias Stella reaction
- Endocervicosis
- Tuboendometrioid metaplasia
- Endometriosis
- Ectopic prostate tissue
- Microglandular hyperplasia

Mesenchymal lesions
- Leiomyoma
- Other benign tumours

Inflammatory lesions
- Infections
- Vasculitis
- Lymphoma-like lesion

HPV and HPV-associated lesions of the cervix

C Simon Herrington, Professor of Pathology, University of Edinburgh, UK

The major aetiological factor for cervical neoplasia is 'high-risk' human papillomavirus (HPV) infection. HPV types are termed 'high risk' (*e.g.* HPV 16) or 'low risk' (*e.g.* HPV 6) according to their prevalence in invasive disease. The natural HPV life cycle is closely linked to squamous epithelial differentiation and productive viral infection only occurs in squamous epithelium. Uncoupling of coordinated viral gene expression from squamous differentiation is central to the development of squamous neoplasia and upregulation of expression of the viral E6 and E7 proteins of 'high-risk' HPV types such as HPV 16 and 18 is key to the induction of genetic and other cellular abnormalities associated with neoplastic progression. The E6 and E7 proteins exert their main effects on cell cycle control proteins, particularly p53 and pRb1 respectively, with disruption of cell cycle machinery and DNA repair mechanisms; the interaction between E7 and the retinoblastoma protein pRb1 is responsible for the marked upregulation of p16 protein expression in lesions infected with high-risk HPVs.

However, HPV infection alone is not sufficient for the development of neoplasia and other factors must therefore be involved. During a productive HPV infection the viral genome is maintained in an episomal (extra-chromosomal, non-integrated) form and the E6 and E7 genes are expressed at low levels. Integration of the HPV genome into cellular DNA has emerged as an important factor in the progression of HPV-associated neoplasia and the effects of integration, notably loss of HPV E2 expression and up-regulation of HPV E6 and E7 expression, can lead to many of the molecular features associated with the development of high-grade intraepithelial and invasive squamous and glandular lesions, for example telomerase activation and chromosome abnormalities. Methylation of several tumour suppressor gene promoters has also been reported during the development of HPV-associated neoplasia. However, the mechanisms of HPV integration are not understood, although the epidemiological association between HPV persistence and risk of disease progression suggests that time may be a factor in the integration process.

The application of improved understanding of the pathological processes associated with productive and non-productive HPV infection (the latter being associated with neoplastic progression) has led to development of the concept of two forms of squamous intraepithelial lesion (SIL). Low-grade SIL encompasses entities such as condyloma acuminatum and papillary immature squamous metaplasia (immature condyloma) and represents productive HPV infection. High-grade SIL correlates with non-productive infection and cell cycle dysregulation. Recent studies have suggested the existence of a population of cells at the squamocolumnar junction that are susceptible to HPV infection; and that LSILs arising in this site are more likely to progress to HSIL. This cell population expresses cytokeratin 7 and it has been suggested that LSILs that express cytokeratin 7 may be more likely to progress to HSIL. However, the data to date are insufficient to support recommendation of this biomarker for routine use.

Invasive squamous cell carcinomas of the cervix are almost always HPV-related, irrespective of morphological pattern, although there are reports of squamous cell carcinomas in which HPV DNA cannot be identified. The majority of adenocarcinomas in situ, and adenocarcinomas, are associated with HPV infection. However, a significant minority of adenocarcinomas are not HPV-associated, particularly gastric-type adenocarcinoma, mesonephric carcinoma and clear cell carcinoma. Recent proposals to re-classify cervical lesions according to their association with HPV infection are logical and will simplify classification of these tumours and their precursors.

Precursor lesions of endometrial cancer

Sigurd F. Lax, MD, PHD, Johannes Kepler University (JKU) of Linz, Faculty of Medicine; Linz, Austria
Medical University of Graz and Styrian Hospital Corporation

So far, the pathogenesis of endometrial carcinoma has been well studied for two types, endometrioid carcinoma and serous carcinoma. Both are considered developing along distinctive pathways. Endometrioid carcinoma and variants, accounting for approximately 80-85% of all endometrial cancers seems to develop from atypical endometrial hyperplasia (AEH), which is the best studied endometrial precancer. In contrast, serous carcinoma seems to originate from a flat highly atypical lesion designated as serous endometrial intraepithelial carcinoma (SEIC). Due to its frequent association with peritoneal disease and, therefore, advanced stage, SEIC is rather considered a superficially spreading carcinoma than a precursor.

AEH is characterized by architectural complexity and nuclear atypia but the latter may be discrete in a small number of cases. The last WHO classification considered the terms endometrioid intraepithelial neoplasia (EIN) synonymously to AEH. AEH needs to be distinguished both from endometrial hyperplasia without atypia (EH) and well differentiated endometrial carcinoma. The distinction from EH is made by the presence of cytological atypia which is based on nuclear enlargement, pleomorphism, coarse chromatin, prominent nucleoli and loss of polarity. Nuclear atypia varies both qualitatively and quantitatively and, therefore, the diagnosis of atypia is subjective. This is reflected by a poor interobserver agreement in many studies and resulted in the condensation of the former four into two categories. Very helpful is the comparison to the adjacent non-hyperplastic endometrium. In addition, EH usually shows a lesser degree of complexity. Both may contain areas of epithelial metaplasia, which often shows very bland cytology. Atypia needs to be assessed ion the non-metaplastic areas. Biomarkers, which may be considered for assistance in the differential diagnosis between EH and AEH are PTEN and Pax-2. The distinction from well differentiated endometrioid carcinoma is based on the absence of destructive infiltrative growth which is characterized by a maze-like or an extensive cribriform pattern, less frequently a haphazard infiltrative growth and a desmoplastic stromal response. SEIC is characterized by replacement of surface and/or glandular epithelium by highly atypical and polymorphic cells with frequent mitosis. These cells often show budding and detachment from the surface. Immunoreactivity for TP53 usually shows a mutant pattern (strongly positive or flat negative), the Ki67 labeling index is increased.

Precursors of and site of origin assessment in high grade serous carcinoma

Naveena Singh, Barts Health NHS Trust, London, UK

Despite growing evidence in support of the Fallopian tube origin of extra uterine high grade serous carcinoma (HGSC)[1-3] there continues to be disagreement on primary site assignment, which in turn results in differences in the staging of low-stage disease[4]. More significantly continuing scepticism is an obstacle to studying the impact of ovary-conserving preventative strategies that have potential to reduce HGSC incidence and mortality. Studies on the origin of sporadic HGSC in the past have been hampered by its presentation with disseminated disease, incomplete tubal examination and technical challenges in performing molecular studies on formalin fixed and paraffin embedded tissues, the last being a prerequisite for identifying and sampling its microscopic precursor lesion, serous tubal intraepithelial carcinoma (STIC). While STIC is reported to be present in 11 to 61 % cases of HGSC in published studies[5], reports on low-stage and optimally examined cases clearly demonstrate that virtually all contain STIC[6-8]. These also show that examples of single-site disease are always tubal, never ovarian. Furthermore, while ovarian involvement in HGSC is typically bilateral, as would be expected in metastasis to a paired organ, tubal involvement is unilateral in the majority of cases[9]. These observations are supported by a variety of molecular results: patterns of telomeric shortening, centrosome abnormalities and CCNE amplification indicate the precursor status of STIC in paired cases of STIC and HGSC[10,11]. Elegant clonal evolution studies demonstrate the same result[12,13]; these also show that, in advanced cases, intraepithelial metastasis can produce lesions indistinguishable from STIC, further demonstrating the futility of studying advanced HGSC to answer questions on its origin. What these and other studies have demonstrated irrefutably is that despite being widely disseminated at presentation in the majority of cases, HGSC arises from a single clone, and there is no molecular evidence of mutifocal origin[14,15]. A proposal for primary site assignment has been put forward for reproducible categorisation (Table A), with its basis in scientific evidence in favour of traditional beliefs[16,17], and has been recommended for use in international ovarian cancer pathology reporting guidelines[18]. This evidence also forms the basis for the recommendations on uniform staging of low-stage HGSC; this is specifically in areas which have been left to the pathologist's discretion in the current FIGO system[19,20], resulting in potential for identical cases to be classified differently[4].

Table A: Criteria for assignment of primary site in Tubo-Ovarian HGSC

Criteria	Primary site	Comment
STIC present	Fallopian tube	Regardless of presence and size of ovarian and peritoneal disease
Invasive mucosal carcinoma in tube, with or without STIC	Fallopian tube	Regardless of presence and size of ovarian and peritoneal disease
Fallopian tube partially or entirely incorporated into tubo-ovarian mass	Fallopian tube	Regardless of presence and size of ovarian and peritoneal disease
No STIC or invasive mucosal carcinoma in either tube in presence of ovarian mass or microscopic ovarian involvement	Ovary	Both tubes should be clearly visible and fully examined by a standardised SEE-FIM protocol. Regardless of presence and size of peritoneal disease
Both tubes and both ovaries grossly and microscopically normal (when examined entirely) or involved by benign process in presence of peritoneal HGSC	Primary peritoneal HGSC	As recommended in WHO blue book 2014[17] This diagnosis should only be made in specimens removed at primary surgery prior to any chemotherapy; see below for samples following chemotherapy.
HGSC diagnosed on small sample, peritoneal/ omental biopsy or cytology, OR HGSC examined post-chemotherapy	Tubo-ovarian	Note: this should be supported by clinicopathological findings including immunohistochemistry to exclude mimics, principally uterine serous carcinoma

1. Piek JM, van Diest PJ, Zweemer RP, et al. Dysplastic changes in prophylactically removed Fallopian tubes of women predisposed to developing ovarian cancer. *J Pathol* 2001; **195**(4): 451-6.
2. Singh N, Gilks CB, Wilkinson N, McCluggage WG. The secondary Mullerian system, field effect, BRCA, and tubal fimbria: our evolving understanding of the origin of tubo-ovarian high-grade serous carcinoma and why assignment of primary site matters. *Pathology* 2015; **47**(5): 423-31.
3. Singh N, McCluggage WG, Gilks CB. High-grade serous carcinoma of tubo-ovarian origin: recent developments. *Histopathology* 2017; **71**(3): 339-56.
4. McCluggage WG, Hirschowitz L, Gilks CB, Wilkinson N, Singh N. The Fallopian Tube Origin and Primary Site Assignment in Extrauterine High-grade Serous Carcinoma: Findings of a Survey of Pathologists and Clinicians. *Int J Gynecol Pathol* 2016.
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6. Gilks CB, Irving J, Kobel M, et al. Incidental nonuterine high-grade serous carcinomas arise in the fallopian tube in most cases: further evidence for the tubal origin of high-grade serous carcinomas. *The American journal of surgical pathology* 2015; **39**(3): 357-64.
7. Morrison JC, Blanco LZ, Jr., Vang R, Ronnett BM. Incidental serous tubal intraepithelial carcinoma and early invasive serous carcinoma in the nonprophylactic setting: analysis of a case series. *The American journal of surgical pathology* 2015; **39**(4): 442-53.
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10. Kuhn E, Meeker A, Wang TL, Sehdev AS, Kurman RJ, Shih Ie M. Shortened telomeres in serous tubal intraepithelial carcinoma: an early event in ovarian high-grade serous carcinogenesis. *The American journal of surgical pathology* 2010; **34**(6): 829-36.
11. Kuhn E, Wang TL, Doberstein K, et al. CCNE1 amplification and centrosome number abnormality in serous tubal intraepithelial carcinoma: further evidence supporting its role as a precursor of ovarian high-grade serous carcinoma. *Mod Pathol* 2016; **29**(10): 1254-61.
12. Bashashati A, Ha G, Tone A, et al. Distinct evolutionary trajectories of primary high-grade serous ovarian cancers revealed through spatial mutational profiling. *J Pathol* 2013; **231**(1): 21-34.
13. Eckert MA, Pan S, Hernandez KM, et al. Genomics of Ovarian Cancer Progression Reveals Diverse Metastatic Trajectories Including Intraepithelial Metastasis to the Fallopian Tube. *Cancer Discov* 2016; **6**(12): 1342-51.
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15. Singh N, Faruqi A, Kommoss F, et al. Extrauterine high-grade serous carcinomas with bilateral ad-

nexal involvement as the only two disease sites are clonal based on tp53 sequencing results: implications for biology, classification, and staging. *Mod Pathol* 2018; **31**(4): 652-9.
16. Singh N, Gilks CB, Hirschowitz L, et al. Primary site assignment in tubo-ovarian high-grade serous carcinoma: Consensus statement on unifying practice worldwide. *Gynecol Oncol* 2016; **141**(2): 195-8.
17. WHO Classification of Tumors of the Female Reproductive Organs. 4th ed. Lyon: International Agency for Research on Cancer (IARC); 2014.
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19. Prat J, Oncology FCoG. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynaecol Obstet* 2014; **124**(1): 1-5.
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SLIDE SEMINAR 1.

PRECURSOR LESIONS

Case 1 C. Simon Herrington

Case 2 C. Simon Herrington

Case 3 Sigurd F. Lax

Case 4 Sigurd F. Lax

Case 5 Naveena Singh

Case 6 Lilla Madaras

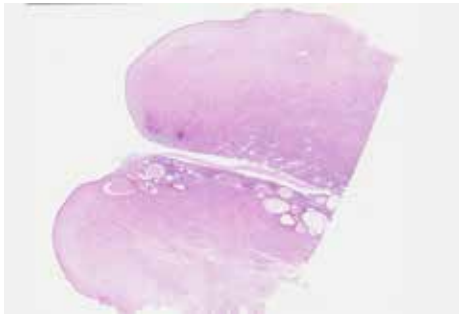
Case 7 Lilla Madaras

Case 8 Pavel Dundr

Case 1

C. Simon Herrington

Female aged 79. History of uterovaginal prolapse. Vaginal hysterectomy performed. Section from the cervix.



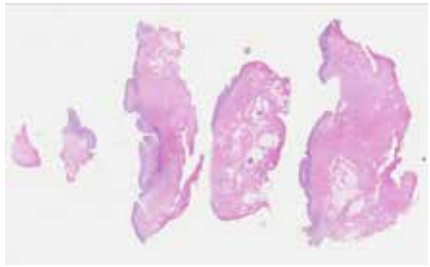
Notes:

Case 2

C. Simon Herrington

Female aged 64. History of VIN. New lesions on left and right side of vulva. Macroscopically the biopsies had an irregular skin surface. The slides are from right (A) and left (B) vulval lesions.

A:



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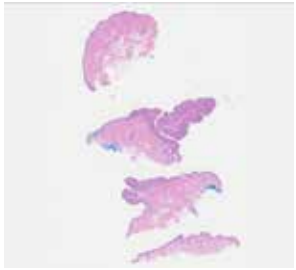
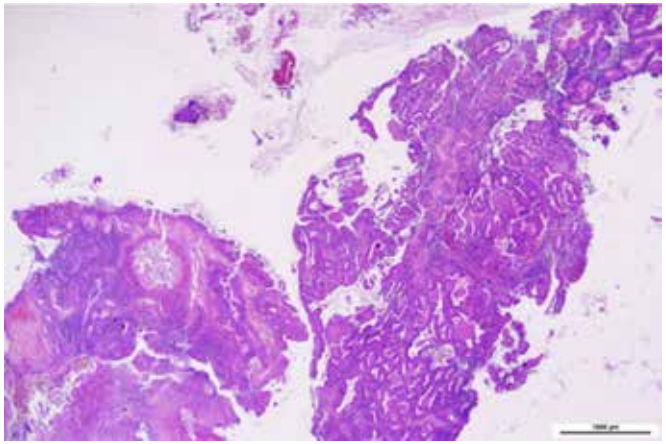


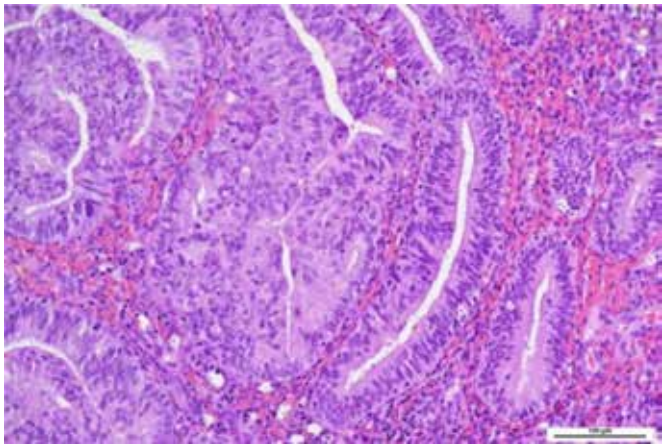
Notes:

Case 3

Sigurd F. Lax

72-year-old female with postmenopausal bleeding. Family history of breast and colon cancer. TVUS: endometrium 11mm thick; right adnexal mass, cystic, 5 cm diameter. A pipelle procedure was performed.



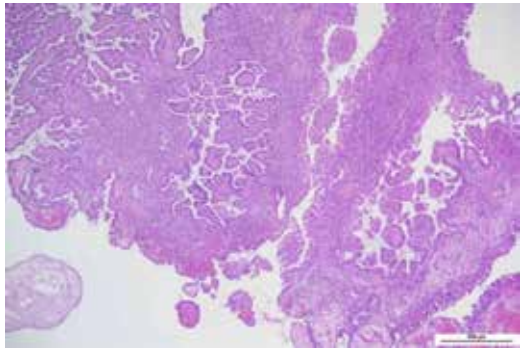


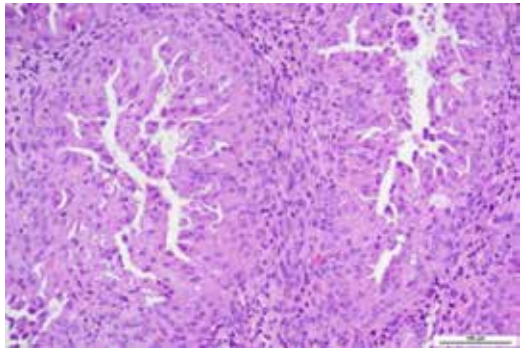
Notes:

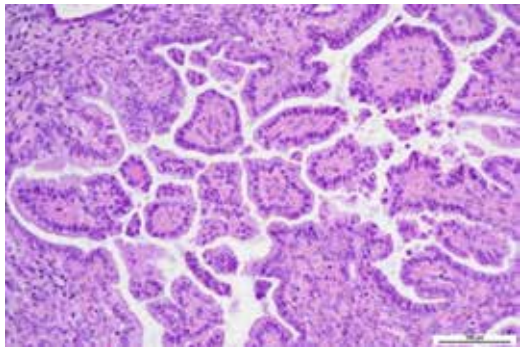
Case 4

Sigurd F. Lax

65-year-old female with postmenopausal bleeding. TVUS: endometrium 8.5 mm thick.







Notes:

Case 5

Naveena Singh

45 y female patient with a suspicious right ovarian mass. CA125 increased – 44; Ca 19-9 increased - 103. RSO and biopsies. Ruptured before surgery but probably on pelvic examination. ?Malignant, if so re-operate later.

Macroscopy: Collapsed and ruptured cystic ovarian mass measuring 90 x 60 x 40 mm. Normal fallopian tube present externally which measures 60 x 8 mm. External surface is otherwise smooth. Internal surface shows multiple, delicate, cauliflower-like projections and solid areas altogether measuring 50 x 40 mm with a maximum thickness of 20 mm.

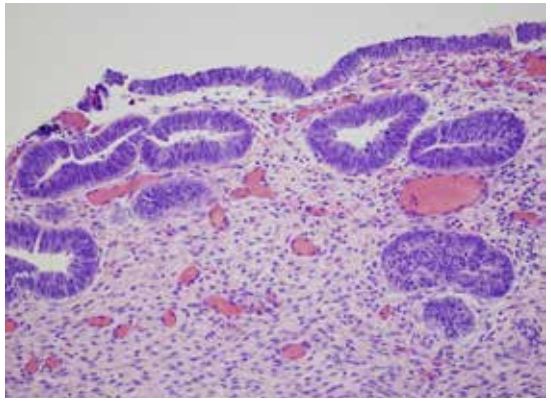
The section is from the second surgery.

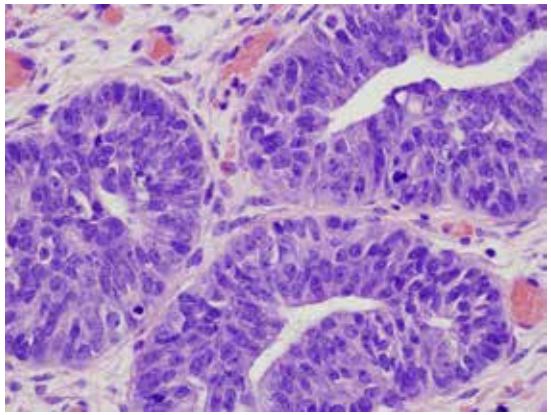
Notes:

Case 6

Lilla Madaras

History: Female aged 66. History of postmenopausal bleeding. Hysterectomy+BSO performed. Section from an endometrial polyp.



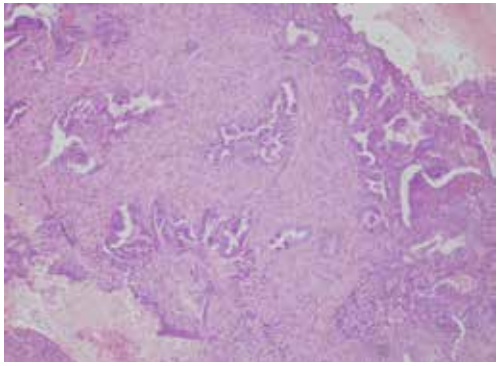


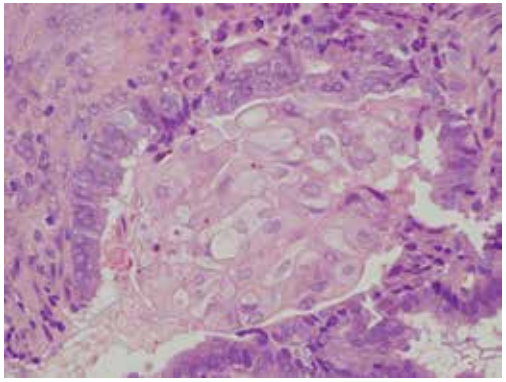
Notes:

Case 7

Lilla Madaras

History: Female aged 50. History of abnormal uterine bleeding. Section from D&C material.





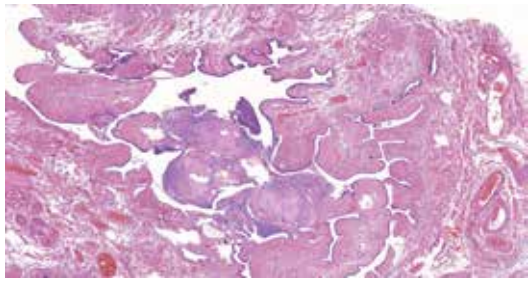
Notes:

Case 8

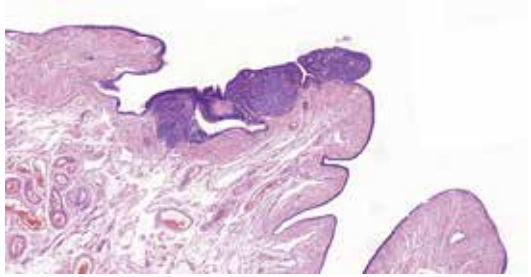
Pavel Dundr

58-year-old female with a repeated cone biopsy for HSIL. Eventually she underwent hysterectomy with bilateral salpingectomy. The lesions in both Fallopian tubes (A - left; B - right) represent an incidental finding.

A:



B:



Notes:

SLIDE SEMINAR 2

EPITHELIAL NEOPLASIA

Case 1 C. Simon Herrington

Case 2 C. Simon Herrington

Case 3 Xavier Matias-Guiu

Case 4 Xavier Matias-Guiu

Case 5 Sigurd F. Lax

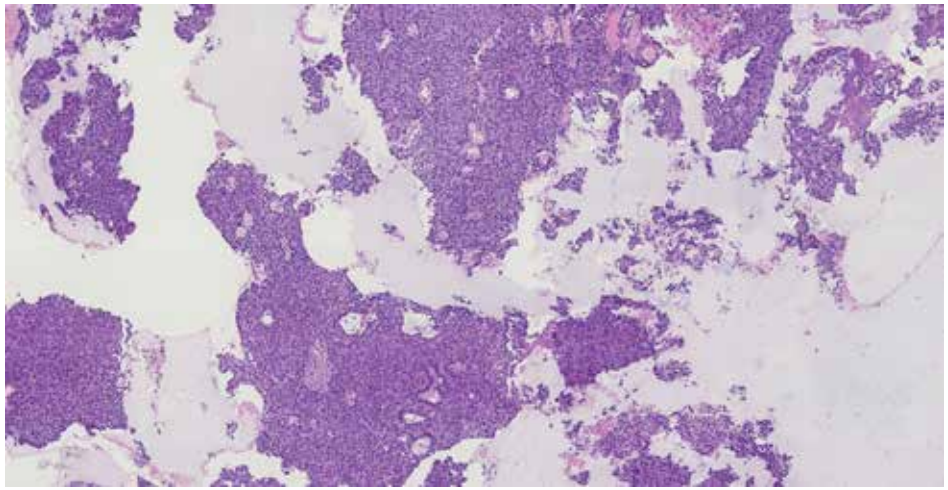
Case 6 Naveena Singh

Case 7 Naveena Singh

Case 8 Pavel Dundr

Case 9 Pavel Dundr

Case 1
C. Simon Herrington
Female aged 54. Previously treated CIN 2 and CIN 3. 2 months of postcoital bleeding. Mass in vagina, suspicious of malignancy. Vaginal biopsy (slide) and subsequent LETZ of cervix.

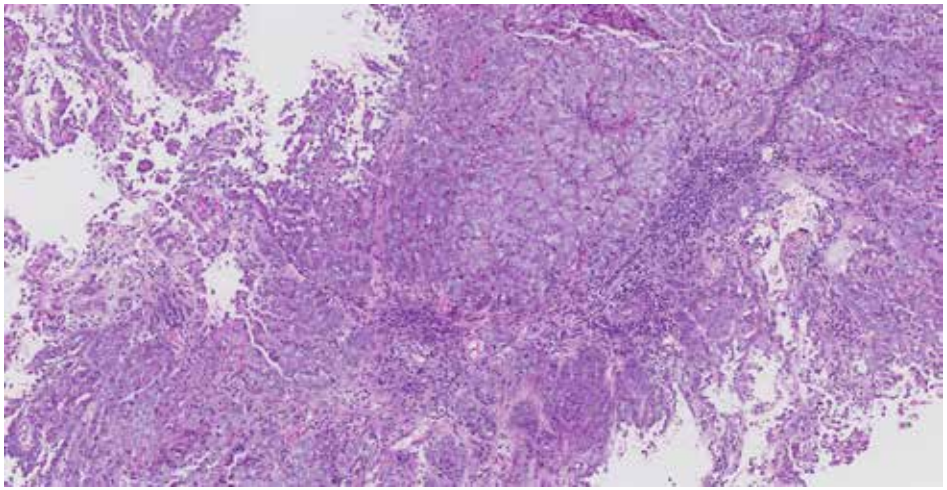


Notes:

Case 2

C. Simon Herrington

Female aged 49. Intermenstrual bleeding. Cervical smear negative. Friable growth on cervix, 2 cm, bleeds easily on touch. Cervical biopsies x 3.



Notes:

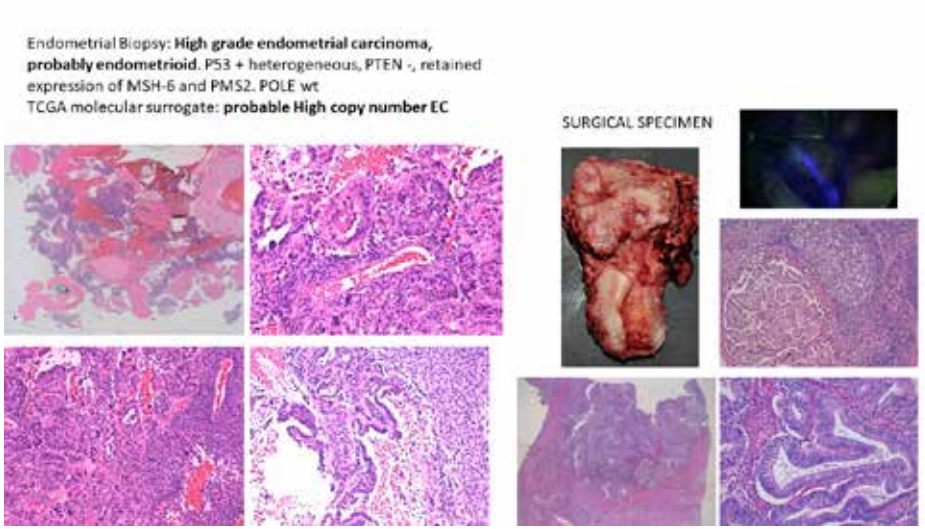
Case 3

Xavier Matias-Guiu

Clinical history: 51-year old woman with unremarcable familial and personal history. Vaginal bleeding. Endometrial biopsy.

Imaging: Enlarged uterus, 8.6 x 4.2 x 5,7 cm, with a mas (4,3 x 3,5 x 2,6 cm) with invasion of less than 50% of myometrial wall. No enlarged lymph nodes

Surgery: Hysterectomy with bilateral salpingoophorectomy. Sentinel biopsy and Lymphadenectomy. Peritoneal washings. Omentectomy and peritoneal biopsy if abnormalities are seen.



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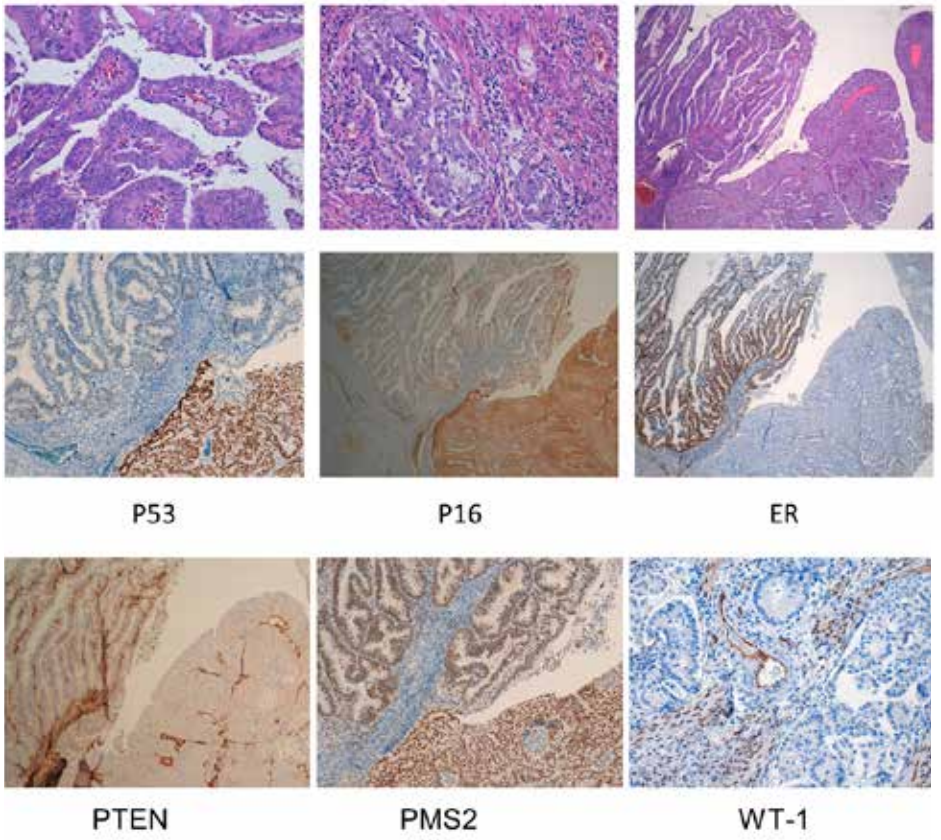
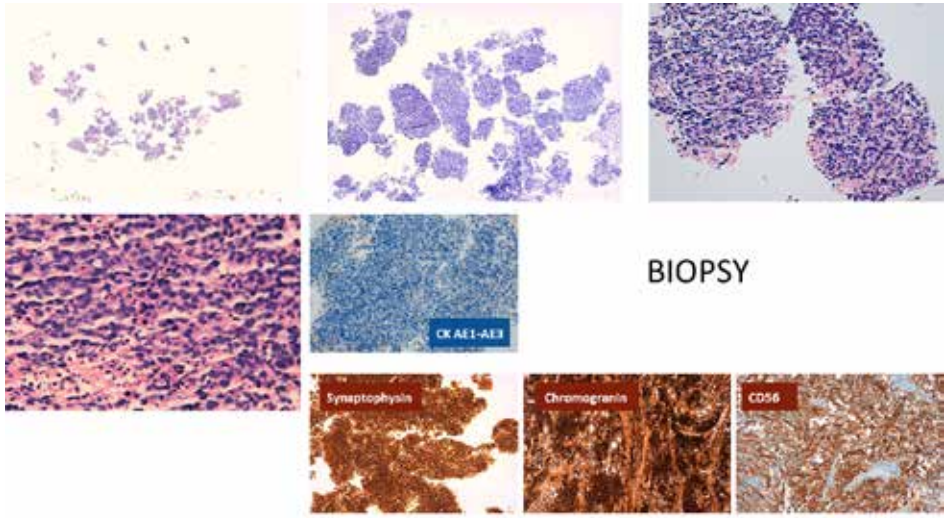


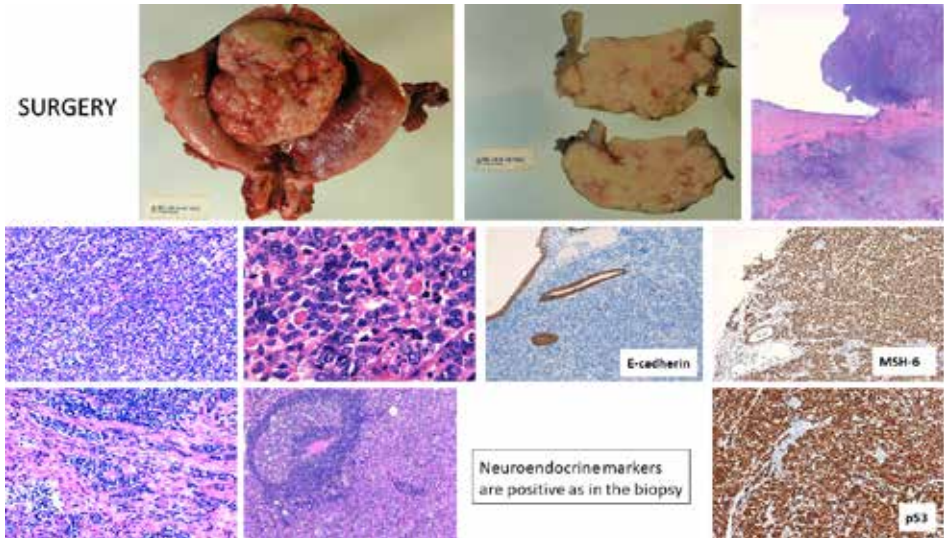
Notes:

Case 4

Xavier Matias-Guiu

52 year old lady. Vaginal bleeding. After biopsy, Histerectomy and bilateral salpingoophorectomy with pelvic and paraaortic lymphadenectomy.

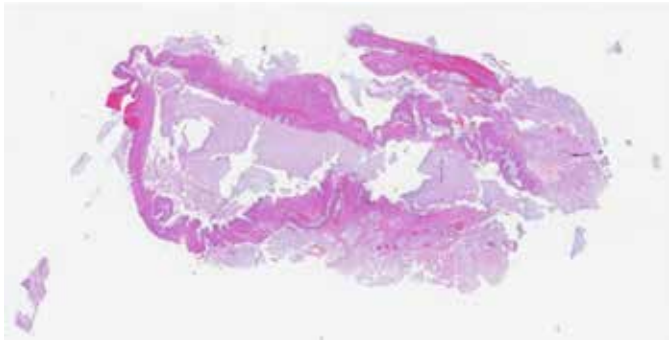


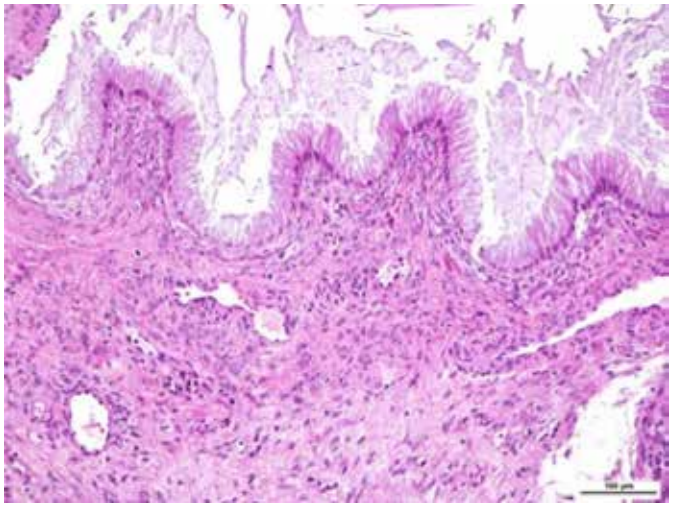


Case 5

Sigurd F. Lax

55 year-old female, St. P. breast cancer. Left-sided colitis with colonoscopy 1 year and 2 weeks ago. TVUS: right adnexal cystic mass, 10 cm, suspicious of malignancy; nodular structures in the cul de sac and plenty of ascites. CA 125 elevated (36). Laparotomy: pseudomyxoma peritonei; right ovarian lesion ruptured > for frozen section



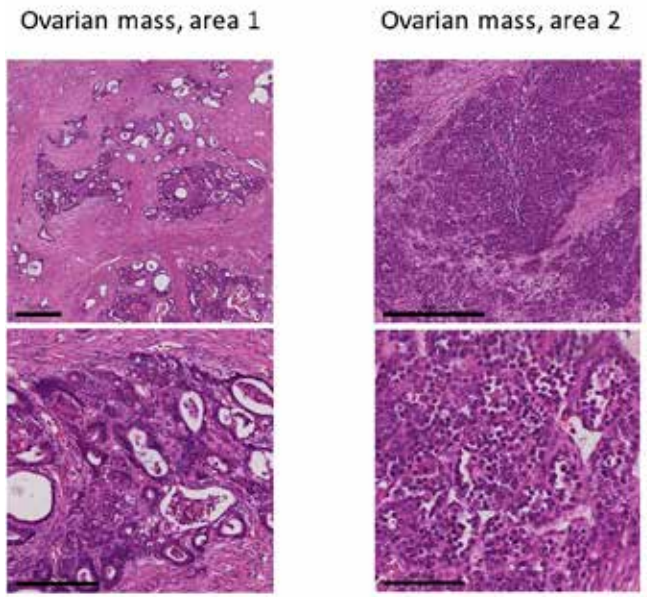


Notes:

Case 6

Naveena Singh

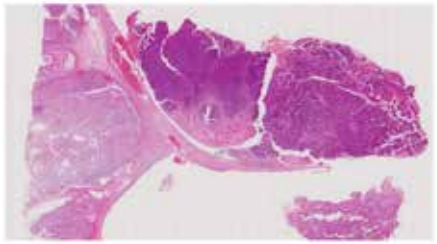
48 y female patient. Ovarian mass. Raised inflammatory markers. Emergency laparotomy.



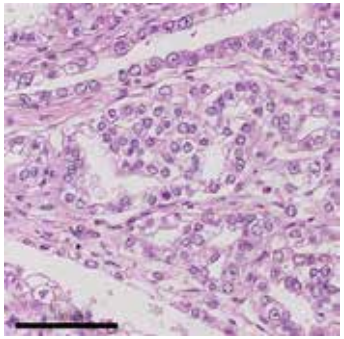
Notes:

Case 7
Naveena Singh
48 y female patient. Bilateral ovarian masses.

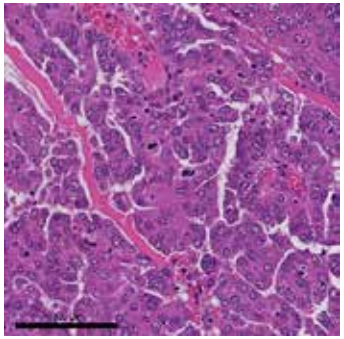
Ovary



Ovary, area 1

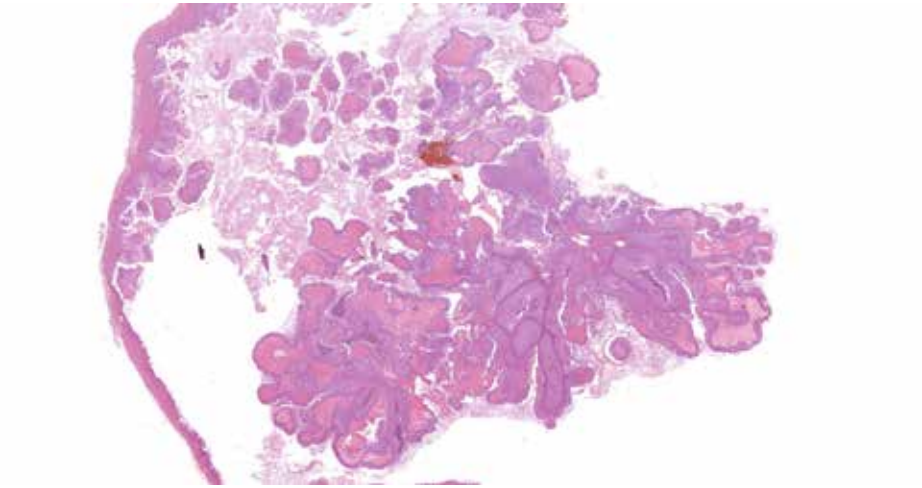


Ovary, area 2



Notes:

Case 8
Pavel Dundr
28-year-old female with a unilateral ovarian tumor. No other clinical data was available (consultation case).

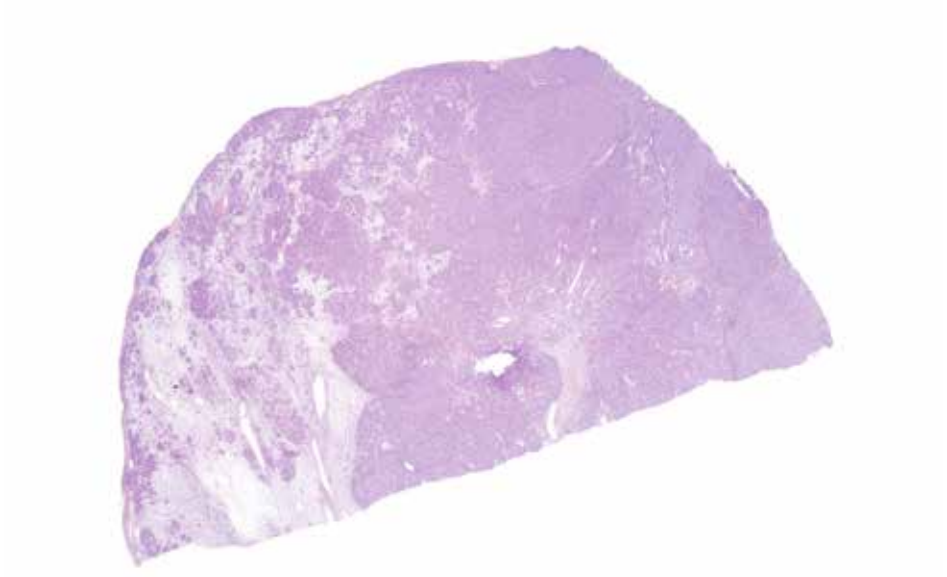


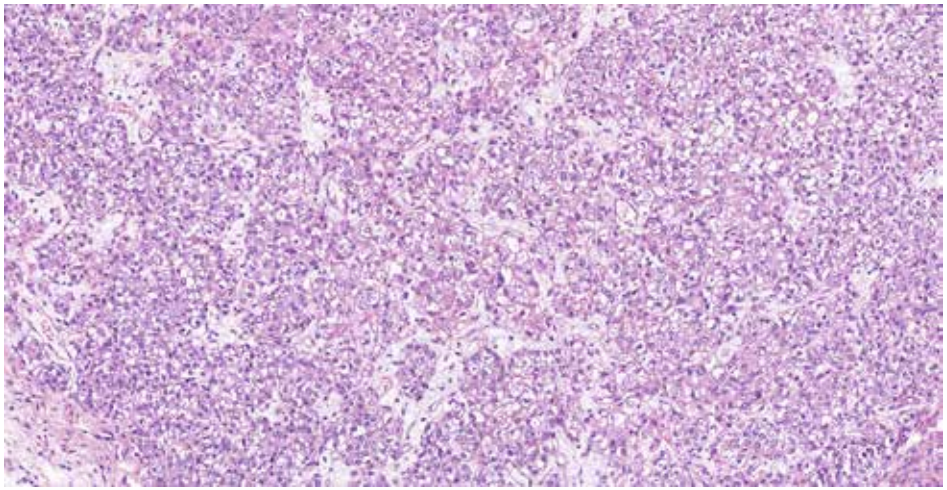
Notes:

Case 9

Pavel Dundr

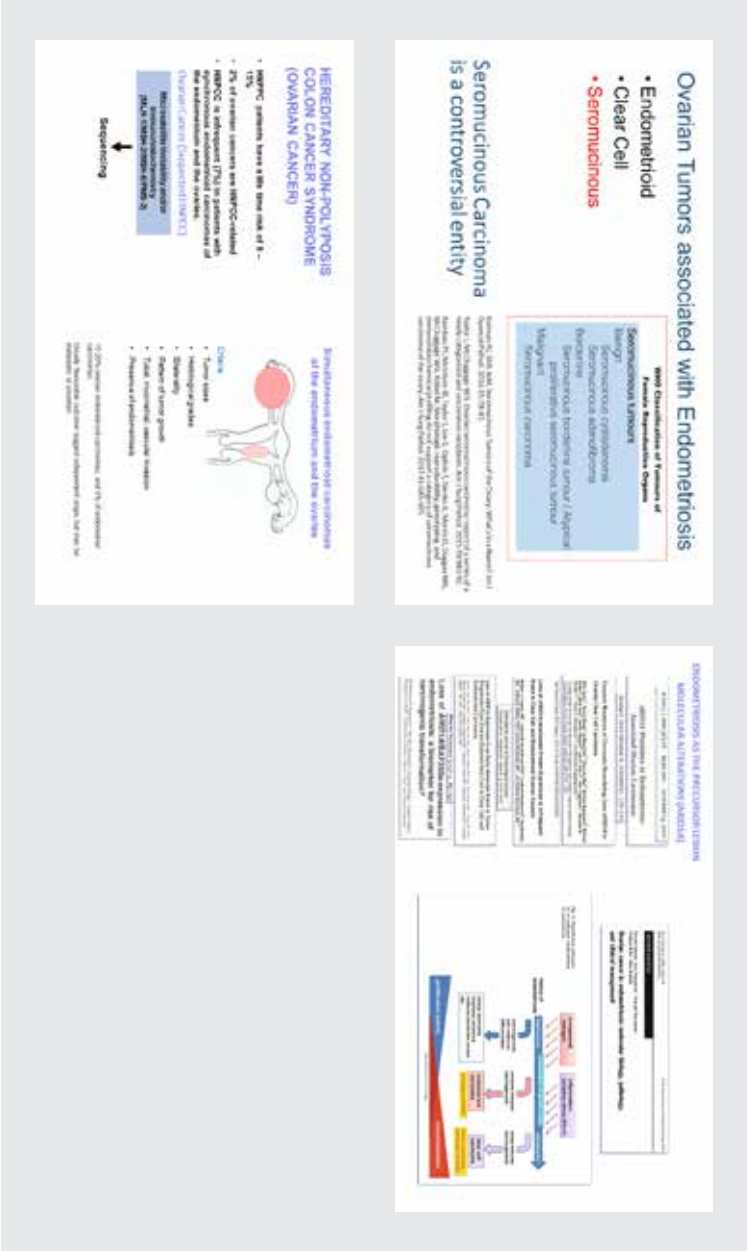
55-year-old female with a unilateral ovarian tumor. No other clinical data was available (consultation case).





Endometriosis and Associated Neoplasms

Xavier Matias Guiu, Hospital U Arnau de Vilanova, Univ Lleida, IRBLLEIDA, Hospital U de Bellvitge. IDIBELL, Spain



Ovarian Serous Borderline Tumours and Prognosis

Naveena Singh, Barts Health NHS Trust

Over the last decade there have been developments in our understanding of the serous borderline neoplasms. While the vast majority of serous borderline tumours have a favourable prognosis, recurrences and progression to low-grade serous carcinoma can each occur in a minority of cases. Recurrence, progression and death occur irrespective of tumour morphology/stage and after long intervals. At the time of diagnosis there are few morphological and no molecular parameters that can predict poor outcome. The morphological parameters tend to co-vary and include a micropapillary pattern and microinvasion. The two most important prognostic factors overall are stage and the presence of extra-ovarian invasive disease, the latter now classified as low-grade serous carcinoma from the outset. It has been shown that the progression of serous borderline neoplasia to low-grade serous carcinoma occurs on a pathway analogous to neoplastic transformation pathways seen in other organs, based on global gene expression profiling, shared mutations in KRAS or BRAF, and the frequent presence of serous borderline tumour in *de novo* low-grade serous carcinoma.

References:

1. Vang et al. Long-term Behavior of Serous Borderline Tumors Subdivided Into Atypical Proliferative Tumors and Noninvasive Low-grade Carcinomas: A Population-based Clinicopathologic Study of 942 Cases. Am j Surg Pathol 2017; 41:725-737.
2. Malpica and Longacre. Prognostic Indicators in Ovarian Serous Borderline Tumours. Pathology 2018; 50: 205-213.

Ovarian carcinoma: The most common mistakes in diagnosis

Pavel Dundr, Department of Pathology, First Medical Faculty Charles University and General University Hospital in Prague

The criteria for the diagnosis of ovarian epithelial tumors have changed over the years, along with changes in classification and expanding knowledge regarding their precursors, immunohistochemical profile, and molecular aberrations. There are currently 5 basic types of ovarian cancer - high grade serous carcinoma (HGSC), low grade serous carcinoma (LGSC), endometrioid carcinoma (EC), clear cell carcinoma, and mucinous carcinoma. The correct classification of these tumors is important because of their different prognosis and treatment. However, in some cases the diagnosis may be difficult. The goal of this presentation is to give an overview of the current problems of histological classification of ovarian epithelial tumors and the most common mistakes which may occur during their diagnosis. Attention is also paid to the evaluation of the significance of auxiliary (immunohistochemical, molecular) methods. The most common diagnostic errors occur especially in the following areas: i) determination of the biological nature of the tumor (benign, borderline, malignant); ii) assessment of the histological type of the tumor; iii) grading; iv) staging; v) assessment of the primary source (primary, metastatic); vi) evaluation of implants in serous borderline tumors. Among these, the most common errors include: i) evaluation of benign serous cystadenoma with focal epithelial proliferation as a serous borderline tumor (S-BTO); ii) classification of S-BTO as an invasive LGSC; iii) classification of HGSC as endometrioid carcinoma and vice versa; iv) assessment of the presence of expansive type of invasion in endometrioid and mucinous tumors; v) distinction between LGSC and HGSC; vi) distinction between primary and metastatic tumors, especially ovarian mucinous tumors. In these cases, clinical-pathological correlation and evaluation of the results of the spectrum of other (especially imaging) examinations are often necessary for a correct diagnosis. Uncommon, but with serious consequences, is a misdiagnosis of HGSC as a borderline tumor, which may happen especially in cases of intracystic tumors without clearly documented invasive growth.

Interpersonal and intrapersonal diagnostic concordance is better than in the past due to the refinement of diagnostic criteria for individual tumor types, but still the diagnosis is complicated and diagnostic accuracy is not optimal. The use of special methods may be very helpful in some cases, and especially immunohistochemical examinations play an irreplaceable role in this context. Molecular examinations may also be beneficial in selected indications.

Acknowledgment: Supported by Ministry of Health, Czech Republic - conceptual development of research organization 64165, General University Hospital in Prague, Czech Republic

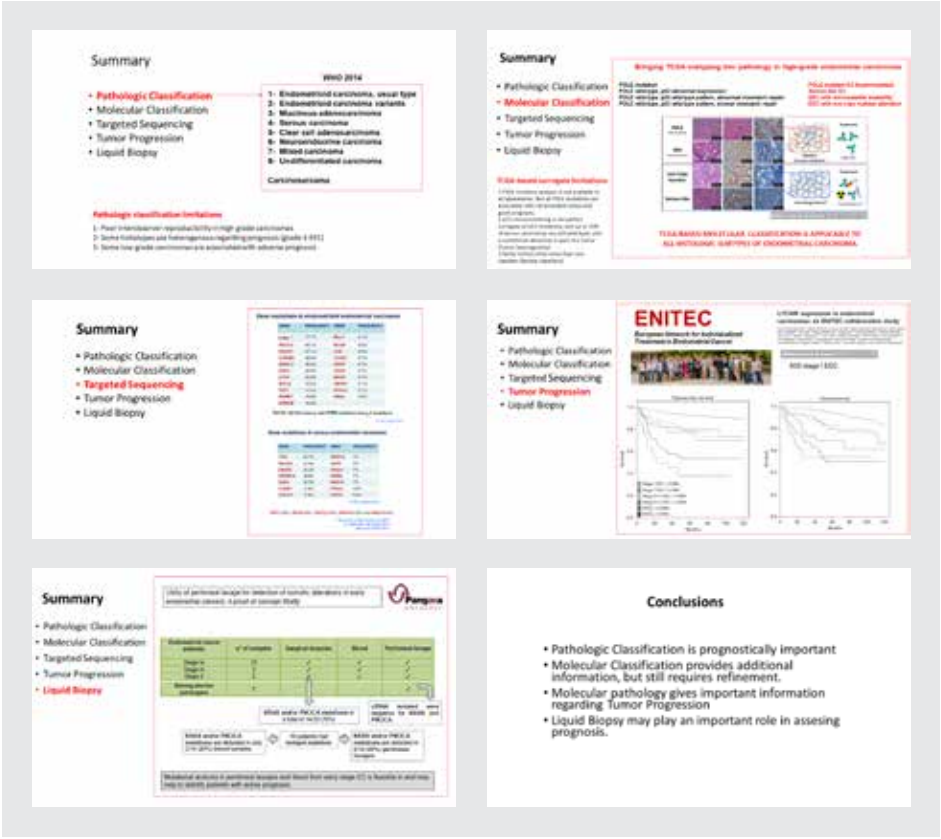
Difficulties in Staging of Gynaecological Neoplasms

Naveena Singh, Barts Health NHS Trust

Staging is the single most important prognostic factor for most cancers. The FIGO staging for endometrial, cervical, vulval and ovarian have all been recently updated to more closely reflect the prognostic impact of pathological findings. Pathological stage directly influences clinical management and assigns patients into a specific prognostic category. For these reasons it is imperative that staging is carried out accurately and reproducibly amongst pathologists. Difficulties in endometrial cancer often relate to the assessment of myoinvasive depth and cervical stromal involvement. In addition there are new insights into the biology of synchronous endometrial and ovarian low-grade endometrioid carcinomas with impact on their staging and management. Cervical cancer staging has been updated in 2018 and offers a clearer approach to areas previously found to be difficult, such as the assessment of horizontal diameter in low-stage disease. Staging in vulval cancer often relates to the identification and measurement of stromal invasion. Ovarian cancer staging needs to reflect our current understanding of the biology of high-grade serous carcinoma.

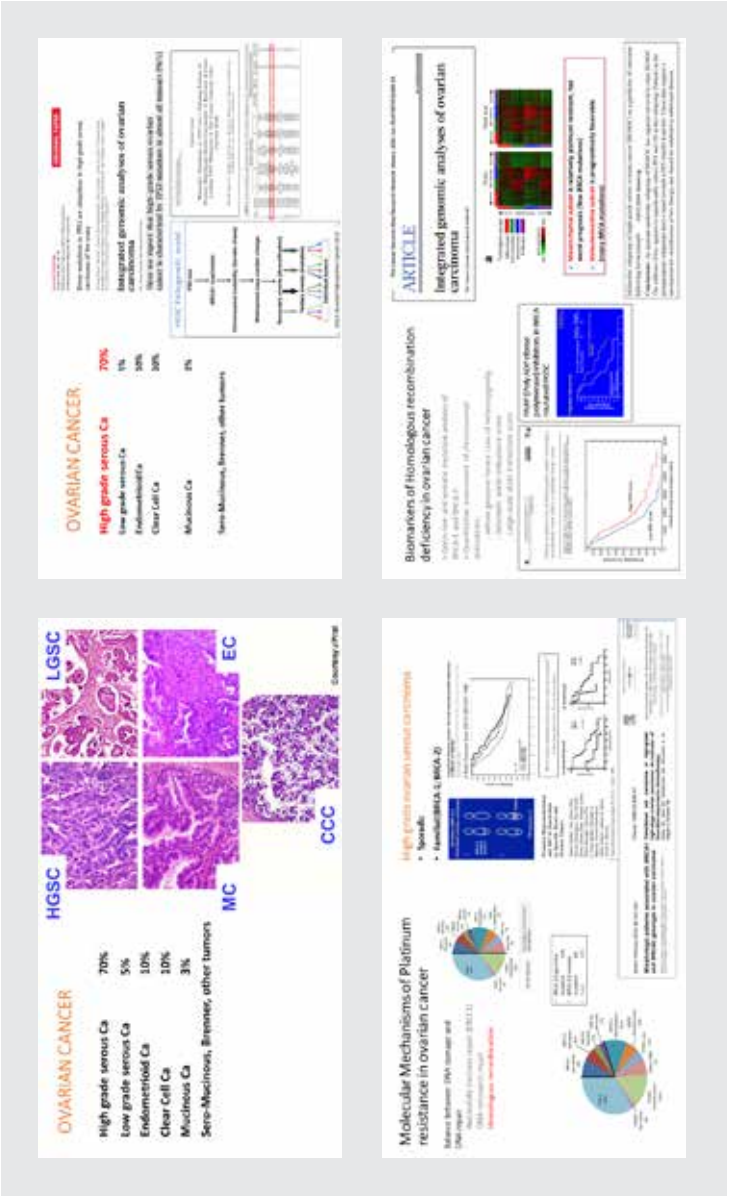
Molecular Pathology and Biomarker Testing in Endometrial Carcinoma

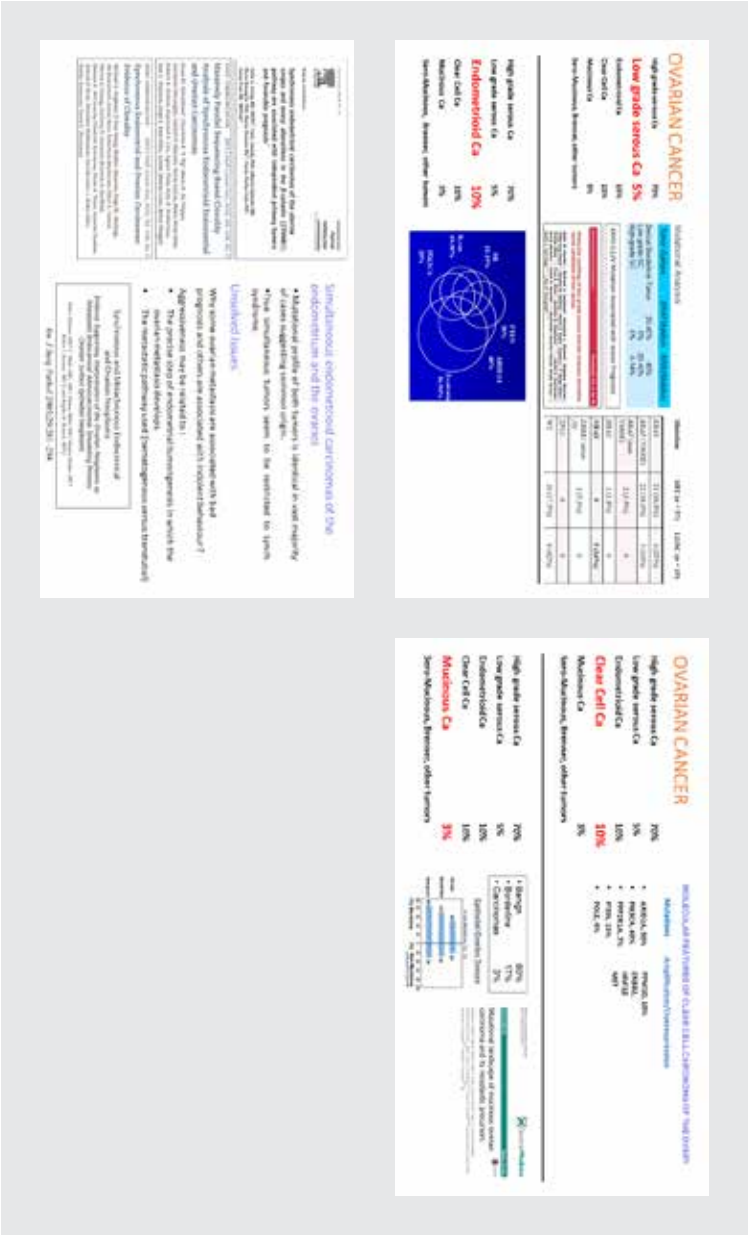
Xavier Matias Guiu, Hospital U Arnau de Vilanova, Univ Lleida, IRBLLEIDA, Hospital U de Bellvitge. IDIBELL, Spain



Molecular Pathology and Biomarker Testing in Different Types of Ovarian Carcinoma

Xavier Matias Guiu, Hospital U Arnau de Vilanova, Univ Lleida, IRBLLEIDA, Hospital U de Bellvitge. IDIBELL, Spain





Morphological features of uterine leiomyomas with bizarre nuclei - poster presentation

András Rókusz, Katalin Dezső, Zoltán Sápi 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary

Introduction: Uterine leiomyomas with bizarre nuclei is a rare but distinct entity, often causing diagnostic challenges. A subset of these tumors show loss of fumarate-hydratase (FH) activity, which can be demonstrated by immunohistochemistry. Beside the bizarre nuclei there are other histological features which can suggest FH-deficiency, e.g. staghorn vessels, prominent nucleloli or pulmonary type oedema. Objective, methods: We examined the morphological features of uterine leiomyomas with bizarre nuclei from the archives of our institute in the period between 2016 and 2019, and applied FH immunohistochemistry on them. Conclusion: Leiomyomas with bizarre nuclei can arise in the setting of either somatic or germline FH mutations. The majority of FH-deficient uterine leiomyomas harbour somatic FH mutation, so routine genetic testing is not recommended in these cases. In young patients with FH-deficient uterine leiomyoma and a familial history of renal cell carcinoma or cutaneous leiomyomas genetic testing can be considered to detect possible FH germline mutations. FH immunohistochemistry is useful in the correct diagnosis of uterine leiomyomas with bizarre nuclei.

Robust expression of EZH2 in endocervical neoplastic lesions - poster presentation

(1) Evelin Makk, (1) Levente Bálint, (2) János Cifra, (1) Tamás Tornóczky, (1) Angéla Oszter, (3) Arnold Tóth, (1) Endre Kálmán, (1) Krisztina Kovács 1 Department of Pathology, University of Pécs Medical School, Hungary Szigeti út 12., Pécs, 7624 Hungary 2 Department of Pathology, County Hospital Tolna, János Balassa Hospital, Szekszárd, Hungary Béri Balogh Ádám u. 5-7, Szekszárd, 7100 Hungary 3 Department of Radiology, University of Pécs Medical School, Hungary Ifjúság út 13., Pécs, 7624 Hungary

The aim of this study was to evaluate the nuclear expression of histone methyltransferase enhancer of zeste homolog 2 (EZH2) in endocervical neoplastic lesions. A total of 54 consecutive neoplastic cases and 32 non-neoplastic endocervical lesions were included in the study. EZH2 immunoreactivity was evaluated semiquantitatively by three independent experts. Robust EZH2 expression was statistically compared among the neoplastic, non-neoplastic and normal glandular epithelium samples. Diagnostic test capability of robust EZH2 expression was calculated. 53 out of the 54 neoplastic cases (98%) showed robust EZH2 expression. Robust EZH2 expression was significantly less often (4 out of 32 cases, 12.5%) found in the non-neoplastic endocervical lesions (p

Giant Condyloma of the Uterus – Case Report - poster presentation

Dóra Hargitai Dr. 1, Áron Somorácz Dr. 1,2 1: SE 2nd Department of Pathology, Budapest, Hungary 2: South-Pest Hospital Centre – National Institute for Infectology and Haematology

54-year-old woman patient with exophytic lesion on the cervix of the uterus. Biopsy was taken and histological examination suggested verrucous carcinoma. PET-CT showed pathological FDG accumulation in the uterus. Oncoteam proposed radical Wertheim hysterectomy due to IB2 stage squamous cell carcinoma. We received a specimen of uterus, cervix, and bilateral adnexae. The surface of the cervix was covered by uneven, verrucous protrusions measuring 0,3-0,5 cm in thickness. The lesion spreaded into the cavity of the uterus, covering its entire inner surface. Histological examination revealed an exuberant squamous proliferation with papillary architecture. The base of the lesion was smooth without any evidence of stromal invasion. Cytopathic changes characteristic for HPV infection were evident in the upper epithelial layers. Immunohistochemistry for P16 was negative. The diagnosis of giant condyloma of the uterus was given, which is a rare entity associated with low risk HPV infection. It shares the same histological features seen in its anal, perineal and vaginal counterpart. The differential diagnosis includes verrucosus carcinoma and papillary immature metaplasia.

Spectrum of HNF1B mRNA splicing variants in various gynecological lesions - poster presentation

Kristýna Němejcová MD, PhD; Jana Rosmusová MD; Radek Jakša MD; Jan Hojný MS; Michaela Bártů MD; Ivana Tichá RNDr, PhD; Prof. Pavel Dundr MD, PhD Institute of Pathology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic.

INTRODUCTION/PURPOSE: The exact mechanism of the involvement of the transcription factor hepatocyte nuclear factor 1-beta (HNF1B) in tumorigenesis has not yet been elucidated. We describe the spectrum of HNF1B mRNA splicing variants in the female genital tract. METHODS: RNA (RQN>8.8) isolated from RNAlater stored tissues (endometroid endometrial/ovarian carcinoma-EEC/EOC, high grade serous ovarian carcinoma-HGSC, and normal tissue) was subjected to cDNA synthesis by SSIII transcriptase and random hexamers. Random samples of each tissue type were pooled and analyzed using in-house multiplex PCR of all present exon-exon junctions and NGS (Illumina). RESULTS: In total, 16/18 of the detected splicing variants were novel, 4 predominant HNF1B transcripts included 2 known (3q, Δ7_8), 2 novel (Δ7, Δ8) splice variants. Only the predominant transcripts were detected in HGSC compared to the multiple variants in EEC/EOC. CONCLUSION: High sensitivity variant detection revealed a series of novel isoforms with a so far unknown function. The expression profiles of the predominant variants will be analyzed to unravel splicing patterns. Supported by projects MZCR RVO 64165 and AZV17-28404A

Case Report: Metaplastic papillary tumour of the fallopian tube, a rare entity. - poster presentation

Dr. Sandra Sunitsch*, Dr. Francesca Sarocchi*, ao.Univ.-Prof. Dr. Peter Regitnig*, Dr. Luca Abete*. *Diagnostic & Research Institute of Pathology, Medical University of Graz, Austria

Introduction/Background: Metaplastic papillary tumours (MPTs) of the fallopian tube are very rare lesions, typically associated with gravidity and uneventful outcome. Objective/Purpose: To report and describe the case of a MPT of the fallopian tube, detected incidentally in a 35 year old woman. Methods: The fallopian tubes were removed post-partum for sterilization, macroscopically described, grossed and routinely stained with H&E according to standard protocol. Results: Histological examination reveals an exophytic lesion within the tubal lumen of the right salpinx, involving only part of the mucosa. The proliferation shows a papillary configuration with loose fibrovascular connective tissue. Epithelial lining consists of one to two layers of plump, nonciliated columnar cells with eosinophilic cytoplasm. Conclusion: MPTs are exceedingly rare lesions. Their nature (metaplastic or neoplastic) has yet to be elucidated. All reported cases have shown no progression, recurrence or metastases. Hence, we remark the importance not to misdiagnose this entity as serous atypical proliferation/neoplasm to avoid overtreatment.

Precision Oncotherapy of Gynecological Malignancies

Istvan Petak, Semmelweis University, Department Of Pharmacology and Pharmacotherapy, Budapest, Hungary University of Illinois at Chicago, Department Of Biopharmaceutical Sciences, Chicago, USA Oncompass Medicine Inc. Budapest, Hungary

On the 26 th of November, 2018 FDA approved lerotrectinib for all human cancers positive for NTRK translocation (3% of all cancers), following the approval of pembrozilumab on the 23rd of May, 2017 for all human cancers with MSI positivity (4% of all cancers). We are officially entering the era of precision oncology, including the oncology of gynecological malignancies. In 2018, 15 novel targeted and immuno anti-cancer therapies in 25 indications were approved. This is an 10X increase in new drug approvals and will surely lead to 100 new drugs in this decade. 75% of novel drugs are linked to molecular diagnostic test results. Since there are no randomized clinical trials to compare each drug in each indications and molecular subtype, we have to use functional molecular evidence for each patients to prioritize between treatments. In precision oncology, our aim is to identify the molecular patho-mechanism of the tumor progression and then we have to find the therapy or combination of therapies based on their molecular mechanism of action. Difficulties of this approach: most genetic variations are variant of unknown significance, many variants have controversial classification due to conflicting evidences, many driver variants are linked to multiple treatments with different level- and often conflicting evidences, most tumors harbor multiple driver alterations (2-8), each driver alterations are linked to multiple druggable or indirect druggable targets, and each drug can be linked to multiple driver alterations and targets in the same tumor. We have developed an AI oncology algorithm, and medical knowledge engine, which can prioritize over 1000 onco-therapies based on 24,000 medial rules. The solution can be also used to prioritize between molecular diagnostic tests based on clinical actionability and mutation frequency. The solution is integrated into a novel medical procedure to enable precision oncology into clinical practice.

Mucinous Ovarian Tumors and Metastases

Sigurd F. Lax, Johannes Kepler University (JKU) of Linz, Faculty of Medicine; Linz, Austria, Medical University of Graz and Styrian Hospital Corporation

Mucinous ovarian neoplasms represent the second largest group of epithelial ovarian tumors after serous neoplasms, of which benign cystadenomas constitute more than 80%. Mucinous cystadenomas and carcinomas cannot be distinguished by the clinical features or the mean age of onset of the disease. They typically occur unilaterally, are confined to the adnexae (FIGO stage I) and clinically present with non-specific abdominal symptoms or are diagnosed by chance. The mean age of disease onset is around 50 years old. The prognosis is excellent. Implants, peritoneal metastases and bilateral occurrence of ovarian mucinous neoplasms should lead to the suspicion of metastasis particularly from a gastrointestinal tumor. Neither microinvasion defined as a maximum extent of invasion of 5 mm, nor intraepithelial carcinoma characterized by high grade atypia without invasion, affect the prognosis of mucinous borderline tumors. Mucinous carcinomas typically show confluent glandular, expansive growth that leads to a labyrinth-like pattern. A destructive infiltrative or nodular growth pattern, however, should lead to the consideration of metastasis. Mural nodules that may reveal a spindle cell sarcomatous or anaplastic carcinomatous pattern occur infrequently in mucinous and do not affect the prognosis. Pax8 positivity is indicative of a primary ovarian neoplasm but positive only in about 50% of cases. In this case, however, mucinous tumors associated with teratomas may show the colonic immunoreaction pattern (CK7−/CK20+/CDX2+). A further marker for colonic differentiation is SATB2. The rare mucinous tumors with endocervical differentiation are now designated as seromucinous tumors and consist of two or more distinct cell types, are frequently associated with endometriosis and seem to show a molecular genetic relationship to endometrioid neoplasms.

New Concepts in Gyneco-Oncological Surgery

Zoltán Novák, Department of Gynecology
National Institute of Oncology, Budapest, Hungary

Cervical cancer: in the recent years, there was a trend towards minimal invasive, less radical procedures. However, 2018 has brought paradigm shifting evidences to light which might reverse this trend. Minimally invasive surgery was associated with worse oncological outcome. Meanwhile, new data are emerging with the use of sentinel lymph node procedures. Endometrial cancer: there is an increasing trend to use minimally invasive techniques and sentinel lymph node procedures in low risk patients, high risk patients are treated with aggressive surgery. Ovarian cancer: ovarian cancer surgery requires a highly specialised team and aggressive cytoreduction remains the gold standard method. Complete cytoreduction to macroscopic no visible disease remains the ultimate goal, and multivisceral resections are frequently used. Vulvar cancer: the lymph node status remains highly important in the stratification of these patients, radical excision with lymph node removal and reconstructive techniques are frequently used.

New Concepts in Cervical Screening

C Simon Herrington, Professor of Pathology, University of Edinburgh, UK

A National Cervical Screening Programme, using cervical smear cytology, has been in place in the UK since 1988. This has been highly successful at achieving its primary objective, namely reducing mortality due to cervical carcinoma. At that time, it was recognised that human papillomavirus (HPV) infection was involved in the development of cervical condylomata but its role in intraepithelial and invasive disease was not well established and there were no simple methods for detecting HPV in clinical material. Improvements in PCR-based HPV testing in the early 1990s led to an explosion in studies examining the relationship between HPV and cervical disease but technical problems (particularly sample contamination) led to overestimation of the population prevalence of HPV infection. Attempts were made to correct for this by analysing viral load in clinical samples, but this did not prove helpful and the true role of HPV in cervical carcinogenesis was not widely appreciated.

The landmark study by Walboomers et al from Amsterdam, published in 1999, changed attitudes towards HPV and its relationship with cervical disease, showing that virtually all cervical carcinomas contain HPV DNA. This is, in fact, likely to be an overestimate, as we now know that HPV-negative cervical carcinomas (particularly adenocarcinomas) do occur. However, this finding indicated that HPV testing had the potential to have very high sensitivity for the detection of cervical carcinoma. This prompted the development of HPV testing strategies to capitalise on this high sensitivity, but with the predictable consequence that the specificity of HPV testing in a population setting was poor. This high sensitivity can, however, be used after treatment to identify women with residual or recurrent disease, the so-called 'test of cure'.

The recognition that HPV testing can accurately predict the absence of high grade intraepithelial, and invasive, disease (a high negative predictive value) led to the concept that HPV testing can be used as a first-line screening test, with no requirement for cytological assessment in those whose HPV tests are negative. This focuses effort on HPV positive samples, which are assessed cytologically; further management is then based on the cytological result. This approach has a number of advantages: it focuses investigative resources on women with a higher probability of disease; and it reduces the burden on laboratories, as the number of smears requiring cytology evaluation is reduced. Potential disadvantages include the inability to detect HPV negative disease, although cervical cytology also has low sensitivity in this situation; and the requirement for reorganisation of services. Nevertheless, primary HPV testing is now being trialled or implemented in several countries.

HPV testing has developed almost in parallel with HPV vaccination, which was first introduced in 2006. Initially, this focused on bivalent (HPV 16 and 18) and quadrivalent (HPV6, 11, 16 and 18) vaccines but vaccines with broader HPV coverage, such as the nonavalent vaccine, are now in use. Vaccination is already changing the epidemiology of intraepithelial and invasive cervical disease and it could be argued that HPV negative cervical disease will become an increasing problem as HPV-associated disease reduces in the population. However, although HPV negative disease may form a greater proportion of cervical neoplasia, the absolute numbers of these uncommon tumours are unlikely to change.

Future cervical screening programmes will almost certainly be based on primary HPV testing with reflex cytology. This has significant implications for pathology services.

Cervical Adenocarcinoma and Precursors

Simona Stolnicu, University of Medicine, Pharmacy, Sciences and Technology (UMFST), Targu Mures, Romania

Squamous cervical lesions are more frequent however there is a higher prevalence of glandular lesion (both precursors and invasive) and new entities have been described recently. The precursor lesion is represented by in situ adenocarcinoma whose morphologic criteria have been described by Friedell and Mackay in 1953. Usual/endocervical, intestinal type and SMILE (stratified mucin-producing intraepithelial lesion) are HPV-related while endometrioid, gastric and tubal/ciliated are HPV-unassociated. Ancillary studies such as p16, ki67 and HPV testing may help in differentiating in situ adenocarcinoma of the cervix from mimics.

Invasive endocervical adenocarcinomas (ECAs) are currently classified according to the 2014 World Health Organization (WHO) system, which is predominantly based on descriptive morphologic characteristics, considers factors bearing minimal etiological, clinical or therapeutic relevance, and lacks sufficient reproducibility. The 2017 International Endocervical Adenocarcinoma Criteria and Classification (IECC) system was developed by a group of international collaborators to address these limitations. The IECC system separates ECAs into two major groups—those that are human papillomavirus-associated (HPVA) and those that are non–HPV-associated (NHPVA)—based on morphology (linked to etiology) alone, precluding the need for an expensive panel of immunohistochemical markers for most cases. The major types of HPVA ECA include the usual (with villoglandular and micropapillary architectural variants) and mucinous types (not otherwise specified [NOS], intestinal, signet-ring, and invasive stratified mucin-producing carcinoma). Invasive adenocarcinoma NOS is morphologically uninformative, yet considered part of this group when HPV positive. NHPVA ECAs include gastric, clear cell, endometrioid, and mesonephric types. The IECC system is supported by demographic and clinical features (HPVA ECAs develop in younger patients, are smaller, and are diagnosed at an earlier stage), p16/HPV status (almost all HPVA ECAs are p16 and/or HPV positive), prognostic parameters (NHPVA ECAs more often have lymphovascular invasion, lymph node metastases, and are Silva pattern C), and survival data (NHPVA ECAs are associated with worse survival). A move from the morphology-based WHO system to the IECC system will likely provide clinicians with an improved means to diagnose and classify ECAs, and ultimately, to better personalize treatment for these patients.

Gynecological Tumours in Familial Syndromes

Pavel Dundr
Department of Pathology, First Medical Faculty Charles University and General University Hospital in Prague

The most common hereditary gynecological tumor syndromes are hereditary breast and ovarian cancer syndrome, and Lynch syndrome. However, there is a whole spectrum of other hereditary tumor syndromes with possible manifestations in the female genital tract, including, amongst others, Cowden's syndrome, hereditary leiomyoma and renal cell carcinoma syndrome, Peutz-Jeghers syndrome, DICER1 syndrome, tuberous sclerosis complex, rhabdoid tumor predisposition syndrome, and nevoid basal cell carcinoma syndrome. Tumors occurring in patients with these syndromes may look like those seen in sporadic cases, but some may have distinctive features (either morphological or related to the age of manifestation), which can be suggestive of an association of the tumor with a particular hereditary syndrome. Pathologists should be aware of these tumors and their possible association with familial syndromes. The role of pathologists in the diagnostics of gynecologic tumors in hereditary syndromes is, however, not in the diagnosis of the hereditary disease itself, but rather in the: i) recommendation for a referral of patients for genetic counseling in distinctive tumors possibly associated with a hereditary disease; ii) involvement in the screening for some hereditary diseases, such as Lynch syndrome, during routine diagnosis of selected tumors (i.e. endometrial and ovarian carcinomas); iii) processing of the gynecology biopsy specimens removed during prophylactic surgery.

The goal of this presentation is to give an overview of gynecologic tumors associated with hereditary syndromes with respect to all the afore mentioned topics. Attention is especially paid to the processing of the specimens in prophylactic surgical procedures, summary of current knowledge with respect to rare gynecological hereditary tumors, and screening for Lynch syndrome. Concerning Lynch syndrome screening, testing endometrial cancer hysterectomy specimens either for MSI or by MMR immunohistochemistry (IHC) with reflex MLH1 promoter hypermethylation analysis for tumors with a loss of MLH1/PMS2 expression is currently a common approach, but not in every country. For example in the Czech Republic this testing is not covered by health insurance companies and is not a standard part of the diagnostic algorithms. However, the Society of Gynecologic Oncologists (SGO) and the American College of Obstetricians and Gynecologists (ACOG) support both targeted and universal screening of endometrial tumors to identify those patients at risk and those harboring germline mutations. Regarding screening for hereditary breast and ovarian cancer syndrome, the situation today is different. Despite the attempts to select patients at risk who are eligible for genetic counseling based on morphological features of HGSC (such as the SET pattern, tumor infiltrating lymphocytes, nuclear atypias, and mitotic count), the current approach endorsed by the SGO is that all women diagnosed with epithelial ovarian, tubal, and peritoneal cancers should receive genetic counseling and be offered genetic testing.

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SLIDE SEMINAR 3

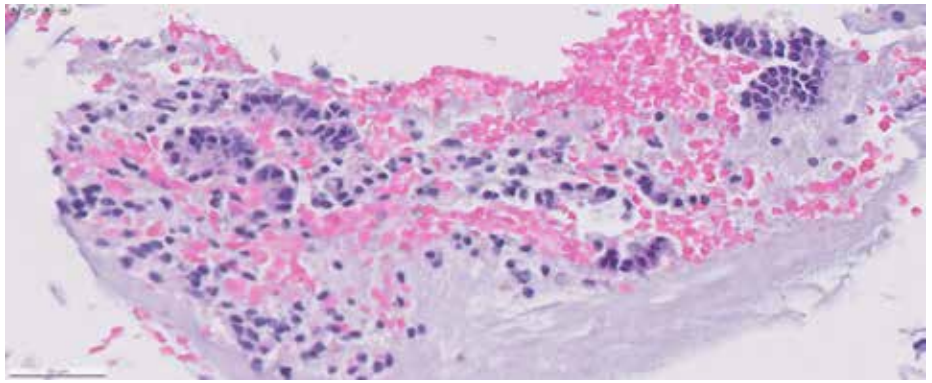
PITFALLS IN SELECTED CASES OF GYNECOPATHOLOGY

Thomas Krausz

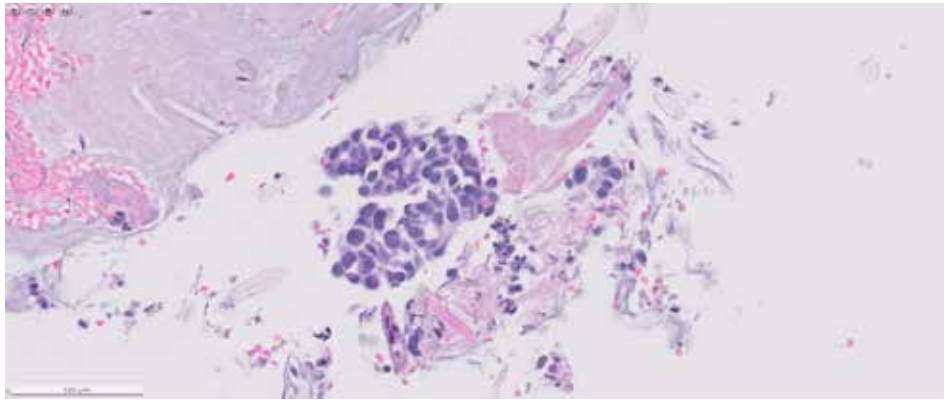
Case 1

65-year-old female, with history of ductal carcinoma of the breast in 2003. A PAP- smear in 2017 showed "atypical glandular cells not otherwise specified". Subsequent endometrial (A) and endocervical curettage (B): rare clusters of malignant cells – ? type.

A.



B.



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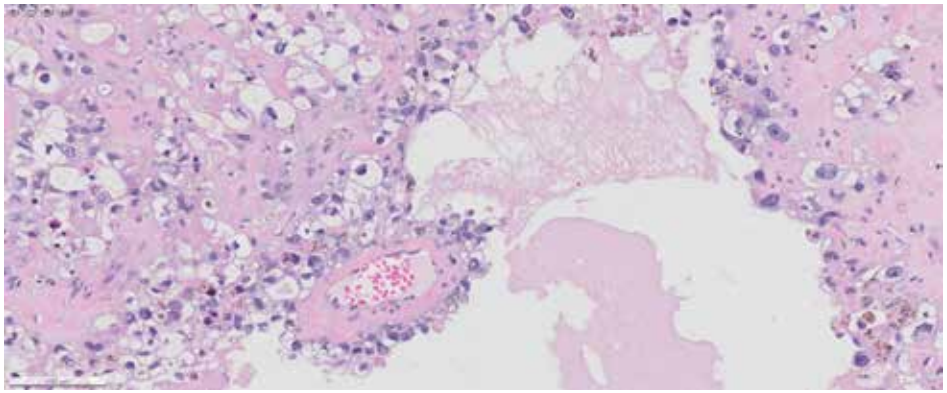
Case 2

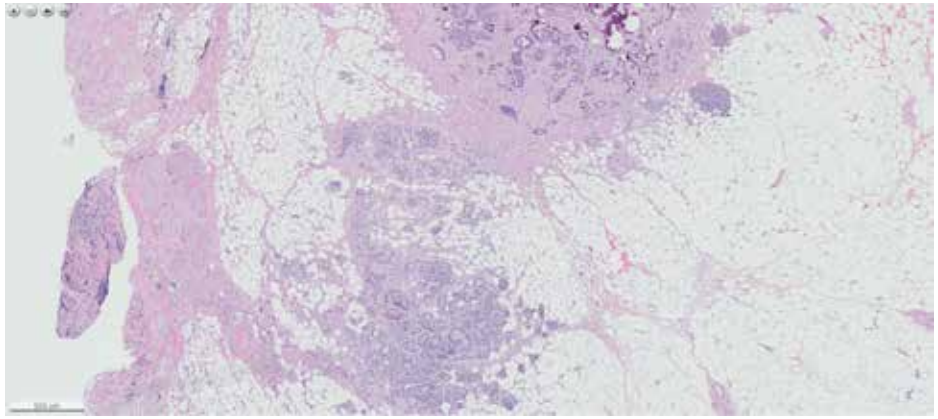
68-year-old female (G3P3003) presenting with uterine bleeding. Transvaginal ultrasound: large, partly necrotic uterine tumor mass (22 cm). Endometrium could not be visualized. The mass appeared to replace the myometrium with metastatic nodules on pelvic peritoneum. She underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal biopsies and pelvic/paraaortic lymphadenectomy.

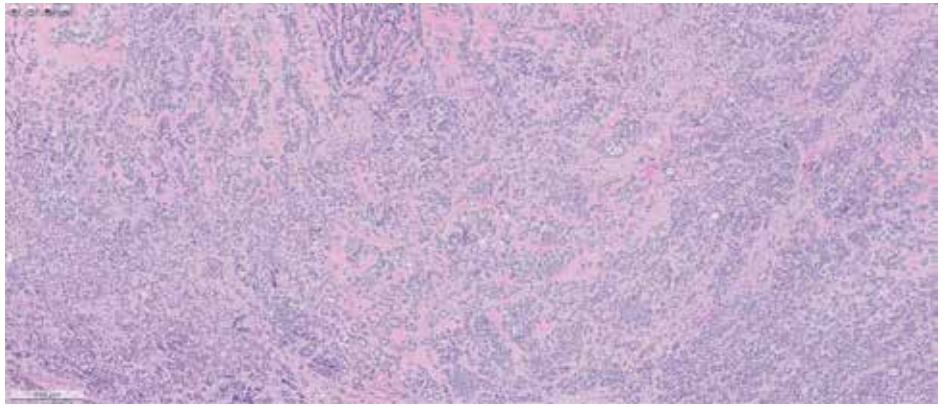


Notes:

Case 3

80-year-old woman with peritoneal tumor deposits. Previous core needle biopsy diagnosed as metastatic “adenoid cystic-like carcinoma”. Right ovarian partly cystic, partly solid mass, 10.5 cm. Submitted slide for the seminar was cut from the metastatic tumor deposit on the peritoneum.





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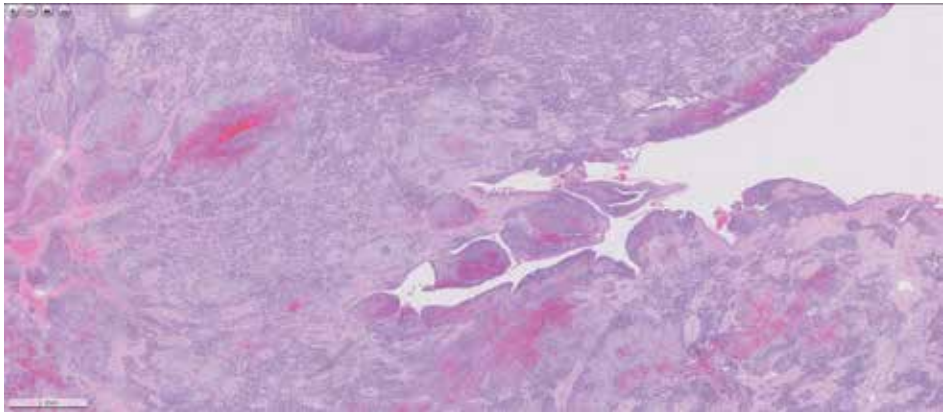
Case 4

17-year-old G0P0 women with past medical history of multinodular goiter and hypothyroidism. Found unconscious at home by parents after acute onset of heavy vaginal bleeding. Physical exam: 10 cm, friable hemorrhagic mass protruding from the introitus. Partial trachelectomy and mass excision was performed. Mass was arising from the ectocervix. Excision was complete. The slide for the seminar is from the cervical mass.



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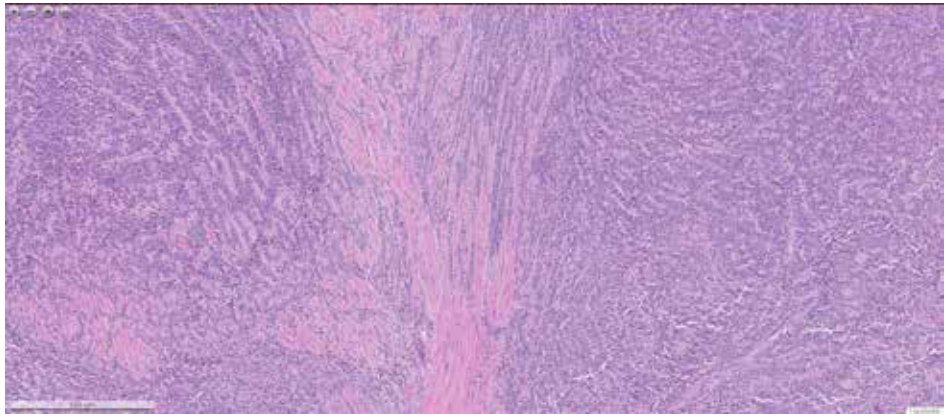
Case 5

57-year-old female with history of uterine bleeding. Previous endometrial biopsy was diagnosed as high-grade carcinoma favoring endometrioid variant. Hysterectomy specimen contained a 5-cm yellow-tan mass in the myometrium.



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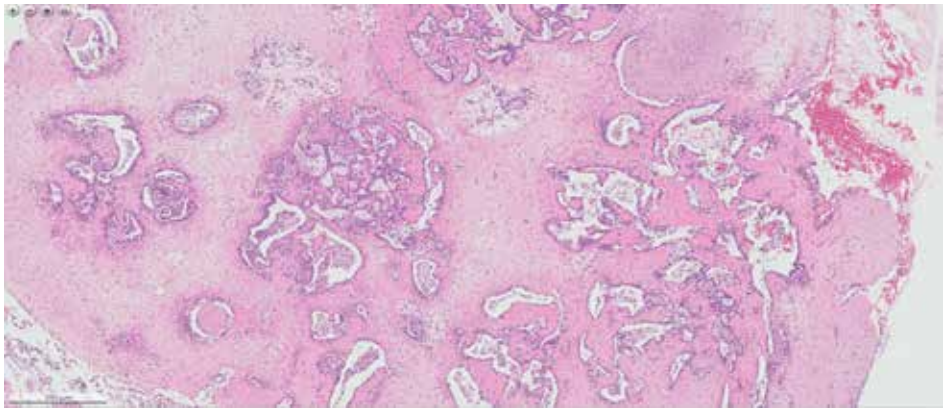
Case 6

39-year-old female with history of vaginal strictures and primary infertility. Biopsies of vaginal stricture diagnosed as clear cell adenocarcinoma arising from vaginal adenosis at two independent institutions (no history of diethylstilbestrol exposure). Patient was referred to University of Chicago for definitive treatment.



Notes:

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	before May 5, 2019	after May 5, 2019
IAP members	150 €	200 €
Non-members	200 €	250 €
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*requires certification from the applicant's institution

Participants are entitled to the following services:
- admission to the scientific program and the exhibition,
- congress bag,
- Handout Book,
- coffee and refreshment during the breaks,
- meals

Cancellation and refund
In case of cancellation before April 30, 2019: 80 percent refund of the fees paid;
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Weather
The weather in June is usually warm in Hungary, however, in Visegrád (height: 352 m) cooler weather may occur. Temperature ranges between 20-24 ºC.

Dress is informal at all occasions.

Currency, exchange, bank cards
The official currency is the Hungarian Forint. Exchange facilities are available at the airport, in hotels, at banks. ATMs are available throughout the country. American Express, Visa, Diner, Eurocard, MasterCard, JCB cards are mostly accepted in hotels, restaurants and city stores, but you should ask before ordering a service, or buy.

Insurance
The Organizing Committee does not assume responsibility for injuries or losses occurring to persons or personal belongings during the conference. Participants are therefore advised to carry the proper travel and health insurance.

Electricity supply and phone
In Hungary electricity is supplied at 230 V, 50 Hz like in most European countries. The 2-pin connecting plug is different from that used in some other countries (e.g. USA, UK, Japan etc.). Phoning and mobile servicing background is according to European standards.

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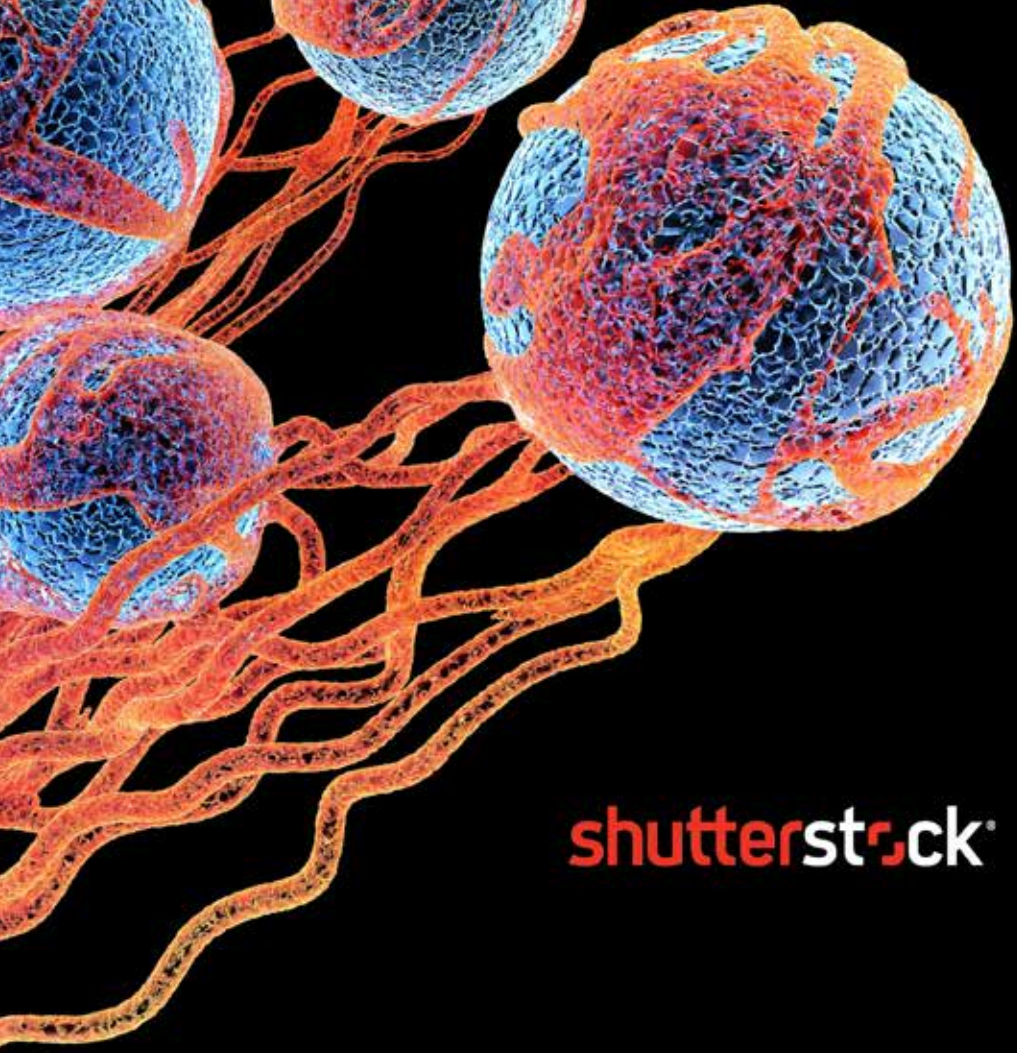

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