

◇ **Invited Lecture**

**The IAC Breast FNAB Structured Reporting System : an Update. JSCC May 2017**

Notre Dame University Medical School and St Vincent's Hospital, Sydney, Australia

○Andrew Field(MD)

**[Objective]** : The aim of the IAC initiative is to produce a standardized approach to breast FNAB, which will include recommended best practice for the FNAB technique, and establish diagnostic categories with specific diagnostic criteria or checklists, that can be used in reporting and assist the establishment of management recommendations.

**[Methods]** : Breast FNAB has been used successfully for more than 60 years to diagnose palpable and more recently impalpable lesions, but its usage varies greatly from country to country, city to city and from hospital to private FNAB clinic. It is a very cost effective and accurate diagnostic tool in the developed world.

**[Results]** : In the developing world where there are limited medical resources including a shortage of diagnostic radiology for mammography and of breast ultrasound and surgical pathology laboratories for breast core and excision specimens, there is a huge potential for FNAB to radically improve the diagnosis and management of breast lesions. But FNAB of breast faces a significant pre-analytical challenge as do all sites for FNAB : it relies on skilled operators performing the FNAB and making the direct smears. As well, there are specific problem areas in diagnosing benign proliferative lesions, such as fibroadenomas and intraduct papillomas, which can show a wide range of features both in surgical pathology and cytopathology.

**[Conclusion]** : Proliferative lesions can produce high cellularity, which is usually associated in FNAB with malignant lesions, and specific diagnostic criteria for proliferative lesions can overlap with malignant lesions in the breast. The distinction of invasive and intraduct lesions has to be addressed.

◇ **Global Asia Forum**

**Diagnostic Efficacy of Rapid On- Site Evaluation (ROSE) with Different Cytology Practice GAF-1 Rapid onsite evaluation of FNA with cyto-histologic correlations**

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**[Objective]** "The Johns Hopkins Hospital" is a world-renowned 1000 bed tertiary care university hospital with a highly acclaimed Cytopathology laboratory. Rapid onsite evaluation (ROSE) for specimen adequacy is routinely practiced in near 100% of FNAs performed at our hospital involving diverse anatomic sites. The presentation will selectively highlight the unique aspects of our FNA practice and will elaborate on the role of ROSE in diagnostics, trainees' education, clinical management and patient care with practical illustrations on cyto-histologic correlations.

**[Methods]** The case material consists of FNAs from Johns Hopkins (~5,500 are performed each year). A group of 10 cytotechnologists (CT), two cytopathology fellows/trainees and five cytopathologists are involved in ROSE. The performance of ROSE not only involves Radiology (ultrasound and CT), but a large number of cases are done at the endoscopy suites (EUS pancreas), bronchoscopy rooms (EBUS lung) and endocrine clinic (thyroid). The cytopathologists are predominantly involved with ultrasound-guided FNAs of liver, kidney/adrenal, soft tissue, lymph nodes and salivary gland. ROSE for all other anatomic sites are managed by CTs. For this presentation, the discussion will be mostly limited to thyroid and pancreas.

**[Results]** Many of our own published studies have shown an excellent diagnostic accuracy for ROSE performed by CTs when compared to the cytopathologists' final diagnosis and cyto-histologic correlation. The advantages of ROSE are universally known such as a higher diagnostic yield, optimum sample triaging for ancillary testing and guiding the radiologist's hands to the more diagnostically significant areas of the mass lesion. However, ROSE offers many unique perspectives and advantages to our practice at Johns

Hopkins, i.e., it ensures a continuing high involvement of our highly trained and efficient CT staff in the FNA cytopathology practice (NOT just a passive “cytoscreening” role), provides an ideal platform to train our fellows in diagnostics and communication skills with strong emphasis on a multidisciplinary approach.

**【Conclusion】** In our practice, the involvement of CTs in ROSE offers diagnostic accuracy comparable to cytopathologists in a variety of anatomic sites. This enable the cytopathologists to handle a much larger case volume for better RVUs for the department. Involvement of trainees in ROSE offers unique teaching opportunities. Interactions of the cytopathology staff and radiologists/clinicians leads to better understanding of the diagnostic issues involved and offers a multidisciplinary approach. Cyto-histo correlations provide a quick quality assurance measure.

## **GAF-2 The practice of ROSE methodology in Russia**

Departments of Clinical Laboratory Diagnostic, Russian Medical Academy of Continuous Postgraduated Education, Moscow, Russia

○Irina Shabalova

**【Objective】** ROSE is able to play an important role in early and precise diagnostics, planning an individual plan for medical examination, management and treatment, and sometimes for type and volume of surgery.

**【Methods】** ROSE in Russia has begun in 70<sup>th</sup> – early 80<sup>th</sup>, in P. A. Herzen Cancer Research Institute (intraoperative diagnostics, fine needle aspiration (FNA) during bronchoscopy), S.P. Botkin Hospital (ROSE during gastroscopy, in FNA of palpable thyroid, breast, lymph nodes etc.), and some other healthcare institutions. Quick MGG, immunofluorescence and other techniques were used.

**【Results】** Nowadays ROSE has demonstrated good results in endoscopy including EUS and EBUS, FNA of thyroid, breast, soft tissues, lung etc. Even if rapid frozen sections can be performed, cytology can be used because of a lot of advantages in rapid assessment of infections, lymphoma, malignant melanoma, Ewing sarcoma, metastases, etc. The usage of telecytology, on-line and off-line consultations gave the additional capabilities for ROSE. Liquid based cytology with subsequent cell blocks, immunocytochemistry, in situ hybridization, and other molecular studies seems to be of a great importance in the future. The possibilities of ROSE will be discussed.

**【Conclusion】** ROSE *per se* and as a method for creation of individual scheme for subsequent examination seems to have the limitless diagnostic opportunities. Rapid assessment of obtained material, morphological diagnosis, opinion or proposal to take more adequate material for cytology and histology is very important. Liquid-based cytology, that is rapidly developing in Russia gives the opportunities for saving cells and tissue fragments for cell blocks, immunocytochemistry, in situ hybridization, and other molecular studies and can be used as a practical tool in personalized medicine.

### **GAF-3 Rapid interpretation of breast cytology in a one-stop multidisciplinary breast unit in a medical center**

Department of Pathology, Taipei Veterans General Hospital, Taiwan

○Chiung-Ru Lai

**【Objective】** High-quality one-stop multidisciplinary breast unit is the most effective way to manage breast diseases, both benign and malignant. The one-stop unit could provide all the required elements of triple assessment and make definitive diagnosis for the majority of patients. The purpose of this study is to assess the efficacy and diagnostic accuracy of a one-stop breast unit in a medical center.

**【Methods】** A total of 378 patients with breast cytology including fine needle aspiration (FNA) and nipple discharge from the multidisciplinary breast unit (composed of breast & plastic surgery, medical & radiation oncology, surgical & cytological pathology, radiology and genetic counseling) of Taipei Veterans General Hospital in 2015 were included. The role and efficacy of cytology in the multidisciplinary team were evaluated by correlated with final histology and clinical patients' outcome.

**【Results】** A total of 321 FNA and 57 nipple discharge specimens were included. The cytology results were benign : 79% ; atypical : 7% ; suspicious : 2% ; positive : 6% ; inadequate : 6%. The results of atypical and up were considered as positive and inadequate specimens were analyzed separately. About 85% of patients could have definitive diagnosis and/or treatment planning in a one-day visit. The overall sensitivity was 93% and specificity was 92%.

**【Conclusion】** Cytology, FNA and nipple discharge, in a one-stop multidisciplinary breast unit can provide quick, efficient, and accurate diagnoses in a one-day visit and serve as a model of standard of care of routine practice in a medical center. It could reassure most patients with benign conditions with no need for further attendance and render definitive diagnosis and/or treatment planning for those who been diagnosed to have cancers.

### **GAF-4 Tissue rinse liquid-based cytology : a feasible tool for the intraoperative cytopathological evaluation of sentinel lymph nodes**

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○Kiyomi Taira<sup>1</sup>, Katsushige Yamashiro<sup>2</sup>

**【Background】** The evaluation of sentinel lymph nodes from a woman with breast cancer is frequently challenging. Since 2008 we have performed the cytopathological evaluation of sentinel lymph nodes of about 3,500 breast cancer patients through Tissue Rinse Liquid-based Cytology (TRLBC).

**【Methods】** Lymph node cut into 2 mm-thick slices is well rinsed in CytoRich™ Red and the cancer cells, if any, washed out in the preservative were pasted on a glass slide by BD SurePath™ technique. The tissue specimens were processed for histological preparation after fixation in formalin.

**【Results】** The cytopathological diagnosis was usually reported in 35 minutes. When we employed the histological diagnosis concurrently using IHC for cytokeratin as a gold standard, overall sensitivity and specificity of TRLBC including isolated tumor cells, ITC was 81.3% and 97.1%, respectively. Only for macrometastasis, micrometastasis, and ITC, the sensitivities were 100%, 94.5%, and 42.5%, respectively.

**【Conclusion】** TRLBC is a feasible and valuable tool for surgical oncology. We present a new on-site approach for the minute tissue material obtained from endoscopic ultrasound-guided fine-needle aspiration. The bloody material soused in CytoRich™ Red was easy to pick up for histological diagnosis by its hemolytic activity and the remaining solution is served for cytopathological diagnosis as an LBC preparation. We have got the cytological and histological preparations containing many targeted cells and successfully made a diagnosis in more than 70 cases.

### **GAF-5 Rapid on site evaluation on FNA of unknown primary tumor to diagnose neuroendocrine tumors**

Department of Pathology, Beijing Hospital, National Centre of Gerontology, Beijing, PR China

○Lan Chen, Shu-rong He, Dong-ge Liu

**【Objective】** Neuroendocrine neoplasms include a group of heterogeneous tumors originated from neuro-ectoderm and neural crest. The tumor cells receive neuronal input of neurotransmitters released by nerve cells or neurosecretory cells and release message molecules of hormones to the blood. They share morphological and immunophenotypic similarities despite the tumor origin. There is usually bland cytopathology and minimal polymorphism, but less commonly there can be anaplasia and tumor cells may mimic other malignancies. In this study we presented the morphological variants of neuroendocrine neoplasms diagnosed on FNA of unknown primary tumors in our collection and emphasized the value of rapid on site evaluation (ROSE) for accurate diagnosis by applying ancillary test of immunohistochemistry (IHC) on smears or blocks for differential diagnosis.

**【Methods】** We reviewed 45 cases suspected of neuroendocrine neoplasms on ROSE in the last four years from FNA of unknown primary tumors. Tumor origin spanned a spectrum of GI, lung, breast, thyroid and paraganglia. 28 cases were diagnosed of neuroendocrine neoplasms or tumors with neuroendocrine differentiation with ancillary test of IHC tested in 26 of them and 18 (100%) had further resection samples to confirm the diagnosis, while 8 patients went on with treatment directly without further biopsy or resection. 17 cases signed out as the suspicious had no cell blocks available for IHC and 11 of them had pathology confirmation to be neuroendocrine tumors for 8 cases and other malignancy or benign lesions for 3 cases (27.3%). The other 6 had no pathology follow-up.

**【Conclusion】** While morphology forms the fundamental bases to recognize the neuroendocrine tumors, IHC on cell block plays an important role for differential diagnosis.

ROSE helps us to triage sample for cell block preparation and make accurate diagnosis possible on cytology samples. A series of cases are demonstrated in the talk to emphasize the potential pitfalls in dealing with this differential diagnosis.

**GAF-6 Role and accuracy of rapid on-site evaluation (ROSE) of CT-guided fine needle aspiration cytology of lung nodules**

Department of Medicine, Surgical Pathology & Cytopathology Unit, University of Padua, Italy

○Ambrogio Fassina, Lorenzo Nicole, Valeria Maffeis, Rocco Cappellesso

**[Objective]** To prospectively investigate the role of trans-thoracic fine needle aspiration cytology (FNA) and the value of rapid on-site evaluation (ROSE) in the clinical management of patients with pulmonary nodules/masses. Computed tomography (CT)-guided FNA is commonly employed for the diagnosis of lung lesions although its position in the diagnostic work-up is still a matter of debate.

**[Methods]** In the last 10 years at the University of Padua we reviewed 611 patients, correlating the results of cytology with the available histological findings obtained from biopsies, surgery or autopsy.

**[Results]** Smears were adequate in 98% of cases and inadequate in 2% ; a diagnosis of malignancy was achieved in 86.2% ; 12.8% were non-malignant ; 1% suspect for malignancy. When correlated with histology, FNA with ROSE discriminated malignant versus non-malignant lesions with a satisfactory concordance (Cohen's kappa 0.78), and high sensitivity (96.3%) and specificity (100%). Moreover, a satisfactory overall agreement of 71.4% was achieved in differentiating the cancer histological types. Pneumothorax, haemoptysis, and chest pain occurred in few patients with poor Performance Status (PS). A single aspiration was sufficient in 79.6% of patients ; two aspirations were needed in 17.4% and three in 3%. Cell bloc preparation and molecular investigation allowed precise and rapid conclusion about the cancer histotypes and the mutation/deletion profiles.

**[Conclusion]** Provided a careful clinical and imaging selection, ROSE FNA demonstrated a safe and useful tool in the diagnostic work-up of lung cancer patients, with minimal or no contraindications, with election as the first diagnostic procedure for patients with peripheral lung lesions or in poor Performance Status. FNA with ROSE should be reconsidered in the guidelines for diagnosing and managing lung cancer.

◇ **Poster Presentation in English**

**PE-1-1 The effectiveness and clinical significance of cytology specimens from pleural effusions for EGFR mutation tests in non-small cell lung cancer**

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○Chien-Chin Chen<sup>1,2,3</sup>

**[Objective]** Patients with advanced non-small cell lung cancer (NSCLC) may benefit from treatment with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) when their tumor harbors an activating EGFR mutation. Malignant effusions frequently occur in patients with advanced NSCLC. Cytology specimens from malignant effusions are available for EGFR mutation testing, but might pose challenges due to low proportion of tumor cells. We aim to better define the suitability and clinical influence of effusion cytology specimens for EGFR mutation testing.

**[Methods]** NSCLC cases in our institution for EGFR mutation testing over a 23-month period were retrospectively reviewed. Specimens were tested for EGFR mutation, using real-time polymerase chain reaction analysis with the Roche Cobas Z480 analyzer and the Cobas EGFR mutation test kit.

**[Results]** A total of 215 specimens were tested, comprising 39 (18.1%) cytology specimens, 122 (56.8%) small biopsy specimens and 54 (25.1%) resection specimens (including 47 lung resection specimens). The average tumor proportion is 32.8% (cytology), 37.2% (small biopsy), and 55.6% (resection), respectively. Except 4 small biopsy specimens, 211 cases had sufficient DNA for mutation testing. EGFR mutations were detected in 22 cytology specimens, 66 small biopsy specimens and 41 resection specimens. There was no significant difference in the EGFR mutation rate between cytology specimens (22 of 39 cases ; 56.4%), small biopsy (66 of 122 cases ; 54.1%), and resection specimens (41 of 54 cases ; 75.9%). Moreover, 12 cases of 22 cytology specimens with drug-sensitive EGFR mutation took TKIs for cancer

control, and most of them (10 of 12 cases) underwent cancer regression or stable disease for 2 to 14 months.

**[Conclusion]** Our results support the effectiveness and clinical significance of effusion cytology specimens for EGFR mutation testing. Careful evaluation of the adequacy of small specimens is required to minimize the risk of false negative or positive results.

## **PE-1-2 Glomus tumor of uncertain malignant potential of lung: A case report of bronchoalveolar lavage cytology, with correlation of surgical pathology specimen and potential diagnostic pitfalls**

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**[Objective]** Glomus tumor in visceral organs is very rare and most of them are of benign nature. Herein we present an unusual case of glomus tumor of uncertain malignant potential in the bronchus of left lower lobe of lung from a 15-year-old adolescent.

**[Methods]** The computational tomography (CT) imaging exam showed a 2.5 cm intra-bronchial mass in the left lower lobe lung. The impression from imaging studies suggested it was most likely a carcinoid. Bronchoalveolar lavage cytology samples were obtained and followed with video-assisted thoracoscopic surgery (VATS) resection.

**[Results]** The bronchoalveolar lavage cytology samples revealed clusters or single of uniform, round to oval-shaped, bland-looking cells with clear cytoplasm admixed with sloughed bronchial epithelium cells. The cytomorphology features are not supportive of the diagnosis of carcinoid or neuroendocrine tumors. A negative diagnosis of was given. However, subsequent histopathologic examination of the surgical resection sample showed the tumor composed predominantly of sheets of ovoid to round cells with clear border, pale cytoplasm and fine granular chromatin with small to inconspicuous nucleoli. The mitotic count was less than 5 per 50 high power fields (HPF). There is no invasion to the surrounding normal bronchial and alveolar tissue. Immunohistochemical staining showed that the cells were diffusely positive for smooth muscle actin (SMA) and collagen IV, while negative for neuroendocrine markers (CD56, synaptophysin and chromogranin A). The Ki-67 proliferation index was approximately 15%. Based on the morphologic features and immunohistochemical profile, the tumor was consistent with glomus tumor of uncertain malignant potential. Re-examination of the bronchoalveolar

lavage cytology samples revealed that those oval-shaped, bland-looking cells with clear cytoplasm are consistent with tumor cells of glomus tumor of uncertain malignant potential.

**【Conclusion】** Glomus tumor has distinct cytomorphologic features in surgical pathology specimen, but it might be overlooked in cytology samples such as fine needle aspiration or as in this case, the bronchoalveolar lavage. Appropriate clinical history and immunohistochemical studies (such as SMA, collagen IV) can further help to confirm the diagnosis.

### **PE-1-3 Lung and pleural effusion metastasis of salivary duct carcinoma**

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**【Introduction】** Salivary duct carcinoma (SDC) is a rare but aggressive form of parotid tumor. It is already known that the cytological features of SDC are large sheet clusters with slight overlapping and abundant granular cytoplasm with light greenphilic cells in the necrotic background. Histopathologically, SDC is characterised by its resemblance to ductal carcinoma of the breast. Although the cytological characteristics of SDC in fine-needle aspiration specimens have been well-described at the primary site, metastasis is rare in SDC. Here, we reported a case of parotid gland SDC metastasis to lung and pleural fluid.

**【Case】** A man in 50's was underwent extended total parotidectomy in 2008, and he was originally diagnosed as having left parotid SDC. Six years later, chest CT identified a mass in the left lung and he was diagnosed with metastatic SDC by both bronchial biopsy and cytology. Subsequently he had a recurrent SDC in the left pleural effusion. Bronchial brushing smear showed small sheet clusters with cribriform-like patterns and isolated cells in the necrotic background. In the plural effusion cytology, tumor cells appeared as clusters of epithelioid cells with apocrine-like cytoplasm. Immunocytochemical staining was strongly positive for HER2/neu and androgen receptor.

**【Conclusion】** Cytological findings may differ between the primary and metastatic tumor, and a diagnosis of histological forms can be especially difficult at a metastatic site. It is important to clarify cytological differences between primary and metastasis, and to confirm the expressions of specific proteins by immunocytochemistry.

#### **PE-1-4 Concordance of lung carcinoma subtypes between liquid-based cytology and tissue specimens : diagnostic aspects of bronchial brushings for lung lesions**

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○Chih-Yi Liu, Hui-Chih Tsai, Yu-Lin Ko, Yi-Jyun Lin

**【Objective】** Liquid-based preparations are proposed to improve the quality of cytologic samples and their diagnostic yield compared with conventional smear cytology. Bronchial brushing cytology is one of several methods for establishing confirmative diagnosis of lung lesions. The purpose of this study was to determine the diagnostic concordance of lung carcinoma subtypes in cytology and tissue specimens. The possible factors related to the diagnostic quality of liquid-based cytology (LBC) were analyzed.

**【Methods】** A total of 85 patients with suspicious lung cancer were enrolled in this study. The bronchial brushing samples were prepared by LBC (SurePath), and both endoscopically visible and non-visible lesions were included. The data were then compared to the histology of lung tissue samples and the clinical factors. The diagnostic concordance of carcinoma subtypes was evaluated. The slides from discordant cases were reviewed, and final diagnoses were made based on immunohistochemical studies. The sensitivity of liquid-based cytology (LBC) were also compared to the outcomes of conventional smear cytology (CSC).

**【Results】** According to the biopsy and resection specimens, malignant tumors were diagnosed in 38 cases. They included adenocarcinoma (42.1%), squamous cell carcinoma (39.5%), non-small cell carcinoma, not otherwise specified (10.5%), and neuroendocrine carcinoma (7.9%). For the diagnosis of histologically confirmed lung cancer, the overall sensitivity of LBC was 63.2%. Concordance in subtype diagnosis was achieved in 70.8% of cases. The diagnostic accuracy was higher in non-adenocarcinoma (75.0%). The mean tumor size in the non-corresponding cases was smaller than the correspond-

ing cases. The diagnostic performance of cytology was also compared with the final diagnoses based on imaging techniques and all clinical information available. The LBC preparations had 75.8% sensitivity and 94.9% specificity in the diagnosis of lung cancer, superior to the performance of CSC samples.

**【Conclusions】** In this study, most patients of lung cancer are diagnosed at advanced stages, with small biopsy or cytologic samples available for pathological assessment. The ability to precisely classify lung carcinoma depends on the procedure, tumor size and tumor type. The results have shown that subtyping of lung carcinoma can be achieved in LBC specimens, with a concordance rate of 70.8%. The diagnostic accuracy of cytologic specimens is higher in the non-adenocarcinomas. Due to the reduction of obscuring elements and the optimal preservation of the cells, LBC preparations allow a more definitive diagnosis in many cases. These findings can provide important clinical implications for selecting the proper diagnostic tools.



**PE-1-5 Metastatic lung cancer of endometrium—detected and confirmed by conventional Papanicolaou (Pap) smear with immunocytochemical (ICC) stains**

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○Chia-Min Wei, Yu-Shi Liu, Shiou-Feng Liu,  
Chiung-Ru Lai

**【Objective】** We described a case of metastatic lung cancer of the endometrium, which was detected by conventional Pap smear. The cytological hints for endometrial lesion and usefulness of ICC on conventional Pap smears were emphasized in the current report.

**【Methods】** A 47-year-old woman diagnosed to have a stage IV lung adenocarcinoma with EGFR L858R mutation and multiple metastases, including bone, brain, adrenal gland and mediastinal lymph nodes. She was referred to GYN section due to abnormal vaginal bleeding. Conventional Pap smear was done. Endometrial sonography and curettage were performed due to malignant Pap smear result.

**【Results】** Clusters of adenocarcinoma cells were degenerated and surrounded by endometrial stromal-like histiocytes, which represented characteristic hints for shedding from endometrium rather than endocervix. ICC stains revealed positive TTF-1 and negative PAX-8 results, which concurred with the origin from lung metastasis. A diagnosis of metastatic lung adenocarcinoma of the endometrium was given by Pap smear, which was further confirmed by pathology of endometrial curettage. Target and chemotherapy continued and further surgery for uterus was not given.

**【Conclusion】** Although it is generally accepted that the aim of Pap test is primarily to detect squamous lesions, endometrial and extra-uterine cancers might appear on the Pap smears in our routine practice. The recognition of cytomorphological hints for endometrial origin and additional ICC stains were important in making correct diagnoses, which could avoid unnecessary surgery.

**PE-1-6 Morphological changes in Doxorubicin resistant small cell carcinoma**

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○Masami Nambu, Hiroki Kameyama

**【Objective】** In most cases of small cell lung cancer (SCLC), SCLC has already spread by the time it is found, so chemotherapy is usually part of treatment if a person is healthy enough. The tumor cells resistant to chemotherapy are considered to show peculiar cellular changes for the action mechanism of the anticancer drug. This time, we confirmed cytomorphological changes seen in Doxorubicin resistant small cell carcinoma.

**【Methods】** Wild type and Doxorubicin resistant type culture cell line of SCLC (H69) were used for this study. The area, the circumference, the major and minor axis length of both cytoplasm and nucleus were measured. And, with the measured values, the mean area, the standard deviation of the area, N/C (nucleus/cytoplasm ratio), the ellipticity, the peround and the pleomorphism were calculated. About nucleolus, number was counted and the area was measured.

**【Results】** In the area of both cytoplasm and nucleus, resistant type was 2 times larger than wild type and showed wider size variation. About nucleolus, resistant type was larger than that of wild type in number and varied in size. The nucleus of resistant type was more pleomorphic than that of wild type.

**【Conclusion】** This study revealed that Doxorubicin resistant type showed quite different feature from wild type small cell carcinoma. There is a possibility of leading to misdiagnosis on histological typing when we make cytodiagnosis in Doxorubicin resistant case of small cell carcinoma. This time, we studied cellular changes only in Doxorubicin resistant SCLC, and it can be considered that there are many patterns of cellular change due to resistance to other anticancer drugs. Therefore we keep it in mind when we make cytological diagnosis of recurrent cases underwent chemotherapy.

### **PE-1-7 The cytomorphological characteristics and clinicopathological features of anaplastic thyroid carcinoma : A case cohort study from Taiwan**

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○Chien-Chin Chen<sup>1,2,3</sup>

**【Objective】** We aim to analyze the cytomorphological characteristics in fine needle aspiration and the clinicopathological features in anaplastic thyroid carcinoma (ATC).

**【Methods】** A retrospective slide review and analysis of eight histologically-proved cases and preoperative six fine needle aspirates with ATC admitted to the Ditmanson Medical Foundation Chia-Yi Christian Hospital, Taiwan, in 2001-2016.

**【Results】** A total of eight cases with ATC are reviewed with a mean age of 71.6 years, mild male predominance (M : F = 5 : 3) and preoperatively euthyroid status (8/8). All patients are died with a mean survival of 6.1 months (range : 1 to 12 months), regardless of different treatment modalities. The average size of tumor is 7.2 cm (range : 5.4 to 9 cm), and all of them have distal metastases (lung : 7/8, bone 1/8). Six of them have preoperative fine needle aspirates, and 1 (16.7%) was inadequate, 2 (33.3%) suspicious for malignancy and 3 (50%) diagnostic of malignancy. On reexamination, they are intermediate or high cellularity, except the inadequate case shows only blood cells. All of the cellular aspirates revealed mixed cellular patterns, including 1) spindle cell (3/5), epithelioid cell (5/5), giant cell (2/5) and squamoid cell (3/5), with necrosis (4/5), leukocytes infiltrate (4/5) and calcification (1/5). No colloidal background, nuclear grooves and pseudoinclusion are found. In the surgical specimens, three (37.5%, 3/8) patients have co-existing minor components of convention papillary carcinoma (5% to 30% of tumor proportion).

**【Conclusion】** Our results support the clinical aggressiveness, mixed cellular patterns and lack of nuclear features of papillary carcinoma in cytology specimens for ATC.

Although the sensitivity of needle aspirate is high, the major diagnostic problem with fine needle aspiration is related to sample quality. Tumor necrosis, hemorrhage, leukocytic infiltration and extensive fibrosis may lead to diagnostic difficulties. It is crucial to diagnose it early, due to the poor prognosis.

### PE-1-8 Cytological Differential Diagnoses between Chronic Thyroiditis and MALT Lymphoma on Thyroid LBC

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**【Objectives】** Chronic thyroiditis with nodular formation may undergo aspiration cytology to distinguish from MALT lymphoma (ML). The cytological distinction between nodular chronic thyroiditis (NCT) particularly associated with predominant lymphocytes and ML has been frequently troublesome. In addition, the morphology in LBC specimens (LBC-S) is not same to conventional specimens (C-S). The aim of this report is to clarify the difference of cytological findings between NCT and ML on LBC-S.

**【Materials and Methods】** We reviewed LBC-S of 19 NCT cases and 21 ML cases confirmed by histologic examination in our hospital. LBC samples were obtained from wash-out fluid of the aspiration needles, fixed with Cytorich-RED™, and prepared by SurePath™ method.

**【Result】** In C-S, the incidence of lymphoglandular bodies was higher in ML (66.7%) than in NCT (21.1%). In 61.9% of ML and 5.3% of NCT cases, lymphoid cells with the nuclei measuring more than 10 μm occupied more than 10% of all lymphoid cells. Lymphoid cells associated with mesh-patterned, elongated, and cleaved nuclei were significantly observed in ML cases (95.2%, 90.5%, and 90.5%) compared with NCT cases (26.3%, 42.1%, and 15.8%). Oxyphilic follicular cell clusters were more seen in NCT (94.7%) than ML (42.9%).

**【Conclusion】** More than 10% of lymphoid cells with >10 μm nuclei, mesh-patterned nuclei, elongated nuclei, and cleaved nuclei are diagnostic clues indicating ML.

### PE-1-9 Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)—A newly proposed terminology

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○Chiung-Ru Lai, Yen-Ying Chen

**【Objective】** Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a new terminology proposed for those tumors previously called encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC). Since it almost behaves as benign lesion, it will be no longer called “cancer”. The aim of this study is to report the frequency, clinical characteristics, cytology results and follow up of such cases in our hospital.

**【Methods】** By reviewing histological slides, cases of NIFTP were retrospectively identified from those tumors originally diagnosed as follicular variant of papillary thyroid carcinoma (FVPTC), well-differentiated tumor of uncertain malignant potential (UMP) and follicular tumor with questionable nuclear atypia, from January 2010 to December 2011. The clinical and pathological correlation and cytology findings were analyzed.

**【Results】** There were 389 patients with pathology proved primary thyroid cancers in the years of 2010 & 2011. Among them, a total of 18 cases of NIFTP (4.6% of primary thyroid cancers) were identified with female predominance, 15 female (age 23-65, median 45) & 3 male (age 15-43, median 21). The tumor size ranged from 1.1 to 4 cm. Median follow up was 62 months, None of these patients received radioiodine therapy. All are alive without evidence of disease. Using Bethesda System for reporting thyroid FNA, over half of the cytology results were intermediate categories (with nuclear enlargement and/or optically clear nuclei and/or nuclear groove) (TBS I : 1 (9%) ; TBS II : 3 (27%) ; TBS III : 3 (27%) ; TBS IV : 3 (27%) ; TBS V : 1 (9%) ; TBS VI : 0 (0%).

**【Conclusion】** The current study supported the reclassification of EFVPTC to NIFTP due to its almost benign behavior. FNA frequently revealed intermediate cytological results and could not reach reliable diagnosis preoperative-ly. More cases are needed for further evaluation.

**PE-1-10 Rapid onsite evaluation is urgent to improve the adequacy rate of thyroid FNA-based on the retrospective study of 2838 cases of thyroid fine needle aspiration from China**

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**【Object】** Fine-needle aspiration (FNA) with ultrasonography guidance is one of the optimal techniques for the diagnostic evaluation of thyroid nodules and it was the initial two years for thyroid FNA in our diagnostic center. This study was proposed to evaluate the adequacy rate and accurate rate of thyroid FNA samples using the Bethesda reporting system for thyroid cytopathology (TBSRTC).

**【Methods】** Retrospective study was perfected on 2838 cases of thyroid FNA with routine H&E staining. They were divided into 6 groups according to TBSRTC, which were : Non-Diagnostic/Unsatisfactory, benign, atypia of uncertain significance/follicular lesion uncertain significance, follicular neoplasm/suspicious for a follicular neoplasm, suspicious for malignancy and Malignancy. The comparison of cytopathological and histopathological samples was performed on 791 cases underwent surgical operation.

**【Results】** Non-Diagnostic/Unsatisfactory samples were 3.56% (101/2838), the benign lesion accounts for 44.68% (1268/2838), FN/SFN accounts for 0.18% (5/2838), suspicious for malignancy accounts for (401/2838), malignancy accounts for 30.58% (868/2838).The risk of malignancy was 34.44% (31/90) for Benign lesion, 70.83% (17/24) for AUS/FLUS, 69% (138/200) for Suspicious of malignancy, 97.03% (457/471) for Malignancy.

**【Conclusion】** FNA is reliable preoperative diagnostic method for thyroid lesion. H&E staining is reliable for the diagnosis of thyroid FNA sample, which is the routine staining for surgical specimens and easy to be paralleled.

Bethesda reporting system is an available diagnostic system and should be applied around the whole country of China. The most accurate diagnosis is the Malignancy group and then the indeterminate group. The diagnosis of indeterminate group was impacted by both the quality and the quantity of the cells. The malignancy risk in benign group is high because of the not so good puncture accuracy. The rate for Non-Diagnostic/Unsatisfactory group was high, which was probably due to the poor cell quantity in initial period. Therefore, rapid onsite evaluation should be applied to improve the adequacy of the FNA and to avoid miss diagnosis and misdiagnosis, especially in the early stage of the FNA center.

### PE-1-11 Atypical adenoma of thyroid gland cytologically mimicking papillary carcinoma ; A case report

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**【Background】** Atypical adenoma of thyroid is a variant of follicular adenoma and shows strong structural and cellular atypia. We present a case of atypical adenoma we suspected of papillary carcinoma in pre-operative cytology.

**【Case】** 78-year-old, male. Ultrasonography revealed a solid mass 2 cm in diameter in right lobe of thyroid gland. Fine needle aspiration cytology (FNAC) was performed and showed a small number of atypical cells appearing to be isolated or forming small follicular cluster. They were almost naked and their nuclei showed anisonucleosis, cleaved shape, groove and intranuclear cytoplasmic inclusion bodies. And eosinophilic nucleoli were observed. With the cytological findings, we made a diagnosis of “suspicious of papillary carcinoma”. In consideration of cytological diagnosis, resection of right lobe of thyroid gland was performed. Histologically, the tumor 1.5 cm in diameter was encapsulated and showed micro-follicular structure and solid proliferation of atypical cells showing irregular shaped nuclei varied in size, nuclear grooves and intranuclear cytoplasmic inclusion bodies. But neither capsular invasion nor vascular invasion was found. Immunohistochemically, tumor cells were positive for thyroglobulin and TTF-1, and negative for CK19, HBME-1, calcitonin and p53, and Ki-67 labeling index was less than 1%, then the pathological diagnosis was made as atypical adenoma.

**【Conclusion】** This case was very difficult to make cytological diagnosis on the ground of poor cellularity and severe cellular atypia mimicking papillary carcinoma. Therefore we should keep this important experience of atypical adenoma in our mind and consider the possibility of atypical adenoma when we suspect of papillary carcinoma on the ground of such cellular atypia as nuclear groove and intranuclear cytoplasmic inclusion body.

### PE-1-12 Diagnostic accuracy of initial benign cytology in thyroid nodules with highly suspicious ultrasonographic features

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**【Objective】** A definite cytology is essential for appropriate treatment of thyroid nodules. However, the diagnostic accuracy of initial benign cytology and the role of repeat fine needle aspiration (rFNA) for nodules with highly suspicious ultrasonographic features (NHSUF) are not well established.

**【Methods】** Retrospective study of 73 NHSUF cases with initial benign cytology and subsequent rFNA was performed. All slides were reviewed with detailed evaluation of the cytological features, diagnostic accuracy and compared with the clinicopathological information.

**【Result】** Upon rFNA, cytological diagnoses of benign and malignancy were 40 (54.8%) and 33 (45.2%), respectively. By reviewing initial benign FNA slides, the false negative rate was 8.2% (5/73). In the cases showing abundant colloid and numerous foamy cells on cytology and no calcification on ultrasound, both initial and repeated FNA were benign. Therefore, these parameters were highly predictive of benign lesions.

**【Conclusion】** The combination of the reviewing the cytology preparations and rFNA can increase diagnostic accuracy and determine the clinical management of NHSUF. However, rFNA is not necessary in NHSUF showing abundant colloid and numerous foamy cells on cytology and nodules without any internal calcification on ultrasound.

**PE-1-13 Anal Cytology Among Men Who Have Sex with Men In Taiwan—Correlation with Pathology, p16/ Ki- 67 Stain and HPV Assay**

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**[Objective]** In recent years, anal cytology has gained acceptance as a tool for anal cancer screening for high risk populations, especially men with sex with men (MSM) with or without HIV infection, in a role similar to the Pap test. The purpose of this study is to evaluate the efficacy of anal cytology for screening anal squamous epithelial lesions and its correlation with HPV assay and p16/Ki-67 stain.

**[Methods]** Patients from special clinics for MSM who completed a detailed sexual behavior questionnaire were included in this study, from August 2015 to July 2016. Anal cytology was collected in one BD SurePath™ vial for liquid-based preparation (LBC). HPV assay (BD Onclarity™ HPV assay) and p16/Ki-67 double staining (*CINtec PLUS*) were performed using residual LBC material. Biopsy was performed in conjunction with high-resolution anoscopy (HRA) for positive cytology or HRA results.

**[Results]** A total of 71 patients were included in the current study. Cytology results were negative in 22 (31%) ; ASC in 11 (15%) ; LSIL in 19 (27%) ; HSIL in 19 (27%). HPV and p16/Ki-67 double staining (*CINtec PLUS*) positivity were statistically correlated with cytology severity : 50% & 6% in negative ; 60% & 20% in ASC ; 94% & 47% in LSIL ; 92% & 60% in HSIL (P value 0.006 ; 0.004). The genotypes of HPV assay were : P2 (39%, HPV 56/59/66) ; P1 (37%, HPV 33/58) ; P3 (26%, HPV 35/39/68), HPV 52 (25%) ; HPV 16 (19%) ; HPV 18 (19%) ; HPV 45 (16%) ; HPV 51 (16%) ; and HPV 31 (12%). Two of 6 (33%) with LSIL and all HSIL (100%) cytology patients show HSIL on corresponding biopsy.

**[Conclusion]** MSM represents high risk population for anal HPV infection but the prevalence (carrier status : 50%) and common HPV types (56/59/66 ; 33/58) are different from those of cervical smears in women. The majority (69%) of anal cytology among this high risk group is abnormal and showed high predictive value of HSIL. The p16/Ki-67 double staining was statistically correlated with anal cytology severity, which might aid the cytology diagnosis.

**PE-1-14 Mucinous carcinoma admixed with neuroendocrine carcinoma of the uterine cervix : cytological features and immunohistochemical profile : Report of a case**

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**[Background]** Neuroendocrine tumor of the uterine cervix generally shows an aggressive clinical behavior. A case is described of intestinal-type mucinous carcinoma of the uterine cervix, admixed with neuroendocrine carcinoma imparting a resemblance to atypical carcinoid.

**[Case]** A 40-year-old woman with abnormal genital bleeding was referred to the hospital, and on admission cervical smear and biopsy were taken. The smear showed clusters of small atypical cells with occasional rosette-like arrangement. Those cells had granular eosinophilic cytoplasm and round nuclei with fine or granular chromatin texture and small nucleoli. Examination of the biopsy specimen demonstrated sheets of cells partially arranged in rosette-like pattern, and the histopathologic diagnosis of well-differentiated neuroendocrine tumor was established based on immunoreactivity for chromogranin-A, synaptophysin. In addition, combined with high Ki-67 labeling index, i.e., exceeding 50%, and empirical evidence, the possible co-existence of adenocarcinoma was suggested, and the attending physicians were advised to manage the patient as such. Consequently, she underwent radical hysterectomy. Grossly the resected uterine tumor showed polypoid appearance, and microscopic examination revealed that the polypoid portion was composed of well-differentiated neuroendocrine carcinoma resembling atypical carcinoid tumor. Underneath the polypoid tumor, we identified mucinous carcinoma of intestinal-type as well as adenocarcinoma in situ showing intestinal phenotype. Small cell or large cell neuroendocrine carcinoma components were not identified.

**[Conclusion]** Non-small cell/large cell neuroendocrine carcinomas rarely arise in the uterine cervix, and appear to be frequently associated with adenocarcinoma. The cytology-pathology correlation is mandatory for optimal patient management.

### PE-1-15 A cytopathological overview of 5 cases of lobular endocervical glandular hyperplasia

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**【Background】** Lobular endocervical glandular hyperplasia (LEGH) is an endocervical lesion with gastric-type metaplasia and also a precursor lesion to mucinous (gastric-type) adenocarcinoma. The most important differential diagnosis of LEGH is adenocarcinoma, including mucinous carcinoma/minimal deviation adenocarcinoma, which has similar clinical, radiological, immunohistochemical features. Five cases of LEGH are reviewed clinically, cytologically, and histologically.

**【Patients】** Recent 3-year period surveyed from 2014 through 2016, LEGH were pathologically diagnosed in a total of 5 patients. The mean age of the patients was 50 years (range, 46 to 59 years). All patients were symptomatic [cervical mass (5), genital bleeding (2), and increased watery discharge (2)] and isolated LEGH.

**【Cytological findings】** Four cases were reported as “AGC” and 1 case as “NILM”. The cytoplasm of all “AGC” cases contained abundant mucin. With a conventional Papanicolaou stain, mucin was stained orange in our facility. In addition, the distinctive cellular clusters surrounded by cotton-candy-like abundant mucin were recognized. Nuclei were round and mildly enlarged with fine chromatin and micronucleoli. Intranuclear cytoplasmic inclusions (INCIs) were also identified.

**【Histological findings】** Small to moderately sized round glands proliferated in a distinct lobular fashion, surrounding larger and dilated central gland. Nuclei were round, uniform, and basally located. INCIs were also identified. Intracytoplasmic mucin was immunohistochemically positive for MUC6 and HIK1083.

**【Conclusions】** It might not be realistic to diagnose LEGH by cytological information only. However, exact understanding and recognition of the cytological characteristics is the key to facilitate further study such as histologic examination, and essential for proper management of LEGH.

### PE-1-16 The various cytological appearances of uterine carcinosarcoma

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**【Introduction】** We will discuss our findings in regard to the cytological appearance of carcinosarcoma which has complicated reoccurrences on the vaginal stump during post-operative chemotherapy.

**【Case】** We examined a 69 year-old woman who had a history of breast cancer stage II A. Two years ago she received a debulking operation for uterine carcinosarcoma at her prior hospital. The patient's post-operative chemotherapy began at our hospital.

**【The clinical course】** The 1<sup>st</sup> line chemotherapy was performed with ‘TC’ therapy. The cytology on the vaginal stump was normal but became worse, and developed atypical squamous cells cannot exclude high grade squamous intraepithelial lesion (ASC-H) and adenocarcinoma over 5 months. Next 6 courses of ‘IFM/CDDP/ADM’ were administered. The cytological report revealed atypical squamous cells of undetermined significance (ASC-US) and atypical glandular cells (AGC). The pathological diagnosis was adenocarcinoma on the vaginal stump. After the 3<sup>rd</sup> line ‘DOC/GEM’ therapy was performed, pathologically the tumor disappeared. AGC, ASC-H and adenocarcinoma were found again during the next chemotherapy. Gradually other small adenocarcinomatous tumors were found on the patient's vulva. We performed the 6<sup>th</sup> line ‘CBDCA/PAC/BV’ therapy which included radiation therapy and the tumors became smaller showing no malignant cells on her vaginal stump.

**【Comment】** We hypothesize that the various histological findings were caused by the effects of the various chemotherapies.

### PE-1-17 A usefulness of cervical cancer screening for cervical adenocarcinoma

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**【Objective】** Although cases of cervical adenocarcinoma have increased, it is said to be more difficult to detect in Pap smear than squamous cell carcinoma. To determine how cervical adenocarcinoma is diagnosed, we retrospectively investigated patients with cervical adenocarcinoma who had received treatment at our hospital.

**【Methods】** We retrospectively investigated 58 patients diagnosed with cervical adenocarcinoma in situ (AIS) or cervical adenocarcinoma at our hospital between April 2011 and November 2016. All the patients were referred to our hospital after either positive findings for Pap smear as cancer screening at previous hospital or being suspected of cervical cancer by a local physician due to signs such as bleeding or vaginal discharge. At our initial examination, Pap smear and biopsy were performed.

**【Results】** The median age of the patients was 53 years (range : 26-87 years). Eight were nulliparous, and the remaining 50 were parous. The distribution of stage was as follows : AIS, n=9 ; IA, n=5 ; IB1-IB2, n=22 ; IIB, n=8 ; IIIA-B, n=5, and IVA-B, n=9. A total of 21 patients were diagnosed in cancer screenings : all of these patients were asymptomatic. Of these, 20 were in stages AIS-IB1, and we could diagnose and treat at early stage. The remaining 37 patients were diagnosed in gynecological examinations : four of these patients had vaginal discharge with no irregular bleeding, and other 33 had abnormal bleeding. In addition, the initial cytological screening revealed NILM for 5 patients, squamous epithelial abnormality for 14 (ASC for 3 patients, HSIL for 5 and SCC for 6) patients, and glandular abnormality for 35 patients (AGC for 11 patients, AIS for 1, adenosquamous carcinoma for 1, and adenocarcinoma for 22).

**【Conclusion】** Overall cervical adenocarcinoma was diagnosed by cancer screenings in 36% (21/58) of patients. In particular, 64% (20/31) of patients up to stage IB1 were diagnosed in cancer screenings with asymptomatic.

### PE-1-18 Primary Malignant Melanoma of the Vagina—Initially Detected by Urine Cytology

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**【Objective】** Primary malignant melanoma of the vagina is extremely rare and accounts for <3% of all primary vaginal malignancies. We reported a case of primary vaginal melanoma initially detected by urine cytology.

**【Methods】** Urine cytology from a 61-year-old woman with hematuria showed a picture of malignant melanoma composed of discohesive epithelioid cells with large nuclei and prominent nucleoli. Cytoplasm is abundant and melanin pigment is identified. Because the background was clean and devoid of apparent tumor diathesis, contamination from GYN tract rather than primary urinary tract melanoma was favored. The patient was therefore referred to GYN and received a Papanicolaou (Pap) test, which rendered identical melanoma cells.

**【Results】** During GYN consultation, the presenting symptom was found to be post-menopausal vaginal bleeding which was mistaken for hematuria by patient herself. After meticulous clinical survey, no other primary sites could be found. Bladder mucosa was free from tumor involvement by cystoscope and repeat clean catch urine was negative, which confirmed that melanoma cells in urine were from GYN contamination. Then, complete staging surgery was performed and confirmed a stage III primary vaginal melanoma.

**【Conclusion】** Abnormal vaginal bleeding could be mistaken for hematuria which might mislead the workup and delay the correct diagnosis. The recognition for possible GYN contamination of cancer cells in urine is very important for tumor origin confirmation. Primary malignant melanoma of vagina, an extremely rare malignancy, may successfully be detected by urine cytology.



### PE-1-19 Primary intestinal-type mucinous adenocarcinoma of the vulva

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**[Background]** Adenocarcinomas of the vulva are rare diseases, and usually arise in a Bartholin gland or occur in association with Paget's disease. Adenocarcinoma of the intestinal type of the vulva is an extremely rare neoplasm, and a few cases have been reported to date. We report a case of primary villoglandular mucinous adenocarcinoma arising in the surface epithelium of the vulva near the urethra.

**[Case report]** A 63-year-old woman, gravid 3, parity 2, was referred to our hospital because of postmenopausal bleeding. A papillary and easy contact bleeding mass with 18 mm in diameter was seen near the urethra. Magnetic resonance imaging (MRI) of the pelvis revealed a 18 mm-sized enhanced mass, and uterus and both ovaries were normal shape and size. Scrape cytologic specimen from the vulvar tumor revealed atypical epithelial cells in mucinous background. Tumor cells formed loose clusters, and the cytoplasm had enrich mucinous material. Nuclei of tumor cells were elongated. Biopsy specimen showed a proliferation of signet ring cells embedded in an abundant myxoid stroma and irregular tubular structures of atypical columnar epithelium were seen. An extensive workup, including systemic positron emission computed-tomography (PET-CT) and gastrointestinal tract fiberscope were performed, but any other cancers or metastases were detected. Radical vulvectomy and bilateral superficial inginal lymph node dissection and Cloquet lymph node biopsy were performed. Mass was 2 cm in diameter and the depth of stromal invasion was 1 mm. The tumor was composed of papillary and complex glandular structures lined by large columnar cells with hyperchromatic nuclei. Cancer cells contained mucinous materials in the cytoplasm. Immunohistochemically, the tumor cells showed diffuse positive staining for

cytokeratin 20 and CDX2. The final pathological diagnosis was intestinal-type mucinous adenocarcinoma of the vulva (pT1bN0M0).

**[Conclusion]** Primary intestinal-type mucinous adenocarcinoma is very rare tumor and the cause is unknown. Further cases need to clarify the diagnostic criteria and to determine a successful treatment modality.

**PE-1-20 The findings of cervical smears in women with endometrial carcinoma- Any hint of endometrial lesions and prognostic significance?**

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**【Objective】** Pap smear is to detect cervical precancerous lesions and cancers. It may also exhibit cytological findings to be the hint of endometrial lesions. This study investigated whether Papanicolaou (Pap) smears show cytological findings leading to detect endometrial carcinoma (EMCa), and is associated with any histologic parameters.

**【Methods】** Among forty three cases of EMCa surgically treated and staged at our institution in a two year period, 40 cases with routine Pap smears within six months prior to surgery were subjected to this study. The Pap findings including interpretation, presence/absence of endometrial cells were recorded for each case, and analyzed in relation to histologic parameters including histologic type, grade, stage and tumor size.

**【Results】** Eleven cases (27.5%) had Pap findings suggestive of EMCa, and 30 cases (72.5%) had negative cytology (NILM). Only one case with negative Pap (2.5%) had the presence of endometrial cells which should be reported as per the Bethesda system (TBS). The positive Pap group comprised 8 low grade endometrioid carcinomas (LGEC), 1 high grade endometrioid carcinomas (HGEC), 1 serous carcinoma (SC) and 1 small cell carcinoma (SCC), and the negative Pap group did 23 LGEC, 2HGEC and 3 SC. Positive Pap or EMCs were not associated with any histologic parameters including cervical involvement and tumor size.

**【Conclusions】** In contrast to previous reports, our study demonstrated lower sensitivity of Pap smear to detect EMCa. Despite TBS category, the presence of EMCs is rare in EMCa cases. There is no specific association between Pap findings and histologic parameters.

**PE-1-21 Characteristics of intraoperative cytology for accurate diagnosis of mucinous borderline ovarian tumor**

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**【Objective】** Accurate and efficient intraoperative diagnosis of mucinous borderline ovarian tumor (mBOT) is challenging. The aim of this study was to evaluate the characteristics and diagnostic capability of cytological techniques such as squash smears and touch imprints for mBOT.

**【Methods】** Our retrospective study included a consecutive case series of 18 patients with mBOT, who were examined using intraoperative cytology at the Saiseikai Noe Hospital between 2006 and 2016. The diagnoses were reviewed with reference to the histopathological analysis of paraffin-embedded tissue section.

**【Results】** Intestinal and seromucinous types of mBOT were diagnosed in 17 (94%) and one (6%) cases, respectively. Touch imprint cytology of 1 case (6%) showed papillary-like tumor architecture, and half of the remaining 16 cases indicated scant epithelial components, while the other half revealed sheet structure. The background was relatively clear without necrotic material. In contrast, the squash smear revealed papillary-like or ball-like architectures in 17 cases (94%), with mild and no cytologic atypia in 2 and 15 cases, respectively.

**【Conclusion】** In the intraoperative diagnosis of mBOT, touch imprints may be suitable for the observation of the background, whereas squash smear may be accurate for the detection of architectural atypia. Combination of both techniques is recommended to improve the diagnostic accuracy.

### PE-1-22 Cytologic features of malignant Brenner tumor : A case report

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**[Background]** Malignant Brenner tumor is uncommon neoplasm. We describe cytologic features of malignant Brenner tumor identified in ascites.

**[Case]** A 80-year-old woman was referred to hospital because of abdominal distension, and imaging studies demonstrated a left ovarian mass. Microscopic examination of the ascitic fluid revealed isolated or small clusters of highly atypical cells, showing heterogeneity in nuclear sizes and shape. Occasional cells showed squamoid appearance as well as intracytoplasmic mucin droplets. These features suggested high-grade adenocarcinoma, but immunohistochemistry for cell-block demonstrated that atypical cells were positive for pancytokeratin (AE1/AE3), cytokeratin 5/6, p63, and were negative for p53, WT1, estrogen receptor, calretinin. Based on these findings, differential diagnosis included squamous cell carcinoma, high-grade endometrioid carcinoma and malignant Brenner tumor. She underwent total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. Extensive sampling identified components of proliferating Brenner tumor, and thus the diagnosis of malignant Brenner tumor was established.

**[Conclusion]** In general, high-grade morphology in ascetic fluid may suggests high-grade serous carcinoma, but features of divergent differentiation, i.e., mucin droplets and squamous differentiation should make malignant Brenner tumor a diagnostic concern.

### PE-1-23 Cytologic features of Papillary squamo-transitional cell carcinoma in Liquid-based cytology : A case report

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**[Background]** Papillary squamotransitional cell carcinoma of the uterine cervix is an uncommon tumor that tends to be recurrent and has metastases. Tumors can be divided three groups based on there histologic appearance : predominantly squamous, predominantly transitional and mixed squamous and transitional.

**[Case]** A 77-year-old female was referred to SNUBH for further evaluation of a cervical lesion diagnosed as "high-grade squamous intraepithelial lesion (HSIL) with papillary pattern" at an outside hospital. Colposcopy was performed, and a protruding neoplastic mass was seen in the exocervix. A punch biopsy with curettage was performed, and a diagnosis of papillary squamotransitional cell carcinoma was rendered. She had a hysterectomy, and on routine colposcopic examination two years later, the vaginal stump was friable and eroded. A cervicovaginal smear and punch biopsy was taken under the impression of a stump recurrence.

**[Results]** The liquid-based cytology preparation of the cervicovaginal smear demonstrated a few papillary tissue fragments and many scattered atypical cells. The papillary fragments contained fibrovascular cores and were lined by loosely cohesive epithelial cells. The background was cellular and showed individually scattered atypical cells with high nuclear/cytoplasmic ratio, nuclear hyperchromasia, irregular nuclear membranes, consistent with high-grade squamous intraepithelial lesion (HSIL) cells. There was no definite evidence of HPV cytopathic effect (koilocytosis). The concurrent punch biopsy tissue demonstrated abundant papillary excrescences with marked cytologic atypia and the tumor cells partly resembled urothelial cells, consistent with recurrent PSTCC. HPV test performed by the real-time PCR method was negative.

**[Conclusion]** PSTCC of the uterine cervix is a rare malignant tumor that should be distinguished from benign papillary lesions such as squamous papillomas or condylomas. The most distinctive feature of PSTCC is the three-dimensional papillary configuration with fibrovascular cores and scattered HSIL cells.

**PE-1-24 Single Claudin-4 immunostain has high sensitivity and specificity to differentiate adenocarcinoma from mesothelial cells in body effusion**

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○Jie-Yang Jhuang, Shu-Chen Chang

**[Objective]** For body cavity effusion specimens, it is important to differentiate metastatic adenocarcinoma from reactive mesothelial cells. Since they may have overlapping cytomorphology, immunohistochemical stains are required to distinguish them. This study aimed to evaluate the diagnostic value of claudin-4 marker in making such a distinction in our institute.

**[Methods]** In this retrospectively study, we searched our database and found a total of 91 pleural/peritoneal effusions have been studied, including 30 cases of metastatic carcinoma and 61 cases of reactive mesothelium without metastatic malignancy. Specimens were from routine body cavity effusion collected from patients. Both cytology slides and cell blocks were prepared. The later was used for immunohistochemical staining. Monoclonal anti-claudin-4 antibody was used for immunohistochemical labeling in conjunction with autostainer (Ventana system). For the interpretation criteria, membrane-bound reactivity was considered as significant and percentages of positive tumor cells were recorded.

**[Results]** Claudin-4 protein was positive in 31 specimens (29 metastatic carcinoma and 2 reactive mesothelial cells), and negative in 60 specimens (1 metastatic carcinoma and 59 reactive mesothelial cells). Positive staining for claudin-4 was significantly more frequent in metastatic carcinoma than in the reactive mesothelium ( $P > 0.0001$ ). The sensitivity and specificity of claudin-4 to distinguish reactive mesothelium from metastatic carcinoma were 96.7% (95% confidence interval [CI], 0.80947–0.998258%) and 96.7% (95% CI, 0.876433–0.994301%), respectively. Furthermore, negative likelihood ratio was 0.035. (95% CI, 0.005012–0.236986).

**[Conclusion]** The results of this study demonstrated that claudin-4 is less frequently expressed in reactive mesothelium and almost always expressed in metastatic adenocarcinoma. Thus, this claudin-4 may be helpful in differentiating metastatic carcinoma from reactive mesothelial cells in pleural and peritoneal fluid cytology specimen with both high sensitivity and specificity.

**PE-1-25 Comparison of three different cell block preparations for malignant body fluid specimens**

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**[Objective]** The cell block (CB) in non-gynecologic cytopathology has gained significance because of its pivotal role in molecular diagnosis and ancillary studies. There are 3 benefits of cell block : it could capture all of the material in malignant body fluid specimens, obtain the highest cellular yield including tissue fragments and free-floating single cells, and preserve the cytomorphology and architecture. CB enables the cytopathologist to know additional cytomorphologic specimen detail including the architecture of the lesion. Most importantly, they allow the evaluation of immunocytochemistry to improve diagnostic accuracy.

**[Aims]** To investigate and find out the best method from three different cell block preparations for malignant body fluid specimens.

**[Materials and Methods]** We analyzed the cytologic findings of pleural effusion and ascites specimens from 35 adenocarcinoma cases using 3 different cell block preparations : 95% alcohol, HistoGel (HG) and Gelfoam technique. Two cytopathologists blindly evaluated H&E and IHC sections of the 105 cell blocks from 35 specimens, and scored them on a scale of 0 (suboptimal, worst) to 3 (optimal, best) evaluating cellularity, cell distribution, morphology, background, pellet size, and overall quality. Averages were then obtained and compared with each of the preparation method.

**[Results]** Our study illustrates that if the specimens are not fixed, the cells cannot concentrate. The staining results show that the method of 95% Alcohol makes chromatin well revealed in H&E stain, but pale in IHC stain. The methods of HG and Gelfoam show a better staining intensity in IHC stains than 95% Alcohol. In HE stain, the cellularity of HG is better than Gelfoam, and the background of Gelfoam disturb the interpretation. The results indicate that the HG technique succeeded in achieving the goals of capturing all the free-floating cells, preserving the cytomorphology and architecture, and better staining results.

**[Conclusion]** Based on our data and technique, we found that it is important to fix the specimens with 10% formalin or cytorich red fixative or 95% alcohol before doing the cell blocks. When there is only a little residual specimen, doing a cytospin would be better than a cell block.

## PE-1-26 Metastatic Embryonal Rhabdomyosarcoma in the Pleural Effusion

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**[Introduction]** Rhabdomyosarcoma (RMS) rarely presents with malignant effusion. Herein we report the cytological features of metastatic embryonal RMS (ERMS) in the pleural effusion with a literature review.

**[Case Report]** An 18 years old woman had presented with toothache and left face bulging for 2 months. Computed tomography showed an 8.1 cm inhomogeneous enhancing mass at left maxillary sinus with soft palate and left frontal sinus involvement. An incisional biopsy exhibited a malignant small round cell tumor (MSRCT). ERMS was diagnosed. Despite chemotherapy, she developed dyspnea from left pleural effusion three months later. Pleural fluid cytology demonstrated high cellular specimen composed of numerous single, round-to oval-shaped neoplastic cells with high nuclear cytoplasmic ratio within diluted blood background. The tumor cell size was variable ranging from 2 to 5 times of the size of neutrophils. The nuclei were hyperchromatic and pleomorphic noticeably, including oval, round, indented, bilobated or multilobated appearance. Large intranuclear inclusion was frequently seen. The cytoplasm was rather condensed. Immunostains for myogenin and desmin on cell block preparation slides corroborated the diagnosis of metastatic ERMS.

**[Conclusion]** Although the cytological features of ERMS are more or less different from the other MSRCTs ; rare encounter of metastatic RMS in body fluids may lead to diagnostic difficulty or error, especially in those unknown cases. Desmin and myogenin stain in cell block material is recommended in such cytology fluids with MSRCT as it is a beneficial and easy technique.

**[Disclosure of Interest]** None declared.

## PE-2-1 Long-term exposure to nicotine derivatives and arecoline accelerates and contributes to the progression of Head and neck squamous cell carcinoma

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Head and neck squamous cell carcinoma (HNSCC) is one of the leading causes of cancer-related death in Taiwan and worldwide. Chewing betel nut, smoking, and alcoholism are the three major risk factors which may contribute to the development of HNSCC. Recent reports have demonstrated that long-term exposure to either nicotine derivatives or arecoline may be associated with tumor progression of HNSCC. However, the underlying nicotine derivatives-or arecoline-mediated mechanism contributing to the aggressiveness of HNSCC has not been thoroughly studied. Therefore, the study is aimed to evaluate the possible phenomenon contributing to the progression of HNSCC, with special emphasis on the reciprocal effects of both risk factors in terms of cellular and molecular changes in the aggressive potential of HNSCC. In this study, the cell model of long-term exposure to nicotine derivatives and arecoline was established. A comparative analysis using SCC-25 and Fadu cells with or without nicotine derivatives and arecoline exposure was performed to evaluate cell proliferation, migration, and invasion as well as the expression of epithelial-mesenchymal transition (EMT) marker, drug-resistance gene expression, cancer stem cell properties, and anti-apoptotic activity. As a result, either long-term nicotine derivatives or arecoline exposure, or exposures to both risk factors was found to stimulate cell proliferation, enhance migration and invasion, induce EMT with morphological alterations in a dose-dependent manner, and attenuate apoptosis. Furthermore, either long-term nicotine derivatives and arecoline exposure, or exposures to both risk factors promoted sphere-forming capacity, upregulation of Snail, and overexpression of CD133, CD24/44+, Nanog, and OCT4, and the drug resistant genes, ABCG2 and MDR1, as well as increased resistance to radiation and chemotherapy. In conclusion, treatment of

HNSCC with nicotine derivatives, in accordance with exposure to arecoline elicited the similar results, whereas exposures to both risk factors accelerated and enhanced almost all the phenomenon in terms of the progression of HNSCC.

**【Keywords】** Nicotine derivatives ; Arecoline ; Head and neck squamous cell carcinoma ; Tumor progression

## **PE-2-2 The Role of Cancer-associated Fibroblast-induced Chemokine (C-C motif) ligand 11 in Tumor Microenvironment Contributes to the Promotion of Head and Neck Squamous Cell Carcinoma**

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Head and neck squamous cell carcinoma (HNSCC) is one of the leading causes of cancer-related death in Taiwan and worldwide. The prognosis of HNSCC is usually poor because of its propensity of extensive invasion, local recurrence and frequent regional lymph node metastasis, even at initial diagnosis. Recent studies showed carcinoma-associated fibroblasts (CAFs), a major type of tumor-surrounding stromal cell, generate certain mediators through which CAFs interact with tumors and contribute to cancer progression in numerous cancers. The orchestration between CAFs and cancer cells is complex and its underlying mechanism needs to be explored. In the present study, we used organotypic culture to investigate CAFs that promote aggressive behavior of cancer cells. Using microarray analysis, we detected abundant expression of chemokine (C-C motif) ligand 11 (CCL11) in CAFs and identify CCL11 as a critical mediator in CAF-induced invasiveness. We validated that CCL11 played a major role in the crosstalk between fibroblasts and HNSCC cells via the paracrine manner. CCL11 was found upregulated in CAFs than in normal fibroblasts via Western blot analysis. HNSCC cells treated with recombinant CCL11 increased capabilities of sphere formation in ten days. Administration of CCL11 promoted migration and invasion abilities through induction of the epithelial-to-mesenchymal transdifferentiation with corresponding morphological alterations of cancer cells. Counteracting CCL11 activity diminished the aggressive phenotype of cancer cells induced by CAFs. We further studied the relationship between the expression of CCL11 in both CAFs and HNSCC cells and clinical outcome in the patients with HNSCC. As a result, a high CCL11 expression level was associated with poor prognosis in

terms of nodal metastasis and survival. These results indicate that CAFs promote cancer invasiveness via a paracrine effect on microenvironmental CCL11 signaling and suggest that CCL11 is a potential prognostic biomarker that could be considered in therapeutic strategies for the treatment of patients with HNSCC.

**【Keywords】** Carcinoma-associated fibroblasts (CAFs) ; Chemokine (C-C motif) ligand 11 (CCL11) ; Microenvironment ; invasiveness ; Head and neck squamous cell carcinoma (HNSCC)

### **PE-2-3 Cytomorphology of Mammary Analogue Secretory Carcinoma of Parotid : A case report and a brief discussion**

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**【Abstract】** Mammary analogue secretory carcinoma (MASC) is a recently described low grade carcinoma of salivary gland that has similar histologic features and immunohistochemical profile to the secretory carcinoma of the breast. They both harbors a recurrent balanced chromosomal translocation t(12 ; 15) (p13 ; q25), which leads to the ETV6-NTRK3 fusion gene. Cytologically, MASC can be confused with other low grade salivary gland tumors, particularly the acinic cell carcinoma (AciCC). It is often difficult to distinguish MASC from other mimics based on cytomorphology alone. Herein, we report a case of MASC in the parotid gland in a 20-year-old man. The preoperative diagnosis of the fine needle aspiration (FNA) is "Acinic cell carcinoma is firstly favored". The diagnosis of MASC is confirmed by detection of ETV6-NTRK3 fusion gene by FISH analysis on the surgical specimen. We will discuss how the cytological features and ancillary studies (immunohistochemical stains and FISH analysis) can help use differentiate MASC of salivary gland from other mimics.

#### PE-2-4 A case of simultaneous occurrence of double cancer (tongue cancer and breast cancer) as two separate primary tumor

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**【Case Report】** The patient was an 80-year-old woman with a medical history of hyperlipidemia and hypertension. The patient visited dental department of a local hospital in 2014, and was found to have tongue cancer, which was diagnosed as well-differentiated squamous cell carcinoma on biopsy. Pre-operative assessment showed cervical lymphadenopathy on physical examination. Fine needle aspiration (FNA) cytology of the enlarged lymph nodes was performed which revealed that squamous cell carcinoma originates in the tongue. Subsequent positron emission tomography (PET) detect a breast mass. FNA cytology of the mass revealed the positive cytology with prominent tubular proliferation. The tumor was diagnosed as solid tubular carcinoma of the breast histologically.

**【Materials and Methods】** FNA cytology of the cervical lymph nodes and breast mass were processed with the liquid-based cytology (LBC) and cell blocks were prepared from the remaining material.

**【Results】** The cytoplasm of tongue cancer cells was orangeophilic, and no histological features of well-differentiated squamous cell carcinoma, such as the so-called cancer pearls or tadpole-shaped cells, were found. Biopsies showed well-differentiated squamous cell carcinoma forming cancer pearls. Breast cancer cells were small, with a high N/C ratio, and proliferated in a solid pattern. Fibrosis was observed in areas of invasion.

**【Discussion】** We encountered a case of tongue cancer with cervical lymph node metastasis and concomitant breast cancer, and report the cytological and histological appearances of these cancers, with a review of the literature.

#### PE-2-5 Mammary Analogue Secretory Carcinoma : A Case Report with Review of the Literature

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**【Objective】** Mammary analogue secretory carcinoma (MASC) is a low-grade adenocarcinoma described in the salivary gland in a 2010 report of mainly parotid tumors with features resembling breast secretory carcinoma. It's a recently described salivary gland tumor that harbors the recurrent ETV6-NTRK3 translocation. Although there is paper described the morphology of cytology, due to its rarity, the cytological characteristics of MASC are still not fully understood. Here, we report the case from parotid gland.

**【Methods】** Fine needle aspiration, smear were fixed in 95% ethanol for Papanicolaou stain and air-dried for Liu's stain. Immunohistochemistry and fluorescence in situ hybridization (FISH) were performed.

**【Results】** Cytological findings were cellular smear, the papillary structures with the vascular cores and loosely cohesive syncytial clusters. The tumor cells were polygonal with abundant bubbly cytoplasm and focal eccentric, round to oval uniform nuclei, vesicular chromatin and small nucleoli, with lack or inconspicuous cytoplasmic granules. The background was clear. FISH shows rearrangement of the ETV6 gene.

**【Conclusion】** MASC can be easily be mistaken with other salivary gland tumors. Cytological morphology appears the papillary structures with the vascular cores, abundant/bubbly cytoplasm and lack or inconspicuous cytoplasmic granules. Immunohistochemical stain is useful for differentiating MASC from other tumors, immunostains positive for S100 and negative for DOG1 would favor MASC. However, to date, only ETV6 rearrangement stands as the defining diagnostic criterion.



## PE-2-6 Cytopathology practice in Hungary

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**[Objective]** Qualification systems for cytopathological diagnostic practice vary among countries. We aimed to differentiate the features of cytopathology practices between Japan and Hungary.

**[Methods]** The author (MS) visited the Second Department of Pathology, Semmelweis University, Szent Janos Hospital, Korányi TB and the Pulmonology Institute in Hungary in 2015 to study their cytopathology practices supported by a grant from the faculty short-term study abroad program of Saitama Medical University.

**[Results]** Medical technologist qualifications do not exist in Hungary, but other occupational categories are available. Qualified pathologists with two years' experience implement cytopathology practices and laboratory technicians are involved in specimen preparation for cytopathology. Cytologists who undergo a two-year training program to obtain a qualification that is superior to that of a laboratory technician perform cytoscreening. Pathologists are involved in medical interviews with patients, ultrasonography and fine needle aspiration, prepare and fix smear preparations that are routinely stained with hematoxylin and eosin (HE) and Giemsa, with occasional Papanicolaou staining usually limited to gynecological and urological specimens. When necessary, cytopathologically diagnosed specimens stained with HE on glass slides are then immunostained.

**[Conclusions]** Cytopathology practices differ between Japan and Hungary. Understanding such differences in other countries will help to improve cytopathology practices in Japan.

## PE-2-7 The liquid based cytology for cervical cancer screening in Mongolia

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**[Objective]** Conventional cytology test is major in Mongolia, but its numerous inflammatory cells, mucus are difficulty. Liquid based cytology (LBC) test is not familiar in Mongolia, then we aimed to assess its sensitivity and accuracy.

**[Methods]** The total 150 cervical split samples were included from 75 women, using cervix-brush. Initially, conventional smears were prepared from brush and brush head was suspended in LBC vial and processed by TACAS™ system, Pap stained, and diagnosed by Bethesda system. Women with the abnormal smears were analyzed by colposcopy directed biopsy.

**[Results]** There were unsatisfactory 14% conventional, and 6% LBC smears ( $p < 0.05$ ). The out of the 13 women with the abnormal conventional smears, 9 true positive, 3 false positive, 1 false negative results were assessed in histology. Thus, conventional cytology test has 90% sensitivity, and 69% analytic accuracy. Therefore, out of the 13 women with abnormal LBC, 10 true positive, 1 false positive, and 2 true negative, no false negative results were in histology. This result shows LBC test has 100% sensitivity and 92% analytical accuracy ( $p = 0.005$ ).

**[Conclusion]** Specimen adequacy was better in LBC test. The sensitivity and analytic accuracy was both higher in LBC test.

## PE-2-8 Current situation in regards to cytology of cervical cancer in Cambodia

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**[Background]** In Cambodia, cervical cancer is the leading cause of cancer deaths among females with an estimated 800 cervical cancer deaths per year. Patients come to the hospital mostly in the very late stage of cervical cancer and the clinicians often performed cervical biopsy directly for suspicious invasive cancer cases without cytology, and performed Pap tests in patients who showed no pathological changes. Some biopsy cases were performed after the abnormal cytology results.

In Cambodia, the process of diagnose cervical cancer has not established such as cytology and colposcopic diagnosis. Here we reviewed the cervical cancer statistics in Khmer Soviet Friendship Hospital.

**[Methods]** Khmer Soviet Friendship Hospital is a national general hospital situated in the capital, Phnom Penh, and working as the only cancer center where comprehensive cervical cancer diagnosis and treatment can be provided. From August to October, 2016, we reviewed and analyzed the pathology and gynecology registration book to reveal the current situation of diagnosing cervical cancer.

**[Results]** 2175 patients consulted with the gynecology outpatient department. There were 175 cervical cytology cases and 127 cervical biopsy cases. Among the 175 cytology cases, there was only one LSIL case and the others were all NILM. On the other hand, the biopsy results revealed 70 SCC, 11 Adeno Carcinoma, 1 lymphoma, 7 CIN1, 3 CIN2, 8 CIN3 (4 were CIS), 2 tuberculosis and 25 cases showed no significant change. The biopsy results showed 82 malignant (64.6%) cases and the cytology specimens, however, there were 25 normal results (19.7%) among the biopsy cases.

**[Conclusion]** There was a big discrepancy between the cytology and biopsy results. The situation in Cambodia cannot be changed unless cervical cancer screening is implemented widely, but pathology departments and gynecology departments need to establish further collaboration to give more feedback to each other for more accurate diagnoses of cervical cancer.

## PE-2-9 Usefulness of liquid-based cytology for the diagnosis of oral squamous cell carcinoma—Comparison of conventional method and liquid-based cytology—

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**[Objective]** Since oral squamous cell carcinoma (OSCC), which represents the greater part of the malignant tumors occurring in the oral cavity, often has hyperkeratosis. This makes it harder to obtain enough cells for the cytological diagnosis on the smear, and this sometimes makes it difficult for us to diagnose. When we observe atypical cells of basal type or cancer pearls in the specimen, it becomes easier. In this study, we focused on some features to be the basis of OSCC such as keratinized superficial atypical cells, cancer pearls and basal type atypical cells. We aimed to evaluate the usefulness of liquid-based cytology (LBC) for the diagnosis of oral lesions with malignant suspicion by comparing the conventional method and LBC.

**[Materials and Methods]** Samples collected from 25 patients were underwent cytological and pathological testing, and were pathologically diagnosed with oral intraepithelial neoplasia (OIN) and OSCC at the department of oral surgery in Iizuka Hospital. Conventional smears were prepared first, using interproximal brush device. Then the brush, containing the residual material, was immersed in a preservative fluid (TACAS Ruby<sup>®</sup>). Both slides were stained by the Papanicolaou method. We investigated whether keratinized atypical cells, cancer pearls and basal type atypical cells appeared in the specimen or not. Fisher's exact test was used to compare differences between the conventional method and LBC specimen using split-sample. When the P-value < 0.05, the difference was regarded as statistically significant.

**[Results]** Cytological diagnosis by the conventional method was positive in 23/25 cases, negative in 1/25 case and inadequate in 1/25 case. Cytological diagnosis of LBC method was positive in 25/25 cases, nothing for negative or inadequate case. In the conventional method, keratinized atypical cells, cancer pearls and basal type atypical cells were observed in 23/25, in 3/25, in 11/28 cases, whereas in

LBC method, they were in 24/25, in 8/25, in 18/25 cases. The frequency of basal type atypical cell was significantly higher in LBC as compared to the conventional method ( $P = 0.04$ ).

**【Conclusion】** As for the results of the current study, it was expected that the LBC improved the diagnostic precision of oral brush cytology because of being excellent for detecting the atypical cells in the oral cavity.

## **PE-2-10 The Usefulness of the Cell Transfer Technique for Routine Cytology Practice in Taiwan**

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**【Objective】** At present, the use of liquid based cytology (LBC) is not so popular in routine cytology practice in Taiwan. Although additional immunocytochemical staining (ICC) is necessary for the workup of cytology diagnosis, the application of ICC is restricted due to limited specimen especially in fine needle aspiration (FNA). The purpose of this study is to evaluate the efficacy of cell transfer technique for its usefulness in daily routine cytology practice.

**【Methods】** A total of 20 cytology samples, with ICC performed on cell transfer slides, were retrieved from the department of Pathology, Taipei Veterans General Hospital and Mackay Memorial Hospital after the introduction of cell transfer technique in 2014. The results and contribution were recorded and analyzed.

**【Results】** Cell transfer technique was performed in 20 cytology samples, including 6 FNA, 1 CSF, 1 pleural effusion, 2 ascites, 1 vitreous fluid, and 9 Pap smears. A total of 34 ICC stains were performed and ranged from one to 3 stains per each case. In 18 cases (90%), ICC stains were contributory for diagnosis : p16 and/or Ki-67 in Pap smears for HSIL and AIS ; CD20 & CD3 for lymphoma in body fluids and FNA ; PAX-8, GATA-3, TTF-1 & CDX-2 for origins of metastases in Pap smears, body fluids and FNA.

**【Conclusion】** Cell transfer technique is very easy and useful in the workup of cytology specimens for those laboratories not using LBC. Although it is not used frequently, it did provide contributory results and helped in getting final diagnosis in 90% of cases using this technique.

### PE-2-11 Rapid on site evaluation on FNA of unknown primary tumor to diagnose neuroendocrine tumors

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**[Objective]** Neuroendocrine neoplasms include a group of heterogeneous tumors originated from neuroendodermal and neural crest. The tumor cells receive neuronal input of neurotransmitters released by nerve cells or neurosecretory cells and release message molecules of hormones to the blood. They share morphological and immunophenotypic similarities despite the tumor origin. There is usually bland cytopathology and minimal polymorphism, but less commonly there can be anaplasia and tumor cells may mimic other malignancies. In this study we presented the morphological variants of neuroendocrine neoplasms diagnosed on FNA of unknown primary tumors in our collection and emphasized the value of rapid on site evaluation (ROSE) for accurate diagnosis by applying ancillary test of immunohistochemistry (IHC) on smears or blocks for differential diagnosis.

**[Methods]** We reviewed 45 cases suspected of neuroendocrine neoplasms on ROSE in the last four years from FNA of unknown primary tumors. Tumor origin spanned a spectrum of GI, lung, breast, thyroid and paraganglia. 28 cases were diagnosed of neuroendocrine neoplasms or tumors with neuroendocrine differentiation with ancillary test of IHC tested in 26 of them and 18 (100%) had further resection samples to confirm the diagnosis, while 8 patients went on with treatment directly without further biopsy or resection. 17 cases signed out as the suspicious had no cell blocks available for IHC and 11 of them had pathology confirmation to be neuroendocrine tumors for 8 cases and other malignancy or benign lesions for 3 cases (27.3%). The other 6 had no pathology follow-up.

**[Conclusion]** While morphology forms the fundamental bases to recognize the neuroendocrine tumors, IHC on cell block plays an important role for differential diagnosis. ROSE helps us to triage sample for cell block preparation and make accurate diagnosis possible on cytology samples. A series of cases are demonstrated in the talk to emphasize the potential pitfalls in dealing with this differential diagnosis.

### PE-2-12 A Novel Method for DNA Cytometry for Exfoliated Cells

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**[Objective]** Understanding proliferative status of samples from precancerous lesions can be difficult when proliferating cells are mixed among majority of normal cells. Here, we report a novel flow cytometry method to enable detection of proliferative cell populations.

**[Methods]** Suspended cells were measured by the flow cytometer, and the acquired signals were used to obtain information corresponding to cell morphology and DNA content. Next, the morphological characteristics of proliferating cells were used to select high N/C ratio-populations, and subsequent DNA ploidy analyses were conducted. Finally, the state of proliferation was indicated by an original cell proliferation index (CPIx) that represents the proliferative characteristics of cell populations.

**[Results]** Human buccal cells and human umbilical vein endothelial cells (HUVECs) were measured to calculate the ratios of nuclear and cell diameters (N/C ratio) of individual cells using the FSC\_W and RFL\_W values, as these values correspond to the lengths of the cell and nucleus, respectively. By drawing scattergrams of cell lengths and N/C ratios using measurement values of buccal cells and HUVECs, respectively, these cells could be discriminated as low-N/C ratio group (buccal cells) and high-N/C ratio group (HUVECs). In addition, CPIx values of HUVECs well represented the proliferative conditions of each cell culture. Finally, when low-proliferative HUVECs and high-proliferative HeLa cells were mixed and measured in this system, CPIx values of mixed samples were well correlated with the proportion of HeLa cells.

**[Conclusion]** CPIx value is suggested to represent proliferative status of samples. Therefore, this method is expected to substantially contribute to know the proliferative status of clinical samples such as cervical dysplasia.

### PE-2-13 The Effects of Formalin Fixing Conditions on Fluorescence in situ hybridization in cell block of effusion cytology

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**【Background】** A cell block method can be applied for immunocytochemical analysis or molecular biological technique of specific biomarkers, and it contributes for accurate diagnosis of effusion cytology. On the other hand, many studies have investigated the effects of formalin fixation for the biomarker expression in tissue samples, there is no study in cytological materials. In the present study, we investigated the effect of formalin fixing conditions on fluorescence in situ hybridization (FISH) in cell block preparation using the cell line.

**【Methods】** The normal human mesothelial cell line (Met-5A) was used. Cells were collected after washing with PBS, and suspended in 0.9% NaCl normal saline solution with 4 mg/dL BSA (albumin from bovine serum) to closely resemble effusion microenvironment. Cell block was prepared by formalin superposition method. The variation of Formalin fixation condition was as follows. 1) Fixing solutions : 10% neutral buffered formalin (NBF), 10% non-buffered formalin or 20% non-buffered formalin. 2) Delay to fixation time : stored at room temperature or 4°C for 0h, 2h, 4h, 8h, 24h, or 48h before fixed. 3) Fixation time : 24h, 72h, 1week or 2 weeks. After embedding in paraffin, the above samples examined respectively by FISH using *p16/CDKN2A* gene probe. Presence of the following factors were observed in each sample. 1) Non-uniform unscorable weakly signal. 2) Decrease or loss of signal. 3) Non-specific signal over nuclei and cytoplasm (autofluorescence or background obscures signal).

**【Results】** The sufficient intensity of signals could be detected in over-fixation samples longer than 72h, however, decreased the number of signals especially *p16* gene (red signals). Specimens left for longer than 4h in room temperature before fixation tended to induce autolysis and increase non-specific background signals. Moreover,

intensity and number of true signals clearly reduced with the passage of time.

**【Conclusion】** Compared with prolonging fixation time, delaying formalin fixation has more serious negative effects on FISH result in cell block. We recommend to perform formalin fix as immediately as possible, and not to leave specimens at room temperature.

## PE-2-14 EBUS-TBNA with ROSE : introducing the procedure to a cancer center

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**【Objective】** Due to practice patterns and concerns about manpower cost and time consume, rapid on-site evaluation (ROSE) of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) appears to be performed at only limited centers. And uncertainty surrounds the optimal number of cases needed to do ROSE for achieving acceptable yields.

**【Methods】** The primary consecutive 400 cases in two years (2009-2011) performed EBUS-TBNA by one operator in Shanghai Cancer Center were retrospectively analyzed. The first 200 cases were performed with ROSE, and the followed 200 cases were performed without ROSE. The first 200 cases were divided into 8 groups by incremental 25 cases aliquots. Except for Smears and cell blocks, any core tissues found in the aspirates were histologically processed. We focused on the diagnostic yield of EBUS-TBNA, inadequacy of first sampling, inadequacy of sampling, cell block (CB)/biopsy success rate, immunohistochemistry (IHC) success rate, and molecular tests carried out on CB and/or core tissues.

**【Results】** 912 lesions were aspirated from 400 patients, including 269 males and 131 females with a mean age of 57.4, a median age of 59, and ranging from age 24 to 84. In cases without EBUS-TBNA biopsy or subsequent mediastinoscopic or surgical staging resections, clinical follow-up was taken as the gold standard. The inadequacy of first sampling and inadequacy of sampling decreased steadily after the initial 25 cases and remained low thereafter. Inadequacy of first sampling were 48% (12/25) and 8% (2/25) of the 1-25 cases and 176-200 cases. With the help of ROSE, inadequacy of sampling were 20% (5/25) and 0% (0/25) of the 1-25 cases and 176-200 cases, respectively. The CB/biopsy success rate and IHC success rate increased steadily after the initial 100 cases. Molecular

tests were performed successfully from 26-50 cases. The sensitivity, negative predictive value (NPV), and diagnostic accuracy for the 8 groups of the first 200 case were relatively stable with ROSE. The overall sensitivity, NPV and diagnostic accuracy for the first 200 cases and the followed 200 cases were 95.4% and 97.7%, 88.0% and 95.5%, 92.3% and 96.9%, respectively. Without ROSE, the diagnostic yield continued to increase slightly after the initial 200 cases.

**【Conclusion】** ROSE provided a clear advantage in providing high diagnostic accuracy for EBUS-TBNA by ensuring adequate sampling. Without ROSE, the diagnostic yield continued to increase slightly after the initial 200 cases. If further sample triaging was not considered, it was cost and time effective that ROSE could be no longer performed when the inadequacy of first sampling was low enough and EBUS-TBNA continued to be accomplished by the same operator.

### PE-2-15 A novel flow cytometry (FCM) based system for cervical cancer testing

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**【Objective】** The aim of this study was to assess the utility of a novel FCM based system for cervical cancer testing through comparisons of measurement results from the system with clinical data.

**【Method】** Cell samples were collected from patients who were treated at our department between September 2011 and February 2013 using the Cervex-Brush Combi. Direct smears were prepared and cells remaining after this process were preserved in preseavation solution to prepare liquid-based cytology specimens (n = 746). Specimens were measured using a prototype FCM system (Sysmex Corporation) and an original index, cell proliferation index (CPIx) was used in this study to calculate cell proliferation. The measurement results were verified against the clinical information. Hybrid Capture II (HC II) was also conducted.

**【Results】** Probability values of correlations between the median CPIx value for each specimen and histological grade were as follows : 0.186 for normal and cervicitis (n = 32), 0.238 for CIN1 (n = 47), 0.351 for CIN2 (n = 18), 0.534 for CIN3, (n = 24), and 0.759 for squamous cell carcinoma (n = 15). The clinical performance of this system was as follows : the sensitivity was 95.2% (58/61) to detect  $\geq$  CIN2 lesions, whereas the specificity was 76.3% (455/596) when NILM and  $\leq$  CIN1 were defined as negative. Compared with FCM system and HC II, the sensitivity to detect  $\geq$  CIN2 lesions by FCM system was 95.2% (40/42), whereas that of HC II was 92.9% (39/42).

**【Conclusion】** The system showed a favorable clinical performance to detect  $\geq$  CIN2 lesions. This shows that it might be utilized to provide healthcare professionals with support information for the diagnosis of cervical cancer.

### PE-2-16 A Case of Plasmablastic Lymphoma

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Plasmablastic lymphoma is a rare malignant lymphoma, which occurs commonly in HIV-positive or immunodeficiency state, including advanced age. We discuss on cytological features of plasmablastic lymphoma with an HIV-negative patient.

**【Case】** The patient is a 63-year-old male, who had been followed up as having nodular goiter of the thyroid. He noticed swelling of the right neck and supraclavicular region. Pharyngeal tumor was suggested by PET. Fine-needle-aspiration (FNA) cytology of the lymph node and biopsy of the pharynx were performed.

**【Cytological findings】** In necrotic background, there were a lot of large atypical cells sparsely. They had cytoplasmic vacuoles and a single or multiple large nuclei with distinct nucleoli and coarse chromatin. Some nuclei located peripherally.

**【Histological findings】** There were some large atypical cells mainly in vessels. They resembled plasma cells, having a single peripherally located nucleus with perinuclear halo. However, some had multiple nuclei and distinct nucleoli. Immunohistochemically, they were positive for EMA and CD138, indicating plasmablastic lymphoma.

**【Conclusion】** The specimen by FNA from lymph node contained rather necrotic and degenerated atypical cells, which had no apparent perinuclear halo in Papanicolaou stain. The diagnosis of plasmablastic lymphoma is difficult without characteristic findings of plasma cell.

**PE-2-17 Fine Needle Aspiration Cytology of Kikuchi's lymphadenitis - Experiences of Korea Cancer Center Hospital**

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**【Objective】** Kikuchi's lymphadenitis (KL) is a benign lymphadenopathy with spontaneous regression. It can be not only clinically but also pathologically mistaken for lymphoma, tuberculosis or SLE. Surgical biopsy is unnecessary if a firm diagnosis can be rendered by fine-needle aspiration cytology (FNAC). In order to find out helpful diagnostic points in the initial diagnostic step FNAC, we examined cytologic details of histologically proven KL.

**【Methods】** Retrospective review was done for 108 patients of FNAC of lymph nodes in which KL was diagnosed or suggested by FNAC and/or biopsy at the department of Pathology, Korea Cancer Center Hospital during the period of January 2010 and June 2016. Histologic sections of FNAC cell blocks and subsequent biopsy specimens were available in 22 and 31 patients, respectively, for confirmation of the diagnosis.

**【Results】** Smears of all the 22 cell block available cases were in concordance with cell block histology and immunohistochemistry of KL. Among 31 biopsy-proven cases, 19 showed diagnostic concordance of FNAC smears with biopsy. Three of the 14 discordant cases were cytologically diagnosed as KL but were histologically proven to peripheral T-cell lymphoma (1), reactive hyperplasia (1) and granulomatous inflammation (1), respectively. The other 11 of the 14 discordant cases were suggested as reactive hyperplasia on FNAC and were finally diagnosed as KL on biopsies.

**【Conclusion】** From our retrospective analysis, we suggest it would be the most helpful to thoroughly find out the characteristic phagocytic histiocytes including crescentic nucleus, especially focusing on the presence of eosinophilic granules in their cytoplasm.

**PE-2-18 Primary Intraocular Lymphoma Masqueraded as Uveitis : A Case Report**

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**【Objective】** Primary intraocular lymphoma (PIL) is a rare hematopoietic malignancy which is difficult to diagnose. PIL predominantly occurs in the elderly and often involves bilateral orbits with central nervous system involvement.

**【Methods】** We used Papanicolaou and immunohistochemistry stains to analyze cytological morphology and differential lymphoid lineage. Flow cytometry was performed as an ancillary test.

**【Results】** Herein, we report a 57-year-old woman with unilateral PIL diagnosed by vitreous aspiration, initially presented as uveitis. Our case illustrated the importance of a careful clinical examination and investigation as uveitis is a common inflammatory eye disorder. PIL should be considered as differential diagnosis for uveitis that is unresponsive to therapy, as PIL could be a great mimicker. Vitreous smear showed atypical lymphocytes with enlarged nuclei, prominent nucleoli, and clumping chromatin. On immunohistochemistry stains, these atypical cells were positive for B-cell marker (CD20) and negative for T-cell marker (CD3), indicating the presence of monoclonality. Flow cytometry showed 45.1% aspirated cells were positive for CD20 surface marker, and 26.1% positive for T-cell surface marker (CD3). Taken together the results of cytological morphology, immunostains, and flow cytometry, intraocular B-cell lymphoma was diagnosed. The CSF cytology and bone marrow biopsy was performed to exclude systemic lymphoma, and there was no evidence of extraocular lymphoma.

**【Conclusion】** Accurate cytological diagnosis of primary intraocular lymphoma via vitreous aspiration affects by specimen quality. Ancillary tests in combination with cell morphology may be helpful to facilitate accurate diagnosis.



### PE-2-19 T-Cell Lymphoma Diagnosed in Sputum in a Patient with Tuberculosis

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**【Objective】** To demonstrate a difficult case of T cell lymphoma diagnosed in sputum cytology in a patient with concurrent mycobacterial infection.

**【Methods】** This 69-year-old female suffered from persistent dry cough without fever for more than one month, associated with progressive short of breath. She also complained poor appetite and weight loss by 4 kg in recent months. After the check-up, the radiographic examination (CXR and CT) revealed patchy infiltration and consolidation over the right lung and enlarged lymph nodes in bilateral hilum and cervical region. Needle biopsy of the cervical lymph node was performed, showing caseous necrotizing granuloma with acid-fast positive mycobacterium. Q-PCR confirmed the mycobacterial infection. After 3-month treatment, the symptoms were persistent and progressive. Cytology specimens from sputum, pleural effusion and ascites were collected and examined in her 2nd time admission.

**【Results】** The sputum smears reveal small and loose atypical lymphoid infiltration scattered between squamous cells or in the background. The atypical lymphoid cells manifest small to medium size with pleomorphism, hyperchromasia and irregular nuclear membrane. The atypical lymphocytes are positive for LCA, CD3 and negative for CD20. The malignant lymphoma cells are also present in the pleural effusion and ascites.

**【Conclusion】** Pulmonary involvement of T cell lymphoma with positive sputum cytology is very rare. Concurrent mycobacterial infection may also distract examiner's focus. Being alert to atypical inflammatory cells is very important not to miss such cases in cytology.

### PE-2-20 NUT Carcinoma with Cytoplasmic Basophilia Mimicking Lymphoma : Diagnostic Pitfall

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**【Background】** NUT carcinoma is a rare, poorly differentiated carcinoma characterized by the presence of NUT gene rearrangement. The cytopathologic features of NUT carcinoma are nonspecific and overlap with other poorly differentiated carcinomas or round cell tumors.

**【Case】** A 36-year-old man presented with cough for two months. Chest CT showed a large infiltrative mass involving left upper and lower lobes of lung, with mediastinal invasion, lymphadenopathy, pleural and pericardial effusion. He underwent LUL wedge resection and the initial diagnosis from another hospital was poorly differentiated squamous cell carcinoma. Our department reviewed the slides and the diagnosis is revised to NUT carcinoma after additional immunostain for NUT. Pericardiocentesis was done to relieve his orthopnea. Cytospins of pericardial fluid show a cellular specimen consisting of noncohesive, monomorphic, large-sized tumor cells with round to ovoid nuclei, open chromatin and prominent nucleoli. The cytoplasm is scant and deeply basophilic in Liu's stain. The tumor cells on cell block are positive for P40 and NUT, while negative for CD3 and CD20.

**【Conclusion】** We present a case of NUT carcinoma which shows intense cytoplasmic basophilia and strongly mimics a lymphoma. Although it is rarely seen in NUT carcinoma, awareness of this feature is important as it can lead to a diagnostic pitfall.

## PE-2-21 Most primary effusion lymphomas in Taiwan are unrelated to HIV and HHV8

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**[Introduction]** Primary effusion lymphoma (PEL) is a HHV8-associated large B-cell lymphoma presenting in body effusion without forming a mass. Cases of HHV8-negative effusion-based lymphoma have been reported with distinct immunophenotype and occasional association with fluid overload status and/or HCV infection. Up to date, there is no large series of PEL with comparison of the two groups from Taiwan.

**[Materials and Methods]** 1. Patients : A total of 18 PEL cases from Taiwan were retrospectively collected, and cell blocks were available in 17 cases for study. 2. Immunohistochemistry : Antibody to bcl2, bcl6, CD3, CD10, CD19, CD20, CD138, cyclin D1, HHV8-LANA (latent-associated nuclear antigen), MUM1 and myc were used. The cut-off value of myc was set as 40% of tumor cells with nuclear staining. 3. EBV in situ hybridization (EBER) Fluorescence in situ hybridization (FISH) : Locus-specific interphase FISH with BCL2, BCL6, IGH and MYC dual color break-apart probes were used on paraffin-embedded cell block section.

**[Results]** The 18 cases included 13 males and 5 females, with M/F ratio of 2.6 and a median age of 77 (range, 46-92). The most common effusion site was pleural (78%). HIV, HBV, and HCV infection were positive in 1/7, 0/8 and 1/11 patients, respectively. Immunohistochemically, 78% cases expressed at least one of the pan B-cell markers (CD19, CD20 or CD79a) ; 35% cases expressed CD30 ; 29% cases expressed CD138. CD10 was negative in all cases. Bcl2, bcl6, MUM1, and myc was expressed in 69%, 38%, 88%, and 40% cases, respectively. Three (18%) were positive for HHV8 : 14 (82%), negative. IGH, BCL2, BCL6 and MYC were rearranged in 69%, 23%, 25%, and 25% cases, respectively. One patient was lost to follow-up. Ten patients received chemotherapy, and 7, supportive

care. In a median follow-up of 3 months (range, 0-33), 13 patients died of disease in 0 to 33 months (median, 2.5 months). The 1-and 2-yr survival rates were 33% and 13%, respectively. The HHV8-positive group (n=3) showed more frequent expression of CD30 (100% vs. 21% ; p=0.0097, Chi-squared test) as compared to the HHV8-negative group (n=14). None of the HHV8-positive cases expressed any of the pan B-cell markers or bcl2, in contrast to 93% (13/14) and 85% (11/13), respectively, in the HHV8-negative group (p=0.0058 and 0.004, respectively). EBER was positive in 33% (1/3) and 15% (2/13) cases, respectively. One HHV8-negative case was a double-hit lymphoma with rearranged IGH, BCL2 and MYC.

**[Conclusion]** 1. There are more cases of HHV8-negative PEL (or effusion-based lymphoma) than HHV8-positive classical PEL (82% and 18%, respectively) in Taiwan. Interestingly, the two HHV8-positive cases tested for HIV were both negative. The clinical settings, including age, sex, infection of HIV, HBV or HCV and fluid overload status, are not significantly different between two groups in our series. 2. The two groups reveal indistinguishable cytomorphology, but distinct immunophenotype. All 17 cases are non-germinal center phenotype without CD10 expression. But HHV8-negative cases reveal more expression of pan B-cell antigens (93% of cases), but less bcl2, CD30 and CD138 (85%, 21% and 21% of cases, respectively). 3. The positive rates of EBER and rearrangement of *BCL2*, *BCL6*, *IGH* and *MYC* loci are not significantly different between two groups in our series. 4. Both groups in our series display dismal prognosis, comparing to better prognosis of HHV8-negative cases in the series of Alexanian et al. (*Am J Surg Pathol* 2013 ; 37 : 241-249)

## PE-2-22 Intraoperative smear cytology of chordoid meningioma : a case report and literature review

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**【Introduction】** Chordoid meningioma is a rare subtype of meningioma displaying a greater tendency of recurrence and locally aggressive behavior. Herein we report features of this rare tumor by an intraoperative smear cytology and do a literature review.

**【Case report】** This 47-year-old woman complained of intermittent dizziness for months. Brain magnetic resonance images revealed a parietal tumor measuring 6.1 x 5.4 x 4.4 cm. Intraoperative smear cytology showed moderately cellular sheets of ovoid to spindle tumor cells. The cells had vesicular nuclei with small nucleoli and moderate amounts of eosinophilic cytoplasm with indistinct cell borders. Some inflammatory cells and myxoid materials were found in the background. Histologically, cords and trabeculae of epithelioid tumor cells were separated by a fibrous and mucous-rich matrix containing delicate blood vessels. Tumor cells were positive for vimentin and EMA but negative for AE1/AE3, S100, GFAP, HepPar-1, CD34 and NeuN immunohistochemically. The final diagnosis of chordoid meningioma was made. Gross total tumor resection was achieved, and no recurrence was detected after a 6-month follow-up.

**【Discussion】** Meningioma is a common intracranial tumor and majority of subtypes behave in a benign clinical manner. Chordoid meningioma is classified as WHO grade II tumors because of a high rate of recurrence and less favorable outcomes. In smear cytology, it is characterized by sheets and clusters of ovoid, vacuolated tumor cells in a background of myxoid materials and chronic inflammatory cells. The differential diagnoses include chordoma, chordoid glioma, chondrosarcoma and metastatic adenocarcinoma. Chordoma is composed of large tumor cells having copious vacuolated bubbly cytoplasm in a discohesive manner. In chordoid glioma, binucleated tumor cells with relatively

long and fibrillary cytoplasmic processes are usually seen. By contrast, bizarre and pleomorphic nuclei are characteristic of chondrosarcoma and metastatic adenocarcinoma. In chordoid meningioma, tumor cells are always bland looking. Chordoid meningioma is immunoreactive for EMA and vimentin. Stainings for S100, AE1/AE3 and GFAP are negative. In conclusion, the diagnosis of chordoid meningioma made by smear cytology is challenging owing to its rarity and different features compared to classical meningioma. A quick, correct diagnosis during intraoperative consultation depends upon successful recognition of the distinctive cytomorphology of this tumor.

### PE-2-23 A case of anaplastic oligodendroglioma that proved difficult to diagnose

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**【Background】** Anaplastic oligodendroglioma is a rare brain tumor, and few cytological reports are available. We report here a case of anaplastic oligodendroglioma diagnosed on squash cytology.

**【Case】** A man in his 70's visited a nearby hospital complaining of pain and numbness in his left hand and right leg. A mass was found in the left parietal lobe by magnetic resonance imaging and oligodendroglioma or astrocytoma was suspected clinically. Squash cytological smears showed loose clusters of tumor cells. Individual tumor cells showed abundant eccentric eosinophilic cytoplasm, like that seen in gemistocytic-like cells. Frozen section findings were consistent with those of squash cytology, and the tumor was diagnosed as gemistocytic atypical astrocytoma. After surgery, about two thirds of the tumor was found to be typical oligodendroglioma, while the remaining third was anaplastic oligodendroglioma with gemistocytic-like cells. The anaplastic oligodendroglioma was positive for OLIG2, IDH-1 and GFAP by immunohistochemistry, and a deletion of 1p19q was detected by FISH analysis.

**【Conclusion】** The intraoperative diagnosis of brain tumors is often difficult because of small sample sizes, and a more comprehensive diagnosis using IHC and FISH analysis is necessary in rare cases. The intraoperative diagnosis of brain tumors can be important to achieve a differential diagnosis.

### PE-2-24 Cytopathologic analysis in pediatric and young adult age group : review of our experiences

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**【Background】** In pediatric and young adult age group, rare various malignant tumors that have an aggressive course can be seen. A rapid accurate diagnosis for them from cytology specimens is important, although cytopathologists are relatively unfamiliar with them. We evaluate the role of cytology for young age group with our cases.

**【Methods】** We conducted a retrospective study of cytology in pediatric and young adult patients  $\leq 29$  years of age. Distribution of cases in different age groups, sample types, histologic types were analyzed.

**【Results】** 379 positive samples (2.3%) from 205 cases (2.0%) in young age group were collected from 16,676 positive samples (10,425 cases) in our institution for 22 years. Sample types were CSF (54.9%), uterine smears (23.5%), body cavity fluid (10.3%), and others. The cytological diagnosis were classified as follows : leukemias 119 (31.4%), brain tumors 90 (23.7%), uterine cervical neoplasms 84 (23.2%). In children  $\leq 10$  years of age, the most common diagnosis were leukemias 19 cases (67.9%) and brain tumors 21 cases (70%). Uterine cervical neoplasms were not found under 15 years of age. Definite diagnosis could be offered on cytology in most cases, while in 16 cases (7.8%) specific diagnosis could not be offered. Most of them were small round cell tumors like rhabdomyosarcoma, AT/RT, etc.

**【Conclusions】** Cytology is a simple and useful diagnostic procedure. This study showed an efficacy of cytology in the pediatric and young adult age group, although cytopathologists should be aware of performing immunocytochemistry and/or FISH to achieve the correct diagnosis of small round cell tumors.

**PE-2-25 A Retrospective Study on the Risk of Malignancy Associated With the Papanicolaou Society of Cytopathology Guidelines in Endoscopic Ultrasound-Guided Fine-Needle Aspiration Specimens of Pancreatic Lesions**

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**[Objective]** The Papanicolaou Society of Cytopathology (PSC) has recently proposed a standardized terminology and nomenclature guidelines for pancreatic cytology. However the risk of malignancy associated with the new guidelines has been scarcely studied. In this study, we investigated the risk of malignancy for endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) cytology according to the PSC new guidelines.

**[Methods]** 294 patients who had undergone pancreatic EUS-FNA procedures were retrospectively studied. The cytologic diagnoses were re-classified according to PSC new guidelines. The risk of malignancy was calculated and the receiver operating characteristic (ROC) curve analysis was performed.

**[Results]** The risks of malignancy were 18.1% for “negative,” 20.0% for “neoplastic,” 57.1% for “nondiagnostic,” 69.2% for “atypical,” 87.5% for “suspicious,” and 100.0% for “positive” respectively. The area under the receiver operating characteristic (AUROC) was 0.93 (95% CI, 0.90-0.96), which was significantly higher than that associated with old classification (0.82 : 95% CI, 0.77-0.87) conventionally used in China.

**[Conclusion]** Our investigation demonstrated that the new guidelines have a greater ability of risk stratification than the old classification system conventionally used in China. This may be helpful in giving better predictions of malignancy, thus leading to more personalized treatment strategies.

**PE-2-26 The Cytological examination of gastric disease for the patients on the emergency department**

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The paper discusses the cytological characteristic of inflammatory, atrophic and dysplastic changes of the gastric mucosa.

**Keywords :** Gastric mucosa, hyperplasia, intestinal metaplasia, atrophic gastritis, gastric epithelial dysplasia, *Helicobacter pylori*.

Chronic gastric diseases are one of the leading places in the clinic of internal medicine diseases. Their share in the total burden of disease is more than 60%.

*Helicobacter pylori* (HP) -one of the most common infections in the world.

Retrospectively analyzed the results of 146 cytological studies of emergency medical patients with gastric pathology for 2 years, which amounted to 584 study.

Cytological samples obtained primarily to biopsy the tissue pieces are also used blind lavage with saline is endoscopy.

**The Results :** Regardless of the method of producing the material in 81.3% cases of cytological material presented multicellular clusters covering epithelium are with severe degenerative changes, elements necrosis and infiltrations with neutrophilic leukocytes that matched the clinical diagnosis of acute gastritis. In 8.8% of cases in cytological smears detected cell secretory type glands, accumulation of covering foveolar type epithelium and intestinal metaplasia with the inflammation signs. In 7.3% of cases severe restructuring epithelial cells with reactive changes. Dysplasia of mild to moderate degree in 1.3% of cases, in 0.7% dysplasia of glandular epithelium severe structural atypia, with increased cell proliferation. In 40% studied by immersion in the epithelium of the mucous glands and surface epithelium revealed different degrees of contamina-

tion H. Pylori. Background -92% of cases, the inflammatory process, and in 8% of cases reactive regenerative epithelial changes. In 0.7% in the case detected stomach cancer.

Conclusion : 1. Application of the method of cytological diagnosis of patients admitted to the emergency hospital emergency gastric pathology, found in 80% of cases of acute gastritis, with varying degrees of inflammation prevalence of severe degree, including 40% of the cases was detected *Helicobacter pylori*.

2. Cytological examination revealed morphologic processes in the form of intestinal metaplasia, atrophy and different degrees of dysplasia epithelium of the gastric mucosa.

3. In severe dysplasia of the epithelium of the mucous membrane of the stomach to prevent gastric cancer patients should be advised to repeat the survey to take the material for histological analysis.

## **PE-2-27 Inconsistency Analysis between Fine-Needle Aspiration Cytology and Imprint Cytology during Hepatic Tumor Sampling- Five -year Experiences in a Tertiary Center**

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**[Background]** The preoperative diagnosis of suspected neoplastic hepatic lesions mostly depends on either fine needle aspiration (FNA) cytology or core biopsy. Under sonographic guidance, hepatic lesions can be detected and sampled properly and safely. The touch imprint cytology can be done at the same time on processing biopsy specimens. Previous studies have shown that both FNA and imprint cytology can yield similar sensitivity and specificity (around 85%, 100% vs. 87.1%, 100% respectively). But there did exist inconsistency of final diagnosis between these two methods. The aim of this study is to investigate the possible causes of discrepancies between FNA and imprint cytology of hepatic tumors.

**[Materials and Methods]** From January 2011 to December 2015, 4,044 cases of liver imprint and 1,245 cases of liver FNA cytology examinations were performed at our institute NTUH. Among these cases, 990 cases out of 938 patients had concurrent FNA and imprint cytology smears. All these cases were sampled under sonographic guidance, and slides were stained with both Papanicolaou and Liu's stain (a kind of Romanowsky stain). The slides of inconsistent pairs were reviewed and were compared with clinical-imaging-histopathological diagnosis.

**[Results]** Thirty seven cases had diagnostic discrepancy between FNA and imprint cytology. After excluding nine cases with consistent clinical diagnosis, cytology specimens of six cases in the FNA (+)/imprint (-) group were reviewed. Most cases (83%, 5/6) had adequate cellularity, but there was no obvious malignant cell after thorough reviewing. Twenty two cytology cases in the FNA (-)/imprint (+) group were also reviewed. Up to thirteen cases (59%) had poor cellularity for interpretation. Four

cases showed degenerated cells in the inflammatory/necrotic background. Five cases showed no obvious malignant cells after thorough microscopic reviewing.

**[Conclusion]** In this study, we've found that cellularity adequacy was one of the important causes for false-negative FNA cytology but not imprint cytology examinations. Technical improvement for proper smear preparation may be helpful for FNA(+)/imprint(-) cases. Adequate FNA sampling passes may decrease false negativity for FNA(-)/imprint(+) cases.

## **PE-2-28 Perivascular epithelioid cell tumor (PE-Coma) of the retroperitoneum diagnosed by preoperative EUS-FNA cytology : a case report**

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**[Background]** Perivascular epithelioid cell tumors (PEComas) are rare mesenchymal neoplasms which can arise from almost any location in the body.

**[Case]** A woman in her 50s with a 3.5 x 2.3-cm mass was observed in the body of the pancreas on abdominal plain CT performed to follow the course after left breast cancer surgery performed 8 years ago. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) cytology of the pancreas was performed. Wet-fixed and cell block preparations were prepared.

**[Results]** On Papanicolaou staining, atypical cells population accompanied by tumor vessels was present with small lymphocytes in the background. Atypical cells occurred cells formed a solid nest with microvacuolated, lace-like cytoplasm. Therefore, the diagnosis of this lesion based on EUS-FNA cytology findings was suspected adenocarcinoma but neither increase in chromatin nor nuclear division were observed. Therefore, it was difficult to make a diagnosis based on the cellular morphology alone. Immunostaining was performed using cell blocks. HMB-45,  $\alpha$ -SMA, and Melan-A were positive, and AE1/3, S-100, c-kit, synaptophysin, CD10, and bcl-2 were negative. Based on these, the lesion was diagnosed as a PEComa. Laparoscopic excision of the tumor was performed. It was located at the retroperitoneum alongside the inferior margin of the body of the pancreas. The excised tumor had a fibrous capsule, the boundary was clear, and the cut surface was solid with a fibrous septum. The pathological diagnosis was PEComa, the same as that on preoperative cytology.

**[Discussion]** PEComas are defined as tumors that differentiate into perivascular epithelioid cells, and angiomyolipoma in lymphangioleiomyomatosis of the kidney and liver are included. The present case was a rare tumor classified as

PEComas-NOS that originated from the retroperitoneum. Ultimately, this patient was diagnosed with EUS-FNA cytology before surgery using the cell block method.

**【Conclusion】** We report the case of PEComa and review the literature on outcomes and the search for markers associated with this rare disease.

## **PE-2-29 Expression of vimentin and high molecular weight cytokeratin in the differentiation between reactive renal tubular cells and low-grade urothelial carcinoma cells in voided urine**

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**【Objective】** Reactive renal tubular cells show features of an atypical repair reaction. Differentiation between reactive renal tubular cells and low-grade urothelial carcinoma cells (LG-UCs) therefore can be a diagnostic challenge based on morphology alone. In this study, we evaluated the diagnostic utility of vimentin and high molecular weight cytokeratin (HMWCK) antibody in differentiating reactive renal tubular cells from LG-UCs.

**【Methods】** We evaluated voided urine cytology and surgical specimens from 40 patients with renal disease, and 17 patients with low-grade urothelial carcinoma. All slides were stained with vimentin and HMWCK.

**【Results】** In the reactive renal tubular cells in voided urine cytology, vimentin showed strong cytoplasmic staining in 39/40 (97.5%) cases, but all forty cases were negative for HMWCK. The LG-UCs showed positive for HMWCK in 3/17 (17.6%) cases, whereas none were positive for vimentin. The reactive renal tubular cells of histological specimens in the renal disease group demonstrated positive for vimentin in all (40/40) cases, but all 40 cases were negative for HMWCK. The low-grade urothelial carcinoma group showed abnormal staining for HMWCK in 4/17 (23.5%) cases, whereas none were positive for vimentin.

**【Conclusions】** Vimentin expression in urine cytology can help to distinguish reactive renal tubular cells from LG-UCs. However, HMWCK does not appear to be a useful adjunct to distinguish these 2 groups in voided urine cytology.



**PE-2-30 Type 2 papillary renal cell carcinoma invasion of the renal pelvis by pelvic irrigation cytology**

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**[Objective]** Papillary renal cell carcinoma (pRCC) is a comparatively common tumor comprising about 7–15% of all malignant renal tumors. However, the previous reports of pRCC were based on fine-needle aspiration or tumor imprint cytology. To our knowledge, there are no reports of using pelvic irrigation cytology to diagnose pRCC.

**[Case]** We here report a case of type 2 pRCC that was diagnosed by pelvic irrigation cytology. The patient was 74-year-old man presented with hematuria during hospitalization in the Coronary Care Unit due to a heart disorder. Renal tumor was detected. After urine and pelvic irrigation cytology, nephrectomy was performed.

**[Results]** On pelvic irrigation cytology, numerous large and small papillary clusters composed of atypical cells having abundant cytoplasm were seen in the necrotic background. The most cytoplasm were granular and a few cells which has clear cytoplasmic features. Macrophages were not found in the background. Histologically, the tumor cells were similar to those of cytology. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) 7, vimentin, epithelial membrane antigen, CD10, alpha-methylacyl-Co A racemase, and negative for CK 20 and CK34βE12, TFE3.

**[Conclusions]** Finally, the tumor was diagnosed as type 2 pRCC. Although, it is necessary to differentiate type 2 pRCC from other diseases on cytology, we consider the diagnosis of type 2 pRCC may be established by meticulous cellular observation.

**PE-2-31 Malignant lymphoma in urine cytology : a report of two cases with B cell lymphoma involving urinary bladder and kidney**

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**[Objective]** Diagnosis of malignant lymphoma in urine cytology is very rare and difficult. We describe the cytomorphological features of lymphoma cells in urine cytology and discuss the differential diagnosis.

**[Methods]** We report two cases with secondary lymphoma involving the urinary bladder and kidney. We also carry out a review of the literature regarding the infrequency of this cytology.

**[Results]** Case1 : A 65-year-old male was admitted because of hematuria. Urine cytology showed individualized single abnormal cells with high N/C ratio and irregular nuclear contour. The final pathologic diagnosis was large B cell lymphoma involving urinary bladder. Case 2 : A 61-year-old male had a history of hepatocellular carcinoma and chronic renal disease. He presented with dysuria, nocturia (about >3–5 times/night), frequency (void >12 times/day) and hematuria. Urine cytology showed many single large pleomorphic cells with high N/C ratio. Mitosis was conspicuous. The background had obvious necrotic debris. The final pathologic diagnosis was large B cell lymphoma involving kidney.

**[Conclusion]** Diagnosis of malignant lymphoma in urine cytology is infrequent and difficult. The most important characteristic is a lack of cellular cohesion, followed by tumor cells with high N/C ratio and scanty cytoplasm. Furthermore, the immunocytochemistry and the clinical history are also very important in differential diagnosis between malignant lymphoma and high-grade urothelial carcinoma.