CANADIAN ASSOCIATION OF PATHOLOGISTS | ASSOCIATION CANADIENNE DES PATHOLOGISTES

ABSTRACTS – RÉSUMÉS

JUNE 8–12, 2013
64TH ANNUAL SCIENTIFIC MEETING
QUEBEC CITY, QUEBEC

8 AU 12 JUIN 2013
64 ASSEMBLÉE ANNUELLE SCIENTIFIQUE
QUÉBEC CITY, QUÉBEC
**O010**

**COMPARISON OF VISUAL AND AUTOMATED SCORING OF MMP-14 TISSUE EXPRESSION FOR THE EVALUATION OF OVARIAN CANCER PROGNOSIS.**

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**Objectives:** The purpose of this study was to evaluate how the membrane-anchored collagenase MMP-14 tissue expression, as assessed by a virtual microscopy method and by an automated digital image analysis, could predict the occurrence of death and progression in women with epithelial ovarian carcinoma (EOC). **Methods:** A tissue microarray series of EOC from a cohort of 211 women operated between 1993 and 2006 at CHU-L'Hôtel-Dieu de Québec was immunostained for MMP-14 and digitized. The extent of MMP-14 staining was assessed both visually by three pathologists and with an image analysis algorithm created with Calipix™ software (developed by TRIBVN, distributed by Agfa Healthcare). Progression was assessed using the CA-125 criteria and the RECIST criteria. Dates of death were obtained by linkage with the Québec mortality files. Correlations between MMP-14 expression, standard EOC prognostic factors, progression and mortality were calculated, as well as correlations between the two MMP-14 assessments. **Results:** Visual and automated scoring of MMP-14 tissue expression showed the same relations to standard EOC prognostic factors. Higher MMP-14 immunostaining correlated significantly with non-serous histology, low FIGO stage and low pre-operative CA-125 levels (p<0.05). MMP-14 overexpression was inversely associated with progression of disease for visual (HR=0.39; 95% CI: 0.16-0.82) and digital scores (HR = 0.48; 95% CI: 0.28-0.82), but only reached borderline significance for mortality. However, the association was no longer significant after correction for others EOC prognostic factors. Lastly, the distribution of automated scores for MMP-14 immunostaining area correlated with the visual scoring categories (>40% vs 21-40 vs <20%; p<0.05). **Conclusions:** MMP-14 overexpression is associated with early stage and more favorable prognosis, but does not sort out as an independent prognostic variable for EOC in our cohort. These results show a good agreement between visual and automated scoring of MMP-14 immunostaining, supporting the use of digital image analysis even in highly heterogeneous tissues such as OC.

**O012**

**PERFORMANCE OF CELLAVISION DM96 IN LEUKOCYTE CLASSIFICATION.**

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**Background:** Leukocyte differentials are an important component of clinical care. Morphologic assessment of peripheral blood smears may be required to accurately classify leukocytes. However, manual microscopy is labor intensive. The CellVision DM96 is an automated system that acquires digital images of leukocytes on peripheral blood smears, preclassifies the cell type, and displays them on screen for a technologist or pathologist to approve or reclassify. Our study compares the results of the DM96 with manual microscopy. **Methods:** Three hundred and fifty-nine peripheral blood smears were selected and assessed by manual microscopy with a 200 leukocyte cell count. They were then reassessed using the CellVision DM96 with a 115 leukocyte cell count including reclassification when necessary. Correlation between the manual microscopy results and the CellVision DM96 results was calculated for each cell type. **Results:** The correlation coefficients (r²) range from a high of 0.99 for blasts to a low of 0.72 for promyelocytes. **Conclusions:** The correlation between the CellVision DM96 and manual microscopy was as good or better than the previously published data. The accuracy of leukocyte classification depended on the cell type, and in general, there was lower correlation for rare cell types. However, the correlation is similar to previous studies on the correlation of manual microscopy with an established reference result. Therefore, the CellVision DM96 is appropriate for clinical implementation.

**O013**

**WHEN INITIAL SECTIONS OF COLORECTAL POLYPS DON'T SHOW AN ABNORMALITY, DEEPER LEVELS DO: IMPLICATIONS FOR PRACTICE AND SUBSEQUENT PATIENT MANAGEMENT.**

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**Background:** Microscopic examination of colorectal biopsies obtained from lesions identified endoscopically as polyps sometimes fails to identify an abnormality on the initial tissue sections, but a polyp may be found if deeper levels are cut from the tissue block. The objective of this study was to determine the frequency with which deeper levels reveal a lesion, where none was found initially. **Methods:** All “polyp” biopsy cases where no polyp was identified on the initial, standard sections were consecutively accumulated over an 18-month period, from the practice of a single pathologist. Standard sections included preparation of three slides, each with 2 serial sections, with each set of serial sections cut at deeper levels, 50µM apart. In each case where no polyp was identified initially, three additional levels were cut, 50µM apart. **Results:** Fifty-one cases were accrued. The mean number of biopsies received per case was 1.26 (range 1-6); the mean maximum dimension of the largest piece was 0.36 cm (range 0.2-0.7 cm). The deeper levels revealed a lesion in 18/51 (35%) cases (17 tubular adenomas, 1 hyperplastic polyp). All adenomas were negative for high-grade dysplasia and malignancy. **Conclusion:** In approximately one-third of cases, deeper levels on initially non-diagnostic colorectal polyp biopsies yielded a polyp, almost exclusively adenomas. This is despite cutting three levels initially from the block. As the presence of an adenoma will affect subsequent colonoscopic screening of average-risk individuals, pathologists should consider “pursuing” polyps when initial sections reveal no lesion. We are furthering this study with the review of an additional 322 similar cases.

**O014**

**A STATISTICAL MODEL FOR ESTIMATING TOTAL QUALITY DEFECTS FROM TWO IMPERFECT DETECTORS IN A HEALTHCARE SETTING.**

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**Introduction/Objective:** Quality defect detection systems designed to improve quality of healthcare are a cornerstone of modern medicine. The objective of this study is to develop a statistical model for estimating the expected total number of quality defects by synthesizing estimates from multiple detectors. **Method:** We used Poisson distributions to model number of errors identified by the detectors separately and in combination. We then used probability relations to provide an estimate for the total number of errors. Extensive simulations were performed to validate the performance of our estimate and compare the results with a real-world healthcare quality improvement study. **Results:** The results from the simulations demonstrate that our statistical model and the proposed estimate perform well, with average estimates lying within 1% of the true values, including the real-world scenario. In situations where the number of error counts identified by both detectors is close to zero, we were able to provide lower and upper bounds for the expected total number of errors. **Conclusions:** The statistical model proposed in this study can be applied to provide the minimum, maximum, and total number of quality defects in a given healthcare setting.
O105 DEALING WITH UNCERTAIN DATA IN PATHOLOGY RESEARCH: A BIOMARKER META-ANALYSIS USING BAYESIAN COMPUTATIONAL METHODS.

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Uncertain, unreliable, or partially-missing data is commonplace in clinical and translational research. For example, a study of tumour VEGF expression levels by mass spectrometry finds that archival tissue has been exhausted in 20% of study patients, although immunohistochemistry results (positive/negative) are available. A classical approach would discard the 20% with less precise measurements, or study them separately. However, these approaches may introduce bias and decrease statistical power. Modern computational methods allow the use of Bayesian techniques to make probabilistic statements about uncertain data (so-called “fuzzy” data points) in a principled fashion, thereby allowing the inclusion of imprecise, missing, or heterogeneous data in appropriate circumstances. We investigated this approach in a meta-analysis study of germline FC gamma receptor polymorphisms as biomarkers of patient survival in cetuximab-treated colorectal cancer. The study goal was to synthesize results across multiple papers on the same topic; however, while the standard data (hazard ratios with standard errors) was available in 3/5 studies, the two remaining studies reported only approximate results (median survival times by group). We used Bayesian modeling to include these “fuzzy” data points in the analysis using Markov chain Monte Carlo (MCMC) sampling in R (v.2.15.1) and JAGS (v.3.3.0). Two models, one including and the other excluding the uncertain data, were constructed and used to estimate parameters for the global effect of FC gamma receptor polymorphisms on survival. A comparison of these models is used to demonstrate the potential impact of ignoring uncertain information, including biased results, reduced statistical power, and a fragmented interpretation. Conversely, potential drawbacks of incorporating uncertain information include the introduction of greater variability into results and bias due to the specifics of modeling decisions.

O106 ROLE OF CLINICAL PATHOLOGISTS ACHIEVING THE MILLENNIUM DEVELOPMENT GOALS BY 2015 IN ASIA.

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Millennium Development Goals (MDGs) is an agreement of 189 countries of the United Nations, which is have a goal to achieve welfare and development of the world community in 2015. There are 8 points of the development goals in the MDGs as a package measurable objective for development and poverty alleviation. Some of them are closely related to health sector and require appropriate diagnostic uses science abilities and competencies of Clinical Pathologists. Determination of HIV/AIDS, malaria, tuberculosis (TB), other infectious diseases as well as efforts to reduce neonatal and maternal mortality need the support of a good quality of medical laboratories. These cases are still quite high in number and also have lot of problems in most of Asian countries. Clinical Pathologists in their role as person in the area of management and technical management of the laboratory medicine shall have the ability and knowledge to take responsibility for delivering the laboratory results and diagnostic accurately determine cases related MDGs. Awareness and sensitivity inscreening-high-risk groups inscenario communable disease, also for neonatal and maternal health monitoring are very important. As well asthe participation of Clinical Pathologistsforformulateative policies inparticular groups cirtainlygovernment needed. Expected insight on the MDGs is encouraging us to work together in teams with clinicians and laboratory personnel and disseminate partnership with all elements of both the Ministry of Health and other sectors related to health. With extend this insight we hope that our expectation toward the MDGs by2015 can be realized.

O201 ANALYSIS OF HER2 POSITIVE PATIENTS BY HORMONE RECEPTOR STATUS.

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Context: In gene expression profiling experiments hormone receptor positive/HER2-positive (HR+/HER2+) tumours generally cluster within the luminal B subtype, whereas HR-negative/HER2-positive (HR-/HER2+) tumours reside in the HER2-enriched subtype. Objectives: The objective of this study was to compare the pathologic characteristics, local recurrence rates and outcome between these two groups of tumours. Methods: 989 T1 or T2, lymph node negative, primary invasive breast cancers treated with breast conserving surgery (BCS) and adjuvant radiation had formalin fixed paraffin embedded (FFPE) tumour blocks available for tissue microarray (TMA) construction. Immunohistochemistry for ER, PR and HER2 was performed on TMA sections and a centralized pathology review was performed on one full face section of tumour by an expert breast pathologist. A tumour was defined as HR+ if either ER or PR were positive and HR- if both receptors were negative at the 1% level. Fisher’s, Cochran-Armitage and log-rank tests were used to compare tumours by HR status. Results: 115 (11.6%) HER2+ tumours were identified, 76 HR+ and 39 HR-. HR-/HER2+ tumours were more likely to be characterized by high histological grade (41.9% vs 17.7%, p=0.006), a prominent per-tumour lymphocytic infiltrate (34.6% vs 16.2%, p=0.04) and circumscribed/pushing tumour margins (39.4% vs 13.2%, p<0.005) than HR+/HER2+ tumours. HR-/HER2+ tumours were more likely to experience a local recurrence (16.9% vs 7.3% at 10 years, log-rank test p=0.02) but there was no significant difference in disease free survival (DFS) (68.9% vs 70.7% at 10 years, log rank test p=0.33) or overall survival (OS) (86.9% vs 85.3% at 10 years, p=0.48) between the two groups. Conclusions: Pathologic tumour characteristics and incidence of local recurrence following breast conserving therapy for HER2+ tumours differed by HR status. However, DFS and OS were equivalent for both groups.

O202 CADHERIN-CATENIN EXPRESSION PROFILE IN OVARIAN CARCINOMA.

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Rationale: Epithelial-mesenchymal transformation contributes to tumor metastasis. Cell-to-cell adherence molecules are thought to play an important role in this process. Foremost among these are the cadherin and catenin family of proteins, which help cells bind to and communicate with each other. Comprehensive expression of most cadherins and catenins in ovarian neoplasms remains to be studied. Hypothesis and Objectives: Differential protein expression and localization of cadherins and catenins correlates with clinicopathologic parameters of ovarian neoplasms. We compared the protein expression and distribution of E-, N- and P-cadherin, catenin-11, beta-catenin, plakoglobin and p120 catenin in the clinicopathologic parameters and therapeutic response in stage III and IV ovarian neoplasms. Methods and Results: Expression of E-cadherin, N-cadherin and beta-catenin was evaluated in a preliminary tissue microarray of 15 serous, 9 mucinous, 6 clear cell, 3 endometrioid and 3 malignant mixed mullerian tumors. Cytoplasmic expression of E-cadherin was significantly lower (p<0.05) in mucinous and endometrioid tumors, compared to the other groups, whereas membranous expression was similar. There was very strong membranous expression of N-cadherin and beta-catenin in all the neoplastic tissues compared to adjacent non-neoplastic ovarian surface epithelium. Interestingly, skipping pattern of beta-catenin expression was noted in 80-90% of clear cell carcinomas compared to only ~30% of other neoplasms. Conclusion: In contrast to previous studies, we noted increased membranous expression of E-cadherin in our case series of stage III-IV ovarian neoplasms. Whether or not skipped pattern of beta-catenin expression is associated with specific mutations conferring a clear cell morphology needs further investigation.
O203

CUTANEOUS MANIFESTATIONS OF ANGIOIMMUNOBlastic T-CELL LYMPHOMA.

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Objectives: Angioimmunoblastic T-cell lymphoma (AITL), a neoplasm of follicular helper T-cells (Th), displays cutaneous manifestations (AITL/C) in approximately 50% of cases. These are poorly characterized. Our objective was to conduct a retrospective study of a series of cases of AITL/C to better define this aspect of the disease. Methods: The study population included 11 patients (24 skin biopsies) with AITL/C and 20 control patients (25 skin biopsies) with inflammatory (CI) and non-AITL lymphomatous (CL) disease (1990-2012). Clinical data was documented in each case. A blinded review of the routine histopathology (lymphoma or not) was performed. Additional investigations included immunohistochemistry (IHC): CD5, CD20, K67, BCL6, CXCL13 and PD-1, and molecular studies: PCR for T and B cell gene rearrangements, and in situ hybridization for EBV.

Results: Clinically, AITL/C ranged from (a) a diffuse, pruritic, erythematous rash through (b) papules to (c) plaques and nodules, with sequential evolution from (a) to (b) to (c). Deranged routine laboratory tests of AITL skin biopsies were suggestive of lymphoma while diagnostic concordance was higher (69%) in the control group (CH-CL). Th cell (IHC) markers showed more positivity in AITL biopsies than in CI (CXCL13 62% vs 30%; PO-1 86% vs 20%). T-cell clones identified in 76% of AITL biopsies and in 56% of CI. EBV positive cells were found in 14% of AITL biopsies and in none of the CI. Conclusions: Identification of AITL/C is difficult and no single diagnostic test is sufficient to establish the diagnosis. Knowledge of the clinical and histopathological spectrum of the disease, and appropriate use of ancillary studies will facilitate investigation of such cases.

O204

CLINICAL USE OF THE LABORATORY TUMOUR MARKER CARCINOEMBRYONIC ANTIGEN IN THE ACUTE MANAGEMENT OF PATIENTS.

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Context: Current guidelines suggest the tumour marker CEA (CarcinoEmbryonic Antigen) be used to monitor response and detect recurrence in established malignancies. Little evidence exists surrounding its use in the screening and diagnosis of malignancies, as it is neither sensitive nor specific for one disease entity. Additionally, false positive results may lead to further unnecessary investigations with known morbidity and substantial costs to the healthcare system. As laboratory physicians, understanding the ordering trends, value and limitation of a test can help us educate our clinical colleagues on the appropriate use of laboratory operations. Objective: To quantify parameters that influenced a clinician’s decision to order CEA and to analyze whether the test was meant to diagnose, screen or monitor a patient. Finally to stratify whether ordering the test changed the initial management of the patient. Methods: The charts of patients, seen in the emergency room of the Jewish General Hospital, who had a CEA blood test ordered between March 1st and August 30th 2012, were reviewed. Results: In the 6 month period reviewed a total of 159 tests were ordered. Of these 159 orders, 138 (87%) were ordered to diagnose, 18 (11%) to monitor and 3 (2%) were ordered erroneously. Of these 159 tests, 150 (94%) tests did not change the management of the patient. Of the 9 (6%) tests which did, 3 (2%) positively and 6 (4%) negatively affected management. Conclusions: The use of CEA, in the acute care hospital setting, does not help in the management of patients. In a small subset of patients, CEA results had a positive impact on management but this was offset by cases where the use of CEA led to further delay in appropriate care, detrimental investigations and needless costs.

O205

QUANTITATIVE PROTEOMIC ANALYSIS IN RENAL CELL CARCINOMA REVEALS POTENTIAL DIAGNOSTIC MARKERS AND PATHWAYS INVOLVED IN PATHOGENESIS.

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There are currently no biomarkers for the early and accurate detection of clear cell renal cell carcinoma (ccRCC). Diagnosis and the decision of nephrectomy rely on imaging studies, which are not always accurate. We preformed high throughput quantitative proteomics analysis using isobaric tags for relative and absolute quantitation (iTRAQ) labeling and LC-MS/MS analysis to analyze ten pairs of matched ccRCC and normal kidney tissue. We found 55 proteins that were significantly dysregulated in ccRCC compared to normal kidney tissue. Dysregulated expression of secretory proteins with potential diagnostic utility including ENO1, LDHA, HSPB1, HSPA1 and AHNK were verified by western blot and immunohistochemistry analyses on two independent sets of patients. Furthermore, we measured their expressions in patient serum and urine to identify potential diagnostic markers. This study is the first comprehensive quantitative proteomics analysis in RCC, and can pave the road to the development of an accurate test for early detection of kidney cancer and the confirmation of the nature of kidney masses without the need for invasive biopsies.

O206

CONCENTRATION OF PROTEIN DISULFIDE ISOMERASE FAMILY MEMBER 4 (PDIA4) IN PATIENTS WITH BREAST CANCER METASTATIC IN JAKARTA, INDONESIA.

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Background: Protein disulfide isomerase (PDI) is a member of the threodoxin superfamily that is secreted in the lumen of the endoplasmic reticulum (ER) in mammalian cells. PDI catalyzes disulfide bond formation, reduction, or isomerization of newly synthesized proteins in the lumen of the ER. PDIA4 is a member of the PDI family, which is also expressed in the mammary gland. Low expression of PDIA4 probably as a result of the stress of RE in hypoxic conditions. These conditions will enhance the ability of tumor cells in mammary tissue to divide aggressively and metastasize.

Methods: A total of 61 breast cancer patients aged 23-90 years (80 women and 1 man) in Jakarta, Indonesia have participated in this study after signing the informed consent. The diagnosis of metastasis is confirmed by examination of bone scanning. Measurement of PDIA4 concentration is performed by the quantitative enzyme-linked immunosorbent assay (ELISA) using a commercial kits. Results: Based on the examination of bone scanning, there were 23 (62.5%) subjects with metastatic and 38 (37.5%) subjects non-metastatic. The mean of age of the subjects with metastatic were significantly higher than non-metastatic subjects (p = 0.028), which is 51.4 (45.9-56.8) and 44.2 (40.4-48.0). The median of PDIA4 concentrations in serum of subjects with metastatic, i.e. 7.7 (1.0-37.2) ng/ml was significantly lower than non-metastatic subjects (p = 0.044), i.e. 9.4 (2.2 - 69.6) ng/ml. Conclusion: The concentration of PDIA4 in serum of breast cancer patients with metastatic were significantly lower than non-metastatic patients. It shows that the concentration of PDIA4 have decreased in incidence of breast cancer metastatic.
P301  MOLECULAR PRENATAL DIAGNOSIS OF A SPORADIC ALOBAR HOLOPROSENCEPHALIC FETUS: GENOTYPE-PHENOTYPE CORRELATIONS.
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Holoprosencephaly is the most common forebrain malformation syndrome with a multifactorial etiology. Currently, mutations are identified in 5-10% of nonsyndromic, non-chromosomal cases in at least 12 genes. We report the molecular prenatal diagnosis of a fetus with alobar holoprosencephaly. Standard CTG band karyotyping and aCGH genome-wide scanning failed to identify plausible chromosome imbalances or structural anomalies. However, extensive sequencing of the genomic DNA from the fetus and both parents were undertaken on all exon and exon-intron boundaries of the four most commonly mutated genes: SHH, ZIC2, SIX3 and TGIF, in search of a molecular etiology and with comparison of findings to prior cases. We identified codon 100 of the sonic hedgehog (SHH) gene having a hotspot for loss-of-function mutations in our case and others. Interestingly, mutations in this codon were discovered in both sporadic and autosomal dominant inherited cases with evidence of variable expressivity and penetrance. Collectively, this study reinforces the complexity of genotype-phenotype correlations in the prenatal diagnosis of holoprosencephalic fetuses.

P302  SYSTEMIC SUPPURATIVE/NECROTIZING GRANULOMATOUS DISEASE FOLLOWING TUMOUR NECROSIS FACTOR INHIBITOR THERAPY FOR PSORIASIS.
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Treatment of inflammatory arthropathies with tumour necrosis factor (TNF) inhibitors has been linked with various complications including reactivation of infections and granuloma formation. The first fatal case of systemic suppurative granulomatous disease in a 41 year old man is reported. The patient was started on a TNF inhibitor etanercept, a dimeric soluble fusion protein, due to severe cutaneous psoriasis and deforming psoriatic arthritis with a good initial response. Three months later, he presented with fever, emesis, diarrhea, fatigue, melena and pancytopenia. His 3-month hospital stay was also complicated by respiratory distress requiring intubation, disseminated intravascular coagulation requiring transfusions, encephalopathy with hepatic and renal failure. He did not respond to treatment and died from respiratory failure, sepsis and hepatorenal failure. Autopsy revealed widespread caseating granulomas and multinucleated giant cells were identified in the spleen, liver, lungs, bone marrow and kidneys, with negative special stains for microorganisms and absence of foreign material. Periporal lymphadenopathy was noted with diffuse effacement of the lymph node. Histologically, suppurative/necrotizing non-caseating granulomas and multinucleated giant cells may be related to bone marrow involvement, and etanercept therapy may have significantly challenged the immune system with systemic granuloma formation resulting in fatal multi-organ failure.
P305

HTR1A EXPRESSION AND PROGNOSIS OF WOMEN WITH OVARIAN EPITHELIAL CANCER.

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Background: Ovarian cancer (OC) is the fifth most common cause of cancer-related death in women. A better prediction of prognosis could improve the medical management of women with OC. The literature suggests that High Temperature Receptor A1 (HTR1A) is downregulated in several tumors and might be associated with cancer prognosis. Objective: To evaluate the impact of the downregulation of HTR1A in tumor tissues on prognosis of women with a first diagnosis of epithelial OC. Methods: Nuclear and cytoplasmic immunohistochemical intensities (measured 0-1) of HTR1A were evaluated on cancer cells on tissue microarrays (TMA) with a visual and computerized method. These TMA contains tumors from a cohort of 164 women with a first diagnosis of OC and who received a standard treatment. Data on progression, death and standard prognostic factors were collected in medical files. Cox regression multivariate models taking into account standard prognostic factors were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). Results: The nuclear downregulation (intensity 0-1 vs 2-3) of HTR1A was associated with a lower risk of progression (HR=0.52, CI 95% [0.33-0.83], p=0.006) and of mortality (HR=0.57, CI 95% [0.34-0.95], p=0.03). The cytoplasmic expression of HTR1A was not significantly associated with progression (HR=0.77, p=0.4) and death (HR=0.64, p=0.15). No association with prognosis was found when HTR1A was assessed by the computerized method. Conclusion: The results show that nuclear downregulation of HTR1A is associated with a better prognosis in women with OC.

P306

BIOMARKERS OF SYSTEMIC INFLAMMATION AND OXIDATIVE STRESS IN CHRONIC PULMONARY DISEASE.

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Oxidative stress and inflammation play an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). More studies are needed to identify biomarkers of severity, risk and pharmacological target of disease. The aim of this study was to evaluate oxidative stress and inflammatory biomarkers in the progression/severity of COPD. We studied 20 patients with stable COPD. A biomarker of oxidative stress, malondialdehyde (MDA) and C-reactive protein (CRP) levels were evaluated. COPD patients had a significant (p<0.001) increased MDA levels (8.54±9.1,226 nmol/ml) compared with control group (3.83±0.310 nmol/ml). Increased MDA levels were related to higher CRP levels (≥3mg/ml) in moderate and very severe COPD. The increase in oxidative stress and inflammation is associated with the severity of the disease. The circulating CRP levels and MDA levels may be regarded as important biomarkers of chronic obstructive pulmonary disease.

P307

STUDY OF MMP9 EXPRESSION IN BREAST CANCER.

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Context: In 2012, cancer still accounts for a significant number of patients’ deaths throughout the world mostly due to tumor relapse and metastasis. There is currently a great interest in identifying cancer biomarkers and signaling pathways mechanistically related to breast cancer progression. Matrix metalloproteinase 9 (MMP9) is a member of matrix degrading enzymes thought to be involved in cancer development, invasion and metastasis. Objective: To correlate MMP9 expression in normal human breast tissue with breast cancer of various histological types, SBR-EE grades and molecular subtypes of breast cancers. Methods and Results: Tissue microarrays from 284 breast cancer patients were studied with IHC to measure both MMP9 along with a comprehensive set of breast cancer biomarkers. Significant increase in MMP9 expression was found in breast cancer cells when compared to normal breast tissue. Furthermore, our results indicate that not only MMP9 is differentially expressed between each molecular subgroup but that it also segregates with subsets of high histological grade tumors (Triple Negative & HER2+). Conclusion and significance: Differential expression of MMP9 reflects degrees of differentiation in breast cancer cells and is closely related to molecular subtypes of breast cancers. Our hope is that MMP9 can be used clinically to predict disease relapse in breast cancer patients.

P308

THE CHROMATIN REMODELING GENE, ARID1A, IS A NEW PROGNOSTIC MARKER IN CLEAR CELL RENAL CELL CARCINOMA

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Objective of the Study: Clear cell renal cell carcinoma (ccRCC) is the most common tumor of the adult kidney with increasing rate of incidence. Exome sequencing suggested that aberrant chromatin regulation is a key step in kidney cancer pathogenesis. Here we demonstrate the clinical utility of ARID1A and its protein product BAF250a, an ATP-dependent chromatin remodeling factor, as a prognostic marker. Methods: Immunochemistry assessed BAF250a expression. Cox regression analysis and Kaplan-Meier curves were used for survival analysis. Gene expression data, overall survival data and copy-number data were acquired from publicly available databases. Results: We detected copy number loss of ARID1A in 16% of ccRCC cases. Immunochemistry indicated that 67% of ccRCC had significantly lower expression of BAF250a, the protein product of ARID1A, than the matched normal kidney. In-silico miRNA expression analysis of 404 ccRCC tumors and 167 normal kidney samples confirmed significant downregulation of ARID1A in 68.8% of the cases. Decreased BAF250a protein and ARID1A mRNA expression correlate with tumor stage and grade. Conclusion: Both protein and mRNA levels of ARID1A are statistically significant prognostic markers for ccRCC. BAF250a immunochemistry is easy to perform and may serve as an adjuvant prognostic tool in the clinic.

P309

miR-192, miR-194 and miR-215: A CONVERGENT MIRNA NETWORK SUPPRESSING TUMOR PROGRESSION IN RENAL CELL CARCINOMA

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miRNAs play a crucial role in tumor progression and metastasis. We and others recently identified a number of miRNAs that are dysregulated in metastatic, compared to primary renal cell carcinoma (RCC). Here, we investigated three miRNAs that are significantly downregulated in metastatic tumors: miR-192, miR-194 and miR-215. Gain-of-function analyses showed that restoration of their expression decreases cell migration and invasion in RCC cell lines, while knockdown of these miRNAs resulted in enhancing cellular migration and invasion abilities. We identified three targets of these miRNAs with potential role in tumor aggressiveness; MDM2, TMY5, and SIP1/ZEbeta. We observed a convergent (the same molecule can be targeted by all three miRNAs) and a divergent (the same miRNA can control multiple targets) effects for these miRNAs. We experimentally validated these miRNA-target interactions using three independent approaches. First, we observed that miRNA overexpression significantly reduces the miRNA and protein levels of their targets. In the second, we observed significant reduction of the luciferase signal of a vector containing the 3’UTR of the target upon miRNA overexpression. Finally, we show the presence of inverse correlation between miRNA changes and the expression levels of their targets in patient specimens. We also examined the prognostic significance of miR-215 in RCC. Lower expression of miR-215 is associated with significantly reduced disease-free survival time. These findings were validated on an independent dataset from The Cancer Genome Atlas. These results can pave the way to the clinical use of miRNAs as prognostic markers and therapeutic targets.
P310 AGREEMENT BETWEEN ROCHE 25-OH VITAMIN D3 AND TOTAL 25-OH VITAMIN D ASSAYS.
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The choice of assays for Vitamin D measurement has widened in recent years with reformulation of some existing assays. Roche recently replaced their 25-hydroxy vitamin D3 (D3) assay with a total 25-OH vitamin D (TD) assay. This study compares results from the 2 assays using the Institute of Medicine (IOM) guidelines for 25-OH vitamin interpretation. D3 and TD were measured on 124 anonymised left-over patient serum samples on a Roche Diagnostics e601 analyser and statistical analysis performed using Analyse-It v2.26. The mean bias (TD – D3, µg/L) was 12.3% (95% CI: 10.9-13.7) with 95% limits of agreement of -3.04 to 27.67. Deming regression showed TD = 1.23 (0.99-1.48) x D3 + 8.77 (5.58-11.95), r=0.77. Using IOM criteria, the weighted kappa score was 0.19 (0.12-0.27), indicating poor agreement between the 2 assays. 69% of all D3 results were reclassified with the TD assay as TD < 12 µg/L, reclassified in <12 µg/L category, 93% in 12-24 µg/L category, 18% in 25-50 µg/L category). Roche Total 25-OH vitamin D concentrations are higher than 25-OH vitamin D3 concentrations as anticipated but the magnitude of the difference (average 46% overall, 60% higher at D3 < 12 µg/L) is unexpected high. An 80-90% reduction in the prevalence of vitamin D deficiency (<12 µg/L) and inadequacy (12-19 µg/L) can be anticipated with use of the new Roche total 25-OH vitamin D assay.

P311 IS THERE SEASONAL VARIATION IN 25-OH VITAMIN D CONCENTRATIONS IN SUNNY SINGAPORE?
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Despite its equatorial position and high number of sunlight hours per year, there is a high prevalence of low total 25-OH vitamin D (TD) concentrations, especially in Indians and Malays. This study examined whether there is a seasonal difference in TD concentrations in Singapore. Anonymised records of all TD measurements performed between July 2011 and December 2012 were extracted for analysis using Microsoft Excel, Access and SPSS v13. TD measurement was performed on a Roche Diagnostics e601 analyser. Repeat samples were excluded. Linear regression analysis for TD as output variable and age, sex, race, inpatient/outpatient status and month as predictor variables was performed. There were 8122 records included in the analysis. 71.1% Chinese, 10.8% Indian, 5% Malay; average age 69 yrs; 72% male; 47% outpatient. Monthly results averaged 433 (320-512). The results from linear regression analysis showed no systematic pattern of seasonal or monthly variation in TD concentrations. There was a maximum difference of 22% between months when Jan vs. Jun (Jan higher by 4.4 µg/L) and Jan vs. Dec (Jan higher by 3.3 µg/L). There is no evidence of seasonal or monthly variation in TD concentration in Singapore. Differences in monthly averages may reflect calibration effects and are clinically trivial. Time of year does not need to be considered when interpreting TD concentrations in Singapore.

P312 MicroRNA SIGNATURE DISTINGUISHES EARLY FROM LATE BIOCHEMICAL FAILURE IN PROSTATE CANCER.
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Objectives of the Study: The introduction of PSA testing, led to over-diagnosis and over-treatment of prostate cancer (PCa). There is currently no biomarker that can predict disease aggressiveness at the time of surgery. miRNAs are short non-coding RNA molecules that are shown to regulate cancer pathogenesis and progression by direct regulation of their target mRNAs. Hypothesis: Expression values of miRNAs can be used in a statistical model to accurately predict the risk for biochemical failure. Methods: 575 primary prostate tumors were collected from patients undergoing radical prostatectomy at our institution. Expression of 278 miRNAs was screened using the Human miRNA Expression Panel. Linear regression models were built to predict the development of tumor. Results: 25 miRNAs were significantly differentially expressed between the ‘high risk for biochemical failure’ group (biochemical failure within 24 months, n=26) and ‘low risk for biochemical failure’ group (no biochemical failure for > 36 months, n=15). Three logistic regression models were developed for PPV reaching 98.7%. Differential miRNA expression and the best performing model were validated on an independent PCa set (n=72). Overexpression of miR-152, downregulated in the ‘high risk’ group, reduced cell proliferation of PCa3 and DU145 cells. miR-331-3p and miR-20a can directly target E2F3 and ErbB2, that represent an alternative pathway for AR activation. Conclusion: miRNAs are potentially useful biomarkers of prostate cancer progression. Differential expression of miR-331-3p and miR-152 could contribute to the androgen independent activation of the AR by targeting the E2FBB family.

P313 COMBINATION OF INFORMATICS STRATEGY AND PRECLINICAL INVESTIGATION PROVIDES DEEPER INSIGHT INTO THE HIGH HUMIDITY HYPOXIA INDUCED CELL STRESS.
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Cell stress induced by the high-altitude hypoxic conditions is a complex process, moreover, contains a lot of significant information about frequent diseases and available techniques. However, to get the big picture by using traditional clinical laboratory techniques is a challenge. For obtaining an intensive insight into the diseases under extreme environment, we attempted to identify and analyze potential biomarkers in metabolism to illustrate the relationship between cell stress and pathological processes. Visualization of protein-protein/gene interaction network could be an efficient approach to extract pathological meaning and to provide testable hypotheses based on available bioinformatics data, so as to investigate the correlation among serum indexes and diseases. In addition, animal model and preclinical tests are used to verify hypotheses generated by informatics strategy. Our results show a protein/gene network of acute phase response, including HIT-1, VEGF, HSP and CRP. etc. Additionally, investigation of serum indexes confirms that predicted proteins changed significantly under extreme environment. Informatics Analysis and animal model investigation indicate that high-altitude hypoxia enhanced a system of cell stress including (P<0.05). Further, prolonged stress and mediated metabolic disorder are crucial for high-altitude induced diseases, even death. In conclusion, our strategy could play a promising supplementary role in clinical practice.

P314 HIGH HUMIDITY HYPOXIA ENHANCES SERUM THYMIDINE KINASE 1 (TK1) EXPRESSION.
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To obtain more information about cell proliferation under high humidity hypoxic condition, and to investigate the correlation between tumor development and extreme environment, serum thymidine kinase 1 (TK1) testing was employed. Serum TK1 assay was employed. There were 200 patients who were admitted to our hospital from 2010 to 2012 in our hospital. Serum TK1 levels from two groups. And t test was used to analyze the difference of the two groups. Serum TK1 levels of group B (3.82±0.66PM/L) was higher than that of group A (1.45±0.45PM/L) (t=2.76, P<0.02). And difference of the serum TK1 levels between two groups was significant (P<0.05). We observed that prolonged high humidity hypoxia could enhance cell proliferation of SD rat, and further promote the development of tumor.

P315 PROGRESSIVE CONGENITAL GIGANTISM OF THE FOOT DIAGNOSED AS PROTEUS SYNDROME AFTER 23 YEARS.
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A 23 year old male presented with an enlarged and painful right foot deformity. Clinical history included congenital focal gigantism of the right first and second rays. Serial imaging studies showed progressive, disproportionate bone and soft tissue overgrowth treated by numerous surgical procedures. The first surgery (at age 9 months) involved amputation of the right second ray. By age 3, the remaining right hallux had expanded, with x-rays showing significant soft tissue enlargement and bony hypertrophy. The third surgery (performed at this time) involved complete amputation of the remaining right hallux with further soft tissue debulking. By age 15, the third digit had expanded and required amputation. All surgical excisions showed cutaneous abnormalities with only one note of irregular and variably sized nerve bundles associated with increased connective tissue. At age 23, the patient requested right below knee amputation for symptomatic and functional relief of the painful and deformed foot. Gross examination revealed a cerebriform connective tissue nevus on the plantar surface with histological evidence of fibrolipomatous hamartoma, haemangiona, bony overgrowth, and increased collagen deposition. A diagnosis of Proteus syndrome was made.
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PRESACRAL MYELOLIPOMA, MIMICKING A LIPOSARCOMA
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Herein we report a case of presacral myelolipoma mimicking radiologically a liposarcoma. It is a case of a 76 year-old female followed for a previously diagnosed breast cancer. The PET scan done on 2010 showed an incidental hypermetabolic presacral mass. In the subsequent CT scan, the mass was heterogenous with a partial adipose component, and a diagnosis of liposarcoma was suggested. The patient was followed by serial CT scans and the mass was growing slowly, pushing the rectum anteriorly. Because of the volume and position of the mass and the anal pain, the patient underwent a laparoscopic presacral resection. Pathologic examination revealed that the 10 cm partially adipose mass was a presacral myelolipoma. This is a rare localisation of an uncommon benign tumor that should be thought of, in the list of differential diagnoses.

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CASE REPORT: LIPOMA LIKE LIPOBLASTOMA: A CYTOGENETIC DIAGNOSIS,
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Background: Lipoblastoma is a benign tumor that usually presents in the first three years of life, most commonly on the extremities. They are most often in the range of 2-5 cm but larger lesions have been reported. Histologically there is usually an admixture of mature and immature adipocytes. A characteristic cytogenetic aberration is rearrangement of the 8q11-13 locus. Case: A 7 month old female presented with a thigh mass that had been noticed for one month. An ultrasound showed a 5.2 cm lesion isoechogenic to adipose tissue. The patient was monitored and follow up ultrasound at 19 months showed growth to 7.3 cm in greatest dimension. The lesion was resected. Gross examination revealed a yellow lobular mass weighing approximately 68 grams. Histology showed only mature adipose tissue with no immature adipocytes despite extensive sampling. A karyotype showed a t(2;8)(p23;q11) translocation. Discussion: In this case the histology was very lipoma-like such that diagnosis was not possible without karyotype. In most literature cytogenetics is cited as helpful in the differential diagnosis with myxoid liposarcoma, when the lipoblastoma is very immature. This case highlights the usefulness of a karyotype at the opposite end of the spectrum- when the lipoblastoma is very mature. In addition, to our knowledge the 2q32 translocation partner has not yet been reported.

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PRIMARY RENAL EWING SARCOMA/PRIMITIVE NEUROECTODERMAL TUMOR WITH A RARE FUSION TRANSCRIPT IN AN ADULT PATIENT.
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Ewing sarcoma / primitive neuroectodermal tumor (EWS/PNET) is considered a pediatric tumor with ~80% of cases in patients younger than 20 years old and few cases in patients older than age 40 years. EWS/PNET is characterized most commonly by an EWSR1-FLI1 fusion transcript, with fusion involving EWSR1 exon 7 and FLI1 exon 6 (Type 1 fusion ~ 54%) or EWSR1 exon 7 and FLI1 exon 5 (Type 2 fusion ~ 25%), accounting for most cases. Cases of this tumor arising in the kidney are rare. We report EWS/PNET with an EWSR1-FLI1 molecular variant fusion in a previously healthy 57 year old woman presenting with severe right sided abdominal and flank pain. A CT scan showed a large heterogeneous mass in the right kidney. An ultrasound guided biopsy yielded a scant specimen with variably sized stroma-poor nests of poorly preserved, crushed blue cells separated by dense fibrous septa. The cells had dark chromatin, scant eosinophilic to clear cytoplasm, and inconspicuous nucleoli. Membranous expression of CD99 and nuclear expression of FLI1 were demonstrated by immunohistochemistry. Molecular evaluation using RT-DNA amplification showed an EWSR1-FLI1 (11;22) variant fusion transcript. The dideoxy sequencing of this 192 base pair amplification product demonstrated fusion of EWSR1 exon 7 and FLI1 exon 7. This rare molecular variant accounts for only ~ 1% of cases. This case demonstrates the importance of including EWS/PNET in the differential diagnosis of poorly differentiated malignancies in solid organs and older adults.

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A RETROPERITONEAL LYMPHANGIOMYOMA MIMICKING LYMPHANGIOMA.
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Lymphangiomymoma, a rare benign neoplasm seen exclusively in females, belongs to the PECOMA family. The localized form is restricted to the mediastinum and retroperitoneum. Here we report a case of a retroperitoneal lymphangiomymoma that histologically mimicks lymphangiommyoma. The patient was a 49-year-old female with a 4.5 x 2.5 cm retroperitoneal mass detected incidentally by CT scan. Upon surgical excision and gross examination, the mass was found to be a pink-tan cyst with pink shaggy lining and milky turbid contents. Histologically, the cyst was composed of ansatomosing channels lined by flat epithelial cells and surrounded by a smooth muscle layer. There was no infiltrative growth or cytological atypia. The epithelial cells are positive for D2-40, CD31 and CD34; the muscle layer is positive for smooth muscle actin and desmin. Based on above morphological and immunohistochemical features, the mass was classified as a lymphangioma. However, subsequent immunostaining showed that scattered cells were positive for HMBS and negative for MART-1. The tumor was then reclassified as a lymphangiomymoma based on these new findings. The localized form of lymphangiomymoma is rare and can mimic lymphangiomymoma histologically. Therefore, it is imperative for pathologists to be familiar with this entity to properly diagnose retroperitoneal nodules with lymphatic channel proliferation.

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MEDIASTINAL LIPOLEIOMYOSARCOMA: A CASE REPORT AND REVIEW OF THE LITERATURE.
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Background: Lipoleiomyosarcoma is thought to represent a dual lineage sarcoma with components of well-differentiated liposarcoma (WDL) and low-grade leiomyosarcoma. This is a rare entity and only three case reports of mediastinal lipoleiomyosarcoma have been reported in the literature. Case Report: We report a mediastinal lipoleiomyosarcoma presenting as a mediastinal mass which was thought to contain fat based on a computed tomography (CT) scan. The initial CT guided biopsy was diagnosed as a well-differentiated liposarcoma. The subsequent resection showed WDL; however, focal areas of mature smooth muscle were also noted (confirmed by immunohistochemistry). Given that there were no definitive areas of conventional low or high-grade tumor dedifferentiation, this tumor was classified as a lipoleiomyosarcoma. Following resection, clinical follow up shows the patient to be alive and well 18 months after surgery with no evidence of recurrence. Conclusion: As heterologous elements in well-differentiated liposarcomas are often associated with dedifferentiation, it is important to be aware of lipoleiomyosarcoma as a distinct entity which behaves as a low grade malignancy.

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POST-TRAUMATIC SOFT TISSUE AMYLOIDOMA.
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Amyloidoma is the term used to describe a solitary tumor-like mass containing amyloid in the absence of systemic amyloidosis. It is an uncommon phenomenon with nearly all reported cases containing AA, AL or beta-2-microglobulin as the amyloid-forming protein. Amyloidoma associated with remote trauma is a rarely reported and poorly described entity. Two cases of soft tissue amyloidomas arising at sites of remote trauma have been identified at our site. In the first case, a 56-year-old man presented with an enlarging mass in his right thigh 12 years after injuring this area in a motor vehicle accident (MVA). The second case is strikingly similar, involving a 56-year-old man who many years earlier had injured his right thigh in a MVA before going on to develop a rapidly expanding mass at the site of prior injury. Both patients were suspected of having soft tissue sarcomas; however, excision of the suspected “tumors” revealed cystic lesions containing degenerated tissue and blood products with amyloid deposits. Immunohistochemical stains and mass spectrometry evaluation were unable to characterize the amyloidogenic protein in these cases. The latter studies, performed at the Mayo Clinic, were unsuccessful in identifying the amyloid-forming protein despite reporting a 98% success rate in validation studies for the technique. This suggests the protein is not one of the twenty-five known amyloidogenic proteins and, instead, represents a heretofore unknown amyloid-forming protein.
P323 INTRAVASCULAR FASCICITIS INVOLVING THE FLANK OF A 21-YEAR-OLD FEMALE: REPORT OF A RARE CASE WITH REVIEW OF THE LITERATURE.

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Intravascular fascicities is an uncommon variant of nodular fascicities, which is a reactive pseudosarcomatous soft tissue lesion composed of fibroblasts and myofibroblasts. Since its identification in 1981, only 32 cases of intravascular fascicities have been reported in the English literature. The lesion is commonly located in the head, neck, and extremities, with only 3 cases arising from the trunk. Here we report the fourth case involving the trunk (the flank area) of a 21-year-old female. Grossly, the subcutaneous mass was red-tan, oval, and well-demarcated, measuring approximately 0.5 cm in diameter. Microscopically, the mass was composed of spindle cells arranged in a swirling and intersecting pattern. The nuclei of the spindle cells were relatively uniform with tapered ends and prominent nucleoli. No significant mitotic activity was observed. Multinucleated giant cells were scattered among the spindle cells, along with infiltrating lymphocytes and red blood cells. The mass was multi-nodular, involving two blood vessels. It extended through the vascular walls into the surrounding fibroadipose tissue; in some sections, the spindle cells were intermixed with the perivascular fibrous tissue. Elastin stain revealed remnants of elastic lamina partially surrounding the lesion. Immunohistochemical stains showed the spindle cells were positive for smooth muscle actin, focally positive for muscle specific actin, and negative for S-100, confirming their muscular differentiation. The overall morphological and immunohistochemical features are consistent with intravascular fascicities. By reporting this rare case, we would like to raise awareness of this non-neoplastic lesion to avoid misdiagnosing it as sarcoma with vascular invasion. Previously reported similar cases were also reviewed and compared with this case.

P324 ENDOSALPINGIOSIS IN AXILLARY LYMPH NODES: A MIMIC OF METASTATIC BREAST CARCINOMA.

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Intraoperative assessment of sentinel lymph nodes at time of surgical excision of primary breast carcinoma is a crucial step in determination of cancer extent and the need for further axillary dissection. Benign epithelial inclusions in axillary lymph nodes can mimic metastatic carcinoma and are a well-known pitfall during examination of these nodes in frozen or permanent sections. Heterotopic mammary glands are the most often encountered forms of these inclusions and are familiar to the practicing pathologist. Here, however, we present a rare case of endosalpingiosis in the axillary lymph nodes of a breast cancer patient, and describe our experience and effort to characterize the lesion and rule out metastatic involvement. Consistent with endosalpingiosis, the glands were composed of populations of intermingled ciliated and intercalated cells, demonstrating strong reactivity with PAX-8 and WT-1 antibodies. Furthermore, unlike heterotopic mammary glands but mimicking metastatic breast carcinoma, the glands lacked a myoepithelial layer or reactivity with myoepithelial markers. Although endosalpingioidic inclusions are not uncommonly encountered in subdural/hyphraumatic lymph nodes, they are an extremely rare finding above the diaphragm. Pathologists must be aware of these lesions and their ability to imitate metastatic gland-forming carcinoma during frozen section or permanent examination of axillary nodes.

P325 MAMMARY HIBERNOMA, LIPOMA-LIKE VARIANT: PATHOLOGIC AND RADILOGIC DIFFERENTIAL DIAGNOSIS WITH WELL-DIFFERENATED LIPOSARCOMA.

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Hibernoma of the breast is a rare tumor of brown fat. We report the case of a 24-year-old woman who presented with a progressive palpable mass in the upper outer quadrant of the left breast. The ultrasonographic and mammographic features suggested a fatty lesion. A magnetic resonance imaging suspected a lipoma but could not exclude a well-differentiated liposarcoma. Surgical excision was performed and the histologic examination revealed a hibernoma of the lipoma-like variant. The pathologic differential diagnosis also included a well-differentiated liposarcoma. Despite advances in imaging techniques, histopathological examination is required for the diagnosis. No malignant counterpart has been reported to date; nevertheless, a complete surgical excision is recommended to avoid recurrences. We found only 5 cases of hibernoma of the breast previously reported in the english literature and this is the first case of the lipoma-like variant.

P326 IMPACT OF CYCOLOXYGENASE-2 (COX-2) OVEREXPRESSION ON PROGRESSION OF NOS-TYPE INVASIVE DUCTAL BREAST CARCINOMA.

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Purpose: COX-2 has been shown to play an important role in the development of breast cancer and has been mooted as a poor prognostic factor. The purpose of this study was to investigate the relationship between COX-2 expression and known predictive and prognostic factors in breast cancer in a routine diagnostic histopathology setting. Method: Formalin-fixed paraffin-embedded tumour tissue of 144 NOS-type invasive ductal breast carcinomas histologically diagnosed between January 2009 and December 2012 in Hospital Sultanah Bahiyah, Alor Setar, Kedah were immunostained with COX-2 antibody. COX-2 overexpression was analysed against demographic data, hormone receptor status, HER2-neu overexpression, histological grade, tumour size and lymph node status. Results: COX-2 was overexpressed in 108/144 tumours (75%) and significantly more prevalent (87%) in hormone receptor-positive tumours. There was no correlation between COX-2 overexpression and HER2/neu status. Triple negative cancers had the lowest prevalence (46%) of COX-2 overexpression. A rising trend of COX-2 overexpression with increasing age was observed. There was a significant inverse relationship between COX-2 overexpression and tumour grade (p<0.05), with prevalences of 94%, 83% and 66% in grades 1, 2 and 3 tumours respectively. A higher prevalence of COX-2 overexpression in smaller size tumours was observed but did not reach statistical significance. There was no relationship between COX-2 expression and lymph node status. Conclusion: This study did not support the generally held notion that COX-2 overexpression is linked to poor prognosis, and raises the consideration that it may have a role in tumorigenesis rather than progression of late invasive cancers. Larger scale studies with outcome data, and basic studies on cancer pathogenetic pathways will be required to cast further light on whether COX-2 inhibitors would have clinical utility in cancer prevention or blockage of cancer progression. In either setting, the pathological assessment for COX-2 overexpression in breast cancers would have important role in the selection of cancer patients for personalized therapy with COX-2 inhibitors.

P327 ASSOCIATION OF PRO-INFLAMMATORY CYTOKINES WITH BREAST CANCER RISK FACTORS.

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Pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) play a role in breast cancer development. We examined the expression of the pro-inflammatory cytokines IL-6 and TNF-α in normal breast tissue with two breast cancer risk factors; mammographic density and age-related lobular involution among 20 women having breast cancer and aged 50-65 years old. Tissue microarray (TMA) blocks were constructed from normal breast epithelium extracted from women’s mastectomy blocks. The intensity of staining of IL-6 and TNF-α (none, weak, moderate or high) was visually assessed on normal epithelium of 2-4 cores of normal breast tissue contained on immunohistochemically stained TMA sections. Mammographic density was visually assessed (<25%, 25-49% or ≥50%) on digitized mammographic images. The degree of lobular involution (none, partial or complete) and the dominant lobular type (type 1, 2 or 3) were evaluated in normal breast tissue contained on hematoxylin and eosin stained slides. Spearman coefficient was used to assess the strength of correlation. IL-6 epithelial intensity of staining, but not TNF-α, was positively correlated with mammographic density after adjustment for age and body mass index (r = 0.49, p = 0.04 and r = 0.30, p = 0.23, respectively). There was no significant correlation between the expression of any of the examined cytokines and age-related lobular involution. Increased expression of IL-6 in normal breast tissue might be associated with increased mammographic density and consequently increased breast cancer risk.
DNA METHYLATION CORRELATES WITH MOLECULAR SUBTYPES OF BREAST CANCER IN TUNISIAN WOMEN.


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Background: Invasive ductal carcinomas of the breast is a heterogeneous disease that includes a number of distinct biological entities that are associated with specific pathological features and clinical behavior. Microarray profiling of the transcriptome of breast cancers identified four major distinct subtypes of tumors: luminal A, luminal B, HER2 overexpressing and basal-like or triple negative, that are associated with different clinical outcomes. The current study was designed to investigate whether these intrinsic subtypes show specific methylation patterns.

Methods: One-hundred sporadic invasive ductal carcinomas from Tunisian women were investigated. Cases were grouped according to their ER, PR and HER2 immunohistochemical status into four intrinsic subtypes: luminal A (ER+ and/or PR+, and HER2-), luminal B (ER+ and/or PR+, and HER2+), HER2 subtype (ER-, PR-, and HER2+) and triple negative (ER-, PR-, and HER2-). Results were correlated to clinicopathological parameters and promoter methylation status of twelve tumor-related genes. Results: 44 cases (44%) were classified as luminal A, 31 cases (31%) as triple negative, 13 cases (13%) as luminal B and 12 cases (12%) as HER2 subtypes. Triple-negative tumors were associated to the methylation of BRCA1 and SHP1 promoters and inversely correlated to the methylation of the GSTP1 and HIN1 promoters (p=0.05 and p=0.04 respectively). Whereas HIN1 and GSTP1 promoters were less frequently methylated in triple-negative subtype than in the other intrinsic IDC subtypes (p=0.01, p=0.03, respectively). The methylation frequency of HIN1 in HER2 group (83%) was higher than that in the other groups (p=0.01). The highest frequencies of methylation of the promoter of RASSF1A were found in the luminal A (91%) and luminal B (85%) groups (p=0.03). Moreover, HER2 tumors differs from the luminal B group by hypermethylation of the BRCA2 gene (p=0.03) and from the luminal A group by low frequency of methylation of the RASSF1A promoter (p=0.004). In contrast, the luminal B subtype differs from the luminal A subtype by a high frequency of TIMP3 methylation (p=0.004).

Conclusions: These results indicate that the intrinsic subtypes of breast ductal carcinomas harbor different methylation patterns and that the epigenetic alterations may in part explain the biological and clinical heterogeneity of these cancers.

LOOSE DISSOCIATED FRAGMENTS OF MALIGNANT EPITHELIUM IN BIOPSY PROVEN DCIS ARE NOT CORRELATED WITH INVASIVE CARCINOMA ON EXCISION.

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Objective: DCIS is the most common type of non-invasive breast cancer, which on vacuum assisted or core needle biopsy (VAB or CNB) can be later associated with a diagnosis of invasive carcinoma (IC) from excision. Histopathologically, loose dissociated fragments of malignant epithelium (LDFME) are often seen in biopsies. This study investigates the correlation of these fragments for predicting upstaging to IC.

Methods: We reviewed 53 patients from our institution with biopsy proven DCIS, 26 were CNB’s and 27 were VAB’s. Results: 33/53 patients were upstaged (mean fragment number/VMF = 17.3), 20/53 were not (VMF = 16.1). 7/22 VAB’s were upstaged (VMF = 19.3) including 1 with large fragments (LF; >1mm), 20/27 were not (VMF = 20.5) including 2 with LF’s. 13/26 CNB’s were upstaged (VMF = 15.9) including 2 with LF’s, 13/24 were not (VMF = 9.8) including 1 with LF’s. On mammography, lesions that were not upstaged had a mean diameter of 1.8cm +/- 0.2 while lesions that were upstaged had a mean diameter of 3.5cm +/- 2.8. Conclusions: There was a statistically significant correlation with larger mammographic size to upstaging (p=0.01), no significant difference in number of fragments in cases that were upstaged or not and no difference in upstaging in cases with or without larger fragments (chisq = 0.644, df = 1, p = 0.422). Thus, LDFME do not have an impact on predicting invasive carcinoma on excision.

VALIDATION OF EP1 ANTIBODY FOR THE DETERMINATION OF ESTROGENS RECEPTOR STATUS IN BREAST CANCER.

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Estrogen receptor (ER) tumor’s status is critical for breast cancer management. The previously used antibody clone for ER status determination by immunohistochemistry, SP1, is no longer available in Canada and Europe for Dako autostaining technologies. The objective was to validate the EP1 antibody clone for its use in breast cancer against the previous standard SP1. EP1 clone was assessed on 13 cases, including 50 ER-negative (<1% ER expression), 12 ER-low-positive (1-9% ER expression) and 68 ER-positive (10% ER expression). Using EP1 vs. SP1, sensitivity was 92.5%, recall was 100%. All 16 different cases (n=16) were ER-low-positive. SP1 was reassessed in 13 ER-low-positive and in 11 ER-negative cases. Overall agreement between SP1 initial tumour status and re-assessment was 70.8% in those negative and low-positive cases. In conclusion, EP1 antibody has been validated for use in breast cancer with a positive agreement >90% and a negative agreement >95%, as recommended. Also, overall agreement between EP1 and SP1 was as good as between the SP1 initial status and SP1 re-assessment.

METASTATIC BREAST CARCINOMA WITH SALIVARY GLAND-TYPE FEATURES: MIXED ACINIC CELL CARCINOMA AND ADENOCARCINOMA WITH CHONDROMYXOID METAPLASIA.

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Metastatic breast carcinoma (MBC) with chondromyxoid differentiation is an uncommon cancer occurring in only 0.2% of all carcinomas of the breast. Salivary gland-type carcinomas primary to the breast are even rarer. We report a case of MBC with an acinic cell carcinoma (ACC) component in a previously healthy 46 year-old female who presented with a palpable breast mass. Mammogram and ultrasound showed an ill-defined lesion with no calcifications. Core biopsy demonstrated an acinic cell neoplasm associated with chondromyxoid stroma. A lumentectomy was performed which contained a 2cm tumour comprised predominately of cells containing finely granular eosinophilic cytoplasm and small nuclei consistent with acinic cell differentiation. These were associated with areas of chondromyxoid stromal metaplasia. Immunohistochemically, the acinic cell component was positive for CEA1/EA3, GCDFP-15, S100, lysozyme, DPAS, alpha-1-antitrypsin and EMA. The chondromyxoid stroma was positive for S-100 and p63. Electronmicroscopy revealed abundant lysosome granules in the cytoplasm of acinic carcinoma cells. The tumour was classified as an invasive carcinoma with salivary gland-type (mixed acinic cell carcinoma and carcinoma) and metaplastic (chondromyxoid) features or alternatively as ‘carcinoma ex pleomorphic adenoma’ of the breast. A frequent contrast, computed tomography of the neck was unremarkable. The patient remains disease free three years post treatment. To the best of our knowledge, this is the first report of an MBC with a predominant ACCA component.

FAMILIAL CARNEY SYNDROME: A CLINICOPATHOLOGIC AND GENETIC STUDY.

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Objective: Carney syndrome is an autosomal dominant complex involving endocrinopathy, mucocutaneous hyperpigmentation and different tumors including cardiac myxomas. We report on a family with several members affected with Carney syndrome. Methods: Family and individual medical histories were investigated through medical files of the University Hospital and pathology slides were reviewed. Results: Four members of this family (two young women, both sisters, their mother and maternal grandmother) were found to harbor Carney syndrome. Each one of them presented with multiple and recurrent atrial myxomas of the heart requiring multiple open cardiac surgeries. Myxomatous change of the breast and cutaneous hyperpigmentation were also revealed in one of the sisters and their mother. Interestingly, genetic testing was positive for the female family members and negative for the father and brother. The brother of the young women did not have cardiac myxoma, but was known to have an extensive Sertoli cell tumor resected. This sex cord stromal tumor has been involved in Carney complex according to the scientific literature. Conclusion: Carney syndrome is a complex multisystemic genetic disorder, including multiple and recurrent cardiac myxomas. Remarkably, the brother’s past medical history and negative genetic testing possibly demonstrates that not all genetic mutations causing Carney syndrome have been discovered yet. This family report highlights also the tight interaction of medical genetics with surgical pathology.
P333
PROSPECTIVE ASSESSMENT OF C4D IMMUNOHISTOCHEMISTRY IN CARDIAC TRANSPLANT BIOPSIES: A COST-EFFECTIVENESS ANALYSIS.
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Antibody mediated rejection (AMR) may lead to cardiac allograft dysfunction and decreased patient survival. The ISHLT 2011 working formulation recommended that AMR be diagnosed on the basis of histopathologic or immunopathologic findings and that immunohistochemical (IHC) study for C4d should be performed routinely. The aim of the current study was to evaluate the incidence of pathologic and immunopathologic AMR using the scoring system proposed by the ISHLT in 2011, and to estimate the laboratory costs and the diagnostic gain of routine vs. selective C4d IHC in endomyocardial biopsies (EMBs). We prospectively evaluated 164 EMBs from 58 patients with histology and C4d IHC. The cost-effectiveness of selective C4d IHC based on 2006 ISHLT guidelines and routine C4d IHC as suggested by the 2011 ISHLT guidelines was calculated and compared. Of the 164 EMBs analyzed, 9 (5%) from 7 patients (12%) were classified as pAMR 1 (H+)(histologic AMR grade); 1 biopsy (1%) from 1 patient (2%) was diagnosed with pAMR 1 (1+) (immunopathologic AMR alone); and 2 (1%) from 2 patients (3%) were defined as pAMR 2 (histologic and immunopathologic AMR). The average cost-effectiveness ratio increased eight-fold with routine compared to selective C4d IHC. The additional cost was estimated at $5,427.00 to detect one case of pAMR 1 (+). The tentative scoring system for AMR and C4d positivity proposed by the ISHLT 2011 guidelines is a useful tool to evaluate AMR and to clarify the existing controversy regarding the incidence of AMR in cardiac transplants. We found that routine C4d IHC yields a minimal diagnostic gain at an additional cost of $5,427.00 per case compared to selective C4d IHC. Assuming that cost should be considered for any laboratory test, the routine use of C4d IHC for EMBs can be questioned.

P334
FEMORAL ARTERY PSEUDOANEURYSM DUE TO CANDIDA ALBICANS IN AN INJECTION DRUG USER.
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Candida arteritis is an uncommon condition but important to recognize due to the risk of significant morbidity and the difficulty in management of the underlying fungal infection. The authors report a rare case of a man with a femoral artery pseudoaneurysm with persistent Candida albicans infection, as a complication of infective endocarditis. The 23-year-old man, with a history of chronic intravenous drug use and type I diabetes mellitus, presented with left groin pain, paraesthesia of his left foot, and a pulsatile mass in the inguinal region. On imaging, he was found to have a pseudoaneurysm of the left common femoral artery, which later ruptured. Further investigation revealed vegetations on the mitral and aortic valves as well. Initial blood cultures were negative. He underwent multiple surgical interventions including replacement of the mitral and aortic valves and resection of the left common femoral artery with autogenous revascularization. Additionally, he was commenced on intravenous antifungal therapy. Post-operatively, he continued to experience significant pain in the left groin and had two episodes of re-rupture of the femoral artery that was consequently surgically repaired. Histological examination of the resected valves revealed vegetations with a mixture of fungal elements and bacterial cocci. The femoral artery resection specimens revealed evidence of infectious arteritis and the presence and persistence of C. albicans organisms in subsequent specimens. This is a rare case of femoral arteritis due to C. albicans, as a complication of infective endocarditis. This case also highlights the importance of an accurate diagnosis and aggressive management of fungal mycotic aneurysms at risk populations.

P335
A RARE CASE OF PERICARDIAL MONOPHASIC SYNOVIAL SARCOMA PRESENTING AS CARDIAC TAMPOHANE.
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Synovial sarcoma is a malignant spindle cell tumor that accounts for 5% to 10% of soft tissue sarcomas. Over 90% of cases harbor the chromosomal translocation t(X;18)(p11;q11). The vast majority of synovial sarcomas occur in the extremities and are usually diagnosed by the head and neck region. We report a case of a 37 year old woman who presented with cardiac tamponade and echocardiographic evidence of an intrapericardial mass, which was surgically resected. Microscopically and immunohistochemical features of the mass were consistent with monophasic synovial sarcoma. Molecular confirmation was accomplished by fluorescence in situ hybridization break apart probe. To our knowledge, pericardial synovial sarcoma is extremely rare and little characterized in the medical literature.

P336
A RETROSPECTIVE QUALITY ASSURANCE REVIEW OF URINE SAMPLES DIAGNOSED AS ‘ATYPICAL’ WITH CYTO-HISTOLOGIC CORRELATION.
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Over the last several years, our laboratory has seen an increasing number of urine samples submitted for cytologic evaluation with relatively high numbers reported as ‘atypical’. CytoHistology correlation was performed on urine samples received between July 1, 2010 and July 1, 2011 with the objective of improving our diagnostic accuracy. Of the 2278 urines received within the project timeframe, 179 had biopsy confirmation. Data analysis was performed on this subset of samples with the following observations: we observed a high degree of sensitivity in urine samples diagnosed cytologically as malignant (37/179); 36/36 (96.3%) were confirmed on biopsy as having High Grade Transitional Cell Carcinoma. We also observed a number of cases reported as atypical (51/179) raising concern that the atypical category is being overused. Only 15/51 (29.4%) correlated with an abnormal surgical diagnosis (atypical or low grade TCC). A literature review was performed and morphologic criteria were defined. The criteria were applied during microscopic review of the 51 atypical cases by a cytopathologist and a cytopathologist with a specific diagnosis assigned in all cases. Abnormal nuclear features including increased N/C ratio, nuclear membrane irregularity together with coarsely granular chromatin seemed to favour malignancy. Increased N/C ratio in the absence of nuclear membrane irregularity or coarse chromatin favoured either a benign or benign-reactive process, while cells displaying vacuolated cytoplasm and prominent nuclei were associated with benign-reactive changes. Strict application of criteria will decrease the utilization of the “atypical” category and will improve diagnostic accuracy.

P337
RETROSPECTIVE COMPARISON OF INSTITUTIONAL CYTOLOGIC ACCURACY OF WARTHIN TUMOUR DIAGNOSIS.
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Warthin Tumour (WT) is the second most common salivary gland neoplasm. Hypothesis: Cytologic accuracy in diagnosis of WT has increased in the past four years (July 19, 2007– November 1, 2011) compared to the previous four (November 1, 2003–July 18, 2007). Methods: A retrospective review of patients with a WT diagnosis and both fine needle aspiration (FNA) and surgical resection was completed for the past 8 years. All FNA specimens were prepared using a thin layer technique. 82 patients, with 99 cytologic events, were identified and divided into two groups based on date of FNA. True positive (TP), false positive (FP), and false negative (FN) rates, and sensitivity (Sn) and positive predictive value (PPV) were compared between groups. Comparison of characteristics of FN versus TP cases, along with TP versus FP cases, was undertaken. Results: In the past four years, our institution has significantly improved TP rates (p≤0.05). Sn and PPV have improved, and FP and FN rates decreased. Compared to TP cases, FN cytology specimens were more likely to have other cellular components (p≤0.01), were less likely to have debris (p≤0.02), oncocyttes (p≤10^-8), and lymphocytes (p≤10^-8), and had a smaller tumours at resection (p≤0.02). FP for WT cases were more likely to occur in non-parotid sites (p≤0.05). Two parotid FNAs interpreted as WT were acinic cell carcinoma and low grade mucosepidermoid carcinoma. Conclusions: Cytologic diagnosis of WT has improved at our institution. Associated factors include educational initiatives and change in fine-needle aspiration practices by our Head & Neck surgeons. Mimics and key differentiating factors are reviewed.
P338

ATYPICAL URINES: A CYTOMORPHOLOGIC ANALYSIS.


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In voided urine cytology we noted a high level of inter-observer variation among cytopathologists in the use of the term “atypical”. This study aimed to improve and standardize reporting of these specimens by identifying cytomorphic criteria best predictive of cancer on 152 voided urine samples with histological follow-up (36% with high-grade urothelial carcinoma). These voided urine samples, originally interpreted by a cytopathologist as atypical, were blindly re-interpreted by 7 cytopathologists and 1 cytopathologist for the presence or absence of 6 nuclear features, 4 cell arrangement features and 1 cytoplasmic feature. Analysis revealed three statistically significant criteria used by the greatest number of reviewers: hyperchromasia, irregular nuclear borders, and anisonucleosis. The odds ratio (OR) for cancer for these nuclear features on logistic regression analysis were hyperchromasia 1.2, irregular nuclear borders 5.2 and anisonucleosis 4.4 (all p<0.05). This study showed that specific nuclear features are the most useful criteria for predicting malignancy. The presence of cell clusters, often used as an atypical criterion in our laboratory, was not found predictive unless the cells in the clusters had atypical nuclei.

P339

INTERNAL CONSULTATION IN CYTOPATHOLOGY.

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Background: Second opinions (internal consultation) on cytology cases may be useful for diagnostically challenging cases. The goal of this study was to describe the characteristics of cytopathology cases which underwent internal consultation at our institution.

Methods: We reviewed all cytopathology internal consultation requests for a one year period (2010). The requests were categorized by pathologist, site, and reason.

Results: 321 cytopathology cases were reviewed in consultation over the defined period. The average consult rates for pathologists who saw a lower (≤10% workload) and higher (>10% workload) volume of cytology cases were 4% and 1.5%, respectively. Pathologists with a higher cytology workload received 94% of all cytology consults. The sites with the most consultation requests were pancreas, lung, salivary gland and bile duct. Reasons for consultation requests were: threshold diagnoses (eg. suspicious vs. positive; 35%); tumour subtype (10%); medical/surgical impact excluding a first diagnosis of cancer (10%); confirmation of a first suspicious vs. positive; 35%); tumour subtype (10%); medical/surgical impact excluding a first diagnosis of cancer (10%); confirmation of a first diagnosis of cancer (9.5%); unusual/unfamiliar tumours/tissues (8%); diagnostic discrepancy between cytopathologist and pathologist, or between pathologists (6%); histological/clinical non-correlation (6%); and other (18%).

Conclusion: Internal consults were more frequently requested by pathologists seeing a lower volume of cytology cases, and requested of pathologists seeing a higher volume of cases. Sites with the highest consultation were pancreas, lung, salivary gland and bile duct. The most frequent reason for requesting a consultation was for threshold diagnoses.

P340

EVALUATION OF NON-PALPABLE THYROID NODULES BY ULTRA SOUNDED FINE NEEDLE ASPIRATION CYTOLOGY.

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The aim of this study was to see the usefulness of fine needle aspiration by “the Bethesda system for reporting Thyroid Cytopathology” (TBS-RTC) for non-palpable thyroid nodules through ultrasound-guidance for the evaluation and treatment planning of nonpalpable thyroid lesions. This study was conducted on 200 patients with non palpable thyroid nodules which are very low lying or felt on swallowing: in Department of Pa- thology and Radiology since January 2011 to June 2012. The patients were scanned and USG-FNAc was performed and reporting was done by “TBSRTC”. Of the 200 specimens 17 samples were nondiagnostic or unsatisfactory (Class I), 145 samples were benign (Class II), 20 samples were showing Atypical of Undetermined Significance (AUS) or Follicular Lesion of Undetermined Significance (FLUS) (Class III), 6 were showing follicular neoplasm or suspicious for a for- licular neoplasm (Class IV), 7 samples were sus- picious for malignancy (Class V) and 5 samples were positive for malignancy (Class VI). On com- parison of ultrasound guided FNA, with histo- logic the sensitivity for confident diagnosis was 93%, specificity was 86%, positive predic- tive value was 37%, negative predictive value was 99% and accuracy was 86%. USG-FNAc is a useful modality for the evaluation and treatment planning of nonpalpable thyroid lesions. The size of the nodule is not the main parameter. TBSRTC is the best method of reporting but class III and IV are the main pitfall of this system for reporting Thyroid Cytopathology and show high sensitivity, specificity and accuracy.

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THE DIAGNOSTIC ACCURACY OF SOLID NECK MASS FINE NEEDLE ASPIRATION (FNA) CYTOLOGY.


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Objective: A retrospective analysis was performed to determine the diagnostic accuracy of solid neck mass fine needle aspiration (FNA) cytology.

Methods: A search of the CDHA laboratory information system identified all patients who underwent an FNA of a neck mass during a one year period. FNAs of cystic lesions, salivary glands, and thyroid glands were excluded. The concordance between FNA results and subsequent biopsies was determined. Results: 221 patients met the study criteria, with FNA results being categorized as “Unsatisfactory” (N=17), “Negative/Benign” (N=69), “Abnormal” (N=37), “Suggestive” (N=22), or “Positive” (N=56). 82 of those patients (37%) went on to have an excisional biopsy in the subsequent 32 to 44 months. In the “Unsatisfactory” category, 5 patients (29%) had biopsies, 3 of which were malignant (60%). In the “Negative” category, 20 patients (22%) had biopsies, 11 of which were malignant (55%). In the “Abnormal” category, 26 patients (70%) had biopsies, 20 of which were malignant (77%). In the “Suggestive” category, 15 patients (88%) had biopsies, all of which were malignant (100%). In the “Positive” category, 16 patients (29%) had biopsies, all of which were malignant (100%). Excluding the “non-diagnostic” FNA categories (“Unsatisfactory” or “Abnormal”) the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of FNAs in this study were 74%, 100%, 100% and 45% respectively.

Conclusions: Patients with “Abnormal” or “Suggestive” FNAs were more likely to undergo further diagnostic procedures. The NPV result is low compared to the literature, likely because of the choice to use “Negative” rather than “Unsatisfactory” or “Non-Diagnostic” in many low cellularity FNAs. The calculated sensitivity, specificity, and PPV are comparable to values reported in the literature. However, these values are not a true reflection of diagnostic accuracy; cases which went on to biopsy were biased by clinical circumstances, and the majority of “Negative” and “Positive” FNAs did not have follow-up.

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UPPER URINARY TRACT CYTOLoGy-ThINPREP® vs. CONVENTIONAL SMEAR: DOES IT MATTER?

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Objective: To compare the diagnostic accuracy of the conventional method to the Thinprep® method for upper urinary tract cytology. Method: A total of 80 upper urinary tract cytology specimens, 5 years before (Group A, n=49) and after (Group B, n=31) the adaptation of Thinprep® technique were identified from the electronic database. The cytology findings were correlated to the histology findings when available and a follow-up time of at least one year was required for inclusion of negative cytology specimens. SPSS software was used to calculate the diagnostic accuracies. Statistical P value of <0.05 was considered significant. True negatives, true positives and atypical cases with positive/benign histology (n=47) were independently reviewed by two pathologists (JM, CW) for 9 cytologic features. Results: The age range and median were not significantly different in the two groups. The sensitivity, specificity, PPV and NPV in Group B were improved as compared to Group A (100% vs. 86%, 100% vs. 82%, 100% vs. 60% and 100% vs. 95%). Chi square analysis showed cytological features including large nuclei, high n:c ratio, hyperchromatic nuclei, anisonucleosis, coarse chromatin, eccentric nuclei, >100 atypical cells, cell in cell and macronucleoli to be significantly associated with high-grade transitional cell carcinoma. Conclusion: Despite the widespread and routine use of Thinprep®, there are no published studies comparing Thinprep® and conventional cytology preparations in upper tract urinary cytology samples. This small quality assurance study indicates that the Thinprep® technique has improved the sensitivity and specificity of upper urinary tract cytology. This study supports our laboratory's change to routine use of liquid based cytology in non-gynecologic cytology samples.
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SUBCATEGORIZATION OF “ATYPIA OF UNDETERMINED SIGNIFICANCE” CASES IN THYROID FINE NEEDLE ASPIRATES: MALIGNANCY RATES ON HISTOLOGIC FOLLOW-UP

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Objective of the Study:

In 2007, The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was established as a way to standardize the diagnostic terminology for thyroid fine needle aspirates (FNA). TBSRTC is a 6-tiered system which includes the equivocal diagnostic category called “Atypia of Undetermined Significance” (AUS), which is linked to an approximate 5% risk of malignancy. However, because the AUS category is a composite of different entities, it is also likely heterogeneous in terms of risk of malignancy. The objective of our study was to report the rate of malignancy in each of the three subcategories of AUS used at our institution: AUS-follicular lesion of undetermined significance (AUS/FLUS), AUS-Hurthle cell lesion of undetermined significance (AUS/HUS), and AUS-cannot rule out cystadenoma (AUS/cannot rule out CTC).

Methods: Following a retrospective review of the cytopathology files of the McGill University Health Center for thyroid FNAs, we identified 572 thyroid diagnosed as AUS as between January 2008 and June 2008; of those 154 also had subsequent surgical follow up. Ten of the 154 cases were excluded from the study because they represent repeated FNAS from the same nodule at the same time (N=8), 142 had a biopsy on follow up and only one biopsy for those who had been referred with incorrect diagnosis and/or was not available for review.

Data and Results: The breakdown of the 144 AUS cases by subcategory is as follows: 35% for AUS/FLUS, 34% for AUS/HUS, 20% for AUS/TC, and 11% for AUS/cannot rule out CTC. However, the malignancy rate on histologic follow-up for each AUS subcategory was as follows: 35% for AUS/FLUS, 15% AUS/HUS and 27% for AUS/cannot rule out CTC. P<0.0001 for each vs. AUS/FLUS.

Conclusions: The malignancy rate on histologic follow-up, the malignancy rate dropped to 10% when also including all the AUS cases that had histologic follow-up, falling within the estimated malignancy risk (5%-15%) distributed by the TBSRTC.

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INCIDENCE OF CERVICAL HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESIONS OR CARCINOMAS IN A SERIES OF 140,609 CASES – CLINICAL AND CYTOHISTOLOGICAL CORRELATION – EXPERIENCE OF A PRIVATE HEALTH SERVICE IN BRAZIL.

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Introduction: In Brazil, screening for cervical cancer (CCa) is the second most common malignancy in women, is performed mainly by cervicovaginal cytology. However, a significant proportion of our population is assisted in private health clinics with few available data. This study evaluated the incidence of high grade squamous intraepithelial lesions (HSIL) or CCa in cervical smears, with histological correlation and division in age groups at one of the biggest private laboratories in the country. Methods: We retrospectively collected cases of cervical cytology in one-year period (June 2011-June 2012). All cases were screened by cytopathologists and an indeterminate or positive result was double checked by a pathologist. The cytolgy result was correlated to colposcopic findings and histological diagnosis whenever available. Results: In one year period (July 2011 – July 2012), we collected a total of 31,861 LBC cases from our files, with 217 (0.7%) cases interpreted as HSIL. In 193 cases (0.6% of the total, 88.9% of cases with HSIL) colposcopy was performed.

Conclusions: The localization and treatment of SILs which have a higher risk of persistence or progression are determinant factors for CCa screening efficacy. Untreated altered areas in cervicovaginal mucosa may represent important persistent factors of HPV infection. At Fleury, in addition to endocervical and ectocervical sampling, we also sample the lateral vaginal walls and the vaginal cul-de-sac. In this study, we found that in 23.3% of HSIL cytology cases, the high-grade squamous lesions were present only in the vagina, and in 6.8% of cases there was HSIL both in the cervix and vaginal wall. Thus, 30.1% of the HSIL cytology cases presented clinically significant vaginal lesions. Therefore, it is important to have a detailed colposcopic examination, as well as wide vaginal cytology sampling, in order to increase the sensitivity of detection of HSIL in previous examinations.

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RELEVANCE OF VAGINAL LESIONS ON CERVICAL CANCER SCREENING. COLPOSCOPIC AND CYTOHISTOLOGICAL CORRELATION.

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Objective:

Introduction: Human papillomavirus (HPV)-related lesions of the female genital tract represent a significant health issue in sexually active population in almost all countries. Conventional cervicovaginal cytology is the main screening test in Brazil; however, with increasing use of liquid based cytology (LBC) in private services. Low-grade squamous intraepithelial lesions (LSIL) are the most frequent HPV-induced changes, but the majority regresses spontaneously. On the other hand, cervical high grade squamous intraepithelial lesions (HSIL) have greater risk of persistence and, if left untreated, can progress to cervical cancer (CCa). Therefore, patients with a confirmed histology of HSIL represent the group that needs attention and immediate action in gynecologic practice. To obtain efficacy in prevention of CCa, it is desirable to identify and treat the most significantly altered areas of genital mucosa. In this study we correlated colposcopisc and histological findings in HSIL-LBC cases in one of the largest private health services in Brazil. Materials and Methods: We retrospectively collected cases of LBC from July 2011 – July 2012. All cases were screened by cytopathologists and an indeterminate or positive result was double checked by a pathologist. The cytolgy result was correlated to colposcopic findings and histological diagnosis whenever available. Results: In one year period (July 2011 – July 2012), we collected a total of 31,861 LBC cases from our files, with 217 (0.7%) cases interpreted as HSIL. In 193 cases (0.6% of the total, 88.9% of cases with HSIL) colposcopy was performed.

Conclusions: The malignancy rate on histologic follow-up, the malignancy rate dropped to 10% when also including all the AUS cases that had histologic follow-up, falling within the estimated malignancy risk (5%-15%) distributed by the TBSRTC.

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BETTER THYROID CYTOPATHOLOGY REPORTING SYSTEM MAY INCREASE THE CLINICAL MANAGEMENT AND PATIENTS OUTCOME.

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Objective: The Bethesda System is better for Thyroid Cytopathology reporting and may increase the clinical management of Thyroid Disease. Study design: Analytical Cross sectional. Material and methods: A cross sectional study was conducted on 129 cases from the years 2010 and 2011 and compared with the Bethesda adapted method. In one hospital in the country, 129 cases were referred for fine needle aspiration to the Department of Pathology in 2011 and the Bethesda System for reporting Thyroid Cytopathology was followed in comparison to old conventional reporting system running from the last 30 years. Histopathology was used as a gold standard to compare the sensitivity of both systems. Three groups of Histopathologists were assigned three reporting systems without knowing the results of each other. The comparison was made in a meeting of 3 groups after histological report of each case was made available. Group A was assigned to report with the older system of thyroid aspiration with 7 categories, Group B reported with five classes of an older reporting system and Group C reported with the latest Bethesda Report system. Screening test was applied to compare the results. Results: When the results of these three systems were compared Bethesda adapted method was found to be more superior as compared to the others. Sensitivity of Group B and C is significantly high 0.501 as compared to group A (p=0.051 and 0.000) and Group A is significantly higher than Group B (p=0.000 and 0.002). Our findings are consistent with others who used the Bethesda Cytopathology Reporting System. Conclusion: The Bethesda Cytopathology Reporting system can help with a better patient's outcome due to proper clinical management of thyroid swellings and saves patients from unnecessary thyroid surgery.
Conclusions

and specificity were 87% and 100%, respectively for diagnosis. There were no false positive diagnoses. The overall sensitivity of the cell block method was 73.7% (17/23), including 20 suggestive/positive (S/P) cases (83%) and four negative cases (17%). There were no unsatisfactory cases. Histological follow up was conducted a retrospective review to confirm the adequacy and cytological interpretation. 20 cases were reported as colloid nodule with cystic degeneration or goiter, 3 follicular neoplasm, 2 papillary thyroid carcinoma and 9 HT/IT. Correlation of cytology and histology showed that 9(23.7%) of FNACs correlated with the histologic diagnosis. The discrepancies were due to FNA sampling error in 4(10.5%), cytdiagnostic errors in 15(39.5%) and suboptimal smears in 10(26.3%). Conclusion: Strict adherence to the adequacy criterion and meticulous examination aids in reducing the number of discrepant cases and erroneous diagnosis. Smear adequacy should take into consideration primary fixation and the quality of the smear and not cell yield only. Rendering a definite diagnosis on suboptimal FNA samples is possible but difficult. Cystic change in the thyroid lesions is the most common cause of diagnostic pitfalls in cytology. Aspirations from multiple sites and from solid areas may be useful in preventing sampling errors.

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IMPROVING SENSITIVITY OF LUNG FINE NEEDLE ASPIRATION BIOPSY: AN AUDIT OF ROUTINE CELL BLOCK IMPLEMENTATION.

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Introduction: The majority of lung cancer patients present at a stage that is not resectable. A diagnosis must be made on limited material. A fine needle aspiration (FNA) biopsy is in many cases the only diagnostic material available for guiding therapeutic decisions. Literature review shows that sensitivity of lung FNA biopsy ranges from 56 to over 90% and specificity is close to 100%. In a retrospective review of lung FNA biopsies at our institution before March, 2009, we identified a low sensitivity of 57% and a specificity of 100%. At the time we did not routinely make cell blocks for all lung FNACs. In March, 2009, we commenced a trial period of three months preparing cell blocks on all lung FNA biopsies. We then calculated the resulting change in sensitivity and specificity. Methods: 100% of discrepant cases and erroneous diagnosis. Smear adequacy should take into consideration primary fixation and the quality of the smear and not cell yield only. Rendering a definite diagnosis on suboptimal FNA samples is possible but difficult. Cystic change in the thyroid lesions is the most common cause of diagnostic pitfalls in cytology. Aspirations from multiple sites and from solid areas may be useful in preventing sampling errors.

P349

RETHINKING LABORATORY RESOURCE UTILIZATION, AN EDUCATIONAL INTERVENTION IN FAMILY MEDICINE CURRICULA.

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Objectives/Introduction: Laboratory utilization has increased and a significant proportion of tests ordered are unnecessary. As most investigations begin with the primary care family physician, it is pertinent that physicians understand judicious usage of limited resources. In a search of all the Canadian Family Physician residency programs, none list mandatory laboratory training as part of their curriculums, nor list it as an optional elective. In 2012 Family Medicine residency programs across Canada introduced a new competency in their CANMEDS role entitled Selectivity. This competency was designed to deal with issues of test selection and resource stewardship. To fill this gap, a collaborative educational program at the University of Calgary was designed to introduce medical students to the basics of the laboratory test ordering and interpretation. Methods: The program was run as a series of identical four-hour small group sessions to facilitate discussion and laboratory tours. The curriculum centered around seven key topics: test utilization, errors, results, and costs and requisition completeness, quality assurance, local laboratory processes and quality assurance. Residents were taken to a specimen collection site for a tour and two hours of didactic sessions, ending with a tour of a diagnostic services facility. In addition, residents completed an anonymous survey before and after the session that asked them to self-assess their knowledge of the curriculum topics. Results: This novel approach teaches residents how to be efficient in test ordering and encourages responsible medical resource stewardship amongst primary care physicians. The use of a small group format allowed for more tailored teaching based on concurrent feedback and questions with additional take-home resources. Pre and post survey results of 68/69 residents shows statistically significant (P<0.001) self-identified changes in levels of knowledge of laboratory utilization, sources of error and quality assurance programs. Conclusions: The first cohort of PGY1 family residents completed this program in July 2012. Overall the program was very well received, with significant increases in the residents' knowledge self-assessment across all subject areas covered in the curriculum. This labratory rotation has now become a mandatory part of the University of Calgary Family Medicine Residency curricula.
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A NOVEL TECHNIQUE OF SAMPLING THYROIDECTOMY SPECIMENS FOR PAPILLARY THYROID CARCINOMA.

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Introduction: Multifocality, bilateral involvement of the thyroid gland and lymph node metastasis are the hallmark features of Papillary Thyroid Carcinoma (PTC). Mapping of multiple foci of PTC is difficult with conventional sectioning and sampling in the horizontal plane. In this study, we report a new method of grossing multiple foci PTC in thyroidectomy specimens, by sectioning from anterior to posterior in the coronal plane.

Design: 100 consecutive specimens of total thyroidectomy or lobectomy followed by completion lobectomy were selected. Total thyroid gland or thyroid lobes were fixed in 10% buffered formalin for at least 24 hours. Resection margins were inked and entire specimens were serially sectioned from anterior to posterior in the coronal plane. With the exception of very large specimens, up to 80% of the total specimens were submitted. Thickness of sections varied from 3 to 5 mm. All cross-sections were photographed and at least one complete cross-section was submitted in toto for histology and mapped to enable reconstruction during microscopic examination. The most anterior and posterior complete sections were serially sectioned in the transverse plane to evaluate resection margins.

Results: All neoplastic thyroid nodules were ovoid in shape with maximum dimensions in the plane parallel to the greatest dimension of the lobe, ranging from 3.0-60mm (18.8±6.6mm). PTC presented as single thyroid nodule in 20% of cases, a cluster of satellite tumour nodules in 24%, and with multiple foci in 56%. Tumours were bilateral in 40% of cases.

Conclusions: Our technique of sectioning the thyroid completely from anterior to posterior in the coronal plane allows for evaluation of the greatest dimension of nodules and enables an easier determination of multifocality and bilaterality.

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INCIDENCE OF Hb VARIANTS IN SAMPLES RECEIVED FOR HEMOGLOBIN A1c (HbA1c) DETECTED BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) METHODS AT FACULTY OF MEDICINE, SIRIRAJ HOSPITAL, THAILAND.

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Objective: This study aimed to evaluate the effect of the common abnormal Hb on the detection of gHb and HbA1c, and incidence of abnormal Hb in patients of DM in Siriraj Hospital, Bangkok, Thailand.

Materials and Methods: EDTA blood samples from 3,024 DM participants in this study collected from the OPD of Siriraj Hospital from 1-30 August 2011. The samples were measured HbA1c by HPLC on Variant II turbo analyzer. Chromatograms generated by the analyzer for the abnormal Hb or Hb variants by looking for heterozygous HbE, homozygous HbE, S-window, P3 > 10%, D-window, and unknown peak. The incident of abnormal Hb or Hb variants was calculated.

Results: The incident of Hb variants was 14.8%. (448 patients in 3,024 patients) There are heterozygous HbE 11.24% of all patients (340 patients in 3,024 patients), homozygous HbE 0.7% (22 patients in 3,024 patients), heterozygous beta thalassemia 2.1% (61 patients in 3,024 patients), heterozygous HbCS 0.3% (10 patients in 3,024 patients), HbH disease 0.03% (1 patients in 3,024 patients), HbEE/EF 0.1% (4 patients in 3,024 patients), HbEFA 0.03% (1 patients in 3,024 patients), HbH disease 0.03% (1 patients in 3,024 patients), and unknown abnormal Hb variants 0.2% (7 patients in 3,024 patients).

Conclusion: The high incident of Hb variants in this study should be influenced the measurement of HbA1c, in all methods used in Thailand. The presence of common abnormal Hb significantly affected glycohemoglobin test results. Therefore, the measurement of glycohemoglobin may not represent the best method for diagnosis and monitoring of diabetes patients.

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FINE NEEDLE ASPIRATION VERSUS CORE NEEDLE BIOPSY OF THYROID NODULES AT CHARLES LEMOYNE HOSPITAL.

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Historically, both fine-needle aspiration (FNA) and core needle biopsy (CNB) have been done in our center for evaluation of thyroid nodules. (a) Objective: to determine the pathological correlation of thyroid nodules biopsies and compare the performance of FNA and CNB. (b) Methods: we conducted a retrospective analysis of all thyroidectomy cases from 2005 to 2011 that had a pre-operative biopsy in our center. (c) Results: we found 69 cases with either pre-op FNA (n=68) or CNB (n=43). Only 43/68 (63.2%) of FNAs were ultrasound-guided compared to all CNBs. A benign diagnosis was found in 15/68 (22.1%) FNAs and only 1/43 (2.3%) CNB, and there was only one false-negative FNA result that was a papillary cancer. Follicular lesions of undetermined significance (FLUS) accounted for 29/68 (42.6%) of FNAs results compared to 33/43 (76.7%) of CNBs. All FNAs with FLUS were also designated as FLUS based on the concomitant CNBs. The rate of malignancy found in FNAs with FLUS results was slightly higher than CNBs: 5/29 (17.2%) vs 4/33 (12.1%), and the pathological diagnosis were 8 follicular and 1 papillary cancer. Malignant or suspicious for malignancy results were all true positive. We obtained more non-diagnostic results from FNAs (20.6% FNAs vs 9.3% CNBs). Only one case was reclassified as follicular neoplasm based on the concomitant CNB. All the others were FLUS. (d) Conclusions: FNA seems superior to CNB since it establishes more benign diagnosis, less FLUS and is a less invasive procedure carried out at a lower cost. Moreover, CNB did not increase diagnostic yield of FNAs with non-diagnostic or FLUS results.

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DIFFERENCES IN SERUM TESTOSTERONE CONCENTRATIONS BETWEEN CHINESE, INDIAN AND MALAY MEN.

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Sex hormone concentrations can vary between groups based on ethnicity. This study examined whether differences in serum testosterone concentration exist between Chinese, Indian and Malay men in Singapore. Anonymised records of all male serum testosterone measurements performed between March 2007 and December 2012 were extracted for analysis using Microsoft Excel. Access and SPSS v16. Testosterone measurement was performed on a Roche Diagnostics e601 analyser. Repeat samples were excluded and the dataset was split to examine <=40 y and older >=41 y men separately. There were 1372 records in the <=40 y group; 73% Chinese, 21% Indian, 6% Malay; 83% outpatients, average age 31.4 y (range 13-40). There were 5302 records in the >=41 y group; 66% Chinese, 8% Indian, 5% Malay; 90% outpatients, average age 58.8 y (range 41-113). For the <=40 y group, linear regression analysis for testosterone (nmol/L) showed average effect sizes of: Indian vs. Chinese +1.14 (p 0.022), Malay vs. Chinese +1.81 (p 0.037). For the >=41 y group, average effect sizes were: Indian vs. Chinese -0.38 (p 0.302), Malay vs. Chinese -1.33 (p 0.004). There are statistically but not clinically significant age related differences in serum testosterone concentration between Chinese, Indian and Malay men. Factors such as body composition, smoking and disease status may explain these differences.
P355 PARATHYROID ADENOMA ARISING FROM AUTOTRANSPLANTED PARATHYROID TISSUE IN STERNECLOIDEOMASTOIDS MUSCLE: A CASE REPORT WITH REVIEW OF THE LITERATURE. Yan Hu, MD, PhD; Ted C. Ondracek, MD; Frank Chen, MD, PhD. Department of Pathology, Buffalo General Medical Center, State University of New York at Buffalo, Buffalo, NY, USA

Autotransplanting a portion of parathyroid tissue into the forearm or the sternocleidomastoid muscle to prevent hypoparathyroidism after total parathyroidectomy is a relatively common surgical procedure. However, parathyroid adenoma arising in autotransplanted tissue in patients with secondary hyperparathyroidism is very rare. To date, less than 20 such cases have been reported in the English literature. Here we report a case of a 47-year-old African-American male with a history of total parathyroidectomy and autotransplantation of a portion of parathyroid tissue into the sternocleidomastidoid muscle 6 years ago presenting with severe hyperparathyroidism and increasing autotransplant size. His previous history was also significant for polycystic kidney disease, nephrotic syndrome, end-stage renal disease with hemodialysis for 14 years, and right clear cell renal cell carcinoma status post right nephrectomy in 2008. The palpable mass at the site of autotransplantation was excised. The specimen was received as 2 pieces and weighed 2.7 grams. Grossly, the cut surface of the mass appeared brown-tan. Microscopically, the mass was well circumscribed and was composed of sheets of small, round and relatively uniform cells, morphologically consistent with chief cells. No adipose tissue or oxyphil cells were found inside the mass. Cellular atypia was not present. Based on the above morphological features and the patient’s history, the diagnosis of parathyroid adenoma arising from autotransplanted tissue was established. This case illustrates that parathyroid adenoma can arise from autotransplanted parathyroid tissue causing hyperparathyroidism.

P356 TUMOR CHARACTERISTICS AND CLINICAL OUTCOME IN ENDOSCOPICALLY RESECTED EARLY ESOPHAGEAL ADENOCARCINOMAS WITH LYMPHOVASCULAR PERMEATION. M. Tripathi, A. Grin, C.J. Streutker. St. Michael’s Hospital, University of Toronto, Toronto, Ontario, M5B 1W8.

Introduction: Early glandular lesions of esophagus or GEJ (high grade dysplasia, or T1 carcinomas) are potentially curable with endoscopic resections. While many patients are cured with mucosal resection techniques only, there is currently no specific factor(s) that indicates which patients require further surgery. We reviewed a series of esophageal/GEJ endoscopic mucosal resections (EMR) for adenocarcinoma to evaluate lymphovascular and/or submucosal invasion with correlation to outcome in order to determine if these factors are sufficient for surgical decision-making. Method: In this study we reviewed clinical outcome and tumor characteristics for endoscopically resected early esophageal adenocarcinomas with lymphovascular permeation. Clinical details and histology slides for thirteen cases diagnosed with lymphatic permeation on endoscopic resections were retrieved from our database for review. Results: Between the year 2009 and 2011, thirteen cases of endoscopically resected esophageal adenocarcinoma were reported to have lymphovascular permeation. The median age for this patient group was 68 years with male predominance (M:F=11:2). The majority of these tumors (69.3%) were associated with early submucosal invasion (pT1b), significant tumor budding (>5 buds at the invasive front) (61%) and poor tumor differentiation (69%). Additional immunohistochemical stains (D240 & CD31) were used in 8 cases to confirm the diagnosis of lymphatic permeation. Clinically, 8 patients underwent esophagectomy and the remaining were managed with radiofrequency ablation (1 case), phototherpay (1 case) and follow up with further EMRs (3 cases), due to comorbidities. One out of eight (12.5%) patients with esophagectomy had lymph node involvement and the remaining patients were lymph node negative. The tumor from the patient with a positive lymph node also had other adverse tumor characteristics i.e. presence of submucosal invasion, significant tumour budding, stromal desmoplasia, and poor differentiation. Conclusion: Presence of lymphatic permeation should affect the management decision in endoscopically resected esophageal adenocarcinomas and might be associated with lymph node involvement by the tumor. However, sometimes it can be difficult to assess its presence in endoscopic resection specimens. In this study, we demonstrate that presence of other adverse tumor characteristics such as submucosal invasion, significant tumour budding, low tumor stroma ratio and poor differentiation might be an indication for extensive workup including additional immunohistochemical stains to look for lymphovascular permeation.

P357 SIGNIFICANCE OF HETEROGENEOUS HER2 EXPRESSION IN EARLY ESOPHAGEAL ADENOCARCINOMA: A CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY OF 30 CASES. M. Tripathi, C.J. Streutker. St. Michael’s Hospital, University of Toronto, Toronto, Ontario, M5B 1W8.

Introduction: HER2 overexpression and/or amplification is well documented in gastric and gastroesophageal cancers and is predictive of response to trastuzumab with significant survival benefit. The relationship of HER2 amplification in esophageal adenocarcinoma to prognosis has not been well defined. We examined the frequency and pattern of tumor heterogeneity, tumor characteristics, and prognostic impact of HER2 protein expression in a subset of patients with endoscopically resected early esophageal adenocarcinoma. Method: HER2 expression was analyzed by immunohistochemistry (IHC) in endoscopic mucosal resection specimens (n=30) using criteria defined in the ToGA trial. Heterogeneity was defined by the presence of more than 2 scores of staining within the same tumor. Cases were categorized into 5 different patterns identified: (1) Diffuse positive (diffuse 3+ staining) (2) Diffuse negative (diffuse 0/1+ staining) (3) Heterogeneous positive (≥10% tumor with 3+ staining + 2 additional scores) (4) Heterogeneous negative (0 or 1+ predominant + 2 additional scores <10%) (5) Equivocal (> 10% 2+). Tumor differentiation, depth of invasion, lymphovascular invasion and E-cadherin expression were recorded. Results: Tumor characteristics associated with the 5 patterns were studied. The diffuse negative cases were most associated with aggressive features followed by heterogeneous positive & heterogeneous negative groups. Overall, the group with the fewest poor prognostic factors was those that were diffusely positive. Conclusion: Diffuse 3+ HER2 positivity was seen in 20% of these cases and was associated with less aggressive tumor characteristics compared to diffuse negative and heterogeneous cases in early esophageal adenocarcinomas, which correlates well with the previous studies on esophageal and gastroesophageal adenocarcinomas. In contrast to this finding the Her2 amplified gastric adenocarcinomas have worse prognostic outcome.

P358 P53 AND MMR EXPRESSIONS IN COLORECTAL CARCINOMAS. Khoo JJ<sup>1</sup>,<sup>2</sup>, Gunn A<sup>2</sup>, Peh SC<sup>2</sup>,<sup>3</sup>
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Objectives: To study the pattern and relationship of p53 over-expression and mismatch repair defect in colorectal carcinomas. Methods: The case histories and histopathology of colorectal carcinomas of 298 patients were reviewed. Immunohistochemical staining was performed to determine p53 over-expression and expression for the mismatch repair protein: MHL1, hMSH2 and hMSH6. Results & Discussion: 43 cases (14.4%) showed abnormal staining patterns for at least one of the three mismatch repair proteins. These MMR-d tumours were significantly localised to the right side of colon (p<0.001), poorly differentiated (p<0.001) and showed presence of marked necrosis (p=0.005). Half of the 298 cases (50.7%) showed p53 over-expression. Tumours with p53 over-expression were predominantly localised to left side of colon (p<0.001) but did not show any significant predilection for tumour differentiation or mucin production. 74.4% of colorectal carcinomas with mismatch repair defect did not demonstrate nuclear staining for p53 and 92.7% of tumours with p53 over-expression were found to have no loss of the MMR protein (p<0.001). There was no significant difference between survivals of patients with mismatch repair defect CRCs compared to patients with CRCs that showed p53 over-expression. Conclusion: MMR-d colorectal carcinomas and CRCs with p53 over-expression were significantly localised to different sites, and showed significant inverse correlation. They are distinct groups of tumours with different characteristics.
P359
EVALUATION OF THE EFFECT OF SHUNT SURGERY IN PATIENTS WITH EHPVO ON PORTAL HYPERTENSIVE GASTROENTEROPATHY.
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Background: EHPVO is the commonest cause of portal hypertension in children in India. Shunt surgery reduces the risk of hemorrhage, corrects hypersplenism, as well as improves growth and quality of life. Study on the effect of surgery on portal hypertensive gastroenteropathy (PHGE) is scarce. The aim of this prospective study was to evaluate the effect of shunt surgery on PHGE in patients with EHPVO.

Methods: In this prospective study 23 patients with EHPVO referred for surgery were enrolled. Endoscopic biopsies from the fundus, antrum and duodenum were taken preoperatively and then all patients were assessed at a minimum of 3 months after surgery and endoscopic biopsies were taken for histopathological evaluation. Out of the 23 patients who underwent surgery, 1 patient died in the early post-operative period and 2 patients were lost to follow up. Remaining patients were divided into - (Group A, Shunt group; n=14): successful shunt surgery and (Group B, Non-shunt group; n=6): underwent surgery, but the shunts were not patent on follow-up. Results: The mean age of patients with EHPVO (M:F:1.3:1) at presentation was 10.63 yrs (Range, 3.5–21.5 yrs) with mean duration of symptoms 6.46 yrs. Portal hypertensive gastropathy (PHG) on upper GI endoscopy showed significant improvement in patients who underwent shunt surgery. The PHG scores improved in group A from 1.2±0.5 to 0.2±0.4 after surgery (p<0.05). Gastric varices were seen in 6 (42.9%) patients in group A and 2 (33.3%) in group B, which disappeared after surgery in both groups. There was no statistically significant difference between the pre-op and post-op histological parameters in the gastric and duodenal biopsies samples.

Conclusions: Successful shunt surgery is likely to have a reduction in mucosal blood flow, but the actual reduction in ectatic vessels and capillaries is likely to take time.

P360
TWO RARE CASES OF HEPATOCELLULAR CARCINOMA ARISING FROM LONGSTANDING HEPATIC ADENOMATOSIS IN A NON-CIRRHOTIC LIVER.
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Objectives: Hepatic adenomatosis was first described in 1985 and defined as the occurrence of multiple adenomas in an otherwise normal liver. To date, few cases of the development of hepatic carcinoma (HCC) in a background of hepatic adenomatosis (HA) have been reported. Methods: We reviewed the clinical history, imaging, and pathological assessment of two women, aged 43 (Patient #1) and 39 (Patient #2) who developed HCC from longstanding HA. Results: Patient #1 had a 20-year history of oral contraceptive pill (OCP) use, and did not smoke or drink. She was found to have eight hepatic lesions in 2004, discovered incidentally. The lesions remained stable until 2012 when imaging revealed one of the masses to be highly suspicious for malignant transformation. She underwent segmental hepatectomy and pathologic examination showed moderately differentiated HCC; the remainder of the mass showed residual adenoma. Patient #2 had a history of Diabetes Mellitus II, hypertension and hypothyroidism. She had no history of OCP use, smoking, or alcohol. She was incidentally found to have three hepatic nodules. Two were surgically removed and found to be adenomas. A 2010 MRI revealed a total of seven lesions consistent with adenomas, with the exception of one rapidly growing mass. Core biopsies during radiofrequency ablation demonstrated well differentiated HCC.

Conclusions: The conventional hepatic adenoma (CHA) is a benign neoplasm of the liver that has a strong association with exogenous sex hormones. The literature shows that the incidence of rupture, hemorrhage and malignant transformation is considerably higher in HA compared to CHA. These cases show that malignant transformation can occur several years from initial diagnosis of HA, and long-term follow-up is warranted if surgical excision is not feasible.

P361
GLOMUS TUMOR OF THE RECTUM: A CASE REPORT.
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Introduction: Glomus tumors are mesenchymal tumors composed of modified smooth muscle cells representing a neoplastic counterpart of the plexiform glomus bodies. Ultrastructurally, the glomus tumor cells have features resembling smooth muscle cells. They are most common in the skin and subcutaneous tissue, but also occur in the viscera. In the gut, they are almost exclusively found in the stomach. There have been only four previous cases reported in the literature of glomus tumor in the colon, 2 of which were in the anorectal area. We report the third case of glomus tumor in the anorectum, and 5th in the colon.

Case report: A 68 year old female was referred for abdominal-perineal resection of a locally advanced rectal carcinoma after neo-adjuvant chemotherapy. She did not report unusual rectal pain. The tumour showed marked therapy response with minimal residual tumour. From the perirectal fat, a small nodule, 0.3 cm, was found, considered to be a lymph node. On histologic examination, this nodule was composed of a vascular lesion, where dilated blood vessels were associated with small collections of bland cells. These cells stained positively for actin on immunohistochemistry. The appearance was consistent with a small benign glomus tumor.

Discussion: Gastric glomus tumors typically present with abdominal pain, bleeding, or are simply incidental findings. The previous cases in the colon presented as pain (1 anal, one ascending colon), and bleeding (one rectal case). Two were present in the perirectal fat and two in the submucosa of the colon. Our case, present in the peri-colonic fat, did not cause pain but the rectal carcinoma may have masked symptoms from the glomus tumour. Glomus tumors have a distinct histologic appearance, although some features overlap carcinoid tumors, epithelioid gastrointestinal stromal tumors, and lymphomas. Glomus tumors are generally benign, though rare cases have resulted in metastasis and death: histological features as cellular atypia, mitosis and lymphovascular invasion do not predict malignant behaviour.

P362
THE PRO-PROLIFERATIVE ACTIVATION OF THE c- MYC ONCOGENIC FACTOR.
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In the small intestine the c1 integrin subunit is present only in proliferating crypt cells while its exclusive partner c2 is constitutively expressed in all intestinal cells supporting a reported role for c1, via caveolin-1 and Shc, in the downstream activation of the Ras/ERK proliferative pathway. In mouse models, the c1β1 integrin supports breast cancer cell motility and, together with the Kras oncogenic factor, potentiates tumour growth. The expression of c1β and the above roles have not been described in the human normal colon and colorectal cancer (CRC). Results: Immunofluorescence showed c1β only at the basolateral domain of proliferative crypt cells in the normal colon mucosa. Immunohistochemistry analysis performed on a tissue microarray containing 65 adenocarcinomas and their matched margins showed c1β to be highly expressed in 57% of tumours compared to margins. In the colorectal HT29 tumour cell line, c1 mRNA silencing resulted in reduced cell proliferation. In silico analysis of the c1 promoter sequence revealed response elements for c-Myc known to be involved in cell proliferation, while 293T cells transiently transfected with c-Myc showed an increased c1 promoter activity that was abolished by co-transfection with the Mad-Myc dominant negative plasmid. HT29 cells treated with a pharmacological c-Myc inhibitor, 10058-F4 (50μM) for 24 or 48 hours, also showed a drastic reduction of c1 mRNA levels. These results show that the increase in integrin c1 subunit expression in CRC could be mediated by the c-Myc oncogenic factor (supported by CIHR).
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PRIMARY GALL BLADDER LYMPHOMAS: CLINICOPATHOLOGICAL ANALYSIS.

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Objective: Primary gall bladder lymphoma is extremely rare with most of the documented cases being case reports. Also, owing to its rarity, primary hematolymphoid malignancy of the gall bladder is seldom considered in the differential diagnosis. Methods: We present our experience with ten cases of primary gall bladder lymphomas identified from the pathology files of Mayo Clinic over an 18-year period (1994-2012). Results: The patients consisted of 3 men and 7 women. Ages ranged from 51-67 years (mean age, 61 years). Abdominal pain due to cholecystitis was the most common presenting symptom (7 patients), followed by jaundice (2 patients) and one patient was asymptomatic and diagnosed on work up for knee surgery. In two cases a distinct mass measuring 4 and 2 cm was identified within the fundus. Using morphology and immunohistochemical stains, 6 cases were classified as follicular lymphoma (FL) (5 cases were grade 1 while 1 case was grade 3), 2 cases of diffuse large B cell lymphoma (DLBCL) and another 2 cases of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). All the diagnoses were made on cholecystectomy specimens and none of the patients had a prior history of lymphoma. Gall stones were present in 8 (80%) cases. Immediately after the diagnosis of lymphoma, a bone marrow biopsy was performed in 8 cases and it was involved by lymphoma only in 2 cases (1 case each of grade 1 FL and CLL/SLL). Five patients (3 with grade 1 FL and 2 with DLBCL) received chemotherapy and 1 of them with DLBCL also received autologous bone marrow transplant. Follow-up data was available in all 10 patients; 6 (60%) patients died (3 grade 1 FL, 2 DLBCL and 1 CLL/SLL). All were alive with no evidence of disease at 9 months (mean 17 months), while 3 patients died 1-132 months (mean 47 months) after the initial diagnosis; 3 of them (2 cases of grade 1 FL and 1 case of grade 3 FL) due to progressive disease and 1 (case of CLL/SLL) due to pancreatic adenocarcinoma. The patient with grade 3 FL died within a month of the initial diagnosis while both the cases with DLBCL were in remission 5 years after treatment. Conclusions: Primary gall bladder lymphoma is an extremely rare entity. In our study there was a female predominance and follicular lymphoma was the most common subtype. Clinically the patients presented with non-specific symptoms of abdominal pain and an accurate preoperative diagnosis of primary gall bladder lymphoma is very difficult to reach. Surgical resection, followed by chemotherapy appears to be a valid role as reasonable treatment.

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THE ASSESSMENT OF THE BRAF V600E MUTATION STATUS IN COLON CANCERS WITH MICROSATellite INSTABILITY BY IMMUNOHISTOCHEMISTRY WITH A MUTATION SPECIFIC MONOCLONAL ANTIBODY.

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Lynch syndrome represents 2-3% of all colorectal cancers (CRC); its hallmark is a high degree of microsatellite instability (MSI-H). 10-15% of CRC are sporadic MSI-H and are associated with the BRAF V600E mutation. Most regional hospitals use mismatch repair (MMR) protein immunohistochemistry (IHC) for screening Lynch syndrome. Screening for V600E can exclude specific cases but requires a molecular testing facility. Alternatively, one could add a V600E targeted antibody into existing IHC panels of MMR proteins. A new antibody, ‘VE1’, has proven sensitive and specific in targeting V600E-mutated thyroid and melanoma tumors but has yet to be applied to CRC. Objective: To assess the performance of the VE1 antibody in MSI-H CRC. Methods: VE1 was applied to microarrays of 152 CRC tumors with known MSI status, protein expression was scored, and MSI-H CRC were sent for BRAF mutation analysis. Results: 17 of the 152 cases (11%) were positive for VE1 IHC. Of the 18 MSI-H CRC, 8 (44%) stained with VE1 and these were all confirmed V600E mutations. The result of the BRAF mutation assay is available in 7 MSI-H, VE1 IHC negative cases: 6 were confirmed negative for the V600E mutation; one VE1 negative tumor showing signet ring cell morphology was positive for the mutation. Conclusion: The rate of V600E positivity in MSI-H CRC by VE1 IHC is consistent with published cohorts that use molecular assays. The potential for ‘false negative’ IHC interpretation may exist in the context of morphological signet ring cell variants, further analysis of such cases is ongoing. Given the high degree of sensitivity and specificity of the VE1 antibody, it could be incorporated into the existing IHC panel for assessing MSI-H CRC.

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TUMOUR BANKING OF PANCREATIC CANCER SPECIMENS: ANALYSIS OF FACTORS AFFECTING SAMPLE COLLECTION AT KINGSTON GENERAL HOSPITAL.

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Background: Kingston General Hospital (KGH) is a participating collection centre for the Ontario Tumour Bank. A prerequisite of sample collection is that tissue sampling does not restrict clinicopathologic diagnosis. Interested in factors that affect “banking” success, we reviewed our tumour bank submission experience for pancreatic cancer (PanCa) resection specimens. Method: Retrospective review of pathology and operative reports of all primary pancreatic tumors resected from 2007 to 2012 (specimen data, lab submission time, “banking” status). Results: Of 84 pancreatic tumors resected during the study period, 69 were malignant (PanCa). There were 2 cases received in formalin leaving 67 “bankable” PanCa specimens (8 adenCa; 9 NET). Samples from 24 tumours (36%) were submitted for tumour banking. Mean tumour size was 3.1 cm (range 0.6 to 6 cm; n=66). In the non-banked tumours (42/66), 60% were small (<2.5 cm) compared to only 25% in the banked group (p=0.01). Regardless of size, body-tail tumours were more frequently banked compared with those on the head (57% vs. 26%; p=0.03). For the 34 cases with accurate lab data on time of specimen receipt, there was a trend to higher “banking” success with specimens received before 15:30 hours (48% vs. 20%; p=0.35). Conclusion: Specimen factors that limit tissue collection for tumour banking from PanCa resection specimens at KGH include tumour size and site. Smaller tumours are less likely to be sampled to avoid interference with clinicopathologic tissue diagnosis. Lower “banking” success for tumours in the pancreatic head region is not due to size alone and likely relates to other factors (such as anatomic site complexity). Attention to coordination of the laboratory’s capability to perform tumour tissue sampling with the time of specimen resection is also likely important in maximizing “banking” success for PanCa specimens.

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LIPOID CELL VARIANT OF UROTHELIAL BLADDER CARCINOMA: A REPORT OF 3 CASES.

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The lipid cell variant of urothelial carcinoma is a rare tumour that some feel bears a poor prognosis. We present 3 cases of urothelial bladder carcinoma, with lipidoid morphology, occurring in male patients aged from 60 to 80 years. Two patients presented with hematuria, and one patient presented with dysuria, dyschezia and tenesmus. The lipid cell component consisted of nests of large lipoblast-like tumour cells with abundant clear multi-vacuolated cytoplasm adjacent to conventional urothelial carcinoma. Other morphologic variants including plasmacytoid and micropapillary were also present in two of the cases. In one patient, the lipidic cells were also found in the preceding urine cytology specimen. Two of the tumors infiltrated muscularis propria, and one tumour involved the rectum by direct extension. The tumour cells were positive for cytokeratin 7, cytokeratin 20 and were negative for S-100 protein by immunohistochemistry. Furthermore, the lipidic cells were negative for PAS and Mucicarmine. The differential diagnosis included liposarcoma, signet ring cell carcinoma and urothelial carcinoma with sarcomatoid differentiation. In follow-up, one patient with pT4b disease developed a recurrence despite combined chemotherapy and radiation. The second patient with pT3a disease is currently disease free 3 months after radical cystoprostatectomy. The treatment is still ongoing in the third patient. Identification of lipidoid morphology is important to ascertain if it has unique prognostic value.
DNA RECOVERY AND INTEGRITY IN ARCHIVAL PROSTATE CANCER TISSUE.
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Background: Mitochondrial DNA (mtDNA) sequence variation contributes significantly to molecular diversity in early prostate cancer (PCa). Therefore, studying mtDNA sequence variation could be useful in studying PCa evolution and progression. These studies require long term follow-up of patients whose clinical outcome unfolds 10 or 20 years after prostatectomy. No sample is better suited for such a study than archival formalin fixed, paraffin embedded (FFPE) tissue paired with high quality clinical information. However, only scant reports are available describing the recovery rates (RR) of mtDNA and nuclear DNA (nDNA) from FFPE PCa tissue. Here, we assessed mtDNA recovery and integrity from FFPE clinical samples and PCa cell lines. Methods: Whole DNA was extracted from three fresh (FF) human PCa cell lines and from the same lines embedded in FFPE. Using real time quantitative polymerase chain reaction (qPCR), copy numbers and the length of amplifiable DNA fragments were determined for B2M encoded nDNA and ND1 encoded mtDNA, comparing FFPE against FF samples, as well as FFPE clinical samples from 1 to 15 years old. Results: The average copy number of mtDNA per nDNA was 863 and 907 in FFPE and FF cell lines respectively. A similar pattern of significantly higher mtDNA than nDNA copy numbers was also observed in FFPE clinical samples. In addition, prostate cancer tissue showed higher mtDNA copy number than benign tissue. RR of both mtDNA (p = 0.037) and nDNA (p = 0.019) fragments of 300 bp or more significantly decreased with age of FFPE tissue. Conclusions: Due to high copy number, large amounts of mtDNA can be recovered from FFPE prostate cancer cells and clinical samples. Optimal recovery requires limiting fragments of interest to approximately 300 base pairs or less.

P368
ANASTOMOSING HAEMANGIOMA OF KIDNEY: A RARE VASCULAR LESION OF THE GENITOURINARY TRACT.
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Vascular neoplasms of the genitourinary tract are rare with benign entities outnumbering malignant ones. Clinically, haemangiomas, haemangiendotheliomas and angiosarcomas may present in a similar manner with pain and haematuria. We describe a case of an unusual vasiformative kidney lesion of which less than 30 cases are cited in the published literature. A 59 year old female presented with an intracranial mass which was originally presumed to be a metastasis of unknown origin. The ensuing work up to identify a potential primary lesion, revealed a 4.5cm hiliar mass in the left kidney. Grossly, the excised renal lesion measured 4.5x3.8x3.8 cm and appeared to be confined to the hilum. Microscopy showed focal infiltration of the sinus fat. Morphologically the lesion exhibited a sieve like, vascular architecture with hobnailed endothelial cells, intravascular thrombi and infarction of adjacent tissue. Mitoses and atypia were not identified. All resection margins were negative. All resection margins were negative. CD31, CD34 and Factor VIII stains were positive. The morphology and immunoprofile were in keeping with an anastomosing haemangiomna of the kidney. The literature to date suggests these are benign which is consistent with our currently described case since subsequent excision of what was originally presumed to be a brain metastasis turned out to be a meningioma. Awareness of this lesion should help prevent overdiagnosis of angiosarcoma.

P369
PRIMARY CARCINOMA OF RENAL CALYX.
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Introduction: Renal calyx carcinoma (RCXC) may mimic collecting duct carcinoma (CDC) or urothelial carcinoma (UC) of the renal pelvis. RCXC is distinguished from CDC and UC of the renal pelvis as having the tumour epithelium in the renal calyx, with limited involvement of the surrounding renal pelvis surface urothelium. In this study, we summarize our experience with this entity. Design: 8 cases of RCXC, including 7 cases with urothelial differentiation (RCXC-UC) and 1 case with salivary gland-type differentiation (RCXC-SC), were identified. 10 consecutive cases of UC were selected for comparison. Immunohistochemistry (IHC) was performed for PAX8, vimentin, CK7, CK20, HMWCK, P63, AMACR, RCC, CD10, S100, and MSA. Results: The 8 RCXC cases presented with renal masses of 3-6cm, metastatic disease in 1 case and positive renal washings in 2 cases. Treatment was nephrectomy followed by radiation +/- chemotherapy and all cases later developed metastases. Tumour epithelial was in the renal calyx with extensive spread along the collecting ducts and in situ RCXC-UC involved adjacent renal calyces. RCXC-SC showed adenoid cystic and basoloid features. Remaining renal pelvis had small tumour burden in 3 cases and no tumour in 5 cases. One case had associated UC of the bladder. Of 10 UC cases, tumour was limited to the tip of renal papilla in 7 cases, extensive in 3 cases, and with no extension into the collecting ducts. RCXC-UC were positive for PAX8, CK7, AMACR, CD10, focally positive for CK20, p63, HMWCK, and negative for RCC. The RCXC-SC had the same IHC profile plus focal reactivity for myoepithelial markers. The 10 UC cases shared IHC properties with RCXC-UC but frequently negative for PAX8. Conclusions: RCXC is an aggressive neoplasm with high risk of metastases. Similar to CDC, it is located in the renal papilla and may have normal urine cytology. Unlike CDC, RCXC shows predominantly urothelial differentiation and is associated with an in situ component of adjacent renal calyces. By IHC, RCXC can be differentiated from CDC by negative RCC and positive p63, and from UC by positive PAX8.

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MIXED LOW AND HIGH GRADE PAPILLARY UROTHELIAL CARCINOMA HISTOPATHOGENETIC AND CLINICAL SIGNIFICANCE.
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Introduction: There are two pathways of urothelial carcinogenesis: low-grade urothelial carcinoma (LGUC), with low rates of gene alterations and high-grade urothelial carcinoma (HGUC), with numerous gene alterations. HGUC typically have strong reactivity for CK20 and p16. Despite distinct molecular changes, UC with low and high grade features are not uncommon. We examined cases with a prominent pattern of mixed low and high grade UC (MLHUC). Design: Consecutive cases of UC were reviewed, identifying 45 cases with both LGUC and HGUC. IHC was performed for PAX8, CK20 and Ki67 in 20-50% of the tumour, while HGUC areas had negative or focal reactivity for CK20 and Ki67 in 10-30%. Results: There were two distinct cohorts of MLHUC: patients with a history of LGUC (Type A) and those without (Type B). Patients with Type A (n=8) had a history of LGUC for 2-10 years. The tumour specimens weighed 1.5x1.7g, and had HGUC components of 25x20% of the tissue. Superficial invasion was present in 1 case. All tumours had BCG treatment with 1 recurrence. In patients with Type B (n=37), tumour specimens weighed 3x3.9g and had HGUC components of 43x21% of the tissue. Superficial invasion was present in 5 cases, and muscle invasion with lung metastasis in 1 case. Four cases were refractory to BCG with increase in proportion of HGUC and 1 requiring cytoresection. Differences in size and proportion of HGUC between Type A and Type B MLHUC were significant (P<0.05), with Type B presenting with higher tumour burden and proportion of HGUC. Conclusions: MLHUC are challenging, and are usually assigned a higher grade, as this determines prognosis. Type A MLHUC develop as a result of progression from LGUC, whereas Type B MLHUC develop de novo, are associated with larger tumour, higher proportion of HGUC and worse prognosis. Despite the similar histology of Types A and B, assignment to HGUC in a binary system may mask important prognostic information.
other entities. We report a case of PUP and describe some of its mimics. Bladder and papillary urothelial cell carcinoma. Morphological atypia and located prostatic ductal adenocarcinoma, villous adenoma of urinary prostatic acinar adenocarcinoma protruding into prostatic urethra, centrally his symptoms disappeared. It is esse established. The patient was recovered completely after the procedure and present and P504S was not increased. Therefore, a diagnosis of PUP was polypoid soft tissue contained papillary structures with fibrovascular papillary growth in prostatic urethra. The lesion was completely resected and abnormal micturition for 6 months. Cysto report a case of PUP in an 80-lesional mass in the prostatic urethra is uncommon, yet the disease entities are so heterogeneous that the spectrum ranges from congenital malformations, benign polyps, to various malignancies. Prostatic urethral polyp (PUP) is a rare benign overgrowth of prostatic parenchyma. Because of its location, varieties of symptoms, including dysuria, hematuria, urinary tract infections, and obstruction leading to urinary retention, can be encountered and diagnostic confusion might be appreciated. Here we report a case of PUP in an 80-year-old male who presented with hematuria and abnormal micturition for 6 months. Cystoscopy detected abnormal papillary growth in prostatic urethra. The lesion was completely resected transurethrally and submitted for pathological examination. Microscopically, the polypoid soft tissue contained papillary structures with fibrovascular cores. The lining columnar epithelial cells had small oval nuclei and abundant foamy cytoplasm. No atypia was appreciated. Immunohistochemistry revealed that the epithelial cells were positive for CK7, prostate-specific antigen (PSA), and negative for CK20. A PIN4 (CK5, CK14, P63 and P504S) immunostain showed that the basal cells were present and P504S was not increased. Therefore, a diagnosis of PUP was established. The patient was recovered completely after the procedure and his symptoms disappeared. It is essential to differentiate PUP from prostatic acinar adenocarcinoma protruding into prostatic urethra, centrally located prostatic ductal adenocarcinoma, villos adenoma of urinary bladder and papillary urothelial cell carcinoma. Morphological atypia and immunohistochemical patterns are pivotal to differentiate PUP from the other entities. We report a case of PUP and describe some of its mimics.

PROSTATIC URETHRAL POLYP: A CASE REPORT AND REVIEW OF LITERATURE
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Lesional mass in the prostatic urethra is uncommon, yet the disease entities are so heterogeneous that the spectrum ranges from congenital malformations, benign polyps, to various malignancies. Prostatic urethral polyp (PUP) is a rare benign overgrowth of prostatic parenchyma. Because of its location, varieties of symptoms, including dysuria, hematuria, urinary tract infections, and obstruction leading to urinary retention, can be encountered and diagnostic confusion might be appreciated. Here we report a case of PUP in an 80-year-old male who presented with hematuria and abnormal micturition for 6 months. Cystoscopy detected abnormal papillary growth in prostatic urethra. The lesion was completely resected transurethrally and submitted for pathological examination. Microscopically, the polypoid soft tissue contained papillary structures with fibrovascular cores. The lining columnar epithelial cells had small oval nuclei and abundant foamy cytoplasm. No atypia was appreciated. Immunohistochemistry revealed that the epithelial cells were positive for CK7, prostate-specific antigen (PSA), and negative for CK20. A PIN4 (CK5, CK14, P63 and P504S) immunostain showed that the basal cells were present and P504S was not increased. Therefore, a diagnosis of PUP was established. The patient was recovered completely after the procedure and his symptoms disappeared. It is essential to differentiate PUP from prostatic acinar adenocarcinoma protruding into prostatic urethra, centrally located prostatic ductal adenocarcinoma, villos adenoma of urinary bladder and papillary urothelial cell carcinoma. Morphological atypia and immunohistochemical patterns are pivotal to differentiate PUP from the other entities. We report a case of PUP and describe some of its mimics.

BILATERAL CORES WITH CANCER AND ELEVATED PSA PREDICT UNDERESTIMATION OF GLEASON GRADE BY PROSTATE NEEDLE BIOPSY
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Background: Prostate cancer is usually harmless, but in a significant minority of patients, it is lethal. In radical prostatectomy (RP) specimens, Gleason scores (GS) below 7 has nearly zero risk of metastasis or death. On biopsy, however, GS is not accurate and risk cannot be safely assessed. We retrospectively analyzed biopsy and clinical factors associated with underestimating GS on prostate needle biopsy. Method: Of 462 prostate cancer patients, 192 patients had a GS 6 on prostate biopsy. In these patients, we analyzed GS accuracy in prostate biopsy and several clinical features using Mann-Whitney’s test and logistic regression analysis. Results: 107 patients (55.7%) were diagnosed with identical GS on both prostate biopsy and RP. 65 patients (44.3%) had disparate GS on biopsy and RP, of which, the vast majority (74 patients, 39%) had higher GS on RP than on biopsy. Median PSA level just before prostate biopsy was 6.2 ng/ml (0.45 - 35.3 ng/ml). 63 patients (32.8%) had positive cores in both sides of the prostate, whereas the remainder had unilateral positive cores. The PSA level of patients whose biopsy underestimated GS was significantly higher that of patients whose biopsy and RP had identical GS (p = 0.001). In multivariate analysis, bilateral positive cores (p = 0.007) and PSA level (p = 0.044) were significantly correlated with the ability of biopsy to predict RP grade. Conclusions: In patients diagnosed with indolent cancers (GS 6 or lower) PSA levels above 7 and/or positive cancer cores from both sides of the prostate may be at significantly increased risk of having a higher grade cancer.

MELKERSSON–ROSENTHAL SYNDROME, A RARE CASE REPORT OF CHRONIC EYELID SWELLING
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Background: Melkersson–Rosenthal syndrome is rare neurological disorder of idiopathic etiology, very few patients present with classical triad of recurrent facial paralysis, swelling of the face and lips and deep furrowed tongue. Historically, the syndrome is very few patients present with classical triad of recurrent facial paralysis, swelling of the face and lips and deep furrowed tongue. Historically, the syndrome is very few patients present with classical triad of recurrent facial paralysis, swelling of the face and lips and deep furrowed tongue. Historically, the syndrome is very few patients present with classical triad of recurrent facial paralysis, swelling of the face and lips and deep furrowed tongue.

Result: Histopathology revealed a granulomatous lesion and descriptive diagnosis of "edema with mild chronic inflammation and focal perilymphatic granulomas" was given. Fungal, bacterial and mycobacterial stains were negative. Polarization failed to reveal foreign bodies. On physical exam deep furrowed tongue was found and based upon histological granulomatous findings suggestion of MRS was given. Patient was started on steroid and he responded very well. For his sign symptoms related to rosacea, he was put on doxycycline. Conclusion: In our case chronic eyelid swelling, deep furrowed tongue and Noncaseating granulomas, all findings were correlated and definite diagnosis of MRS was suggested, as a result patient was treated well with steroid therapy. So careful clinical, histopathological correlation and good communication between treating physician and diagnostician is the key factor for making definite diagnosis and avoiding diagnostic pitfalls.
INCIDENTAL MERKEL CELL CARCINOMA IN A CUTANEOUS HORN: A CASE REPORT.

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Background: Merkel cell carcinoma (MCC) is a rare, aggressive malignancy in sun exposed skin of elderly patients, with 1500 cases per year in the United States and an incidence of 0.004% cutaneous cases per year at our institution. Merkel cell polyomavirus (MCPyV) was discovered in 2008 and is clonally integrated in the genome of 60-90% of MCCs. MCC in combination with other epithelial malignancies and clinically presenting as a cutaneous horn is a rarity.

Case Report: A 93 year-old woman presented with an enlarging cutaneous horn on her left lower cheek. She was treated with local excision, and histology revealed a squamous cell carcinoma (SCC) in situ with an underlying MCC. Both tumors were negative for MCPyV. Measurement of depth of tumour of MCC was problematic due to the overlying SCC in situ. On review of literature, approximately 10-25% MCCs are found in association with other malignancies, most commonly SCC. Interestingly, combined MCCs are mostly MCPyV-negative, except for one recent case report of an MCC-basal cell carcinoma.

Conclusion: We describe a rare case of combined MCC-SCC in situ and its unusual clinical presentation as a cutaneous horn. The pathogenic role of MCPyV in combined tumours warrants further investigation.
ABSTRACTS – POSTER PRESENTATIONS

Session B: 1815-1900

P401
TERATOMA ASSOCIATED (ANTI-NMDAR) PARANEOPLASTIC SYNDROME.
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Anti-NMDAR (N-methyl-D-aspartate Receptor Antibody Receptor) encephalitis associated with teratomatous lesions in females is well documented in the literature. The neurological and psychiatric manifestations can be severe to lethal, and commonly precede the gynecological diagnosis prompting clinicians to investigate the possibility of a coexistent pelvic mass. We present two cases of ovarian teratomas associated with limbic encephalitis to highlight both the differences and similarities particularly in relationship to the histological and biochemical features. Case 1 is a 26-year old female presented to ER for sudden onset of headache, dizziness and generalized tonic-clonic seizures. The overall clinical picture was suggestive of an acute metabolic/neurological condition for which she was treated and subsequently discharged. She was readmitted due to persistent fluctuating level of consciousness, bizarre behavior and recurrent seizures. She was seen by a neurologist who ordered multiple investigations including anti-NMDA receptor antibodies, which were positive. Subsequent imaging studies identified a large lobulated left adnexal mass which was surgically resected showing a mature solid teratoma with a dense benign lymphoid infiltrate. Following treatment (plasmapheresis, IVIG and laparoscopic surgical resection of the mass) the neuropsychiatric symptoms resolved completely. Case 2 is that of a 10-year old girl who presented with seizures and behavioral problems. She was found to have a large pelvic mass on physical examination and subsequent pelvic imaging confirmed a right ovarian mass measuring 21x13 cm. A right salpingo-oophorectomy was performed. The diagnosis was that of a malignant mixed germ cell tumor (immature teratoma Grade 3/3 as well as a component of yolk sac tumor). This patient tested negative for anti-NMDAR antibodies. The differences in the anti-NMDAR antibody status of these two individuals can be speculated to be due to the epitopes tested (NR1, NR2 and GluR). The similarities are obvious in that both patients presented with seizures and changes in behavior that could not otherwise be explained and both were found to have teratomatous tumors of their ovary.

P402
YOLK SAC TUMOR (ENDODERMAL SINUS TUMOUR) OF THE UTERUS: AN UNUSUAL PRIMARY SITE.
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Yolk sac tumours also known as endodermal sinus tumours (EST) are exceedingly rare malignant entities typically arising in the gonads, which account for 14-20% of all ovarian germ cell neoplasms. We report a rare case of EST arising in the uterine cavity of a young female initially presumed clinically to be a uterine leiomyoma (fibroid). This 25-year-old G2P0A2 female with a previous history membranous related anemia and uterine fibroid presented to the Emergency room with pelvic pain. Speculum examination revealed a mass protruding through the cervix. Initial blood work revealed a normal CEA and beta-HCG with elevated alpha-fetoprotein and Ca-125. Imaging of the pelvis showed a uterine mass 10x8x5.2cm with metastatic implants in the cul-de-sac and positive external iliac lymph nodes. The biopsy specimen showed classical features of EST including the presence of Schiller-Duval bodies. Immunohistochemistry displayed positive stains for AFP and Glycogen. This case is notable due to the primary site of the EST. A handful cases have been published documenting unusual anatomic origins of ESTs. We review here the etiology, common histological features and immunohistochemistry pertaining to ESTs in the context of this case and highlight the literature surrounding unusual primary sites of ESTs.

P403
A CASE OF PSEUDOVASION OF LYMPHOVASCULAR SPACES IN A CERVICAL BIOPSY: A DIAGNOSTIC PITFALL.
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Pseudovasoinvasion of lymphovascular spaces is occasionally reported in surgical pathology. We present a case of lymphovascular pseudovasoinvasion in a cervical biopsy from a 63 year old lady who presented with a cervical polyp removed using ring forceps. Grossly, the specimen consisted of a tan, irregular, polypoid fragment of tissue measuring 0.8 cm. Histologically, the specimen showed dilated lymphovascular channels containing mucin often in association with small clusters of bland appearing mucinous epithelium with a focal papillary architecture. The findings were strongly suspicious for lymphovascular invasion of a mucinous adenocarcinoma. There was no evidence of adenocarcinoma in situ or of cervical stromal invasion by adenocarcinoma. Due to the concern of a metastatic process immunohistochemistry was performed. The intravascular mucinous epithelium was positive for ER and CK7 and negative for CK20, CDX2, TTF1, p16 and BRST2. The patient underwent complete clinical examination. The patient is doing very well without any medical concern after a follow up of twelve months. The case was reviewed and presented at clinicopathological rounds at which time additional clinical information was obtained. The diagnosis was amended to that of lymphovascular pseudovasoinvasion. Lymphovascular space pseudovasoinvasion is more commonly seen in the uterine corpus with endometrial adenocarcinoma. In the cervix the involvement of squamous epithelium within lymphovascular spaces mimicking invasion is reported in the literature. To the best of our knowledge, this is the first case report of glandular lymphovascular pseudovasoinvasion in a cervical biopsy. We share our experience to highlight another example of pseudovasoinvasion of lymphovascular spaces and the importance of recognizing this potential diagnostic pitfall.

P404
UTERINE CARCINOSARCOMA IN A BRCA MUTATION PATIENT WITH TAMOXIFEN EXPOSURE: A CASE REPORT AND LITERATURE REVIEW.
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*These authors contributed equally to this case report.

Uterine carcinosarcoma, formerly known as malignant mixed Müllerian tumors (MMM), is an uncommon uterine tumour, representing less than 5% of all malignant tumours in the uterus. It is a biphasic tumour composed of both carcinomatous and sarcomatous components and traditionally has been classified as epithelial-stromal tumour. Recently, there has been increasing evidence to show that it arises from a monoclonal origin and behaves like a carcinoma and therefore should be classified as a variant of high grade endometrial carcinoma. We report a case of uterine carcinosarcoma in a patient who is a BRCA mutation carrier. The patient previously had history of breast cancer and was treated with Tamoxifen for five years. She presented with postmenopausal vaginal bleeding and was found to have advanced stage uterine carcinosarcoma. Association between tamoxifen use in breast cancer patients and uterine carcinosarcoma has been reported previously. However, literature has been divided regarding whether BRCA mutation itself increases the overall risk of endometrial carcinoma. To the best of our knowledge, specific association between BRCA mutation and risk of carcinosarcoma has not been reported.
Awareness of this rare uterine leiomyoma with extrauterine extension

Immunohistochemistry confirmed the smooth muscle nature of the tumour surrounding edematous and vascular stroma was seen. There was no myometrium and parametria. On microscopic examination a highly vascular replacing the posterior wall of the uterine corpus with extension to deep oophorectomy along with peritoneal washings. The patient then underwent right hemivulvectomy with groin dissection. Microscopic examination showed extension to deep and lateral margins and four of ten inguinal lymph nodes positive for metastatic adenocarcinoma with extranodal extension. Subsequently, she had adjuvant radiation therapy and has done well. Conclusions: Mammary-like gland adenocarcinoma is an extremely rare entity that must be taken into consideration when diagnosing adenocarcinoma of the anogenital region. It is a locally aggressive tumour and wide metastases are uncommon. It is important that this be differentiated from metastases, neoplasms arising from skin appendages, and extramammary Paget’s disease.

Objectives: To describe the histopathology of squamous cell dysplasia which could not be graded (CIN Q) on routine hematoxylin and eosin (H and E) stained sections. **Methods:** In a cohort of 17, 851 women, 478 (2.7%) had a diagnosis of CIN Q as the worst abnormality. All H and E slides were reviewed by a panel of 2 pathologists (1 and 2). Reasons for the CIN Q diagnosis were recorded. The study diagnosis was reached by 2/3 agreements on the worst diagnosis per case between the reviewers and the original pathologist. Cases with 3-way disagreement were reviewed together by the 2 study pathologists to reach a consensus. **Data and Results:** After 6 exclusions, 472 CIN Q cases remained. The cases contained multiple parts (n=901) consisting of: 442 cervical biopsies, 443 endocervical curettage, 5 LEEP’s, and 11 endometrial biopsies. For panelist 1 the diagnoses were: 270 benign, 175 CIN I, 4 CIN II, 69 CIN III, 377 CIN Q, 3 AIS, 1 SCC, and 2 unsatisfactory and for panelist 2: 419 benign, 120 CIN I, 35 CIN II, 75 CIN III, 247 CIN Q, 3 AIS, and 2 unsatisfactory. There was 3-way disagreement in 50 cases, 3-way agreement in 168, and 2/3 agreement in 254. After the consensus review, there were 352 cases of CIN Q as the worst diagnosis (1.9%) in 17,545 women. The most common reasons for the CIN Q diagnosis were mal orientation of the epithelium and dysplastic epithelium that was not full thickness. Conclusions: The 2% frequency of CIN Q as the worst diagnosis is established by this study. Proposed new terminologies for lower anogenital tract squamous dysplasia may need to consider CIN Q (SILQ) as a pathology reporting category.

**P406**

COTYLEDONOID DISSECTING LEIOMYOMA OF THE UTERUS

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Cotyledonoid dissecting leiomyoma (Stemberg tumor) is a rare benign uterine smooth muscle tumor. Patients are often of reproductive age and present with abnormal uterine bleeding, pelvic mass or enlarged uterus. This rare variant of uterine leiomyoma has an unusual growth pattern (placenta-like). It often grows as a bulky vascular uterine mass with involvement of the broad ligaments and pelvic cavity. The imaging and gross appearance of this leiomyoma are alarming for a malignant process. We report a 39 year old female presenting with prolonged vaginal bleeding. Ultrasound and consequent MRI were both reported as a malignant process involving parametria with high suspicion for a malignant mixed Mullerian tumor. Total abdominal hysterectomy, bilateral salpingo-oophorectomy along with peritoneal washing were performed. On gross examination there was a large multinodular polyloid haemorrhagic mass replacing the posterior wall of the uterine corpus with extension to deep myometrium and parametria. On microscopic examination a highly vascular smooth muscle neoplasm dissecting and replacing the myometrium with surrounding edematous and vascular stroma was seen. There was no evidence of atypia, increased mitotic activity or necrosis. Immunohistochemistry confirmed the smooth muscle nature of the tumor. Awareness of this rare uterine leiomyoma with extratubercule extension especially at the time of frozen section prevents overdagnosis and subsequent overtreatment in a young female.

**P407**

A RARE CASE OF MAMMARY-LIKE GLAND ADENOCARCINOMA OF THE VULVA.

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Objectives: Mammary-like glands of the anogenital region are currently a poorly understood variant of cutaneous glands that combine morphologic and immunohistochemical features of eccrine, apocrine and mammary glands. Herein, we describe a case of the rare occurrence of a vulvar adenocarcinoma arising from these glands. **Methods:** We reviewed the clinical history, operative findings, pathological assessment and follow-up in a 71 year old female diagnosed with mammary like adenocarcinoma of the vulva. **Results:** In January 2010, a 71 year old female presented with a one-year history of a tender, indurated area on the right side of the vulva for which symptomatic treatment was offered. In January 2011, examination revealed a 1x1cm solid, mobile mass in the previously indurated area that was subsequently removed by wide local excision. Pathological assessment revealed a partially mucinous, well differentiated adenocarcinoma. Immunohistochemistry showed positivity for Mammoglobin, ER and EMA, whereas BRST-2, CK-7, CK-20, Vimentin, PR, and S100 were negative. Further investigations, including abdomen/pelvis/chest CT, PET scan, and mammogram revealed no other primary site or metastases. The patient then underwent right hemivulvectomy with groin dissection. Microscopic examination showed extension to deep and lateral margins and four of ten inguinal lymph nodes positive for metastatic adenocarcinoma with extranodal extension. Subsequently, she had adjuvant radiation therapy and has done well. Conclusions: Mammary-like gland adenocarcinoma is an extremely rare entity that must be taken into consideration when diagnosing adenocarcinoma of the anogenital region. It is a locally aggressive tumour and wide metastases are uncommon. It is important that this be differentiated from metastases, neoplasms arising from skin appendages, and extramammary Paget’s disease.

**P408**

OSSEOUS METAPLASIA OF THE ENDOMETRIUM: A CASE SERIES.

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Objectives: Osseous metaplasia of the endometrium is a rarely encountered condition in which mature bone is found within the endometrial tissue. The majority of cases reported in the literature follow the pattern of focal endometrial ossification with subsequent abortion and secondary infertility. We discuss three cases of this phenomenon recently encountered in our institution. **Methods:** The clinical history, hysteroscopic findings, and pathologic assessment of three women who were found to have bone formation in their endometrial tissue samples were reviewed. **Results:** Patient #1 was a 39 year old female with a history of remote therapeutic abortion who was found to have an intrauterine foreign body on ultrasound. Hysteroscopy revealed two bony structures. Pathological assessment demonstrated osseous metaplasia of the endometrium. Patient #2 was a 36 year old female with a history of dilation and evacuation for missed abortion 5 months prior. Subsequently, she suffered dysfunctional uterine bleeding and infertility. Hysterectomy was unremarkable but microscopic pathological evaluation showed evidence of osseous endometrial metaplasia with mature bone formation. Patient #3 was a 23 year old female with primary infertility and an intrauterine calcification on ultrasound. The calcification was removed hysteroscopically and microscopic evaluation demonstrated fragments of devitalized bone tissue. **Conclusions:** Awareness of osseous metaplasia of the endometrium is important because: 1. In the vast majority of cases, removal of the bony material results in the restoration of normal menstrual function and fertility potential. 2. This benign condition must not be mistaken for a sarcomatous neoplastic process, which may arise in the endometrium, especially in the postmenopausal age group.
Adenocarcinoma of the uterus is a rare neoplasm composed of benign epithelial and malignant stromal components. Here we describe a case of adenocarcinoma with chondrosarcomatous and rhabdomyosarcomatous stromal differentiation and stromal overgrowth. The patient is a 48 year old woman who presented with a mass protruding through the vagina. The biopsy revealed malignant adenocarcinoma. Total abdominal hysterectomy and bilateral pelvic lymphadenectomy were performed. Microscopic examination revealed benign endometrioid glands with underlying hypercellular malignant stroma. The tumor exhibited areas of sarcomatous overgrowth with chondrosarcomatous and rhabdomyosarcomatous stromal differentiation. Lymph nodes were negative for tumor. The patient received adjuvant pelvic radiation therapy. During the following 9 months, the patient developed pulmonary metastases. Histology of the metastatic lesions confirmed the diagnosis of adenocarcinoma with predominance of the chondrosarcoma element. Sarcomatous overgrowth, either with homologous or heterologous elements, confers aggressive tumor behaviour in adenocarcinomas. Long-term follow-up is essential to provide future experience with these unusual neoplasms.

Objective: Persistent HR-HPV infection has been found to be associated with several human cancers such as head & neck, skin, breast and cervix. Epidemiology studies show that the major type of HR-HPV in Cervical malignancy are 16 and 18. On average, it takes 12–15 years before a persistent HR-HPV infection may ultimately, via consecutive premalignant stages (ie CIN lesions), lead to an overt cervical carcinoma. This argues that HPV-induced cervical carcinogenesis is multi-step in nature. The objectives of the study were for finding the distribution of HR-HPV positive in biopsy and cervical swab samples that submitted to Clinical Lab Dharmais Cancer Hospital, Jakarta during 2009 – 2010, and to know the correlation between cytology and the positivity of HR-HPV. Method: Samples are 117 cervical swab and cervical biopsy that submitted to Clinical Lab Dharmais Cancer Hospital during 2009 – 2010. All samples were tested for cytology using PAP smear test and for HPV DNA Genotyping test using Linear array HPV Genotyping Test. The test uses amplification of target DNA by PCR and nucleic acid linear hybridization for the detection of 37 high- and low-risk HPV genotypes qualitatively. It targets an HPV genome sequence of 450 bp long within the L1 region of the HPV genome. Data was analysed descriptively. Results: There were 18 HR-HPV positive in normal and Ascus samples. The positivity of HR-HPV test according to cytology of samples were as follows in CIN 1 32%, CIN2 60%, CIN3 82% and in Cervical Ca 96%. Conclusion: The result of our study showed the main type of HPV were 16, 18, and 52 consecutively. Percentage of HR-HPV positivity increase in conformity with the increase of CIN (Cervical Intra Neoplasia) stage. Clinical utility of HPV-DNA Genotyping testing are identification of HR-HPV type, as primary screening test combined with cytology, confirm the unclear cervical cytology result, predict the risk of Cervical Ca and for colposcopy follow up.

PRIMARY AND INCIDENTALLY DISCOVERED HEMATOLOYMPHOID NEOPLASMS DIAGNOSED IN GYNECOLOGIC SPECIMENS: A CASE SERIES.

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Background: Primary gynecologic lymphomas are rare and most commonly affect the ovary, with diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) being the most frequent adult subtypes. We present a case series from one institution illustrating our experience with both primary and incidental gynecologic hematolymphoid neoplasms.

Methods: a search for terms including “ovary”, “cervix”, “uterus”, “lymphoma” and “leukemia” in the diagnosis section of our final reports encompassing the years 2002-2012 was performed using the our institution’s Meditech database. Clinical information was gathered through the Meditech and ClinicalConnect databases. Results: There were 18 cases of adult gynecologic hematolymphoid neoplasms with patient ages ranging from 24 to 84, including aggressive DLBCL, intravascular DLBCL, and FL of the uterus, DLBCL of the cervix, and ovarian Burkitt lymphoma. Two cases of primary granulocytic sarcoma were identified after endocervical curettage and gynecologic surgery. Lesions that were incidentally discovered in gynecologic nodal dissections include one case of nodular lymphocyte predominant Hodgkin lymphoma and nine cases of in-situ FL. A case of a biopsy-discovered primary Epstein-Barr virus-positive lymphoma-like lesion of the cervix is included. Conclusions: Although rare, a variety of hematolymphoid lesions can be found in gynecologic specimens and accompanying nodal dissections and can prove challenging to diagnose, particularly during intra-operative consultation, but are important to identify because their management differs significantly from that of other lesions of the gynecologic tract.

PERPLEXING DOUBLE EXPRESSION OF NAPSIN A AND TTF-1 IN OVARIAN TUMOR OF A 27 YEAR OLD: A DIAGNOSTIC PITFALL.

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Objective and Methods of the study: Double napsin A and TTF-1 positive immunostaining pattern has been considered highly specific for lung primary adenocarcinoma and has not been reported in extrapulmonary adenocarcinoma in the literature. We report an unusual ovarian tumor of a 27 year old with aberrant double expression of TTF1 and napsin A and review literature on immunomarkers. This case is instructive for pathologists to avoid a possible diagnostic pitfall in their clinical practice.

Data and Results: A 27 year old previously healthy woman presented with a 4 day history of right lower quadrant pain and was found to have torsion of a right ovarian cyst. Ovarian wedge resection and cystectomy was performed to reveal a moderate differentiated adenocarcinoma. Entire specimen was thoroughly examined and failed to reveal evidence of teratoma. The neoplastic cells are positive for CDX2, CEA, CK20(patchy), TTF1, napsin A and negative for PAX8, ER, PR, CA125, CK7, P16, calretinin and inhibin. Given the immunoprofile, a diagnosis of metastatic adenocarcinoma, possibly originated from either colorectal or lung is rendered. Clinical follow-up revealed a 9.0 cm sigmoid colon tumor with metastases to liver, omentum, lymph node, and ovary. Conclusions: This is the first case which showed a double staining with TTF1 and napsin A in colon adenocarcinoma and reiterates that interpretation of IHC requires correlation with clinical, radiologic, and microscopic findings.
A UNIQUE CASE OF UTERINE CARCINOSARCOMA WITH PROMINENT DIVERGENT DIFFERENTIATION.
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Introduction: Divergent differentiation in uterine tumors can take the form of mixed epithelial tumors, with mixtures of different Mullerian and non-Mullerian epithelia, or carcinosarcomas, biphasic tumors with both epithelial and mesenchymal components. History: We report a unique case of an 86-year-old woman who presented with vaginal bleeding. Subsequent endometrial biopsy showed Grade 2 endometroid adenocarcinoma for which she underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, but no staging lymphadenectomy due to her age. Findings: Pathological examination of the resected uterus revealed a carcinosarcoma. Interestingly, the carcinomatous component was composed of equal proportions of clearly demarcated small cell carcinoma and endometrioid carcinoma. The small cell component stained diffusely for neuroendocrine markers, including CD56, synaptophysin and chromogranin along with TTF-1; whereas the endometrioid carcinoma component was completely negative for these markers but was positive for ER and vimentin. The sarcoma component was admixed with the small cell carcinoma and showed mitotically active atypical spindle cells in a background of myxoid stroma and foci of chondroid and lipoblastic differentiation. Extensive lymphovascular invasion by the small cell carcinoma was also present. Discussion: Uterine small cell carcinoma and carcinosarcoma are both rare, aggressive tumors with poor prognoses. The optimal management of neither lesion is defined and no evidence-based therapeutic regimen exists for this mixed tumor. Treatment targeted to the most aggressive component – the small cell carcinoma – seems appropriate. It is important to consider divergent differentiation in mixed tumors in order to avoid misdiagnosing small cell carcinoma as merely dedifferentiated carcinoma.

BONE MARROW HISTOLOGIC FINDINGS IN SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING WITH PANCYTOPENIA.
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Patients with systemic lupus erythematosus (SLE) frequently have hematologic abnormalities such as aplastic anemia, thrombocytopenia, and leukopenia. Bone marrow abnormalities may precede a clinical diagnosis of SLE, or may occur in patients with an established diagnosis of SLE. Knowledge of the accepted histologic and immunohistochemical bone marrow findings in SLE is important for correct diagnosis and clinical management. Presented is the case of a 37 year old female with a five day history of fever, pleuritic chest pain, nausea and vomiting. She was found to have severe pancytopenia with no known history of a bleeding disorder. A physical exam was non-contributory. Initial investigations revealed a right sided pneumonia and blood work showed a pancytopenia with Hb 73, WBC 3.9, Plts 26, reticulocyte count 3 and MCV 82. Hemolytic work-up including haptoglobin and direct Coombs’ test were negative. The patient was commenced on antibiotics and received multiple blood transfusions. A bone marrow biopsy showed features consistent with a diagnosis of “myelodysplastic-like syndrome” (MDS). On further investigation, it was found that the patient had an established diagnosis of AML and the spectrum of hematological disease manifestations in this disorder is important in not making a diagnosis of MDS or other hematopoietic neoplasms. Molecular cytogenetics is often but not always helpful in distinguishing mimics from true MDS. Awareness of patient history of SLE and the spectrum of hematological disease manifestations in this disorder is important in not making a diagnosis of MDS or other hematopoietic neoplasms, for appropriate patient management and treatment.

HAIRY CELL LEUKEMIA INVOLVING BILATERAL FEMORA, AND MEDIASTINAL AND PARAVERTEBRAL SOFT TISSUE: AN UNUSUAL MANIFESTATION.
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Hairy cell leukemia is a rare indolent B-cell lymphoproliferative disorder that usually presents with splenomegaly, pancytopenia, and bone marrow involvement. We describe a rare case of hairy cell leukemia in a 50 year old man that initially presented with isolated right hip pain that was diagnosed as bilateral avascular necrosis of unknown origin based on magnetic resonance imaging (MRI). At the time of presentation the patient had no splenomegaly or bone blood abnormalities. A whole body scan was normal. The patient subsequently underwent right hip decompression and iliac crest bone grafting followed by three years of physiotherapy until he had a repeat hip MRI which showed marrow replacing lesions in both proximal femora, worse on the right. A CT scan of the thorax and abdomen/pelvis additionally demonstrated anterior mediastinal and paravertebral soft tissue masses. The paravertebral mass was biopsied. Pathology reported a low-grade B-cell lymphoma not otherwise specified. There was insufficient material for flow cytometry. A bone marrow biopsy was negative and the blood work remained normal. The patient refused treatment but his pain progressed. A repeat biopsy was done one year later of the right hip lesion. This time the flow cytometry confirmed hairy cell infiltrates (CD10+, CD20+, CD11c+, CD25+, lambda light chain restricted). Hairy cell leukemia presenting with isolated boney involvement and soft tissue masses in the absence of splenomegaly or pancytopenia is very rare, and as far as we know, has never been reported. In retrospect, the initial paravertebral mass biopsy was consistent with hairy cell leukemia, but the possibility was not entertained at the time because it did not fit the clinical picture. It is important to be aware of the possibility of this type of presentation. The patient received a 5 day course of cladribine and his hip pain improved.

COMPOSITE LYMPHOMA OF HODGKIN LYMPHOMA AND MANTLE CELL LYMPHOMA.
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Objectives: Composite lymphoma continues to pose great diagnostic and therapeutic challenges for pathologists and clinicians. Accumulation of these cases will help future diagnostic endeavors. Composite lymphoma composed of Hodgkin lymphoma and mantle cell lymphomas are extremely rare. Here we report a case in a symptomatic female patient who had extensive lymphadenopathy and splenomegaly. Methods: We received a biopsy sample from a peripheral site in Nova Scotia. The case was examined with data from histology, immunohistochemistry, flow cytometry, and molecular study from our institution. Results: H&E biopsy of a left inguinal lymph node showed complete obliteration of normal architecture of a lymph node, replaced by a dense, diffuse infiltrate of small lymphocytes. Areas with large atypical cells are present, some of which resembles Reed-Sternberg cells. Flow cytometry analysis of the lymph node demonstrated a clonal population of CD5+ B cells. Immunohistochemistry showed that the small B cells are CD5+ and strong nuclear staining for cyclin D1. The large atypical cells show typical phenotype of Reed-Sternberg cells, namely, LCA+, CD20−, CD30+, CD15+ and characteristically very weak PAX5; they are negative for cyclin D1, suggesting different origins of clonality from the small B cell component. Bone marrow is involved by the mantle cell lymphoma, but not the Hodgkin lymphoma. Molecular study of bone marrow also showed a B cell clone. Conclusion: This is a case with both Hodgkin lymphoma and mantle cell lymphoma. Patient has received chemotherapy and continues to be observed.
SARCOMATOID ANAPLASTIC LARGE CELL LYMPHOMA (ALCL): DIAGNOSTIC PITFALL WITH SARCOMA, NOT OTHERWISE SPECIFIED (NOS).

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Background: Extramedullary Anaplastic Large Cell Lymphoma (ALCL) has many histologic variants but consistently demonstrates strong diffuse CD30 staining with or without ALK-1 positivity by immunohistochemistry. Sarcomatoid ALCL, a rare variant, is often misdiagnosed as a sarcoma of soft tissue. The distinction between sarcomatoid ALCL and Sarcoma, NOS is critical as the treatment is very different. Morphology is often misleading, particularly in small biopsies. Knowledge of the proper staining pattern of CD30 is important, when used in a panel, in the differential diagnosis of Sarcomatoid ALCL versus Sarcoma, NOS. To our knowledge, there are no series addressing CD30 and ALK-1 immunostaining in sarcomas versus Sarcomatoid ALCL. Design: We present two cases of sarcomatoid ALCL of soft tissue mimicking pleomorphic sarcoma comparing morphology and immunohistochemistry. A retrospective review of departmental archival material of all pleomorphic sarcomas and Sarcoma, NOS (30 cases) was undertaken. The immunohistochemical staining pattern of CD30 and ALK-1 were reviewed in all the sarcomas to compare and contrast with Sarcomatoid ALCL. Results: Both cases of Sarcomatoid ALCL showed diffuse strong membrane positivity in the tumor cells. One case was ALK-1 positive. In comparison, all our sarcomas were either CD30 negative or showed focal weak staining. All sarcomas had negative staining for ALK-1. Conclusion: Extramedullary Sarcomatoid ALCL in routine practice may be misdiagnosed and treated as Sarcoma, NOS. The staining pattern of CD30 and ALK-1 help reach the correct diagnosis. Sarcomatoid ALCL should be entertained in the differential diagnosis of sarcomas which have an inflammatory background. CD30 and ALK-1 immunostains with T cell gene rearrangement studies are important ancillary tests to avoid this diagnostic pitfall and mismanagement of the patient.

WHO ORDERS AUTOLOGOUS BLOOD? A RETROSPECTIVE ANALYSIS OF PREOPERATIVE AUTOLOGOUS BLOOD UTILIZATION IN A MEDIUM-SIZED PROVIDER.

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Background: The utilization of preoperative autologous blood donation (PABD) peaked in the 1990s in response to concern about the risk of transfusion-transmitted infection (TTI). Allogeneic transfusion is currently associated with a very low risk of TTI. Consequently, PABD has a limited set of clinical indications while being associated with higher cost than allogeneic transfusion. This study seeks to determine trends in PABD utilization. Methods: A retrospective chart review of all autologous donations from 2000 to 2011 at a medium-sized blood provider was performed. Data reviewed included requesting physician name, physician specialty and date of graduation from medical school, requesting institution, number of autologous units requested and collected, and number of autologous and allogeneic transfusions received by the donor/patient. Results: 338 autologous donations occurred over the study period and a declining trend was observed. 626 autologous units were collected of which 188 (30%) were transfused. Requests for PABD were made by 99 individual physicians. 10 physicians accounted for 51% of all autologous requests. The average date of medical school graduation for this group was 1982. The most common procedures were gynaecologic (53%) and orthopaedic (35%). Conclusion: A declining trend in PABD utilization is observed over the study period. Residual demand appears to be physician-driven. The majority of residual PABD utilization is attributable to a small group of physicians that graduated from medical school prior to the development of highly sensitive tests for blood-borne pathogens. This suggests that the majority of PABD requests at out centre are being made without reference to recent utilization guidelines.

BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM: A CASE REPORT.

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Objective: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare subtype of acute leukemia. Once postulated to originate from NK lineage precursors, accumulating phenotypic, functional, and genetic evidence has pointed to derivation from hematopoietic precursors with commitment to the plasmacytoid dendritic cell (pDC) lineage. Here we describe a case of a young woman who presented with fever, skin rash, anemia and multiorgan failure. Initial clinical and pathological findings were consistent with secondary HLH and therapy was started. BPDCN was not identified. Data and Results: The morphological features of the skin tumour, that recurred 18 months after her first presentation, coupled with the CD4, CD56 and CD123 positivity indicated a BPDCN. Bone marrow fibrosis, megalakaryocytic dysplasia and CD4, CD56, and CD123 positivity supported this diagnosis. Interestingly, many cells in the skin biopsy also showed lysozyme/muramidase intermediate positivity suggestive of monocytic/myeloid differentiation and possible disease evolution. Conclusions: Due to the rarity of BPDCN and recent change in the WHO classification scheme, both the diagnosis and management of this disease is challenging. It is reported that 10-20% of cases of BPDCN are associated with or develop into myelomonocytic leukemia or acute myeloid leukemia. Therefore for all cases of BPDCN one needs to consider leukemic transformation, which shows an overlapping immunophenotype with pDC neoplasms. Due to the patient’s poor performance status and advanced disease, she was treated palliatively and recently succumbed to her disease.

CARDIAC TAMPOONADE AS INITIAL MANIFESTATION OF ACUTE LEUKEMIA.

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Objective: Here we describe a case of a previously healthy 74 year old gentleman presenting with acute onset exertional dyspnea. Initial workup to rule out pulmonary embolism revealed a large pericardial effusion and urgent pericardiocentesis was performed. Cytologic evaluation of the pericardial fluid showed many blast cells consistent with acute leukemia. The only hematological abnormality on presentation was a mild anemia and thrombocytopenia. Results: Cytoplogic evaluation of the pericardial effusion revealed 90% blast cells, medium to large with round to irregular contour, prominent nucleoli and scant blue cytoplasm. Flow immunophenotyping showed the blast cells were positive for CD3, CD34, HLA-DR and TdT and showed partial expression of MPO and CD2. Interestingly, only a small proportion of blasts (0.7%) of the leukemic clone were identified in the peripheral blood by flow cytometry. The bone marrow trephine biopsy was hypocellular and contained 30% blast cells. Discussion: Tamponade as the initial presentation of acute leukemia is rare although post-mortem findings of leukemic infiltration of the pericardium is frequently documented. In this case, subsequent flow immunophenotyping and bone marrow examination supported the initial morphological diagnosis. The pericardial effusion was treated conservatively with pericardiocentesis followed by intrapericardial bleomycin. Due to the patient’s age and performance status, the acute myeloid leukemia was treated conservatively with hydroxyurea for symptom control.
P421 EXTREMELY SOLID FOCAL COMPOSITIONS IN THE HEAD SUPPRESSED BY IMMUNE RESPONSES OF T H P 1 ST-phylum and Heterotrophic Bacteria in the Bloodstream of Patients with Acute Lymphoblastic Leukemia

Objective: The aim of this study was to investigate the presence and characteristics of extremely solid focal compositions in the head suppression of immune responses of T H P 1 st-phylum and heterotrophic bacteria in the bloodstream of patients with acute lymphoblastic leukemia.

Methods: We studied 50 patients with acute lymphoblastic leukemia and 50 healthy controls. We used PCR amplification and sequencing to detect the presence of extremely solid focal compositions in the head suppression of immune responses of T H P 1 st-phylum and heterotrophic bacteria in the bloodstream of patients with acute lymphoblastic leukemia. We also used PCR amplification and sequencing to detect the presence of extremely solid focal compositions in the head suppression of immune responses of T H P 1 st-phylum and heterotrophic bacteria in the bloodstream of healthy controls.

Results: We found that the presence of extremely solid focal compositions in the head suppression of immune responses of T H P 1 st-phylum and heterotrophic bacteria in the bloodstream of patients with acute lymphoblastic leukemia was significantly higher than that in healthy controls (P<0.05).

Conclusion: The presence of extremely solid focal compositions in the head suppression of immune responses of T H P 1 st-phylum and heterotrophic bacteria in the bloodstream of patients with acute lymphoblastic leukemia is higher than that in healthy controls, which suggests that these bacteria may play a role in the pathogenesis of acute lymphoblastic leukemia.

P422 DISSEMINATED HISTOPLASMOSIS IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA: CASE REPORT AND LITERATURE REVIEW.

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Background And Objective: Disseminated histoplasmosis is rare, but may occur in patients with immune compromised status (9/20, 45%) without preceding or concurrent acute myeloid leukemia (11/20, 55%). The most common morphological feature of disseminated histoplasmosis is the presence of histoplasma capsulatum, which is a yeast-like organism. The most effective IHC markers were CD43 (12/14, 86%), CD15 (6/6, 100%) and CD68 (11/12, 92%). Conclusion: MS is a poorly recognized lesion having multifaceted manifestations and not usually considered in the differential diagnosis of lymphadenopathy and hepatosplenomegaly. An expanded immunohistochemical panel including additional markers such as CD117, CD68, CD15, CD56 and CD34 are useful in recognizing this lesion. Correct diagnosis of this entity is important in the context of optimal patient management and further prognostication.

P423 CHRONIC LYMPHOCYTIC LEUKEMIA CELL SEGMENTATION USING A MACHINE LEARNING ALGORITHM.

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Chronic lymphocytic leukemia (CLL) is the most common type of blood cancer in North America. White blood cell morphology in CLL may be similar to normal lymphocytes and therefore require hematopathologist examination for diagnosis. Despite being a common disease, there are a low number of studies examining the automated detection of CLL from digitized peripheral blood films. Development of hematopathology software tools for the early detection of CLL will help significantly increase the survival rate. This work focuses on CLL cell segmentation using the support vector machine (SVM) algorithm. The most important aspect of the SVM as a machine learning algorithm is its capability to overcome the ‘occlusion problem’ when lymphocytes are tightly bound to the surrounding RBCs. Over and under-segmentation problems are thereby significantly reduced. Peripheral blood smear images used in this research were pathologist-referenced images of CLL and normal lymphocytes. Stained peripheral blood smear slides were used to acquire 140 images using the commercial CellVision™ DM900 system. We used all the images for segmentation accuracy measurement and 12 of these images are used for training of the SVM algorithm. The algorithm obtained 97.06%±0.50 average accuracy for nucleus segmentation, and 97.45%±0.79 for cell segmentation. The cytoplasm region can be extracted by 90.7%±11.94 average accuracy with simple mask subtraction. The success of this segmentation process could play a significant role in the success of subsequent cell classification software systems.

P424 MICROORGANISM AND ANTIMICROBIAL RESISTANCE PATTERN IN PATIENTS ISOLATED IN LOW IMMUNE STATUS WARD IN A NATIONAL CANCER HOSPITAL IN JAKARTA.

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Cancer patients who received chemotherapy and radiation therapy or those with leukemia often present with neutropenia and immunosuppression. This is a common situation in hospitals, especially in cancer hospitals. These patients are treated in special ward for low immune status, and blood specimen, throat, nasal and rectal swabs for culture was taken at regular interval. Microorganism and resistance pattern will help guide empirical therapy in these patients, especially because infection may be life-threatening in these patients. Here we report the microorganism pattern and antimicrobial resistance in these patients. We observed the microorganism pattern during July 2012 until December 2012 and compared it with the pattern during the 2nd semester of 2011. All specimens submitted for culture during the period were included. Analysis was performed using the WHONET software version 5.6. In the 2nd semester of 2011, total number of isolates was 1243, 710 of which were Gram positive microorganism. The most prevalent microorganism species were S. aureus (27%), S. xylosus (21%) and S. aureus (14%). Most prevalent Gram positive microorganism was K. pneumoniae (17%), followed by E. coli (17%). Acinetobacter baer was comprised of 5.6% of total isolates, while Pseudomonas sp. were found in 7.9% of isolates. The result of 2nd semester of 2012 showed a shift from Gram positive to Gram negative as dominant organism (637 Gram negative vs 561 Gram positive, total 1198 isolates), with S. hicus (16%), E. coli (9.5%) and S. epidermidis (7.8%) as the most prevalent microorganisms. During July-December 2011, antimicrobial resistance pattern in S. aureus showed 40% isolates were resistant to oxacillin, but 100% susceptible to vancomycin. Susceptibility to carbapenems ranged between 22.2% (meropenem) to 71.4% (doripenem). Similar result was observed in S. epidermidis (susceptibility to oxacillin 46.7%, vancomycin 100%, carbapenems 37.5 – 68.4%). E. coli showed susceptibility to cefotaxime, ceftiraxone and ceftazidime in 25, 20 and 66.7% of isolates, respectively, and 100% to all carbapenems and amikacin. Similar pattern was showed by K. pneumoniae with 0%, 11.1% and 20% isolates susceptible to ceftriaxone, ceftazidime, and ceftazidime, and 100% to carbapenems and amikacin. In the 2nd semester of 2012, Gram positive organisms showed susceptibility to oxacillin in 24.2% isolates, cefoxin in 25%, carbapenems in 54.1 – 58.8% and vancomycin 81.2%. These results showed that resistance, especially methicillin resistance was increasing, and vancomycin resistance was emerging. Gram negative organisms showed susceptibility to ceftriaxone in 3.5%, cefotaxime in 9.1%, ceftiraxone in 35.3%, amikacin in 70.6%, and carbapenems in 80 – 85.7% isolates, which showed that resistance in Gram negative organisms was also becoming an increasing problem. We concluded that resistance both in Gram positive and Gram negative organisms found in immunosuppressed patients in our hospital’s isolation ward, and use of antimicrobials must be controlled to prevent further creation of multi-resistance microorganisms.
**P425 DISSEMINATING HISTOPLASMOSIS: A CASE REPORT.**
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Histoplasmosis is a disease caused by the dimorphic yeast *Histoplasma capsulatum*. This infection is endemic in North and Central America, but can also be found in other regions of the world. Most infected patients were asymptomatic, and the few symptomatic patients showed varied clinical manifestation. In this case report, we reported a case of histoplasmosis in a child presenting with pancytopenia. **Case:** NM, 5 years 11 months old, was referred to Harapan Kita Woman and Child Hospital with suspected malnutrition, anemia and hepatomegaly suspect leukemia. On anamnesis, there were history of relapsing fever since 4 months before, weight loss and productive cough. The child’s parents also observed increasing pallor. Patients had been diagnosed and treated as tuberculosis, but was not adherent to treatment. Physical examination revealed pallor, fever, rales and hepatomegaly. Laboratory examination showed hemoglobin level of 4.7 g/dl, WBC count 2300/ul, platelet count 47000/ul. Peripheral blood film showed pancytopenia with microwurus hypochromic anemia. Albumin level was low, with prolonged PT and aPTT, high ESR and increased CRP. Bone marrow aspirate revealed numerous *Histoplasma* yeasts in the histocytes. Patient was then diagnosed with histoplasmosis and treated accordingly.

**Discussion:** We reported a case of histoplasmosis which manifested with pulmonary manifestation and pancytopenia. Disseminated histoplasmosis was found in 4-27% infected children, and only in 1 in 2000 immunocompetent adult. Diagnosis of histoplasmosis can be confirmed with several tests including culture, histopathologic, and serology for antigen and antibody detection or by PCR method. In this case, diagnosis was confirmed by cytomorphologic evaluation of bone marrow aspiration which was indicated because of pancytopenia. **Conclusion:** Diagnosis of histoplasmosis might be considered as a differential diagnosis in cases of hematologic disorders with pulmonary manifestation.

**P426 STUDY ON COLONIZATION OF NUC-MECA GENE IN THE ARMPIT OF CEREBRAL PALSY CHILDREN AT DIFFERENT SEASONS.**
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**Objective** To investigate the colonization of nuc-meca gene in the armpit of cerebral palsy children at different seasons. **Methods** 58 axillary swabs were collected from cerebral palsy children in summer and autumn. E. coli mecA gene was examined by using multiple-PCR and sequencing. **Result** No mecA gene was amplified from these samples, and the incidence of mecA gene colonization in A and B group was 31.03% and 48.28%, respectively. There were no significant difference in the groups. **Conclusion** No mecA gene was in the armpit showed the well-hospitalization environment and the daily bathing was effective for removing the mecA gene in the armpit.

**P427 THE VALUE AND CLINICAL SIGNIFICANCE OF THE COMBINE OF ENDOTOXIN QUANTITATIVE DETECTION AND WHITE BLOOD CELL DETECTION MONITORING BACTERIAL INFECTION.**
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**Objective** To study the value and clinical significance of the combine of endotoxin quantitative detection and white blood cell detection monitoring bacterial infection. **Methods**: Using dynamic photometric turbidity method to detect 4 cases of a hospital medical persons’ blood endotoxin and using cell analyzer to test the white blood cells. **Results**. In 4 cases, two case of patients with bacterial endotoxin raised while leucocyte stay normal, one case with normal bacterial endotoxin while white blood cells increased, and one case is all normal. **Conclusion** Joint of testing to the bacterial and leucocyte detection can improve the detection rate of bacterial infections.

**P428 HERASIM©: AN OPEN SOURCE, EXTENSIBLE SOFTWARE PROGRAM FOR MODELING CANCER CELL CLONAL EVOLUTION.**
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Several computer models of cancer cell growth and clonal evolution have been published but there is no free, extensible model available. To fill this need we wrote the HeraSim software package. HeraSim is written in Java and utilizes an agent based design where each cancer cell is represented as a state machine which advances through the stages of the cell cycle based on resource accumulation and user-defined rules. The cells participate in a complex 3-D model representing the growing tumour. This model allows each cell to calculate its position relative to all other cells and thereby determine its rate of resource accumulation and its competitive advantage relative to neighboring cells. The user can begin a simulation with any number of starting clones in a heterogeneous configuration. The software can model mutation acquisition, stem-cell like properties of certain clones, Hayflick limits, cell to cell competition, apoptosis, necrosis due to hypoxia, and response to treatment. For each of these parameters the user defines the starting variables and the state machine rules. The graphical interface displays clones as different colours and with built in functions to summarize cell ages and attributes. Each cell can also be clicked to reveal the cell attributes. The graphical interface allows the user to view the virtual tumour to be sliced in the x, y or z planes. The program is fully extensible to allow future modules to be added to reflect new discoveries in cancer biology. The software is available to researchers for free through a web repository.

**P429 FINDING THE DISTRIBUTION OF CANCER MUTATIONS: EVALUATING AN INFORMATICS-BASED APPROACH.**
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The catalogue of somatic mutations in cancer (COSMIC) database (maintained by the Wellcome Trust Sanger Institute) is a comprehensive database of published mutations in cancer, and due to its huge number of documented samples is an often-quoted reference for statistics about these mutations, such as their frequencies. However, for many genes which display mutation "hotspots", inclusion of studies that fail to sequence the entire gene may lead to biased numbers. KRAS is one such gene where the overall mutation rate and per-mutation rates also have specific clinical relevance as predictive biomarkers. We evaluate KRAS in colorectal cancer as a test case, comparing three different ways of calculating mutation frequencies using COSMIC data: (1) simple frequencies, (2) per-mutation weighted averaging, and (3) per-mutation frequencies based on abstracted study methodology. Method 1 is the most obvious method (dividing the number of mutations by the number of assayed tumors) and yields the number displayed on the COSMIC website. We propose method 2 to help correct for varying study methodologies by calculating a weighted average of each non-zero within-study frequency. Method 3 uses a subset of studies with manual review of study methodology to determine the correct denominator, and represents a labour-intensive gold standard. Overall mutation frequencies by these methods are 36.3%, 39.6%, and 39.0%, respectively, with the simple method showing a distinct underestimate. Per-mutation frequencies are calculated as well. Our proposed method 2 is quite accurate overall and does not require manual review, but shows a small upward bias for frequencies of mutations occurring less often than 1/200, which future refinements may be able to address. In conclusion, caution should be employed when calculating straight mutation frequencies using COSMIC data (or adapting straight frequencies from the COSMIC website), and a more nuanced approach is often preferable.
P430
cytoscape and ingenuity ipa in an illustrative case of neurofibromatosis type ii with jak2(v617f) mutation and bcr-abl translation.

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We hereby present one of two validated network visualization programs Cytoscape and IPA to elucidate biomolecular interactions of three genetic aberrations. The illustrative clinical case is that of a 90 year old man with Neurofibromatosis type 2, who subsequently developed JAK2 (V617F) positive Polycythemia vera, then followed by translocation t(9;22) positive Chronic myelogenous leukemia. Cytoscape version 2.83 (http://www.cytoscape.org), an open source, java-based collaborative project and trial IPA version 7.6 (ingenuity systems: http://www.ingenuity.com), a commercially available web-based proprietary product were analyzed. Cytoscape generated pathways were generated by selecting NCBI, Biocyc, and Pathway Commons databases, limiting searches to human pathways. Resultant pathways were then subject to select plugins like “BiNoM 2.1”, “Reactome” and GeneMANIA from a selection of over 150 publicly available sources. IPA use involved progressive addition of select Ingenuity pathway results obtained from the proprietary “Knowledge Database” to a blank network and subjecting these to proprietary tools like “Grow” and “Path Explorer”. Select visual results from both methods will be used to demonstrate the valuable contribution of such programs towards our understanding of the underlying biological processes in carcinogenesis. In our opinion, both Cytoscape and IPA provide substantial biomolecular information to further our understanding of disease processes and effectively communicate within the field. Differences between pathways include cost, functionality, databases, computer-system requirements, data formats, interface, output, and customizability with cytoscape providing a more articulated, at times complex experience, while ingenuity IPA is a one-stop shop network more user-friendly visualization tool.

P431
Squamous Cell Carcinomas of the Anterior Oral Cavity are Commonly Associated with Simplex Intraepithelial Neoplasia.


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Invasive squamous cell carcinomas (SCC) of sun-exposed and non-exposed skin often develop from dysplastic cells limited to the basal (parabasal layer as seen in actinic keratosis and differentiated or simplex intraepithelial neoplasia (SIN) of the genital areas. In these areas, Bowen’s disease or Bowenoid erythroplasia are rarely associated with invasive SCC. We investigated the occurrence of SIN associated with invasive SCC of the anterior oral cavity and its clinicopathological significance. Methods: 69 consecutive cases of invasive SCC of the anterior tongue (54 cases), hard palate (8 cases), mandible, and floor of mouth (7 cases) were categorized into 3 groups: Group 1: comprised cases associated with SIN-in-situ exhibiting classical features of high grade intraepithelial neoplasia (HGIN) with atypical cells involving more than the lower third of the squamous epithelium; Group 2: consisted of cases with features intermediate between Groups 1 and 3. Results: 53 cases (76.8%) were classified as Group 3 with only 13 (18.8%) Group 1 and 3 (4.3%) Group 2 cases. Group 3 showed a female predominance [35/53 (66.0%) vs. 2/13 (15.4%) in Group 1], were more often poorly differentiated [23/53 (43.4%) vs. 3/13 (23.1%)], larger (2.3±1 cm vs. 1.0±0.6 cm), and associated with a higher rate of lymph node metastases [21/53 (39.6%) vs. 3/13 (23.1%)] and local recurrence [4/53 (7.5%) vs. 0/13 (0%)] than invasive SCC associated with conventional HGIN. There was no difference in age of presentation (6° decade) or frequency of staining with p16 or p53 between tested cases in Groups 1 and 3. Conclusions: SIN lesions are more commonly associated with invasive SCC of anterior oral cavity and aggressive disease than conventional HGIN lesions. Due to the subtle histopathological changes in SIN as compared to conventional HGIN, SIN lesions pose potential diagnostic difficulty with differentiation from mild dysplasia or reactive atypia.

P432
DicEr1 Rnase Iii Domain Mutation Contributes to the Pathogenesis of Wilms Tumour Without Background nephrogenic rest.

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Wilms tumor (WT) is the most common pediatric renal malignancy with an incidence of ~1/10,000 live birth. 30% to 44% of kidneys removed for WTs show nephrogenic rests. While the periblolar nephrogenic rest serves as a morphologic marker of loss of heterozygosity or imprinting for IGFI-2 and is associated with Beckwith-Wiedemann syndrome, the intralobar nephrogenic rest functions as an indicator of WT-1 mutation and is linked to WAGR and Denys-Drash syndrome. Here we reported three cases of trisomic WTs as a rare manifestation of DICER1 mutation-associated familial pleuropulmonary blastoma syndrome. Somatic DICER1 mutations were detected in either the RNase IIIa (n = 1), histologically with diffuse anaplasia) or RNase IIIb domain (n = 2, histologically without anaplasia). Interestingly, none of the three cases showed nephrogenic rests or nueroblastomatosis in the adjacent kidney. We also screened for mutations in the DICER1 RNase IIIa and RNase IIIb domains using formalin-fixed paraffin-embedded tissue from 28 cases of apparently sporadic WTs. One case (3.6%) of trisomic WT without background nephrogenic rests contained a silent somatic DICER1 mutation in the RNase IIIa domain. This study has demonstrated that a subset of WTs harboring germ-line and/or somatic DICER1 mutation, and the WTs in this setting are typically trisomic without background nephrogenic rest. We concluded that the DICER1 Rnase III domain mutation could be a key event in the pathogenesis of WT independent of the background nephrogenic rest.

P433
A Rare Case of Mucoepidermoid Carcinoma Arising in a WarthIn Tumor.

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Warthin tumor (cystadenoma lymphomatous papilliferum) is the second most common benign tumor of the parotid glands. It can rarely undergo malignant transformation of the epithelial or lymphoid component. Here we report the case of a 56-year-old male, who had undergone parotidectomy for a tumor of the left parotid gland. The 4.5 cm encapsulated nodule showed the typical histological features of a Warthin tumor. Upon review, we identified several areas, 0.1-0.2 cm, consisting in a proliferation of squamous and glandular epithelium with marked cellular atypia (large nuclei with prominent nucleoli and vesicular chromatin, high N/C ratio) and numerous mitotic figures. Special stains (PAS+ and mucicarmine+) highlighted the presence of mucin in the glandular cells. Immunohistochemical analysis showed a distinct staining of the tumoral cells for EMA and CK14 and an increased proliferation index (ki-67 up to 30%). P63 and CK7 were positive both in Warthin and carcinoma cells, while vimentin, S100, GFAP, and α-fetoprotein were all negative. All these findings lead to a diagnosis of mucoepidermoid carcinoma in a setting of a Warthin tumor. Only a few cases of mucoepidermoid carcinoma within Warthin tumors have been reported so far in the literature. Interestingly, a t(11;19) translocation which generates a CRTC1/MAML2 fusion transcript has been implicated in the development of a subset of Warthin tumors with mucoepidermoid carcinoma. Ongoing genetic analysis will determine if this translocation is present in the patient described herein.
P434
ADÉNOME PÉLOMORPHE DU PALAIS SIMULANT UN CARCINOME EPIDERMOÏDE.
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L’adénome péloromique est le néoplasme bénin le plus fréquent des glandes salivaires, dont la présentation au niveau des glandes salivaires mineures du palais reste rare et souvent atypique. Le cas d’un homme de 36 ans présentant une lésion primaire du palais dur qui s’avère un adénome péloromique en métaplasie malpighienne extensive est rapporté. Les biopsies initiales ont permis de porter le diagnostic d’un carcinome épidérmique à deux reprises. Par conséquent, le patient subit une chirurgie de résection complète de la lésion, dont l’examen extemporané corrèle avec les données biopsiques antérieures. Cependant, l’histologie définitive de la totalité de la tumeur, permet de reclasser la lésion en un adénome péloromique en métaplasie malpighienne extensive, et ceci sur la base de nouveaux aspects observés sur la pièce chirurgicale. Il s’agit d’une tumeur de localisation et d’histologie atypiques. La particularité anatomo-histologique de cette lésion et les pièges diagnostiques seront traités dans cette communication.

P435
MUCEOEPIDERMOÏDE CARCINOMA OF THE LACRIMAL SAC.
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Tumours of the lacrimal sac are rare. These include squamous and transitional cell carcinomas and less commonly mucoepidermoid carcinoma (MEC). We describe a case of MEC in a 70 year old male referred to the ophthalmology clinic with a three month history of progressive left medial canthal swelling and globe displacement. On examination a firm, non-mobile, minimally tender mass was noted in the left medial canthus. Computed tomography (CT) revealed a large lobulated well defined solid medial, anterior orbital tumour measuring 2.4 x 1.7 x 1.4 cm with suspected bony erosion and invasion of the anterior ethmoid air cells. Subsequently an ophthalmic plastic surgeon performed a left medial orbitotomy and removal of the tumour along with upper part of the lacrimal duct. The specimen consisted of an ovoid firm fragment of dark brown tissue measuring 2.5 x 1.8 x 1.6 cm. Microscopic examination revealed a carcinoma comprised of nests of cells showing areas of squamous differentiation with focal keratinization and dyskeratotic cells and admixed intermediate and clear cells with vacuolated cytoplasm. Some of these cells contained mucin and were demonstrated by mucicarmine stain. There was prominent mitotic activity including atypical mitoses. The tumour extensively involved the inked surgical margins. The findings were most consistent with a mucoepidermoid carcinoma of intermediate to a focally high grade differentiation. The nasal lacrimal duct was involved by the tumour. A left orbital exenteration, left medial maxillectomy and left external ethmoidectomy was performed to obtain clear margins following by adjuvant radiotherapy. Histological examination is the most important diagnostic tool in the diagnosis of MEC which requires the coexistence of 3 cell types: epidermoid, intermediate and mucin-secreting cells. In summary, although rare, MEC should be kept in the differential diagnosis and extensive sampling of the lacrimal duct apparatus should be undertaken to ensure that these tumours are not misdiagnosed as a squamous cell carcinoma.

P436
CEREBELLAR MEDULLOBLASTOMA IN A 57-YEAR OLD MAN.
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Cerebellar medulloblastoma is a rare neoplasm in adults. We report here a case of a medulloblastoma in a 57-year-old man who presented with a 7-week history of progressive loss of coordination involving the right body, slurred speech and lightheadedness. MRI of the brain revealed an enhancing tumor with mass effect and a large cystic component within the substance of the right cerebellar hemisphere. Bilateral suboccipital craniectomy with microsurgical gross total resection of the tumor was performed. Frozen sections showed sheet-like small blue cell tumor. Permanent sections showed a malignant tumor composed of small blue nuclei with nuclear molding, crowding, frequent mitoses, and scant cytoplasm. Immunohistochemical staining showed that the tumor was positive for chromogranin and synaptophysin. Ki-67 was positive in about 20% of the tumor cells. Negative were GFAP, HMW keratin, and Pankeratin. The initial diagnosis was malignant small blue cell tumor with neuroendocrine features, in favor of medulloblastoma. Due to the patient’s age, the case was sent out to Mayo Clinic for consultation. The consultant result was medulloblastoma, WHO grade IV. The patient was subsequently treated with chemotherapy with vincristine concurrent with craniospinal irradiation. He did well without recurrent tumor two years after the diagnosis and treatment. In conclusion, cerebellar medulloblastoma may occur in adults in their fifties and patients may survive well with appropriate treatment.

P437
RAPID DEVELOPMENT OF AN UNDIFFERENTIATED INTRACRANIAL MYXOID SARCOMA IN A GLOBLASTOMA PATIENT TREATED WITH CHEMORADIOTHERAPY. 
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The occurrence of two separate primary intracranial malignant neoplasms is a rare event. Secondary neoplasms such as sarcomas have been linked to radiation therapy used for treatment of a primary tumor. We describe a case of a 47 year old male with glioblastoma who developed an aggressive undifferentiated myxoid sarcoma less than one year after tumor resection followed by the Stupp chemoradiation protocol (60Gy in 30 fractions and temozolomide). Imaging showed a dural based lesion believed to be a chronic subdural hemorhage. Subsequent changes within the lesion suggested glioblastoma recurrence. However, histological examination revealed large atypical undifferentiated cells that were highly mitotic with a myxoid and vascular background. Differential diagnoses included metastatic undifferentiated carcinoma, melanoma, anaplastic meningioma, histiocytic or hematopoietic neoplasms. Immunohistochemistry showed strong positivity for CD68 and vimentin while AE1/AE3, HM4B4, EMA, CD1a and CD20 were negative. This lesion proved to be an undifferentiated dural-based myxoid sarcoma. The possibility of an association with a Li-Fraumeni syndrome is raised to explain the rapid development of the sarcoma. The objectives of the presentation are a review of radiation induced sarcomas and their association with genetic disorders.

P438
PEDIATRIC PRIMARY ALK1+ ANAPLASTIC LARGE CELL LYMPHOMA OF THE BRAIN.
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Anaplastic lymphoma kinase-positive anaplastic large cell lymphoma (ALK+ ALCL) is a 7-cell lymphoma that accounts for 10% to 20% of childhood lymphomas. ALK+ ALCL frequently involves lymph nodes and extranodal sites including the skin, bone, soft tissues, lung and liver. However, primary brain ALCL is exceedingly rare. We describe the case of a 6-year-old male who presented with acute headache and vomiting and chronic absence seizure-like symptoms. Gadolinium-enhanced magnetic resonance imaging (MRI) of the brain showed an avidly enhancing 4.4 cm x 2.8 cm x 2.5 cm mass in the parasagittal region of the left parietal lobe with adjacent leptomeningeal seeding. He underwent left parieto-occipital craniotomy and stereotactic lesion removal through an interhemispheric approach. Histologic and immunophenotypic features were consistent with ALK1-positive anaplastic large cell lymphoma, lymphohistiocytic pattern. Presence of the (2:5) ALK translocation was confirmed by fluorescence in situ hybridization. The patient completed induction chemotherapy with no MRI evidence of residual tumor at 4 months post-op.
P439
THE COMPLEXITY SCORE MODEL: A PATIENT-CENTRED, KNOWLEDGE-BASED, DATA-DRIVEN APPROACH TO PATHOLOGIST WORKLOAD EVALUATION IN THE AGE OF PERSONALIZED MEDICINE.
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As personalized medicine (PM) shifts clinical practices, our traditional approach to pathologist workload measurement must also shift to align with this new practice paradigm. The role of pathologists in PM is to provide diagnoses relevant to the current disease state of the patient and to identify specific characteristics that will predict response to therapy and prognosis. The ability to capture actual work performed is problematic in models where measurements are based on "number of cases" as defined by particular specimen types. As PM evolves, pathologists will need to perform increasingly complex analyses on the same "cases", with no concomitant increase in number of cases or specimen types. To address limitations of traditional models, the University Health Network (UHN) and its geographically diverse partner institutions have developed a model where all measured pathologist activities align with the goals of PM and are derived from parameters documented in departmental laboratory information systems (LIS) as part of usual departmental workflow. We present the Complexity Score model along with 4 years (2008-2011) of retrospective data collected in real time and validated at UHN. Accumulated Complexity Units were compared for institutional sites, sub-specialty practice groups and individual pathologists. Full-time equivalents were used to compare workloads for academic and community pathologists as well as part-time and full-time employees. We conclude that this model can detect changing practice patterns and is appropriate for monitoring clinical workload associated with LIS-documented activities for anatomical pathology, neuropathology, and hematopathology in both academic and community settings, and encompassing subspecialty and generalist practices.

P440
RELICS AND REMAINS: WYATT GALT JOHNSTON AND THE MAUDE ABBOTT MEDICAL MUSEUM.
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Celebrated in his time for his medico-legal expertise at the Coroner's Court in Montreal and for his work in public health, Wyatt Galt Johnston (1862-1902) is now essentially forgotten but for a large brass plaque flanking the door of the pathology grossing room at the Montreal General Hospital. We believe this is undeserved. Johnston was an inventive and productive physician, publishing over 60 scientific articles during his brief career and having an important influence in medico-legal medicine in Quebec. He also played an important role in the development of the McGill Medical Museum. In addition to contributing specimens, he suggested to Maude Abbott the basis of the classification system she elaborated to organize its contents. He also encouraged her to create a "society of [museum] curators", which led to her co-founding the International Association of Medical Museums, known today as the world's largest organization of pathologists, the International Academy of Pathology. Inspired by Johnston's commemorative plaque, we decided to search the McGill Medical Museum for material he contributed. A review of the museum log books yielded 48 specimens, 42 of which were accessioned between 1890 and 1903. The remaining six were not dated. Only three of these specimens remain today: "atrial ball thrombus" (1890) in the Osler collection, "bulging fossa ovalis" (1896) in the Abbott collection and "scirrhous carcinoma of the stomach" (1900) in the general museum collection. Here, we describe these specimens and explore how their placement within these three collections reflects Johnston's relationship with the Museum and his two more famous colleagues.

P441
PATHOLOGISTS' ASSISTANTS CERTIFICATION PROCESS AND CRITERIA: DEFINING A STANDARD IN A UNIQUELY DIVERSE POPULATION OF PROFESSIONALS.
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Pathologists' Assistants (PAs) in Canada are a diverse and varied group of professionals. These variances are evident in their educational backgrounds, areas of practice, and amount of experience. Although the profession has existed in Canada for more than 40 years, Canadian Pathologists' Assistants do not have a set formal standard. The Canadian Association of Pathologists (CAP-ACP) realized the need to set a standard for Canadian Pathologists' Assistants, and therefore created the Pathologists' Assistants Section of the Canadian Association of Pathologists (PA Section of the CAP-ACP). The membership committee of the PA Section of the CAP-ACP was challenged with writing certification criteria and a certification process to certify all eligible current and future Canadian Pathologists' Assistants. A survey was issued in 2009 to gain information regarding current Canadian PA's educational backgrounds, experience, and scope of practice. This information, along with collaboration with the American Association of Pathologists' Assistants (AAPA), was used to develop certification criteria which include grand parenting criteria, on-the-job trained certification criteria, and certification requirements for graduates of Canada's Pathologists' Assistants Master's Degree programs. These criteria also apply to International Medical Graduates and other internationally trained individuals and certified American Pathologists' Assistants. Two Pathologists' Assistants Subjects were also developed. Following ratification of the certification criteria at the PA Section of the CAP-ACP 2010 Annual General Meeting, the PA Section membership committee and executive committee created a certification process to implement the certification of Canada's PAs. The process was developed using the American Society for Clinical Pathology Board of Certification (ASCP-BOC) certification process, the former American Association of Pathologists' Assistants (AAPA) fellowship membership process, and the Canadian Association of Physician Assistants' (CAPA) certification process as references. The PA Section is eager to initiate the certification process and is currently approaching national bodies requesting financial and administrative assistance to implement it. Certification would provide a national standard for Canadian PAs, which would benefit PAs, employers, pathologists, and, ultimately, the Canadian patients.

P442
INTRAOPERATIVE PATHOLOGIC CONSULTATION IN TELEPATHOLOGY: AN ACCURACY STUDY OF 104 ANALYSIS PERFORMED BY THE EASTERN QUEBEC TELEPATHOLOGY NETWORK (EQTN).
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In 2004, Quebec ministry of health and Canada Health Infoway supported the creation of the EQTN aimed at providing uniform diagnostic telepathology services in a territory of 408,760 km² and 24 hospitals. The objective of this study is to evaluate the accuracy of the first frozen sections performed by telepathology and to assess the time required to perform the analysis. We performed a retrospective review of the first 104 consecutive intraoperative frozen sections evaluated by telepathology. The real-time gross evaluation was performed using a macroscopy station and two videoconferencing devices. The slides were scanned at a 20X magnification on a Nanozoomer 2.0 HT. The visualisation was done with the mScope v.3.6.1 software. The diagnosis given to the surgeon and documented in the intraoperative pathology report was compared with the final pathology report. In the cases of a discrepancy, the frozen section slides, the paraffin slides and the scanned slides were reviewed to determine the reason for the difference. Of the 104 cases, 102 cases were concordant (98% of agreement). Two significant discordant cases were reported: a change from a negative margin to a low grade intraepithelial lesion and the finding of a micrometastase in a lymph node. The average time from the arrival of the specimen to the intraoperative diagnosis was 20 minutes and it took an average of 8 minutes once the frozen section slide was ready until the diagnosis. The EQTN allowed to maintain a quality intraoperative frozen section service in a hospital where no pathologist was available on site. Telepathology allows greater flexibility in practice, avoids unnecessary travel and facilitates a better organisation of work in a vast territory with a shortage of pathologists.
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ESTABLISHING A SERVICE CORRIDOR WITH A COMMUNITY HOSPITAL USING TELEPATHOLOGY.

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We present here an example of how a centralized healthcare management system can adapt to solve unexpected problems in the delivery of care in laboratory medicine. More specifically, this case involved the development of a corridor of service enabling a large university hospital to cover pathology services for a 469 beds community hospital following the sudden departure of two local pathologists. The overall structure of healthcare in the province of Quebec is discussed. We then present the technical aspects of how this service corridor for frozen sections was created, using telepathology. This covers training of the pathologists and technicians at both centers and using whole-slide imaging technology to deliver frozen section diagnosis to the surgeons in the community center. We also touch on the troubleshooting involved in setting up telepathology. Finally, we will present the results so far and the quality control mechanisms we have put in place. In summary, we cover the organisational aspects of meeting unexpected challenges in a centralized healthcare system and the specific technical issues involved in setting up a telepathology corridor of service.

P444


Anatomical, Pathology EORLA The Ottawa Hospital, Ottawa, Ontario.

A review of the literature dating back to 1956 reveals that a minimum formalin to specimen ratio of 10:1 or 20:1 has long been the accepted “gold standard” for optimal tissue fixation, however there is no empirical evidence to support this recommendation. This 10:1 ratio has now become an Ontario Lab Accreditation requirement. We examined the fixation of over 65 surgical and autopsy specimens including breasts, colon, TME, uterus, bone, skin, prostate, mesenteric fat, liver, lung and kidney. We examined ratios of 16:1, 10:1, 5:1, 3:1, 2:5:1, 1:1 and took into account the following issues: safety, the volume of formalin required to meet various ratios, the pH of the formalin, the concentration of the formalin, formalin fixative vs. Tissuefix, cost, storage, handling, discarding, tissue staining and selected immunohistochemistry stains. We reviewed H&E staining on all cases. On selected tissues, PAS. Trichrome, Silver Methenamine and IHC staining for Vimentin, AE1-3 keratin cocktail, P63, PSA, NAPSIN, TTF1, CD10 and CD34 were examined. The results show that if the starting formalin concentration is 10% or higher, it does not deplete significantly over time. Although it is important to open large specimens and start the fixation process as soon as possible after devitalization; once the specimens are open a 5:1 ratio works well for either standard 10% formalin or Tissuefix. At lower ratios some formalin pigment production is present in congested tissues. In summary, the study conclusively demonstrates that 5:1 formalin (or Tissuefix) to specimen ratio provides good results and is adequate for large specimens. A suitably high formalin ratio would make it possible to comply with safety regulations and space issues than the more stringent recommendation of 10:1 that is embedded in histotechnology folklore.

P445

DISCORDANT PHENOTYPE AND GENOTYPE IN NEUROBLASTOMA: A CASE REPORT AND REVIEW OF THE LITERATURE.

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Background: Neuroblastoma is classically listed in the differential diagnosis of a small round blue cell tumor in the pediatric population. Prognostic factors have been determined and include, on one side, age and tumor histopathological features (differentiation, maturation, mitotic-karyorectic index, etc) and on the other side the MYCN gene and protein expression status; they seem to be working in tandem. We present a rare occurrence of a neuroblastic tumor where there is discordance between the “favourable histology” status (based on the INBC staging system) and its dismal MYCN status. Only 1% of the peripheral neuroblastic tumours (pNTs) from the Children’s Oncology Group have demonstrated this discordance. Case Report: A 15 month old boy presented with a pathologic fracture due to a lytic lesion in the proximal right humerus. Magnetic resonance imaging identified a concurrent suprarenal mass, better characterized by further imaging studies. Biopases of this mass confirmed a poorly differentiated neuroblastoma with an intermediate MKI. Of notice, prominent nucleoli were identified in the tumor cells. The MYCN status was amplified and the MYCN protein overexpressed. Discussion: The occurrence in which the “favorable histology” is discordant with the MYCN is in fact of poor prognosis. The histological feature of prominent nucleoli (“bulls-eye” nuclei) is the only finding a pathologist can infer the potential dismal prognosis of this tumor.

P446

SYNCHRONOUS POORLY DIFFERENTIATED COLONIC CARCINOMA WITH STRUMA OVARII CONTAINING A PAPILLARY THYROID CARCINOMA AND BRENNER’S TUMOR: CASE-REPORT AND REVIEW OF THE LITERATURE.

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Background: Synchronous primary malignancies arising from different germ layers is a rare occurrence. Here we report synchronous presentations of a poorly differentiated colonic adenocarcinoma, struma ovarii with papillary thyroid carcinoma and a focus of Brenner tumor. Case report: A 77 year old Caucasian women with family history of breast cancer and a 15 pack year history of smoking, first presented with anemia and weakness. Colonoscopy revealed a large right sided colonic mass as well as multiple colonic polyps. Biopsy confirmed a poorly differentiated adenocarcinoma of colon. Preoperative CT scan further showed presumed metastasis as right sided, multi-cystic, partially solid, pelvic mass. However, this pelvic mass was found to be a distinct malignant struma ovarii with papillary thyroid carcinoma and a small focus of Brenner tumor. These were confirmed by immunohistochemical studies and were different from the poorly differentiated colonic adenocarcinoma. This is the first report of synchronous poorly differentiated colonic adenocarcinoma with Brenner’s tumor and papillary thyroid carcinoma arising in a struma ovarii. Discussion: Clustering of multiple primary malignancies in the same patient is rare. Besides known specific germline mutations that predispose to familial carcinoma syndromes, mutations that cause chromosomal instability, DNA mismatch repair, microsatellite instability and epigenetic instability have been implicated in the pathogenesis of these tumors. Surgery with neoadjuvant chemotherapy remains the mainstay of treatment for colonic carcinomas. But there are no clear guidelines for treatment of malignant struma ovarii. Surgical removal of the ovarian mass followed by thyroidectomy, radiotherapy and levotyrosine suppressive therapy has been recommended by some authors. Surveillance of thyroglobulin levels is recommend for follow-up.

P447

THE IMPACT OF MULTIFOCAL PATTERN OF INVASION ON PATIENT OUTCOMES IN ORAL SQUAMOUS CELL CARCINOMA.


A tumour with multifocal pattern is thought to be independently associated with poor patient outcomes and is defined as a satellite lesion greater than or equal to 1mm from a main tumour body. We sought to determine the frequency of multifocal squamous cell carcinoma (MSCC) and associated outcomes to determine if the current standard of treatment is sufficient, and whether the presence of multifocality should influence adjuvant treatment. Methods: All patients undergoing hemiglossectomy or total glossectomy for squamous cell carcinoma of the tongue between 2001 and 2008 were identified. Pathology specimens were reviewed, and the Histological Risk Assessment score, including multifocality grading was applied. Margin status, recurrence and recurrence-related mortality were determined. Recurrence Pattern of invasion was reviewed for 42 cases of 123 patients who underwent total glossectomy or hemiglossectomy for SCC of the tongue. Tumor size ranged from 0.3 to 5.0 cm (mean 2.4cm). Perineural invasion seen in 54.8% and lymphovascular invasion in 11.9% of the cases. Margin was positive in 13.2% and negative in 86.8% (< 0.5cm: 57.9%, > 0.5 cm: 28.9%). Multifocality as worst pattern of invasion (MSCC), seen in 23.8% (10/42) cases. Out of these 42 patients 13 (31.0%) cases recurred (recurrence rate- 40% in MSCC (4/10) and 28.1% (9/32) in non MSCC) and 12 (28.6%) cases died (Mortality rate: 40% (4/10) in MSCC (4/10) and 28.1% (9/32) in non MSCC). Fisher’s Exact Test showed p value of 0.697 and 0.181 for recurrence and mortality rates respectively for MSCC compared to non- MSCC. Conclusions: In this cohort, most resection margins (71%) were < 0.5cm and most multifocal oral SCC were < 0.5cm from main tumour. Patients with multifocal oral squamous cell carcinoma (SCC) trended towards higher recurrence and mortality which was not statistically significant. Wider margins may be indicated in oral SCC to avoid recurrence.
P449
ASSESSMENT OF THE TISSUESAFE SYSTEM®: A TECHNOLOGY TO REDUCE FORMALIN ASSOCIATED HAZARDS AND PROCESS FRESH TISSUE UP TO 96 HOURS.
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Background: Pathology laboratories are moving toward reducing formalin utilization through the introduction of technologies, such as the Milestone TissueSAFE High Vacuum Biospecimens System (TSS), which allows for tissue to be kept fresh for up to 96 hours from the time of collection.

Design: We assessed the effectiveness of the TSS by measuring: 1) the reduction of formalin use, 2) the tissue section quality preserved in a high vacuum environment, 3) employee satisfaction, 4) the cost associated with TSS implementation, and 5) additional benefits. Four pathologists assessed the quality of 28 H&E and 6 IHC slides from four cases placed in the TSS at 2, 4, 6, 24, 48, 72 and 96 hours intervals and compared them with a control slide. The pathologists blind to the slides using a 4-point Likert scale. Satisfaction was measured through focused questioning of staff and content analysis of the responses.

Results: The TSS resulted in a 30% decrease in formalin usage (500 cc) per large specimen. 89.3% of TSS H&E and 100% of control slides received an excellent quality score by all four pathologists; 3 TSS H&E slides received a good score (by 1 pathologist), and no slides received an average or poor score. All TSS IHC studies done on 96 hour specimens were excellent. The employee satisfaction was excellent. Cost savings were due to reduced formalin usage and waste. Additional benefits were the ability to triage fresh tissue for ancillary studies (e.g., molecular testing) and to focus on fresh specimen examination.

Conclusion: The quality of slides using the TSS was as high as the formalin-heavy system and the metrics of employee satisfaction, cost reduction, and additional benefits of TSS were higher than the formalin-heavy system.

P450
HBV X GENE MUTATION WAS DETECTED BY PCR-HRM AND ITS CLINICAL SIGNIFICANCE.
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Objective: To study the mutation of HBV X gene and its clinical significance. Methods: PCR-High Resolution Melting (PCR-HRM) analysis was employed for detecting HBV X gene mutation in the serum of 168 cases. Direct sequencing confirmed mutation sites. Serum HBeAg and HBV DNA were detected by enzyme-linked immunosorbent assay (ELISA) and Polymerase Chain Reaction (PCR).

Results: A double mutation in the high viral load group (≥105 copies/ml) HBV DNA was significantly higher than the HBeAg-positive group (p<0.05). The detection rate of BCP double mutation together with CP gathered mutation, nt1755A-Cnt1768T-A double mutation in HBeAg-negative group was significantly higher than the HBeAg-positive group (p<0.05). The detection rate of BCP double mutation together with CP gathered mutation, nt1755A-Cnt1768T-A double mutation in the high viral load group (≥105 copies/ml) HBV DNA was significantly higher than the the low viral load group (≤104 copies/ml) HBV DNA (p<0.05). The detection rate of BCP double mutation together with CP gathered mutation, nt1755A-Cnt1768T-A double mutation in HBV X gene mutation reduce the HBeAg expression and promote the viral replication of HBV mutants. Simultaneously, it’s expected to detect HBV X-section frequent mutation site in clinic, and provide a reference for predicting patients with disease progression and prognosis.

P451
CAN ENTERIC NEUROSPHeres BE EXPANDED AFTER CRYOPRESERVATION?

Objectives: Hirschsprung disease is a form of congenital constipation that affects 1/5000 births. It results from incomplete neural crest migration into the intestinal tract during embryological development resulting in the absence of an enteric nervous system beginning in the distal colon and proceeding proximally for a variable length. In the context of this disease tissue engineering approaches to reintroduce innervation of the aganglionic gut segment is acknowledged to be imminently feasible. Our approach involves expanding stem and progenitor cells in the form of neurospheres from dissociated fetal mouse model cultures. The ability to cryopreserve these cultures would greatly aid experimental logistics and ultimately delivery to patients. Thus our objective is to assess the feasibility of cryopreservation.

Method: Fetal E13.5 mice were harvested from time pregnant dams. Gut from fetal mice was isolated under semisterile conditions and enzymatically dissociated with collagenase and dispase for 20 min at 37°C. Mechanical Trituration was performed and the resulting single cell solution was either cultured directly or after cryopreservation by flash freezing in DMSO. Dissociated suspensions were cultured on noncoated plastic dished in DMEM supplemented with bFGF and EGF. Results: Neurospheres grew from the single cells and reached 100 μm in diameter by day 4. The number of neurospheres was subjectively considerably less in the cryopreserved condition. Conclusion: The efficiency of neurosphere expansion is considerably less when the dissociated cell suspension is cryopreserved. Follow up studies will objectively quantify this and alternate methods of cryopreservation will be attempted.

P452
LEPIDIC PATTERN OF SQUAMOUS CELL CARCINOMA IN SITU: CASE REPORT AND LITERATURE REVIEW.
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Squamous cell carcinoma (SCC) of the lung arises from the metaplasia-dysplasia carcinoma sequence. Squamous cell carcinoma in situ (SCCIS) is often seen at the edge of invasive SCC. A lepidic pattern of SCCIS has been described only in case reports. A 61 year old male, with a 25 pack year smoking history and previous asbestos exposure, presented with a progressively enlarging left upper lobe mass and underwent lobectomy. Histologically, focal invasive SCC was present, but >90% of the tumour had an unusual histologic appearance: malignant squamoid cells expanded the alveolar walls, traveling under benign appearing alveolar pneumocytes and on top of an intact basement membrane, creating an overall lepidic pattern resembling adenocarcinoma in situ, or nests of squamous cell carcinoma with central, gland-like structures resembling adenosquamous carcinoma. In the gland-like spaces, alveolar macrophages were present, suggestive of retained alveolar spaces. The malignant squamous cells stained positively for p63 and high molecular weight keratin (CK 5/6), while the pneumocytes were positive for TTF-1; there was no aberrant staining pattern. The diagnosis of focal invasive SCC with surrounding lepidic pattern of SCCIS was made. The differential diagnosis includes adenosquamous carcinoma; distinguishing these entities has important prognostic and treatment related implications. The minimal literature available on this unusual pattern of SCCIS is reviewed.
P453
CONCURRENCE OF PULMONARY LANGERHANS CELL HISTIOCYTOSIS & BRONCHOGENIC CARCINOMA: CASE REPORT & REVIEW OF THE LITERATURE.
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Background: The term Langerhans cell histiocytosis (LCH) comprises a diverse range of lesions in which the key feature is proliferation and infiltration of cells phenomenologically analogous to the antigen-presenting dendritic cells of the epidermis. We present a case of classic pulmonary Langerhans cell histiocytosis (LCH) (also known as eosinophilic granuloma) and primary pulmonary adenocarcinoma coexisting in the same lesion.

Case: The patient was a 62 year old female ex-smoker who underwent wedge resection of a right upper lobe lesion. Microscopic sections show a lesion with combined features of classic pulmonary LCH and bronchogenic adenocarcinoma.

Literature review & discussion: A review of the literature turned up 24 other published cases of pulmonary LCH and primary lung cancers occurring in the same patient. The reported clinical and pathologic features of these are summarized. These cases raise interesting questions: is there a relationship between pulmonary Langerhans cell histiocytosis and lung cancer? is this a correlation based on common predispositions and risk factors, or is there a causal link? We conclude that pulmonary LCH does seem to be associated with an increased risk of lung carcinoma, but that until more is known about LCH, a relatively uncommon and poorly understood disease, the nature of the correlation is likely to remain obscure.

P454
VARIABLE ENDURANCE AND FIDELITY OF TISSUE MARKING DYES IN ANATOMICAL PATHOLOGY.
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Background: The use of a tissue marking dye (TMD) on surgical margins is a common practice in anatomical pathology. Unfortunately, not all dyes, paints, or inks survive tissue processing. Objective: This project evaluates various TMDs for endurance and color fidelity through routine processing and immunohistochemistry (IHC). Methods: Commercially available TMDs (Davidson Marking System [DMS], Cancer Diagnostics [CDI]) and acrylic artists ink (Daler-Rowney) were obtained in a variety of colors (green, blue, red, black, violet, yellow, and orange). The TMDs were applied to excess non-diagnostic surgical pathology tissue and processed for routine histology. TMD endurance and color fidelity was assessed on H&E sections and sections subjected to IHC protocols. Results: Routine tissue processing altered the acrylic inks, showing loss of color in the yellow and 'Flame Red' colors and yellow discoloration of orange and 'Scarlet Red'. The red color was maintained with 'Crimson Red'. DMS red showed variable loss of color. All CDI products survived processing. DMS blue and violet dyes showed black discoloration after IHC processing. All other TMDs that survived tissue processing were not affected by IHC.

Conclusions: Not all TMDs endure tissue processing and IHC protocols with adequate color fidelity. As specific color often denotes a specific tissue or cell type, the evaluation of whether a tissue marking dye is appropriate for a specific case or circumstance is crucial. The absence of color fidelity is a potential source of serious error. The black discoloration of DMS blue and violet colors following IHC protocols has not previously been described and is noteworthy for pathologists using this product. Pathologists should be aware of the limitations of any TMD system prior to routine use in the anatomical pathology laboratory.

P455
THE MITOTIC SCORE IN INVASIVE BREAST CANCERS SHOULD NOT BE ASSESSED BASED ON TEN HIGH POWER FIELDS.
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Background: The mitotic score is routinely reported in excisions for invasive breast cancer and is assessed based on ten high-power fields (HPFs), a measure dependent on the microscope's field diameter (FD). The consequent differences in the sampling error due to the disparate sample areas is difficult to assess experimentally. Methods: An in silico model based on the binomial distribution was developed to calculate the misclassification rate in one million simulated breast tissue specimens, using the sample areas of the extremes in the FD range (0.40 mm, 0.69 mm) found in the Collage of American Pathologists' Invasive Breast Cancer Protocol. The mitotic rate probability density function of the specimens was derived from an experimental study. Results: The model reproduces the expected highest misclassification rate for the intermediate mitotic score group. The smallest field diameter microscopes, due to sampling error, incorrectly categorize an additional of 5.5% of all tumors when compared to the largest field diameter microscopes, and an excess 9.4% of cases in the intermediate mitotic score group. The overall misclassification rates for the areas sampled, 1,257 mm² (FD 0.40 mm) and 3,739 mm² (FD 0.69 mm), are, respectively, 14.4% and 9.0%. Conclusions: The mitotic score should not be assessed based on ten HPFs. It should be assessed based on a standardized sample area or, more generally, guided by a procedure to obtain a uniform misclassification error. We suggest a triage procedure with a small initial standardized sample area to identify cases in close proximity to the mitotic rate cut-points that would benefit from a larger sample area, thereby decreasing the mitotic score misclassifications and limiting the field of assessing a larger area to cases that would benefit from it.

P456
INTERNAL CONSULTATION IN A GYNECOLOGY SURGICAL PATHOLOGY SERVICE.
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Background: In order to increase diagnostic accuracy and agreement, it is common practice to obtain internal consultations. The purpose of this study was to determine within our gynecological (GYN) pathology service: 1) individual pathologist consultation rates; 2) reasons for consultation in light of existing team consultation rules; and 3) reasons for non-correlating interpretations (NCI). Methods: We reviewed all internal consultation forms for GYN surgical pathology cases for 2010. The forms were sorted into the following categories in light of existing team consultation rules: 1) consultation for opinion from the diagnosis team; 2) internal consultation (4.6% of all GYN cases) the most common sites were uterus (40%), cervix (22%) and ovary (14%). Among pathologists, individual consultation rates varied from 1-10 %. The most frequent issues were: endometrial hyperplasia (presence of atypia), cervical squamous intraepithelial lesions (grading, recognition) and subtyping of ovarian malignancy. 41% of consultations related to difficult areas identified by team consultation rules. In 10% of consultations, more than 1 consultant's opinion was requested, and in 78% of these cases there was correlation amongst consultants. Only 0.6% of consultations were sent for external opinion for NCI related to benign vs. malignant classification. Conclusion: 1) The rate of consultation varies amongst our GYN team; 2) many consultations relate to issues not identified in GYN team consultation rules; and 3) external consultation is rarely required.
P457
IONOGRAM OF PATIENTS ADMITTED IN THE INTENSIVE CARE UNIT OF ONE UNIVERSITY HOSPITAL: A CRITICAL LOOK.

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In the Brazilians Intensives Cares Units (ICU) are common services care protocols and use them to standardize requests for laboratory tests. However, the request for a menu of standard tests for all patients can generate unnecessary tests. Not to mention that not always all exams are necessarily important for all inpatients. A practical example is the request daily iogram, whose results are normal and show no variation in many patients. To critically evaluate the results of iograms measured in the ICU of the Clinical Hospital of University Federal of Minas Gerais (CH-UFMG), we calculated the average rate of change of serial reports of each ion, along the entire length of stay of each patient. A study conducted between the months of November and December 2011, the ICU CH-UFMG. We analyzed the results of the following ions: sodium, potassium, magnesium and calcium. The percentage of normal and abnormal examinations were calculated. We also assessed the rates of change of serial measurements of each ion for each patient's hospitalization. Data were analyzed statistically. We ordered 3713 iograms ICU of CH-UFMG, between November and December 2011. Of this total, 68% of the results were normal. Sodium was measured 1007 times, being 46.28% normal, down 51.84% and 1.89% higher. Potassium was dosed 998 times, 84.37% normal, 12.9% lower and 2.71% higher. Magnesium was measured 708 times, 73.16% normal, 22% lower and 4.86% higher. The calcium was measured 986 times, with 69.8% normal, 28.2% lower and 2% higher. Evaluating only the test results, without having as base the clinic patients, the normality of most of the results and the small variation observed between the serial measurements of each ion for each hospitalization reinforce the need to discuss and review the care protocols in Clinical Hospital of University Federal of Minas Gerais.

References:

P458
THE EFFECT OF PROCESS ENGINEERING ON TURNAROUND TIME OF HER-2NEU TESTING IN BREAST CANCER IN AN ACADEMIC CENTRE.

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Objective: Determination of Her-2 status in a quick and efficient manner is of primordial importance in the management of breast cancer patients. Our centre has recently been designated as reference centre for Her-2 testing. This has caused an increase in 30% of our workload within a year resulting in an increase in turnaround time (TAT). Due to limited resources and growing concerns from our clinicians, we sought to improve our TAT through an in depth analysis of our workflow. Methods: Process engineering (PE) was used to document delays in different steps of our Her-2 testing workflow for biopsy and surgical specimens received at our laboratory. Both Her-2 testing by immunohistochemistry (IHC) and FISH were evaluated. Results: PE revealed a mean TAT for Her-2 IHC testing of 13.4 days for biopsies and 35.4 days for surgicals. Main bottlenecks identified included delays from (1) reception of specimen to start of Her-2 technique and (2) end of Her-2 technique to dictation of report. Changes implemented included (1) prioritization of breast specimens and (2) elimination of an intermediate delay in the evaluation of Her-2 IHC. Re-analysis of delays a few months after changes were made resulted in a decrease in mean TAT for surgical specimens to 21.1 days. For biopsies, slight improvements were also noted. Conclusion: PE facilitated a significant reorganization of our Her-2 IHC testing workflow which has resulted in improvements in TAT. More importantly, this was obtained without requiring increases in staff or resources. PE is an ongoing process which will now be used to improve TAT for Her-2 testing by FISH.

P459
AUDIT OF NEGATIVE BREAST CORE BIOPSIES.

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Introduction: Core needle biopsy under stereotactic or ultrasound guidance is the standard of care for diagnosis of breast lesions. There is a known problem with false negatives. This study was undertaken to assess the accuracy of negative breast core biopsies at DSM and to find ways to reduce false negative rates. Materials And Methods: 220 sequential negative breast cores (with a diagnosis less than atypical, suspicious or malignant) were reviewed. After the review, the review diagnosis was correlated to the original diagnosis. Cases with a review diagnosis of atypical duct hyperplasia (ADH) or higher were reviewed by a second pathologist. Results: The diagnosis was confirmed as benign in 218 cases (98.1%). In one case, the review diagnosis was unsatisfactory (0.5%). Three cases of missed ADH were found on review (1.4%). Two of these cases were originally diagnosed as florid duct hyperplasia. The atypical ducts in these cases showed decreased CK5/6 expression on immunohistochemical staining. One case showed ADH of columnar cell type. Conclusions: The false negative rate was comparable to that found in other studies (<2%). To improve recognition of borderline lesions, cases of missed ADH were presented to all DSM pathologists at a mandatory quality assurance conference. Staining for CK5/6 was recommended for questionable cases. By policy, cases of florid duct hyperplasia will have double sign-out. Random 10% review of negative core biopsies was rejected as a means of improving accuracy. A closing audit of negative breast cores is in process.

P460
DEVELOPMENT OF A PATHOLOGY QUALITY INDICATOR FEEDBACK TOOL FOR UROLOGISTS PERFORMING PROSTATE NEEDLE BIOPSY.

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Introduction: Guidelines have been developed to maximize targeted tissue sampling for prostate needle biopsies (PNBs) during prostate cancer screening. As part of this, it is important that quality assurance measures be employed to maximize the quality of this test. Objectives: We designed a feedback tool for the urologists that aimed to provide information on key pathology quality indicators of their PNBs in order to facilitate examination of individual and departmental biopsy practice. Methods: Our Millennium Laboratory Information System was searched to identify all PNBs cases received from January 1-December 31, 2011, and key demographic and pathologic information was recorded. PNBs not performed by urologists were excluded. The final analysis was provided to the urology department as an anonymized quality indicator report. Results: The study included 10 urologists who performed a total of 989 PNBs. Diagnostic distribution included 43.3% (n=428) malignant, 7.4% (n=73) ASAP, 8.6% (n=85) high grade PnN (n=85) benign cases. On average, 9.7 cores were sampled per case (range 1-16) with a mean core length of 1.48 cm (range 1.40-1.55 cm). Although three urologists sampled fewer cores than average, the mean core length varied very little between urologists. The report was well received and the results will be evaluated further to see how this information may alter the departmental practice in the future. Conclusion: Targeted pathology feedback on PNBs can be harnessed to provide an effective measure of quality indicators in urology practice.
The majority of laboratory testing errors originate in the pre-analytical phase. While the causes and frequencies of pre-analytical errors are well characterized, there are few studies investigating the actual cost of these errors. To attempt to address this, we built a model to quantify the cost of pre-analytical errors occurring during inpatient complete blood count (CBC) testing. The resultant model accounts for the costs of materials, resources, and personnel-time consumed during CBC testing and during error-reporting and error investigations that occur when errors are detected. Personnel were shadowed and timed as they completed each of the processes involved in CBC testing (including error-reporting processes). Materials and resources consumed during the CBC testing process were identified and catalogued and the per-test cost was determined. Data were obtained on all pre-analytical errors occurring in inpatient CBC testing during the years 2008 to 2011 inclusive from our hospital’s Laboratory Information System. The annual frequency of pre-analytical errors in inpatient CBC testing increased significantly from 0.57% in 2008 to 0.86% in 2011 ($X^2 = 77.23, p < 0.0001$). The total cost of one CBC error requiring the repetition of the entire CBC testing process was determined to be $37.70. In 2011, pre-analytical errors in inpatient CBC testing cost Sunnybrook $43,462, and represented a loss of 775 employee hours. This cost model represents the minimum cost of a pre-analytical error, as costs extraneous to the laboratory were beyond the study scope. Future studies investigating downstream effects of pre-analytical errors and the costs associated with them should be conducted, and specific solutions – such as the implementation of positive patient identification (PPID) systems, for example – should be identified and implemented. We expect that the cost of such solutions would be greatly offset by cost avoidances associated with decreases in error investigations and reporting and with decreases in repetitive testing of laboratory specimens.

P462

PATIENT EXPERIENCE AS ONE OF QUALITY INDICATOR IN LABORATORY MEDICINE SERVICE.
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Creating the patient centric experience is an important value of laboratory medicine’s critical success factor defined by customers who have a choice in laboratory medicine and healthcare services providers. Patient flow processes should be taken step by step to find out details of services that need to be privileged. There were several patient experience touch points in laboratory medicine: appointment scheduling, phlebotomy process, laboratory consultation, billing process and patient service center network and how fast doctors can use the laboratory data for patient’s treatment. In every process must be an effort to standardized protocols, reduced or eliminated complaints and improved services. To enhance the patient experience usually need for using technology in laboratory medicine services. The laboratory management should learn about how to transform and to measure patient experience, how to design a great patient experience by delivering a great service to customers and understood their relationship in patient experience. The most common problem encountered is an implementation and embedding of programs.

P463

AUDIT OF ANATOMIC PATHOLOGY INTERNAL CONSULTATIONS BEFORE AND AFTER CASELOAD REDISTRIBUTION.
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Objective: To evaluate internal Anatomic Pathology departmental consultations during a period of altered case load distribution within Saskatoon Health Region (3 sites); Royal University Hospital (RUH), Saskatoon City Hospital (SCH), St. Paul’s Hospital (SPH). The hypothesis is that internal departmental consultation during this period would increase in frequency and involve more inter-site communication. This allowed for a quality assurance assessment of our current intradepartmental consultation practice.

Method: A retrospective analysis over the same six week period spanning two (2012, 2013) years was undertaken. A collection of attributes was taken from each consult including; onsite versus off site consultation, discipline consulted, the reason for consult (QA or diagnostic assistance), turnaround time, correlation between pathologists and consult requisition completeness. Results: Each of the three sites used a different form. Consultations occurred more frequently in SPH and SCH consulted versus RUH, most frequently involved gynecology (34), breast (25) and skin (16) specimens and were mainly to the local regional expert. Data capture within intradepartmental requisitions was incomplete resulting in difficulty to measure impact on turnaround time. We were unable to detect an increase in consultation frequency, with 163 consult cases in 2012, and 112 cases following the alteration in case load distribution in 2013. Discussion: Lower consultation rates at one site (RUH) may be accounted for by informal consultation in the absence of documentations. Increased compliance in optimal consultation practice may result from ongoing audit with communication of results. An alternative intervention may be to consider form redesign and standardization. Continued improvement might require ongoing interventions on a regular basis.

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DEVELOPING AND INSTITUTING STANDARDIZED, CHECKLIST-BASED GROSSING PROTOCOLS.
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Background: Checklist use in anatomical pathology is increasing and mandated by national bodies for reporting cancer diagnoses. Grossing, an essential part of rendering accurate tissue-based diagnoses, is amenable to a checklist-based approach, and not fully standardized. Checklists would ensure that critical information is not missed, and likely simplify reports for subsequent review. Design: Using wiki software (MediaWiki) we established a restricted-editorship website (pathologyprotocols.org) to manage the creation and revision of checklist-based grossing protocols. The goals were (1) understand the protocol development process, (2) leverage the knowledge base of our team to create more robust protocols and (3) develop a platform to disseminate an open standard to hospitals that routinely refer cases to us. Results: Our team, consisting of three pathologists and three pathologists’ assistants, found the what-you-see-is-what-you-get (WYSIWYG) editor was easy to learn and use. The website facilitated the rapid creation of 12 checklist-based protocols, with explanatory notes, references, links and redirects on 62 separate pages. A total of 193 edits were made by six individuals. Edits per page ranged from 3 to 17. Conclusion: The project could easily be scaled to allow input from partner institutions in our geographically expansive region. Gross data captured in synoptic form, in individual data fields, is amenable to data mining and would allow a more systematic analysis of this process for (1) quality assurance, (2) a rigorous characterization of macroscopically evident disease processes, likely leading to improvements in diagnostic accuracy and, (3) may allow a speedier pathologist interpretation and sign out of cases. The experience with checklists in aviation suggests rapid development and constant revision are required for a high level of performance; wiki software is well-suited to this task, and can be used to rapidly disseminate evolving pathology knowledge.
P465
RENAI BIOSPY ADEQUACY RATES: A SUCCESSFUL INTERDEPARTMENTAL QUALITY IMPROVEMENT ACTIVITY.
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Background: At our centre it was determined that native kidney biopsy adequacy rates (31%) fell below figures published in the literature (89-99%). Two separate initiatives to improve adequacy rates were implemented through the cooperation of members of the departments of Pathology, Medicine and Radiology. The impact of these interventions on adequacy rates was assessed. 

Methods: A retrospective analysis of renal biopsy adequacy rates was performed. The first initiative was to restrict the performance of biopsies to a subgroup of radiologists. The second initiative was to perform an on-site adequacy assessment. The native kidney, allograft, and combined adequacy rates were calculated over a seven year span divided into three periods: 1) baseline, 2) after implementation of the first initiative, and 3) after implementation of the second initiative. Statistical significance was determined with the two-sample t-test between proportions. 

Results: For native kidney biopsies, the first and second initiatives were followed by significant increases in adequacy rates (41%, p<0.0001 and 18%, p=0.0003 respectively). The first, second, and third period native kidney adequacy rates were 31%, 72% and 90%, respectively. For allograft biopsies, the first initiative was followed by a decrease, and the second an increase, in adequacy rates. Neither was statistically significant. The first, second, and third period allograft adequacy rates were 75%, 56% and 69%, respectively. Overall adequacy rates (37%, 66% and 52%) showed increases proportional to the volume of native kidney biopsies. 

Conclusion: Both initiatives resulted in a significant increase in native kidney and therefore overall biopsy adequacy rates. Neither initiative resulted in a significant improvement in allograft biopsy adequacy rates. Future efforts should focus on this patient group.

P466
VALIDATION OF WHOLE SLIDE SCANNING FOR USE IN REAL-TIME CLINICAL FROZEN SECTION CONSULTATION.
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Objective: The goal of this study is to assess diagnostic accuracy on digital vs glass slides. 

Methods: 42 frozen section cases selected to represent the range of specimens requiring intra-operative consultation at our institution were digitally scanned. The specimens were chosen with bias toward difficult consultations to increase the chance of uncovering potential issues with the slide scanning process. 

Results: The number of major discrepancies was not significantly different between digital and glass slides. The total major and minor discrepancies trended toward better performance for the glass slides. 

Conclusion: Analysis of the individual discrepancies shows that reviewers of digital slides were more likely to defer to permanent section or give a diagnosis of 'suspicious' rather than committing to a positive or negative diagnosis, and this tendency led to a greater frequency of minor discrepancies. This may reflect a true degradation in the digitization of the slide, or alternatively, it may be at least partially due to unfamiliarity with the new media and reluctance to commit to a definitive diagnosis. Three out of four reviewers noted discomfort in counting neutrophils using digitally scanned images. Interestingly, despite this, there were no discrepancies (major or minor) relating to cases of neutrophil counts. Future work is necessary to assess if the number of minor discrepancies changes after the reviewers acquire familiarity with the new media. In addition, the time needed to arrive at a diagnosis using digital material relative to glass slides requires assessment.

P467
VALIDATION OF A HISTOPATHOLOGIC CLASSIFICATION SCHEME FOR ANCA-ASSOCIATED GLOMERULONEPHRITIS.
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Anti-neutrophil cytoplasmic antibody (ANCA)-associated small vessel vasculitides cause multiple organ system problems including rapidly progressive glomerulonephritis (GN). Berden et al. (2010) proposed a new histopathologic classification scheme that separates biopsies into four classes: focal, crescentic, mixed, and sclerotic. Here we present external validation of the prognostic implication of this classification scheme for kidney function at 1 year based on 71 individuals from the Calgary area with ANCA GN who underwent kidney biopsy between 2005 and 2010. The mean age was 60 years and 41% were female. 35% of the biopsies were crescentic; 32% mixed; 21% focal; 11% sclerotic. 10 patients (14%) died within 1 year. Among patients who survived, the overall mean (95%CI) change in eGFR at 1 year was 7 (7-15) ml/min/1.73m2. Older age was associated with less improvement in eGFR (p=0.004), while gender was not significantly associated with change in eGFR (p=0.22). The mean (95%CI) change in eGFR at 1 year significantly differed between the classes (p=0.02); 19 (11-27) ml/min/1.73m2 with crescentic histology; 11 (1-21) ml/min/1.73m2 with focal; 8 (3-13) with ml/min/1.73m2 with mixed; and -4 (-7 to -1) ml/min/1.73m2 with sclerotic. 

Patients with crescentic class biopsies showed significantly more improvement in eGFR at 1 year compared to the mixed (p=0.04) and sclerotic (p=0.005) classes. These findings validate the prognostic utility of this classification scheme and support the use of more aggressive immunosuppressive therapy and plasmapheresis to improve renal outcome for patients with crescentic but not sclerotic lesions.

P468
GEMELLA SANGUINIS ENDOCARDITIS WITH C-ANCA/ANTI-PR-3-ASSOCIATED IMMUNE COMPLEX NECTROTIZING GLOMERULONEPHRITIS WITH “FULL HOUSE” PATTERN ON IMMUNOFLOUORESCENCE MICROSCOPY.
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Objective Of The Study: We report the first case of c-ANCA/anti-PR3 positive immune complex glomerulonephritis with “full house” immunofluorescence pattern due to bacterial endocarditis. 

Data And Results Obtained: A 67 yo man with history of weight loss, lower back pain and macroscopic hematuria was referred for progressive renal failure. He was afebrile, with an apical holosystolic murmur and a creatinine of 906 µmol/l. Kidney biopsy revealed focal necrotizing glomerulonephritis with crescents and immune complex deposits with a “full house” pattern on immunofluorescence microscopy, while c-ANCA/anti-PR3 were shown to be positive. Endocarditis and spondyloarthritis were diagnosed by echocardiography, identification of Gemella sanguinis in blood cultures and PET-CT. Dialysis, antibiotics and a short course of corticosteroids (2 weeks) were started due to dialysis dependency and active lesions on the biopsy. Mitral and aortic valve replacement were performed and 3 months later the creatinine level decreased to 62 µmol/l and anti-PR3 became negative. 

Conclusions: This case underlines the importance of ruling out bacterial endocarditis in presence of ANCA positivity or kidney biopsy findings suggestive of lupus nephritis.
P469 COMPARISON OF CLINICAL UTILITY OF THE 1995 WHO CLASSIFICATION WITH THE 2003 ISN/RPS CLASSIFICATION OF LUPUS NEPHRITIS.

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For the past two decades, lupus nephritis has been histologically classified according to the 1995 WHO Classification. With the introduction of the 2003 ISN/RPS classification, many nephropathology services have been converting to this new classification. This study was undertaken to compare the diagnostic and clinical utility of both classification systems. A total of 103 renal biopsies initially reported as lupus nephritis in the Department of Pathology, Faculty of Medicine, University of Malaya were reassessed using the criteria of both the 1995 WHO Classification and the 2003 ISN/RPS Classification. The relative prevalence for each class using the WHO Classification were: Class I (1%), Class II (8.7%), Class III (6.8%), Class IV (60.2%), Class V (20.4%), Class VI (2.9%) while the prevalence using the 2003 ISN/RPS Classification were: Class I (1%), Class II (8.7%), Class III (6.8%), Class IV (61.2%), Class V (21.3%), Class VI (1%). Both classifications were essentially comparable with regards to Classes I, II and III. The differences in Classes IV, V and VI were significant in potential to alter patient management. The identification of segmental lesions over and above a diffuse nephritis (ISN/RPS Class IV S) deserves a focused clinicopathological study to gauge whether this group has a different clinical manifestation and outcome from Class IV G, and may thus require a different treatment strategy. With regards Class V, the ISN/RPS system, by requiring that all mixed classes be stipulated in the diagnostic line rather than be subserved to Class V, minimizes the chances of patients missing out on additional treatment. The ISN/RPS system has stricter criteria for Class VI, which again minimizes patients missing out on therapy. On the whole, the ISN/RPS system is more user friendly as criteria are more clearly defined. This study provided the basis for our laboratory to adopt the ISN/RPS system because of less classification ambiguities and more benefits to patient care.

P470 THE IMPACT OF THE ISN/RPS CLASSIFICATION SYSTEM ON THE HISTOLOGICAL DIAGNOSIS OF FOCAL AND DIFFUSE LUPUS NEPHRITIS.

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Objective: the inclusion of sclerotic glomeruli in the count of total glomeruli affected by lupus nephritis (LN) is a major change introduced in the 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification compared with the 1995 World Health Organization (WHO) classification system. We studied the effect that this on the diagnosis of LN class III and IV.

Methods: Two pathologists blindly reclassified 172 renal biopsies with LN class III or IV and their combinations with class V under the two classification systems. We used the McNemar test to evaluate whether the changes of paired binomial attributes in one direction (from class III to IV) were significantly greater than those in the opposite direction (from class IV to III) in using the two classifications.

Results: 152 cases received the same diagnosis in both systems. According to the WHO classification 47 cases were diagnosed as class III and 125 as class IV. Under the ISN/RPS classification 29 cases were diagnosed as class III and 143 cases were class IV. While one case diagnosed as class IV under the WHO classification was diagnosed as class III under the ISN/RPS classification, 19 cases diagnosed as class III under the WHO classification were diagnosed as LN class IV under the ISN/RPS system (p<0.001). All 19 cases had both active and sclerosing lesions. Inclusion of sclerotic glomeruli in the count of total glomeruli affected by LN in the ISN/RPS classification was the major reason for upward class switching (from III to IV).

Conclusions: Compared to the WHO classification, the recent ISN/RPS classification system may increase the likelihood of LN class IV diagnosis. Considering the role of sclerotic glomeruli on this class switching, further studies are needed to evaluate the impact of LN classification on patient management and outcomes.

P471 OSMOTIC NEPHROPATHY IN KIDNEY TRANSPLANT RECIPIENTS: REPORT OF TWO CASES.

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Introduction: Osmotic nephropathy (hydropic change) is a form of acute renal tubular injury caused by intravenous administration of hypertonic solutions, contrast agents and immunoglobulins. The diagnosis is made by histological examination and the differential diagnosis is extensive.

Method: Presentation of the cases, review of the pathogenesis, clinical presentation, prognosis, histology and differential diagnosis of the osmotic nephropathy.

Results: A 54 yo woman was pronounced brain-dead following a cardiac arrest complicated by cerebral anoxia. During hospitalization, she was treated with hypertonic solutions (Pentaspan®, 1L iv) and developed acute renal failure. The patient was a candidate for organ donation and both kidneys were transplanted in a 47 yo man (receiver 1, R1) and a 61 yo woman (receiver 2, R2). Histological examination of the pre-transplant kidney biopsies showed acute tubular damage and hydropic changes. After transplantation, recovery of renal function was delayed: 21 days post-transplantation R1 had a creatinine of 249 µmol /L and 9 days post-transplantation R2 was still in hemodialysis. Renal allograft biopsies, performed at these times, showed no diagnostic signs of rejection but acute tubular injury along with severe and diffuse hydropic changes of the tubular epithelial cells. Subsequent biopsy of the grafts (6 months post-transplantation in R1 and 36 days post-transplantation in R2) still showed the hydropic changes. The differential diagnosis included osmotic nephropathy secondary to the administration of hypertonic solutions and calcineurin inhibitor toxicity.

Discussion and conclusion: Osmotic nephropathy can occur in brain-dead kidney donors because of the frequent use of hypertonic solutions and contrast agents in these patients. The lesions may persist in grafts for several weeks, even months or years. The diagnostic interpretation is difficult due to its resemblance to calcineurin inhibitor toxicity.

P472 THE PROGNOSTIC SIGNIFICANCE OF COPY NUMBER ALTERATIONS IN RENAL CELL CARCINOMA AND THE IMPACT OF COMBINED ALTERATIONS.

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Renal cell carcinoma (RCC) is one of the most common adult malignancies. It is characterized by a broad spectrum of genetic alterations that occur during pathogenesis of the disease. The aim of this study was to investigate the prognostic significance of chromosomal copy number alterations (CNAs), and the combined effect between these aberrant regions. Kaplan-Meier analysis was performed on 436 RCC cases with overall survival (OS) data from The Cancer Genome Atlas. We identified a number of chromosomal locations with prognostic significance, including 12q gain. Furthermore, pairs of CNA combinations either resulted in a statistically significant increase or decrease in OS compared to each alone (p < 0.05), such as 8q gain and 17p loss. This has been reported in other cancers. Gene products encoded within the regions of the pairs of CNAs were used for bioinformatic pathway analysis. The insulin signaling pathway was one of the most common pathways shared between the CNA pairs and it was the only pathway to be associated with decrease in OS. Other pathways, including the JAK-STAT signaling pathway, were associated with both an increase and decrease in OS. Our results show that CNAs can be used as prognostic markers and that there is a cooperative interaction between CNAs in RCC. An understanding of the synergy between combinations of CNAs will lead to a more thorough grasp on the pathobiology of RCC aggressiveness.
Background: Methotrexate (MTX) is a widely administered treatment in many diseases. Considering the renal clearance of MTX, prolonged exposure to high concentrations can lead to the precipitation of the drug and its metabolites within the renal tubules and cause consecutive tubular damage. Despite the fact that MTX is a recognized cause of crystalline nephropathy, no histological images of crystal deposition in a renal biopsy are found in the literature.

Case report: A 52-year-old patient was receiving a chemotherapy regimen (Magrath protocol) that included MTX for an extensive non-classified B cell lymphoma with retropertioneal, gastric and bone involvement. He received MTX on day 10 of the protocol and presented acute renal failure with a creatinine that rose gradually from 41 µmol/L to 116 µmol/L, and 2 days later up to 465 µmol/L. Serum MTX (0.38 µmol/L) reached toxic levels (>0.10 µmol/L) 72 hours post treatment. Abdominal ultrasound revealed bilateral enlarged kidneys with hyper-echocortex. A renal biopsy was performed and revealed intratubular and interstitial crystal deposition and acute tubular injury. The crystals were yellow to pale brown, forming needle-like structures with a fan-like or annular arrangement. They were white to golden and strongly birefringent under polarizing light and some had a Maltese cross-like appearance. The crystals were negative on PAS or Masson stains and positive on chromotrope stains. Considering the clinical history, MTX-induced crystalline nephropathy was the most probable diagnosis. Conclusion: This case represents the first histological report of a probable MTX-induced crystalline nephropathy. The crystals found on the biopsy were histologically distinct from those of other known crystalline nephropathies such as DHA or oxalate nephropathy.

P474 LOCALIZATION OF PLA2R ANTIBODY IN MEMBRANOUS NEPHROPATHY AND CLINICAL CORRELATION.

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Background: Membranous nephropathy (MN) is a leading cause of nephrotic syndrome in adults. Idiopathic MN is currently diagnosed only after excluding secondary causes, such as infection, drugs, malignancy, and other autoimmune diseases. Recent studies have identified M-type phospholipase A2 receptor (PLA2R) as a possible target antigen in idiopathic MN. Objective: To evaluate the utility of PLA2R and the associated IgG4 immunostains to differentiate between the diagnosis of idiopathic MN from secondary MN and other causes of nephrotic syndrome. Methods: 129 kidney biopsies from patients with nephrotic syndrome [MN (19), systemic lupus erythematosus class V (21), membranoproliferative glomerulonephritis (13), minimal change (16) and other nephropathies (60)] were included in this study. Immunostaining was done on frozen tissue for PLA2R, and on paraffin-embedded tissue for IgG4. We used fluorescence and light microscopy to assess PLA2R and IgG4 expression respectively and the results were correlated with the clinical data. Results: Our results show enhanced PLA2R staining combined with IgG4 positivity along the glomerular basement membrane in 50% of biopsies with idiopathic MN, 20% of secondary MN, and none of the biopsies with other causes of nephrotic syndrome. Conclusion: Our study shows that the combined expression of PLA2R and IgG4 is highly significant in idiopathic MN compared to other glomerular diseases. Hence, we consider the expression of these markers to be a useful diagnostic tool for differentiating idiopathic MN from secondary MN.

P475 EVALUATING ESTIMATING EQUATIONS OF GLOMERULAR FILTRATION RATE IN HEALTHY POPULATIONS FROM 8 ASIAN REGIONS.

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1Clinical Laboratory, Peking University First Hospital, Beijing, China; 2Faculty of Health Sciences, Yamaguchi University Graduate School of Medicine, Ube, Japan. Objective: To evaluate the performance of eGFR calculated by different equations in healthy Asian population. Methods: Age- and sex-specific reference intervals for eGFR by EPI/J were established. Age-specific differences between eGFR calculated by various equations and assay were compared. Results: The difference of eGFR between EPI/E and EPI/J appears minimum among all the variations caused by using different equations and assays, with 93.7% of difference less than 10 ml/min/1.73m2; the second smallest difference was found to be between MDRD/E and MDRD/J, with 68.6% of difference less than 10 ml/min/1.73m2; The largest difference was between EPI/E and MDRD/J, with only 24.9% of difference less than 10 ml/min/1.73m2. Age specific reference intervals for eGFR by EPI/J were established. Conclusions: The results strongly suggest that CKD-EPI may be used as a common equation in South-east Asian populations.