CANADIAN ASSOCIATION OF PATHOLOGISTS | ASSOCIATION CANADIENNE DES PATHOLOGISTES

ABSTRACTS – RÉSUMÉS

JUNE 4-8, 2011
62ND ANNUAL MEETING
VANCOUVER, BRITISH COLUMBIA

4-8 JUIN 2011
62IÈME ASSEMBLÉE ANNUELLE
VANCOUVER, COLOMBIE-BRITANNIQUE
O211 HISTONE DEACETYLASE 1 AND 2 IN MESENCHYMAAL TUMORS.
M. Pacheco, T.O. Nielsen. Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia.

Objective: Histone deacetylases (HDACs) are a group of enzymes implicated in epigenetic gene silencing, a mechanism of transcriptional regulation important in the pathogenesis of many soft tissue sarcomas associated with translocations. The efficacy of HDAC inhibitor drugs has been proven preclinically in this type of tumor and has inspired a Canadian clinical trial (IND.200). Nevertheless the in situ expression of their target HDAC proteins has not been comprehensively assessed in surgically-excised mesenchymal neoplasms. The aim of this study is to survey the immunohistochemical expression of HDAC1 and 2 in a large collection of mesenchymal tumors and tissues, to assess if there is high expression of HDAC isoforms in translocation-associated sarcomas that supports their sensitivity to this class of drugs.

Methods: In-situ expression of HDAC1 and 2 was surveyed by immunohistochemistry in 2169 specimens spread over 10 tissue microarrays representing 74 categories of malignant and borderline mesenchymal neoplasms and 40 normal tissues that were included in the analysis. A score system was established based on percentage of tumor cells stained and intensity of staining, resulting in a final score from 0-6. Comparison of the distribution of the staining scores between groups was made using the Wilcoxon rank-sum test. The proportion of tumors expressing HDAC1 and HDAC2 was compared using Pearson’s chi-square test. A p < 0.05 was considered statistically significant.

Data and Results:

<table>
<thead>
<tr>
<th>Specimen group</th>
<th>Normal tissues</th>
<th>Translocation-associated sarcomas</th>
<th>Other mesenchymal neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen group</td>
<td>HDAC1</td>
<td>HDAC2</td>
<td>Specimen group</td>
</tr>
<tr>
<td>Total specimens</td>
<td>285</td>
<td>237</td>
<td>Total specimens</td>
</tr>
<tr>
<td>THL, L, normal</td>
<td>1.7</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>THL, L, normal</td>
<td>0.6 (0.6-1.3)</td>
<td>0.6 (0.6-1.3)</td>
<td></td>
</tr>
<tr>
<td>HDAC1, mean</td>
<td>4.8 (4.4-5.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDAC2, mean</td>
<td>4.0 (3.7-4.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD, mean</td>
<td>3.7 (3.6-3.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Asterisks denote significance: * less than normal tissues, p<0.05 (Wilcoxon).

Conclusions: HDAC2 is present and intensely expressed in a very high proportion of mesenchymal tumors, and particularly among sarcomas associated with fusion transcription factors being assessed in IND.200. HDAC1, consistently with the literature, is less expressed than HDAC2 in normal tissues, and appears even lower in mesenchymal tumors. Results support the choice of HDAC inhibitor SB939 in IND.200, as it has activity against HDAC2. Tissue from accrued patients will be assessed for HDAC expression using these assays, and correlated with drug response.

O212 MEMBRANOUS EXPRESSION OF PHOSPHO-EZRIN/RADixin/MoEsin (ERM) PROTEINS: A POTENTIAL BIOMARKER FOR TRIPLE NEGATIVE BREAST CANCER.

Background: Ezrin is a member of the ezrin/radixin/moesin (ERM) family and has apical expression in normal breast lobules, but, strong cytoplasmic expression in breast carcinomas. Another ERM protein, moesin, is a distinguishing marker of triple negative (ER/PR/Her2 -ve) breast cancers. We postulate that the activated forms of ezrin and/or moesin may have a better predictive power and therefore, we examined the expression of activated ERM proteins (pERMs) in breast cancers.

Design: A TMA from 63 breast cancers (16% triple -ve) and 20 mammoplastes was made. IHC was performed with antibody for pERM (which shares epitope specificity with ezrin pT567 and moesin pT588). The % of positive area and intensity staining were scored by two evaluators independently. Cases were dichotomized into triple -ve versus all other subtypes. pERM staining was categorized as -/+, +/+, and analyzed using two-sided exact Fisher test. Double immunofluorescence was also performed on a smaller TMA of 8 triple -ve cases to assess the co-localization of ezrin and moesin. Results: pERM showed continuous membranous staining in 19% of cancers, whereas only apical in normal lobules. A statistically significant association of pERM with triple -ve cases was observed; the prevalence of triple -ve cases was 42% in the pERM +ve and 10% in the -ve cases (p<0.017). Double IF staining showed striking cytoplasmic co-localization of ezrin and moesin within the tumour cells; in contrast to reports of other breast cancers wherein moesin localizes to the stroma and ezrin remains in tumour cells. Conclusion: The unique association of membranous pERM in triple -ve breast cancers suggests that the presence of activated ERM proteins may be a distinguishing feature of triple-ve breast cancers.

O213 BASAL-LIKE CARCINOMAS OF THE BREAST IN ASSOCIATION WITH TUMORAL STROMAL FIBROSIS, TUMORAL FIBROSIS NEOANGIOGENESIS, AND INTRATUMORAL LYMPHOVASCULAR INVASION.
K. Chung, J. Hanson, S. Silverman. Department of Laboratory Medicine, Misericordia Hospital, Edmonton, Alberta.

Objectives: We hypothesize that tumoral fibrosis, intratumoral lymphovascular invasion and tumoral neoangiogenesis in basal-like carcinomas (BLC) are predictors of distant metastases via hematogenous spread.

Methods: We evaluated 11 cases of BLC and 16 controls of invasive ductal carcinoma not otherwise specified (IDC NOS) for tumor fecality, tumor size and grade, lymph node status, presence or absence of central and peripheral tumoral fibrosis, presence or absence of intra and/or peritumoral lymphovascular invasion, tumoral neovascular density, and breast biomarkers. We performed immunohistochemistry (IHC) using D240/P63, CD31, and CD5/6 antibodies.

Results: Tumor stromal fibrosis was identified in 91% of BLC and in 6% of the controls (p < 0.001). Intratumoral lymphovascular invasion was identified in 82% of BLC and 19% of the controls (p = 0.002). The other associations for BLC and IDC NOS were not statistically significant. All the cases, including BLC and control cases showed CD31 positivity in the tumoral fibrous or central aspect of IDC NOS. Conclusions: The above findings show that BLC is associated with tumoral fibrosis, tumoral neoangiogenesis, and intratumoral lymphovascular invasion. These histological features may be markers of hematogenous pattern of distant metastatic spread. We are unclear of the findings associated with CD31 and their significance.

O214 P16 EXPRESSION IN ENDOMETRIAL CLEAR CELL CARCINOMA.
J. Makowians, R.G. Stovel, S. Nofech-Mozes, R.S. Saad. Department of Pathology and Laboratory Medicine, Sunnybrook Health Sciences Centre, Toronto, Ontario.

Clear cell carcinoma (CCC) of the endometrium is a rare neoplasm and often associated with an aggressive clinical behavior and poor outcome. Furthermore, the molecular pathways involved in the development of CCC are still unclear. Both uterine serous and CCC characteristically express p53, suggesting that they may share common molecular pathways. Recent studies have shown that p16 is widely expressed in the majority of serous carcinoma. However, there is no/minimal data available regarding p16 expression in CCC. In this study, we investigated the expression of p16 in endometrial CCC. Forty five cases of endometrial CCC and 50 endometrial serous carcinomas were retrieved from the archives of anatomic pathology during the period between January 2002 and December 2010 and a representative block was chosen for p16 staining. P16 was considered positive when tumor showed both nuclear and cytoplasmic staining. Percentages of cells staining was recorded as follow: Negative (0-5%), weak (1+, 6-25%), moderate (2+, 26-50%) and strong (3+, >50%). A case was considered positive if more than 50% of the tumor cells were stained. Amongst the CCC, 24/45 (53%) presented as pure CCC and 21/45 (47%) as mixed tumors. The majority of serous carcinomas (48/50, 96%) demonstrated diffuse/moderate-strong expression (score 3+, >50%). In the CCC group, only 9/45 (20%) were strongly positive for p16. In the endometrioid component of mixed tumors, staining was weak and/or patchy. Interestingly, p16 expression showed a significant correlation with lymph node metastases (r =0.45, P< 0.001). Our data indicate that p16 may play a role in the tumorigenesis of a subset of CCC and serve as prognostic marker by its correlation with lymph node metastases. In contrast to p53 which is expressed in the majority of clear and serous carcinomas, p16 is expressed in only a fraction of CCC, indicating a possible different molecular pathway.
O215
ASSESSMENT OF CORRELATION BETWEEN p16INK4A STAINING, SPECIFIC SUBTYPE OF HPV AND PROGRESSION OF CINI LESIONS: FIRST COMPARATIVE STUDY.

M. Razmpoosh MD1, A. Sansregret MD2, L.L. Olligny MD3, D. Bouron-Dal Saglio MD1. 1Department of Pathology, 2Department of Gynecology-Obstetrics, CHU Sainte-Justine, Université de Montréal, P Québec.

Objective: To confirm the interest of p16INK4A staining as a prognostic marker in cervical intraepithelial neoplasia grade 1 (CINI), to compare p16INK4A immunostaining, specific subtypes of HPV and evolution of CINI in order to adapt patient follow up.

Method: 74 cervical biopsies with a histologic diagnosis of CINI were reviewed. CINI diagnosis was confirmed and they were stained with p16INK4A. HPV status was assessed for 38 of these cases by PCR-direct sequencing, using the same paraffin-embedded specimens. The results of the follow up biopsies were noted in order to determine the progression of the CINI lesions according with the p16INK4A and the HPV subtypes.

Results: Out of the 74 CINI biopsies, 50 were p16 negative, of which 19 regressed and 19 remained the same; none progressed. 12 were lost to follow up. Out of the 24 p16 positive biopsies, 10 were lost to follow up, 3 regressed, 8 remained the same, and 1 progressed. 6 different high risk HPV subtypes were identified in 7 of the 24 p16 positive lesions (HPV39 was observed twice). 16 subtypes (12 high risk and 4 low risk) were found in 26 of the 50 p16 negative samples.

Conclusion: We confirm that p16INK4A negative CINI seldom progress to a CINII-III lesion. In our series, p16INK4A positive CINI were only associated with high risk HPV subtypes, whereas both high and low risk HPV were detected in p16INK4A negative CINI lesions.

O216
NEUTROPHIL DNA NET FORMATION IN APPENDICITIS AND OTHER ACUTE INFLAMMATORY CONDITIONS.

D. Salina1, C. Gwozd1, F.H. Pilsczek1, F.H. Green1,2, M. Kelly1,2, A. Sansregret1, L. Hornberger1, S. Lozanoff1, 1Snyder Institute of Infection, Immunity and Inflammation, 2Department of Pathology and Laboratory Medicine.

Background: Neutrophil extracellular traps (NETs) are webs of DNA covered with antimicrobial molecules that constitute a newly described killing mechanism in innate immune defense (Brinkmann et. Al, Science 2004 Vol. 303). NET formation involves a complex process of nuclear envelope breakdown and extracellular release of DNA and granular enzymes (J.Immunol. 2010 Vol. 185).

Objectives: The purpose of this study was to confirm NET formation in appendicitis and also to identify the spectrum of NETs in various acute inflammatory conditions.

Methods: Neutrophils were purified from humans, activated with S. aureus and then fixed at various time points for TEM. TEM images from the in vitro study were correlated with those obtained from human appendicitis. Cases of purulent appendicitis, cholecystitis, pneumonia and random abscesses were selected for analysis based on light microscopy findings suggestive of NET formation.

Results: TEM showed an extensive release of numerous DNA containing vesicles and NETs with lysis of collagen fibers in appendicitis. These changes seen are similar to previously published in vitro studies. The NETs formed in these tissues, and other acute inflammatory conditions, are positive for histones and neutrophil proteolytic enzymes (including elastase, myeloperoxidase and lysozyme).

Conclusion: Neutrophils form DNA NETs from a highly complex process when activated by S.aureus and other bacteria. This includes nuclear envelope breakdown, exocytosis of DNA containing vesicles, and NET formation. The release of NETs is likely harmful to the surrounding tissues, and causes destruction of collagen fibers. This mechanism is an important part of the acute inflammatory response to microbial infection, and likely plays a major role in supplicative appendicitis and other inflammatory disorders.

O221
THREE-DIMENSIONAL RECONSTRUCTION OF AN ORGANIC STRUCTURE FROM HISTOLOGICAL SLICES.

B. Falkenberg1, S. Lozanoff1, L. Hornberger1, C. Sergi1. 1Dept. of Engineering, University of Alberta, Edmonton, Alberta; 2Dept. of Anatomy and Reproductive Biology, University of Hawai’i School of Medicine, Honolulu, USA; 3Dept. Pediatric Cardiology, University of Alberta Hospital, Edmonton, Alberta; 4Dept. Of Lab. Medicine and Pathology, University of Alberta, Edmonton, Alberta.

Background: Three dimensional reconstructions (3D) of morphological structures provide useful information for instructive purposes and animations. This aim of this study was to develop three dimensional, interactive models organic structures from histological sections.

Methods: The image analysis suite Imaris was used along with the software ImageJ produce digital models of 3 different embryonic hearts. A digital camera was used to obtain images of the slices, where after the slices were aligned and composed to form a 3D model. Our study also examined the advantages and disadvantages of this approach of imaging. By analyzing and cataloging structural defects in a sample, 3D reconstruction may be used to improve the understanding of failure modes within a structure such as the heart, and track the development of congenital defects.

Results: Qualitative observations showed that the morphological features of our models may be comparable with those displayed by ultrasound diagnostics emphasizing this technique during regular examination.

Conclusion: Our data supports the use of both software programs for generating files useful for 3D computerized modeling.

O222
QUALITY ASSURANCE PROGRAMS FOR HEMATOPATHOLOGY MORPHOLOGY. ASSESSMENT OF PROGRAMS OF FOUR COUNTRIES.

R. Padmore1,2, 1Division of Hematopathology, The Ottawa Hospital, Ottawa, Ontario; 2Vice-Chair, QMP-LS Hematology Scientific Committee, Toronto, Ontario.

Objective: Assessment of morphology skills is an integral part of external quality assessment (EQA). This study assesses hematopathology morphology EQA programs from four countries.

Methods: The author is personally enrolled in hematopathology morphology EQA programs from Royal College of Pathologists of Australasia Quality Assurance Program (RCPA-QAP), United Kingdom National External Quality Assessment Service digital morphology (UK-NEQAS-DM), American Society for Clinical Pathology CHECKPATH-Hematopathology (ASCP), and participates in Quality Management Program-Laboratory Services (QMP-LS) through the laboratory workplace. Programs were assessed using defined criteria including size, access, format, material, evaluation and feedback.

Results: All programs are available to individual participants, including QMP-LS available through Institute for Quality Management in HealthCare (IQMH). Materials consist of 3–20 peripheral blood and/or bone marrow cases/year with 180 (QMP-LS) to 1050 (UK-NEQAS-DM) participants. All programs have online data entry.

Participation is available for individual pathologists for all programs or as a laboratory for 2 programs (RCPA-QAP, QMP-LS). Preferred features are excellent glass slide sets (RCPA-QAP, QMP-LS, ASCP), quickness of reviewing the scanned slide (UK-NEQAS-DM), providing the participant with ancillary test results for diagnosis (ASCP) and lymph node morphology cases (ASCP). For all programs useful features are the assessment of the individual or laboratory performance compared with other participants, educational feedback, prompt turnaround time, use of clinically relevant cases and rare disorders.

Conclusions: EQA programs vary in features providing the hematopathologist with choice depending on individual needs and objectives associated with skill assessment and education.
Background: Digital Morphology (Virtual Microscopy) uses computers to review digitized images of microscopic preparations. This technology allows pathologists and cytotecnologists to review images from any computer and enables consultation within and among different facilities. Material and Methods: A small pilot survey was conducted by Quality Management Program Laboratory Services (QMP-LS) in 2010. The participants were asked to download the viewing software Image Scope provided by Aperio. QMP-LS distributed the software to 51 participants within Ontario. The participants were asked to view and analyze eight digital images obtained from various preparation techniques and body sites. Results: Over 85% of participant responses matched the assigned value, except for the conventional respiratory bronchial wash smear. The results showed that liquid-based preparation slides are better suited for digital microscopy since they have smaller areas to scan. The image quality and ability to focus on the image and cells are the two most important factors for digital morphology. One of the main hurdles was downloading the Image Scope software because of hospitals’ and community laboratories’ firewall issues, though after reconfiguring firewall and proxy settings all participants were able to proceed with the survey. Conclusions: By using digital images, External Quality Assurance (EQA) programs can provide the means for participants to view and interpret microscopic preparations of small volume, unique or difficult to obtain patient material for assessment and/or education. The survey comments and feedback will help guide QMP-LS in using digital morphology. The committee plans to continue to explore digital morphology in future surveys and to remain well informed of advances in digital morphology.

O224
STANDARDS 2 QUALITY – DEVELOPING PATIENT SAFETY CHECKLISTS TO STANDARIZE SURGICAL PATHOLOGY PROFESSIONAL PRACTICES.

Background: Path2Quality, a collaborative initiative of the Ontario Medical Association’s Section on Laboratory Medicine and the Ontario Association of Pathologists, has developed a draft set of guidelines for internal quality assurance, focused on professional interpretive processes. These guidelines include a set of patient safety checklists (PSCs) analogous to those currently employed by surgical services to reduce errors in the operating room. Methods: The surgical pathology PSCs were developed after a review of pertinent literature, published quality assurance guidelines, and regulatory monitoring requirements. The checklists focus on steps in the interpretive process where critical hand-offs and complex processes need to be optimally accomplished to allow accurate, timely, and complete reporting. Results: Surgical pathology PSCs delineate steps for intraoperative consultation, gross examination, and pre- and post interpretive practices. The draft quality management program including checklists was circulated for review to the laboratory physicians of Ontario, as well as to national and international experts. The final version of the checklists will include modifications based on this feedback. Conclusions: PSCs have not previously been published for surgical pathology interpretive practices. The utility of these checklists will require field evaluation but they have the potential to reduce errors and clarify expectations for optimal surgical pathology practices. The checklists form one component of a comprehensive quality management program for surgical pathologists.

O225
DIGITAL PATHOLOGY: ATTITUDES AND PRACTICES IN THE CANADIAN PATHOLOGY COMMUNITY.
M. Bellis1, A. Pollett1, S. Jothi1, C. Naugler1, G. Yousef1, 2, 3, 4. 1Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario; 1Department of Pathology and Laboratory Medicine Mount Sinai Hospital, Toronto, Ontario; 1Keenan Research Centre of the Li Ka Shing Knowledge Institute, St. Michael’s Hospital Toronto, Ontario; 1Department of Pathology and Laboratory Medicine, University of Calgary, Calgary, Alberta.

Digital Pathology is a rapidly evolving niche in the world of Pathology and will likely only increase in popularity as technology improves. By attaining opinions of Pathologists and Pathology residents across Canada we hope to determine:
1. Their current attitudes towards and experiences with digital pathology;
2. Which modalities digital pathology is best suited for;
3. The need for training in digital pathology amongst Pathology residents and staff. An online survey consisting of 24 yes/no, multiple choice and free text questions regarding digital pathology was sent out via email to all members of the CAP-ACP and Pathology residents across Canada. Telepathology (TP) is used in approximately 48% of institutions, primarily for teaching purposes (62%), followed by OR/frozen consults (50%). Seventy-two percent of respondents believe there is a need for TP in their practice. Eighty-five percent use digital images in their practice. The top two favoured applications of digital pathology are teaching and consultation service, with its main advantage being easier access to cases. The disadvantages of using digital pathology are cost and image/diagnostic quality. Sixty-five percent of respondents would attend training courses in pathology informatics and 92% think informatics should be part of resident training. The results of the survey indicate that Pathologists and residents across Canada do see a need for telepathology and the use of digital images in their daily practice where they would be most useful in teaching environments and consultation services. Integration of an informatics component into resident training programs and courses for staff Pathologists would be welcomed.

O226
MISMATCH REPAIR IMMUNOHISTOCHEMISTRY USE AMONG CANADIAN PATHOLOGISTS.
G. Allro1, S. Kalloger2, A. Pollett1, A.M. Mulligan1, E. Torlakovic1, B.A. Clarke1, 2.
1University of Toronto, Toronto, Ontario; 1University of British Columbia, Vancouver, British Columbia.

Background: Mismatch repair immunohistochemistry (MMR-IHC) has recently been proposed as the primary tool to triage patients with colon (CRC) and endometrial cancer (EC) for Lynch syndrome screening. The aim of this study is to determine the current status of MMR-IHC testing in Canada in academic and community settings and within specialized referral centres. Methods: Online surveys of CAP-ACP members and seven referral centres were conducted and responses analyzed using JMP software. Results: Among CAP members (n=74), there is provincial variation in access to in house MMR-IHC and to referral centres (32.33% ± 21.99%, range: 0%-66.67% vs. 61.93% ± 23.12%, range: 40%-100%). Practice is divergent amongst pathologists and tumour types with regards to recommending testing or initiating reflex testing (50.1% CRC vs. 18.6% EC) and (21.88% CRC vs. 8.2% EC). Up to 50% consider MMR-IHC as a germline test, but 64% favour using it without consent. 80% of specialist labs classify this as type II test and participate in proficiency testing. Only 28% offer MSI testing. Most common cases tested are CRC, EC, ovary, gastric and sebaceous carcinomas. There is lack of consistency in reporting results to pathologists in non-specialist centres. Conclusion: There is variable availability and practice among Canadian pathologists regarding MMR-IHC. Consensus guidelines for performance and reporting should be established.
P701
TWO UNUSUAL PRESENTATIONS OF CLOSTRIDIUM SEPTICUM AORTITIS.

Background: Clostridium septicum aortitis is a rare life-threatening infection that has a strong association with malignancies, in particular adenocarcinoma of the ascending colon. Autopsy case findings: We present two unusual cases of C. septicum aortitis at autopsy with blood cultures that grew C. septicum. The first patient was an 81-year-old man with right scrotal pain. CT scan of the abdomen was negative. He died before an exploratory laparotomy could be performed. Autopsy showed a dilated and dissected aorta, mycotic aneurysms and thrombosis of proximal right testicular artery and ischemic colitis. No malignancy was identified. The second case was an 80-year-old man who presented with nausea and vomiting. A CT scan of the abdomen showed a mycotic aneurysm and he underwent a resection of the infrarenal aortic aneurysm, retroperitoneal debridement plus axillobifemoral bypass. At the completion of surgery he arrested. At autopsy an occult invasive adenocarcinoma of the terminal ileum was identified and confirmed microscopically. Conclusion: We report two additional cases of C. septicum aortitis, which are rarely reported in the English literature and review the pathogenesis. The unusual presentations for these cases are: epididymitis with ischemic colitis and adenocarcinoma of the small bowel.

P702
ABNORMALITIES IN THE PRB-CYCLIND1-CDK4/6-P16 PATHWAY IN PRIMARY SQUAMOUS CELL CARCINOMA OF THE ENDOMETRIUM.
N. Bures MD, M.A. Duggan MD FRCP, G. Nelson MD FRCS, Q. Duan MSc, A. Magliiocco MD, FRCP, D. Demetrick MD PhD, FRCP. 1. Department of Pathology and Laboratory Medicine and 2. Obstetrics and Gynecology, Faculty of Medicine, University of Calgary, Calgary, Alberta; 1Clinical Research Unit and 1Translational Laboratories, Tom Baker Cancer Centre, Calgary, Alberta.

Objective: The pathogenesis of primary squamous cell carcinoma of the endometrium (PSCCE) was recently reported to have abnormalities in the pRb-cyclinD1-cdk4/6-p16 path independent of the Human Papilloma Virus (HPV). This study examined PSCCE cases for alterations in this pathway. Methods: This case control study, compared cases of PSCCE (n=5) to controls of endometrioid cases of PSCCE (n=5) to controls of endometrioid cases. We examined the expression of EADC, pRB, p18, p19, CDK6 and HPV 16 by immunohistochemistry (IHC) was based on summed averages of both reviews were calculated for each antibody and differences between cases and controls were tested for significance using the Student T test. Results: The mean case and control scores respectively were H2AX (7.25, 6.25), pRB (7.25, 6.25), p18 (7.25, 7), p19 (7.5, 7.5), CDK6 (7.5, 6.5) and HPV16 (0.75, 0). Differences were insignificant (p= 0.679). Discussion: Based on these limited investigations, the PRB-Cyclin D1-CDK4/6-P16 pathway may play a role in the pathogenesis of PSCCE. The similarity in expression with EADC; a Type 1 cancer suggests the role is independent of the HPV.

P703
MALAKOPLAKIA OF THE LIVER: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE.
N. Botros MD, D.R. Yan, I.R.Wanless MD. Department of Pathology, Dalhousie University, Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, and Department of Pathology, Dr. Chalmers Regional Hospital, Fredericton, New Brunswick.

Malakoplasia is an unusual chronic inflammatory condition characterized by the presence of Michaelis-Guttman bodies that most commonly affects the genitourinary tract. It is believed to be associated with an altered immune response with features of defective macrophage phagocytosis in response to a bacterial infection. Therefore, there is a high incidence of malakoplasia in immunocompromised patients. Malakoplasia confined to the liver is rare, and only 5 cases have been described in the literature. We report two cases of malakoplasia of liver, both were incidental autopsy findings. The first case involves a 53 year old male with systemic lupus erythematosus and chronic refractory pancytopenia who presented with with severe febrile neutropenia. His blood culture was positive for Stenotrophomonas and Enterococcus and he subsequently developed invasive pulmonary aspergillosis. The second case involves a 60 year old homosexual male who was found to have a mass in periorbital tissue involving the sphenoid bone which, on biopsy, showed inflammation and occasional treponema-like spirochetes. He had a sudden unexpected death at home and autopsy findings included adrenal gland abscess and pulmonary edema. Both cases had normal-appearing liver with incidental microscopic findings of small, round to oval, solid targetoid structures consistent with Michaelis-Gutmann bodies. These stained positively with periodic acid-Schiff, and Von Kossa stain. The first case also showed numerous hemosiderin positive granules resembling bacteria singly and in clumps. These might represent nucleation sites and an early phase of development of Michaelis-Gutmann bodies. It is important to be aware of the existence of malakoplasia in unusual locations.

P704
STUDY OF ENDOCERVICAL CURETTAGE IN COLPOSCOPIc EXAMINATION.
F. Siadat, S. Bradshaw, S. Islam. Department of Pathology and Laboratory Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario.

Background: Opinions regarding the use of endocervical curetage (ECC) in high risk female patients range from performing ECC regardless of colposcopic findings to omission of the ECC as it may not reduce colposcopic accuracy. Based on one meta-analysis, published in 1992, the positive and negative predictive values of ECC in women who had satisfactory colposcopy were 2.4% and 99.4%, respectively. Design: The pathology reports of 310 consecutive female patients with endocervical curettage performed between 2008 and 2010 were reviewed. The presence of any other procedure in the same report was noted. This included cervical biopsy, cone biopsy, and loop electrical excision procedure (LEEP). The pathology diagnosis of each procedure recorded. Results: In total number of 310 female patients reviewed (mean age of 40.5 years old and SD of 12.1), 234 (75.5%) had no remarkable pathological findings. 30 (9.7%) had squamous intraepithelial lesion (SIL) of any grade. 1 (0.3%) had adenocarcinoma in situ and 2 (0.6%) had frank adenocarcinoma. In 170 cases, another procedure other than ECC was done. Conclusion: It appears that ECC may add some additional diagnostic information when performed in high risk patients. However, the importance and clinical implications require larger and preferably randomized studies.
PL06 microRNA PROFILING IN KIDNEY CANCER: ACCURATE MOLECULAR CLASSIFICATION OF SUBTYPES AND CORRELATION WITH CYTGENETIC AND mRNA DATA.
Y.M. Youssif1, N.M.A. White2, J. Grigull2, K. Krizova1, C. Samy2, S. Mejia-Guerrera1, A. Evans3, C. Streuther5, G.M. Youssif1. 1Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario; 2Department of Laboratory Medicine, and the Keenan Research Centre in the Li Ka Shing Knowledge Institute, St. Michael’s Hospital Toronto, Ontario; 3Department of Mathematics and Statistics, York University, Toronto, Ontario; 4Department of Pathology, Toronto General Hospital, Toronto, Ontario.

Objectives: Renal cell carcinoma (RCC) encompasses different histological subtypes. Distinguishing between subtypes is usually made on morphological basis but this is not always accurate. The aim of this study was to identify microRNA (miRNA) signatures that can distinguish between the different RCC subtypes and to explore their biological pathways. Methods: miRNA microarray analysis was performed on three common RCC subtypes (clear cell, chromophobe and papillary), and oncocytoma. Results were validated on the original as well as an independent set of tumors using quantitative RT-PCR analysis. Results: Microarray data were analyzed by standard approaches. Relative expression for qRT-PCR was determined using the ΔΔCt method and expression values were normalized to RN44. We found unique miRNA signatures can distinguish between the different RCC subtypes and also oncocytoma with very high sensitivity and specificity. Conclusions: miRNA expression patterns can accurately distinguish between RCC subtypes. miRNA profiles indicate the presence of both shared and unique pathways among different subtypes.

P070 DISTINCT mTOR SIGNALING IN HEPATOCELLULAR CARCINOMA CELL LINES.
M.G. Neuman. In Vitro Drug Safety and Biotechnology Laboratory, and Department of Pharmacology & Toxicology, University of Toronto, Toronto, Ontario.

Introduction & Objectives: Hepatocellular carcinoma (HCC) has become the third leading cause of cancer-related death worldwide, a trend paralleled by an increase in advanced hepatitis C virus (HCV)-related liver disease. Targeted therapies in HCC have a stellar importance in identifying novel molecular targets for treatment. Based on its role in cell growth and differentiation, aim to evaluate mTOR-signal activation in human HCC cell lines, as well as the anti-tumoral effect of a dual-level blockade of the mTOR-pathway. Methods: The mTOR-pathway was assessed using molecular immune and electron microscopy markers. The effects of dual blockade of mTOR-signalizing with everolimus were evaluated in normal human hepatocytes and liver cancer cell lines HepG2 cells and HuH7 in the presence or absence of replicon (HCV active). Results: Aberrant mTOR-signalizing (phosphorylated RPS6) was present in cancer cell lines and was associated with insulin-like growth factor pathway activation, epidermal growth factor up-regulation, and changed the tumor cell viability in vitro. Blockage of mTOR-signalizing with everolimus shows a higher apoptotic activity in replicon cells when compared with the control HuH7 and HepG2 cells by biomarkers and electron microscopy. mTOR-inhibitor reduced vascular endothelial growth factor and tumor necrosis factor levels. Conclusions: mTOR-signalizing has a critical task in the pathogenesis of HCC, supporting that mTOR-everolimus blockade is effective especially in the HCV-related tumor cells. These findings establish a rationale for targeting the mTOR-pathway in HCC and stratifying the patients based on their primary liver disease.

P078 IGfG4 PLASMA CELL INFILTRATION OF COLONIC POLYPS IN AN ASYMPTOMATIC PATIENT AND OTHER IGfG4-RELATED DISEASE CASES.
L.H. Lee1, E. Shaffer2, S. Urbanski3, M. Kelly4, 1Department of Pathology, University of Calgary, Calgary, Alberta; 2Department of Medicine, University of Calgary, Calgary, Alberta.

Objective: IgG4-related disease (IRD) is a recently recognized disorder, first described in relation to autoimmune pancreatitis (AIP), in which numerous IgG4 plasma cells and fibrosis are present. Non-pancreatic manifestations have recently been identified, but their significance is unclear. We report an index case of colon polyps infiltrated by IgG4 cells in a patient without evidence of AIP. We also identified four additional cases of IgG4 cell infiltration in various tissues.

Results: Our patient is a 33 year old female with neurofibromatosis type 1, who had a single episode of acute pancreatitis 12 years ago. Screening colonoscopy, performed due to a family history of colon cancer, resulted in the removal of two polyps. Histology showed ulceration with granulation tissue and numerous plasma cells infiltrating the submucosa. There were 576 IgG4+ cells/HPF with an IgG4+/IgG- cell ratio of 80%. The polyp bases showed a fibroblast response. Stains for neural tissue and gastrointestinal stromal tumor were negative and there were no signs of neurofibroma, granuloma, or dysplasia. Her serum IgG4 and autoantibody levels were normal, and MRCP revealed a normal biliary tree, pancreatic duct, and pancreas. The other cases of IgG4 cell infiltrated tissues identified were: epiploysis granulatation tissue, tissue associated with metastatic adenocarcinoma, inflammatory myoglandular polyp and MALT lymphoma. Conclusions: Various manifestations of IRD are still being described. Our primary patient is unusual as she is young, asymptomatic, and has no evidence of AIP or autoimmune disease. The only two cases of IgG4+ polyps previously reported are in elderly symptomatic patients with AIP. Our cases illustrates that IRD may be more common than currently reported since they may be asymptomatic and may occur in a variety of conditions and tissues. IRD may be a manifestation of a systemic disorder that requires followup or may represent a localized disease entity that will not manifest elsewhere.

P079 “PROGRESSING” MULTICYSTIC MESOTHELIOMA OF THE LIVER.
M. Caragea1, P.M. Smith1, C. Howlett1, J.R. Parfitt2, T.Krausz1 and S. Chakrabarti1.
1Department of Pathology, University of Western Ontario, London, Ontario; 2Department of Pathology, Windsor Regional Hospital, Windsor, Ontario; 3Department of Pathology, The University of Chicago, Chicago, Illinois.

Background: Benign multicystic mesothelioma (BMM) arising in the liver is an extremely rare lesion that usually affects young women. Only a few cases have been described to date. Malignant transformation in a BMM has been reported only twice. We present a case of BMM arising in the liver, showing evidence of progression to a malignant mesothelioma. Case presentation: A 44-year-old woman presented with a palpable abdominal mass. Her past medical history is unremarkable. Ultrasound revealed a 10 cm complex cystic mass in the left lobe of the liver. A partial liver resection followed. Grossly, the tumor was composed of multiple cysts containing gelatinous and clear fluid. Microscopically, microcysts lined by flat or cuboidal cells were set in an edematous and fibrous stroma with numerous bizzare atypical cells with hyperchromatic nuclei and multinucleation. Scattered atypical mitoses were noted. Immunohistochemistry confirmed the mesothelial origin of both the cells lining the cysts, as well as the stromal cells. Conclusion: BMM undergoing malignant transformation is extremely rare; to the best of our knowledge, this is the third case described. Knowledge that this tumor may occur in the liver, as well as recognition of bizarre cytologial atypia and atypical mitoses are helpful to make the diagnosis of a “progressing” multicystic mesothelioma of the liver.

P070 AN UNUSUAL PRESENTATION OF SYNVOIAL SARCOMA, A CASE REPORT.
J. Gruchy MD, MSc; K. Dakin Hache MD, PhD, FRCP. Dalhousie University, Laboratory Medicine, Anatomical Pathology Division, Halifax, Nova Scotia.

Introduction: Synovial sarcoma accounts for 5 to 10% of soft tissue sarcomas and over 80% arise in the extremities of younger adults. Primary synovial sarcoma of the heart is an uncommon entity, and primary pericardial synovial sarcoma is exceedingly rare with only a few case reports documented. Case History: A 16 year old female presented with a large pericardial effusion. She was otherwise healthy with only a brief history of generalized malaise. Imaging studies revealed a 5cm solid tumor in the pericardium, medial to IVC at the base of the right ventricle. There was no evidence of a peripheral primary. Drainage of the effusion led to fulminant cardiac and pulmonary failure, characterized by worsening biventrical dysfuncton, severe hypoxia, and end organ damage. She was taken to the OR and underwent partal resecton of the tumor. During the case, her cardiac and pulmonary functon was critcal requiring BVAD and ECMO. Cardiac transplant was considered.  Five weeks afer presentaton, she has stabilized. Conclusions: This report describes a rare biventricular dysfunction, severe hypoxia, and end organ damage. She was taken to the OR and underwent partial resection of the tumor. During the case, her cardiac and pulmonary dysfunction was critical requiring BVAD and ECMO. Cardiac transplant was considered. Five weeks after presentation, she has stabilized.

Results: Gross examination revealed a 6.2 cm piece of tan soft tissue with a homogeneous cut surface. Microscopic evaluation demonstrated a hypercellular neoplasm composed of a monotonous population of spindle cells arranged in intersecting fascicles with herringbone configurations, a rich hemangioepicytoma-like vasculature, and focal ossification. The nuclei were closely packed, plump, elongated and mostly blunt ended. An epithelial component was not identified. The tumors cells expressed vimentin, CD99, CD56, bcl-2, and NSE. FISH evaluation was positive for the loss of the 5'telomeric) SS18 (5q74;18q11.2) region (93.5%). Molecular evaluation was positive for SS18/SSX2 fusion transcript by RT-DNA amplification. Conclusion: This report describes a rare location and unusual presentation of monophasic synovial sarcoma arising in the pericardium and associated with fulminant cardiac and pulmonary failure.
P711 PLEURAL MYOPERICYTOMA – A CASE REPORT.
M. Carapea1, R. Inculet1, B. Wehri1, K. Kwan1. 1Department of Pathology, LHSC, University of Western Ontario, London, Ontario; 2Department of Thoracic Surgery, LHSC, University of Western Ontario, London, Ontario.

Background: Myopericytoma is part of the spectrum of perivascular tumors, showing myopericytic differentiation. It is frequently encountered in the skin and superficial soft tissue of the extremities. Rare cases have been described in the deep soft tissues and in the trunk. We report a case of myopericytoma arising in the pleura. To the best of our knowledge, a primary pleural myopericytoma has never been reported.

Case presentation: A 55 year old woman presented with left subscapular pain. A subsequent chest CT demonstrated a 1.5 cm nodule located in the left pleural base. The wedge resection specimen showed a well circumscribed, un-encapsulated tumor composed of a proliferation of plump-oval to spindle cells with monomorphic nuclei and a prominent concentric perivascular growth pattern with the typical spilling off from the vessel wall. At the periphery of the lesion multiple stag horn vessels were present. Cyto logic atypia, mitoses and necrosis were not noted. The immunohistochemical studies performed confirmed the myopericytic origin. The neoplastic cells are positive for smooth muscle myosin and Bcl2.

Conclusion: Although myopericytoma is a relatively common tumor in the skin and superficial soft tissue of the extremities, a primary pleural myopericytoma has not previously been described.

P712 LYMPHOMA ARISING IN PAGET’S DISEASE OF BONE – RARE CASE REPORT.
D. El Demellawy MD, PhD, FRCP. Pathology Department, Northern Ontario School of Medicine, Sudbury, Ontario. William Osler Health Center, Brampton, Ontario.

The malignant potential of Paget’s disease of bone is well recognized; however, primary involvement by lymphoma is extremely rare. We present a rare case of concomitant occurrence of Paget’s disease of bone and lymphoma. A 94-year-old male presented with a right hip displaced subcapital fracture. His medical history is significant for limited cardiac functional capacity, and chronic renal insufficiency. His Peripheral blood shows mild microcytic anemia but no other abnormality. Imaging reveals left upper lobe atelectasia and focal sclerosis in the lateral left 7th rib but no other aggressive bone lesions. Multiple right renal cystic hypodensities are noted, largest measures 2.4 x 2.2cm. There is a solitary hypertensive cyst in the liver segment 8 measuring 1.1cm. There are multiple splenic cystic hypodensities, largest is at the superior pole with partial thin rim calcification measuring 6.6 x 5.1 cm. No evidence of lymphadenopathy or organomegaly. Right hip cemented bipolar hemiarthroplasty is performed which revealed microscopic evidence of Paget’s disease of bone and intervening bone marrow involvement by low grade B cell lymphoma. We present a rare case of synchronous B cell lymphoma and Paget’s disease of bone occurring in the same site. The absence of peripheral absolute lymphocytosis, lymphadenopathy, organomegaly and masses raises the possibility that the lymphoma, in the current case is primary rather secondary. Though Paget’s disease is known to have malignant potential particularly with osteosarcoma, association with lymphoproliferative disorder is extremely rare.

P713 DETECTION OF SERINE 105 PHOSPHORYLATION ON ER-β AND ITS CORRELATION WITH PATHOLOGICAL STATUS OF THE BREAST CANCER.
Y. Liang MD, PhD1, I. Sidiqui MD1, H.-M. Lam PhD1, Y.-K. Leung PhD2, S.-M. Ho PhD1, J. Wang, MD, PhD1. 1Department of Pathology and Lab Medicine, and 2Department of Environmental Health, University of Cincinnati College of Medicine.

Estrogen receptor-β has been established as an anti-proliferative factor in breast cancer cells. A recently described human ER-β serine105 (S105) phosphorylation site was identified. The current study was to investigate the expression of ER-β and S105 phosphorylation in normal breast and breast cancer cells, and correlate the expression levels with tumor grade and stage. Twenty-five breast cancer cases were analyzed by immunohistochemical staining using an antibody specific to phosphorylated S105 (pS105) ER-β and using a scoring system similar to Allred scoring. pS105 signal was localized in both nuclei and cytoplasm of the benign myoepithelial, luminal secretory, as well as breast cancer cells. A stronger, however not statistically significant nuclear staining was detected compared to the cytoplasmic staining. No significant difference of pS105 staining was identified between breast cancer cells and benign tissues (Nucleus: 7.0±0.1 vs 7.0±0.2; cytoplasm: 6.5±0.1 vs 6.5±0.3). No correlation was identified between pS105 staining intensity and ethnicity, status of ER, PR, Her2/neu, and Ki-67, ER-β positivity or TNM staging. In contrast, both nuclear and cytoplasmic ER-β1 signal was significantly reduced (p<0.01) in cancer cells vs. adjacent benign epithelium. Since S105 is common in all ER-β isoforms (β1-5), the increased phosphorylated S105 signal of ER-β in breast cancer cells could be due to the phosphorylation of other ER-β isoforms. Further studies with more breast cancer cases are needed. It is also critical that the phosphorylation patterns of other ER-β isoforms are analyzed.

P715 FIXATION TIME EFFECTS ON IMMUNOHISTOCHEMICAL ASSESSMENT OF HER-2/NEU EXPRESSION IN BREAST CANCER.
S. Robertson, W. Parks. Department of Pathology, The Ottawa Hospital, Ottawa, Ontario.

Objective: Published guidelines for assessment of Her-2/neu overexpression in breast cancer (BC) include fixation time of 6 (or 8)-48 hours in neutral buffered formalin. Weekends/holidays can make this difficult to ensure; furthermore there is little in the literature to support the upper limit of acceptable fixation time. As a first step in validating an increased upper limit to fixation time, we investigated effects of more prolonged fixation times on immunohistochemical assessment of Her-2/neu expression status in BC. Method: 47 cases of BC tissue were harvested, controlling ischemic time to <60 minutes. Samples from each specimen were fixed in 10% neutral buffered formalin for 8, 12, 24, 72, 100, &120 hours. Samples from each BC fixed for different times were embedded in the same block in a random order. Her-2/neu testing of each case was thus done with all variables other than fixation time held constant. IHC testing was performed on the BOND MAX platform using antibody SP3 (Abcam) 1/25 and H2 retrieval for 10 minutes. FISH status for gene amplification was assessed using the Vysis kit. Slide assessment was done blindly; individual fragments were scored as 0-1 (negative), 2+ (indeterminate) or 3+(positive) by IHC and FISH ratios of HER2/ CEP17 on 60 cells calculated. Results: 47 cases had an adequate 24 hour sample although a full range was not present for all specimens. The 24 hour samples included 7 at 3+, 19 at 2+ and 21 at 0-1+. None of the tissues with shorter or longer fixation time showed an alteration in IHC status and there was no drop off of % of 3+ positive cells. FISH signals also showed no drop off in staining quality. Although all cases were concordant across the entire fixation range; full implications of longer fixation time require assessment of effect on other breast predictive markers as the same sample must be used for all testing.

P716 METASTATIC CK-7 NEGATIVE, INVASIVE LOBULAR CARCINOMA OF THE BREAST IN AN OBESE, GENOTYPIC MALE.
M. Kinloch, B. Wilde Department of Pathology, St. Paul's Hospital, Saskatoon, Saskatchewan.

Male breast carcinomas represent approximately 1% of all diagnosed breast cancers. Of this small percentage, less than 1% is subtyped as lobular carcinoma. It is hypothesized that the most important risk factor for lobular carcinoma in male breasts is exogenous or endogenous estrogen that causes a cytoarchitectural change in the breast; but there are very few cases in the literature (~20) to show a causal relationship. Factors that have been associated with invasive lobular carcinoma of the male breast include obesity, endogenous estrogen therapy and Klinefelter’s syndrome (46XXY). The histological diagnosis of an invasive lobular carcinoma in a male requires E-cadherin negative staining. Our case is of a 64 year old obese, Caucasian, male presented with a metastatic neoplasm and a query breast primary. An ultrasound guided needle biopsy of a suspicious left breast mass showed malignant low grade cells, following a single-file architecture and E-cadherin negativity. ER and PR stained positively, as expected. TTF-1, PSA were also negative, as was CK-7. The patient did exhibit features consistent with Klinefelter’s, but genotyping was normal. BRCA-2 testing is pending, but there is no family history of breast cancer. This case exhibits peripheral obesity as a risk factor for lobular carcinoma in a male and is immunohistochemically the first documented case in the literature of a male invasive lobular breast carcinoma to be CK-7 negative.
**P717 HISTOLOGIC PREDICTORS OF MALIGNANCY IN BREAST CORE BIOPSIES WITH ATYPIAL DUCTAL HYPERPLASIA.**
M. Mashhour, A. Shehata , R. Saad. Department of Pathology, Sunnybrook Health Sciences Center, Toronto, Ontario.

**Background:** Percutaneous core needle biopsy (CNB) is the standard technique for histological diagnosis of breast lesions. However, a significant number border-line diagnoses such as atypical ductal hyperplasia (ADH) may be challenging for the clinicians. Previous studies have shown that a proportion of ADH (up to 30%) may have a significant lesion on subsequent resection. We studied the diagnostic implication of various histologic features in breast core biopsy diagnosed as ADH to predict malignancy in subsequent resection.

**Design:** We retrieved core biopsies with ADH from the hospital archives of a large academic center from 2002 to 2010. One hundred and twenty eight cases diagnosed as ADH with their subsequent surgical resection were retrieved. All cases were evaluated for nuclear grade, calcifications, predominant histologic architecture and size of ADH. Histologic findings were tabulated and correlated with the final diagnosis of the resection.

**Results:** Out of 128 cases diagnosed as ADH, 10/128 (8%) cases showed high nuclear grade (Grade 3), 56/128 (44%) cases as intermediate nuclear grade (Grade 2) and 62/128 (48%) as low nuclear grade (Grade 1). The ADH size ranges from 0.1 to 1.4 mm, with an average of 0.6-0.4 mm. Microcalcifications were identified in 54/128 (42%). Regarding the architecture pattern, 44/128 (34%) showed solid pattern, 42/128 (33%) cribriform pattern, 12/128 (9%) micropapillary pattern, and 30/128 (23%) were mixed pattern. On resection, 10/128 (8%) showed invasive carcinoma, 4/128 (3%) cases DCIS with microinvasion, 32/128 (25%) cases DCIS, 17/128 (13%) ADH, 18/128 (14%) as flat epithelial atypia and 47/128 (37%) as fibrocystic changes with ductal hyperplasia.

All cases with high nuclear grade showed malignancy on resection (6 DCIS and 4 IDC), cases with intermediate nuclear grade showed DCIS in 18/56 (32%) and DCIS with microinvasion in 4/56 (7%), and IDC in 6/56 (11%) cases, while cases with low nuclear grade, only 4/62 (6%) showed DCIS. There was a significant correlation between nuclear grade and detection of malignancy in the resection specimen (P< 0.001).

**Conclusion:** Our study showed association between the degree of nuclear grade in ADH in core biopsy and histologic findings in subsequent lumpectomy. The likelihood of finding more advanced lesions is lower in cores with low nuclear grade. Reporting nuclear grade in pathology report may give insight to the clinicians for appropriate management of these patients.

**P718 PROGNOSTIC SIGNIFICANCE OF CD8+ T LYMPHOCYTES IN BREAST CANCER DEPENDS UPON BOTH ESTROGEN RECEPTOR STATUS AND HISTOLOGICAL GRADE.**
J. Lachapelle* 1, K. Baker 1, 2, J. Zlobec 1, 2, T. Bismar 1, 2, L. Terracciano 1, W. Fouilkes 1, 2.
1Pathology, McGill University, Montreal, Quebec; 2Human Genetics, McGill University, Montreal, Quebec; *Oncology, McGill University, Montreal, Quebec. *These authors contributed equally to this work.

Results of previous studies on the influence of infiltrating lymphocytes on prognosis of women with breast cancer have been mixed. This study evaluates the role of CD8+ tumor infiltrating lymphocytes as a prognostic marker in women with breast cancer. Immunohistochemistry staining of CD8+ T cells was performed on a tissue microarray of 1953 breast carcinomas. In order to select the most discriminating cut-off score with which to classify tumors as “high” or “low” CD8+ cell counts, ROC curve analysis was performed using the endpoint survival (death/alive at 5 years). When all tumors were considered, no association between the lymphocyte count and women survival was found. In univariate analysis, there was a reduced disease-specific survival for women with ER-positive tumors with high intraepithelial lymphocyte count (p = 0.004). In those with ER-negative tumors, the disease-specific survival was improved when the intraepithelial, stromal and total lymphocyte counts were high, the total lymphocyte count being also an independent prognostic marker on multivariate analysis (p = 0.031). When stratified by histological grade, on univariate analysis, the previously observed inferior outcome in women with high lymphocyte count and ER-positive tumors stayed significant only if tumors were also of low grade and the superior outcome in those with ER-negative tumors stayed significant if tumors were also of high grade. Our results raise the possibility of different immune-tumor interactions based on ER status and histological grade.

**P719 FIXATION TIME EFFECTS ON ESTROGEN RECEPTOR (ER) IN BREAST CARCINOMA.**
S. Robertson, W. Parks. Department of Pathology, The Ottawa Hospital, Ottawa, Ontario.

**Objective:** Published guidelines for ER assessment of breast cancer (BC) include fixation time of 6-72 hours in neutral buffered formalin. Weekends/holidays can make this difficult to ensure; furthermore there is little in the literature to support the upper limit of acceptable fixation time. As a first step in validating an increased upper limit to fixation time, we investigated effects of more prolonged fixation times on ER expression in BC.

**Method:** 67 cases of BC were harvested, controlling ischemic time to <60 minutes. Samples from each specimen were fixed in 10% neutral buffered formalin for 8, 12, 24, 72, 100, & 120 hours. Samples of each BC fixed for different times were embedded in the same block in a random order. ER testing was thus done with all variables other than fixation time held constant. IHC testing was performed on the BOND MAX platform using antibody clone ERG11, 1/150 and H2 retrieval for 40 minutes. Slide assessment was done blindly; the number and intensity of cells positive in 300 cells was recorded and % positive, H Score and Allred score calculated. Results: 67 cases had an adequate 24 hour sample although a full range was not present for all specimens. H scores of samples fixed at 8-100 hours showed no statistical difference compared to a 24 hour gold standard (Paired T-test). There was a statistically significant decrease in H Score from 8, 12 and 24 hours to 120 hours (p = .01, .03, .04) consistent with some degradation of signal with time. This might be important if ER were used quantitatively. Current recommendations do not require quantitative scores but use 1% as an ER positive cutoff. Using this criterion 7 (10.5%) cases were negative in the 24 hour sample although low range positives were included (mean Hscore 167). Only 1 case with low range positivity (3.3% positive cells) at 24 hours converted to negative at 120 hours. Although most cases are concordant for ER across the full fixation range, full implications of longer fixation time require assessment of effect on other breast predictive markers as the same sample must be used for all testing.

**P720 LYMPHOEPITHELIOUIMA-LIKE CARCINOMA OF THE BREAST EXPRESSING CD117: COULD GLEVIC BE USED AS A TARGETED THERAPY FOR THESE PECULIAR CASES IN FUTURE?**
M. Mashhour, R.S. Saad, W. Hanna. Department of Pathology, Sunnybrook Health Sciences Center, Toronto, Ontario.

**Case report:** The patient was a 56-year old female who presented with a slowly growing left breast mass at the upper outer quadrant. The provisional diagnosis was Non-Hodgkin's lymphoma, large cell type. On gross examination, serial sections revealed a large lobulated mass which occupies 80% of the lumpectomy specimen and measures 4.0 x 3.5 x 2.0 cm. Microscopic examination revealed dense nodular aggregates of lymphocytes and plasma cells interspersed and surrounded by fat and hyalinized stroma. Germinal centers were observed in some aggregates. High power magnification showed sheets of large loosely cohesive and highly atypical cells. These cells have pale eosinophilic cytoplasm and moderately pleomorphic nuclei with inconspicuous nucleoli in a background of dense lymphoplasmacytic infiltration. The lymphoplasmacytic infiltration overshadowed the epitheloid cells in some areas. There was no in situ ductal or lobular carcinoma identified in the specimen. These histologic features lead one to the suspicion that this is a large B-cell lymphoma.

**Immunohistochemistry:** Immunohistochemical study performed using avidin-biotin-peroxidase complex method and monoclonal antibodies against low molecular weight cytokeratin, cytokeratin 5/6, CK7, estrogen and progesterone receptors, c-erb-b2 (Her2/neu), epidermal growth factor (Her1), CD117, B-cell marker CD20, and T-cell marker (CD3). The stains for lymphoid markers such as CD20, CD3 were positive in the lymphoid infiltrate. Light chains kappa and lambda were positive indicating non-clonal lymphocytic proliferation. The large epithelioid cells in the center of the lymphoplasmacytic infiltrate were strongly positive for CK7 (fig.2), weak positive staining for low molecular weight cytokeratin and high molecular weight cytokeratin 5/6. Tumor cells were negative for both estrogen and progesterone receptors, Her2/neu and epidermal growth factor receptor (Her1). There was diffuse and strong positivity for CD117 (c-kit) (Fig. 3). In situ hybridization: In situ hybridization by the ISH NIEW blue detection kit from Ventana was used for the detection of EBV in tumor epithelial cells and PCR was used for the detection of HPV. Both tests were negative results.

**Conclusion:** We are reporting another case of lymphoepithelioma-like carcinoma of the breast, which showed diffuse and strong expression for CD117 (c-kit).
P722
ONCOTYPE DX RECURRENCE SCORES: PREDICTABLE WITH BIOMARKERS?

Background: Stage, grade, estrogen receptor (ER), progesterone receptor (PR) and HER2neu status are established prognostic and predictive markers in breast cancer. Many, but not all, low stage, lymph node (LN) negative, ER positive patients have a good prognosis without chemotherapy. Thus a demand exists for predictive tools to stratify patient risk within this subgroup. The Oncotype Dx test is one of several multi-gene assays that attempt to fill this gap. This test produces a recurrence score (RS) validated in prospective clinical studies and for this reason it is publicly funded in Ontario. The Oncotype Dx test is expensive but several genes tested can be measured by standard immunohistochemistry (IHC). This has led to interest in developing more cost effective strategies to predict recurrence in LN- ER+ patients. As several genes analyzed for Oncotype Dx RS relate to ER, PR, HER2 & proliferative status, it is reasonable to try to incorporate clinical-pathological variables and these IHC scores into a predictive model. Design: A cohort of 62 women aged 35-77 with ER +, HER2 negative breast cancer completed Oncodx testing between March 2010 & February 2011. This sample reflects the population selected at our institution for Oncotype testing. The variables investigated for inclusion in a model to predict RS score included tumor grade, patient age, Allred ER & PR and Ki67 scores. Results: A predictive model for Oncotype RS was developed using stepwise multiple regression incorporating Allred ER, PR & Ki67 scores. This model accounted for 43% of the RS variability (R2 = 0.43, p = 0.02). Discriminant Analysis failed to predict TailorRx categories of RS but individually high Ki67 scores correlated with the highest (>25) TailorRx RS category (p = 0.001). Although validation of ideal Ki67 cut-offs are required, this suggests that for some cases of ER- low stage breast cancer with high Ki67, Oncotype DX testing may not be necessary.

P723
GRANULOMATOUS MYOCARDITIS WITH CORONARY ARTERY INVOLVEMENT.
F. Saeed Kamili, J. Butany. Department of Pathology, University Health Network, Toronto, Ontario.

Objectives: Present a case of granulomatous myocarditis with coronary artery involvement and to discuss differential diagnoses as well as the challenges in differentiating these entities. Methods and Results: Review of UHN records showed four cases of granulomatous myocarditis (last five years). Three were diagnosed as sarcoidosis isolated to the heart and the fourth as granulomatous myocarditis with coronary artery involvement. This last patient is a 44 year old man who underwent orthotopic heart transplant for giant cell myocarditis, diagnosed at endomyocardial biopsy (EMB). The explant heart showed cardiomyegaly and biventricular dilatation (marked on the left) with, extensive, transmural and transseptal myocardial fibrosis involving much of the heart with chronic inflammation and numerous non-necrotizing granulomata. The coronary arteries showed atherosclerosis and granulomatous involvement of the heart with chronic inflammation and numerous non-necrotizing granulomata. The degree of myocardial fibrosis seen is considerably greater than what is usually seen in such cases and in addition, would account for the patient’s symptoms. The left ventricular involvement is truly striking. Conclusions: This is the first report of granulomatous myocarditis with involvement of the coronary arteries. The identification of granulomatous myocarditis can be very difficult at EMB and highlights the need for multiple deeper sections at biopsy. The distinction between granulomatous myocarditis, sarcoidosis and giant cell myocarditis, has management implications and every effort should be made to come with a definitive conclusion, especially regarding the etiology of the patient’s symptoms.

P724
LEFT ATRIAL PSEUDOTUMOR CAUSED BY CASEOUS CALCIFICATION OF THE MITRAL ANNULUS, CASE REPORT WITH REVIEW OF LITERATURE.
S. Gill MD, F. Chen, MD, PhD. Department of Pathology, Buffalo General Hospital, The State University of New York at Buffalo, Buffalo, New York, USA.

Caseous calcification of the mitral annulus (CCMA) is a rare form of periannular calcification, occurring in 0.06% of all echocardiographic studies and in 0.63% of all patients with mitral annular calcification. Here, we report a case of CCMA manifesting as a left atrial mass. The patient is a 78-year-old African American female with multiple co-morbidities, who presented with symptomatic coronary artery disease and chest pain. A pre-operative echocardiogram revealed a mass in the posterior wall of the left atrium which did not appear to affect the mitral valve or protrude into the left atrial chamber. Intra-operatively, white toastypaste-like material was removed from the mass lesion. Gross examination revealed multiple fragments of grey-white friable caseous material, measuring 3 x 2.5 x 1 cm in aggregate. Bacterial and fungal cultures from this material were both negative. Microscopic examination showed this material to be amorphous, non-viable, basophilic, and acellular with foci of calcification. These morphological features were diagnostic for CCMA. Review of the literature indicated that CCMA is a very rare benign lesion, presenting as a round, tumor-like mass with central echolucencies on echocardiography. We believe our case report will further raise the awareness of CCMA so that pathologists and radiologists can get familiar with this rare disease to avoid potential misdiagnosis.

P725
MITOCHONDRIAL DNA DEPLETION SYNDROME AN UNUSUAL REASON FOR INTERSTAGE ATTRITION AFTER THE MODIFIED STAGE1 NORWOOD OPERATION.
W. Bahiham1, D. Cave1, D.B. Ross MD, FRCS(C), C. Sergi MD, PhD, I. Adatia MBChB, FRCP(C). Department of Laboratory Medicine and Pathology, Departments of Anesthesia and Pediatrics, Cardiac Surgery,Pediatrics, Stollery Children’s Hospital, Mazankowski Institute, University of Alberta, Edmonton, Alberta.

Introduction: Mitochondrial DNA depletion syndromes are clinically heterogeneous disorders characterized by a severe quantitative reduction of total mitochondrial DNA. We report here, for the first time to the best of our knowledge, a patient affected with mitochondrial DNA depletion syndrome and a variant of hypoplastic left heart syndrome who died 16 weeks after a modified stage 1 Norwood. Case presentation: A term baby weighing 3.6 kg was delivered by Caesarean section. A prostaglandin E1 infusion was started in the delivery room because a prenatal ultrasound had demonstrated a duct dependent systemic circulation with small left heart structures. A postnatal echocardiogram diagnosed a variant of the hypoplastic left heart syndrome with a large muscular ventricular septal defect. The aortic valve and mitral valve annulus measured 3 and 4 mm respectively. The left ventricle from mitral annulus to apex measured 1.4 versus 3.1 cm for the right ventricle from tricuspid annulus to apex. There was an aortic coarctation with an unrestricted patent ductus arteriosus and atrial septal defect. Bilateral superior vena cavae were present, with the left draining to the coronary sinus. Chromosome analysis revealed a 46, XY karyotype. Neonatal metabolic screen, liver function tests and INR were normal. Conclusion: Interstage mortality after the Norwood stage 1 remains a serious problem and should be considered in the congenital disorders of the outflow tract of the heart.

P726
CYTOLOGY IMMUNOMARKER VALIDATION STUDY: A COMPARISON AND EVALUATION WITH IMMUNOHISTOLOGY.

Background: Immunohistochemistry (IC) is a useful ancillary tool for the interpretation of cytologic samples. The cell block (CB) rather than a ThinPrep (TP) sample is usually used. In the literature, there are few studies comparing IC on TP, CB and histologic (H) samples. Purpose: To validate cytology IC by comparing: 1) TP & CB routine patient samples; and 2) TP, CB and H optimally prepared samples. Methods: 1) 23 TP & CB preparations from routine patient samples (13 fluids, 2 lymph nodes, 8 respiratory exfoliative) were stained with 9 IC markers: CD3, CD10, CD23, CK20, CKCAM5.2, CKAE1/3, and CDX2. IC was performed either manually or using the Ventana BenchMarkXT system. IC slides were reviewed by two authors for intensity (INT 0-3+), % cell distribution (CD 0-100%) and 4Q score (addition of INT & CD). An immunomarker was considered validated when the Q score was 5 or higher, in > 75% of cases, and had a Q score variation within 2 points. Results: On routine patient samples: 83/107 validated on TP & CB; MOC-31 validated only on TP; all other markers were validated on TP & CB. On optimally prepared samples: CD45, CD68, CK7, BerEP4, B72.1, MOC-31 & TTF-1. 2). Fresh tissue from 10 tonsils, 4 lungs, 3 colon carcinomas was obtained for TP, CB & H preparations to which, in addition to the IC markers used in part 1, seven additional markers were applied: CD3, CD10, CD23, CK20, CKAM5.2, CKAEL1/3, and CDX2. IC was performed either manually or using the Ventana BenchMarkXT system. IC slides were reviewed by two authors for intensity (INT 0-3+), % cell distribution (CD 0-4+) and Q score (addition of INT & CD). An immunomarker was considered validated when the Q score was 5 or higher, in > 75% of cases, and had a Q score variation within 2 points. Results: On routine patient samples: 87/107 validated on TP & CB; MOC-31 validated only on TP; all other markers were validated on TP & CB. On optimally prepared samples: CD45, CD68, CK7, CK20, CKAM5.2 & CKAEL1/3 validated on TP, CB & H; BerEP4 & B72.3 did not validate on any preparation; CD3,CD10,CD20,CD3, MOC31, CDX2, & TFF-1 validated only on H. Conclusions: Routine patient samples had fewer validated samples (33%) than optimally prepared samples (44%). Rare markers could not be validated on TP, CB or H. Revalidation of some IC markers is merited at our institution.

Note: Authors are listed in alphabetical order.
Carcinoma (PTC), were determined by a literature search. Probability was then the most common well-differentiated thyroid malignancy, papillary thyroid carcinoma. However, evidence upon which to base a minimum number of epithelial cells necessary to establish adequacy is debated, with epithelial quantitation gaining acceptance. However, there is little agreement in the assessment of posterior mediastinal lesions and requires close cooperation of endoscopist and cytopathologist.

**ENDOSCOPIC ULTRASOUND GUIDED FNA OF POSTERIOR MEDIASTINAL LESIONS: CYTOPATHOLOGY ASPECT.**

**P728**

Methods: Diagnostic and adequacy rates were compared for samples from an 18 month period following reduction of centrifugation times from 5 minutes to 1 minute, to those rates from the 3 years preceding the change. The frequency data.

**Results:** There was an increase in the detection of abnormal cells in Uroes (1 min = 12.1%, 5 min = 10.1%, p<0.001). There was a decrease in unsatisfactory rates for Uroes (1 min = 3.3%, 5 min = 3.9%, p<0.022). There were no statistical differences in detection of abnormal cells or in the adequacy rates for Bronchial or Body cavity fluid specimens. Conclusion: Shortening centrifugation times during processing of NGC specimens that undergo ThinPrep slide production increases the detection of abnormal cells, while decreasing the rate of unsatisfactory cases in Uroes. In the majority of specimens however, there is no significant difference in diagnostic rates, and therefore a reduction of the duration of centrifugation expedites processing of samples and conserves laboratory resources, without compromising diagnostic utility.

**P727**

**Reduced Centrifugation Time Conserves Laboratory Resources, While Improving Diagnostic Utility in Some Samples.**

A. Adamiak1, S. MacDonald1, and S. Boerner1,2. 1Laboratory Medicine Program, University Health Network and the University of Toronto, Toronto Ontario.

Background: Certain non-gynecologic cytology (NGC) specimens require centrifugation prior to ThinPrep slide production, however, the optimum duration of centrifugation has not been established. AIM: To determine the effect of reducing centrifugation time from 5 minutes to 1 minute on the diagnostic and adequacy rates of NGC specimens undergoing ThinPrep slide production.

Methods: Diagnostic and adequacy rates were compared for samples from an 18 month period following reduction of centrifugation times from 5 minutes to 1 minute, to those rates from the 3 years preceding the change. Specimen types included Bronchial (washings and brushes), Body cavity fluids (pleural fluid, peritoneal fluid, pericardial fluid, peritoneal washings) and Uroes (voided and bladder washings). Results: There was an increase in the detection of abnormal cells in Uroes (1 min = 12.1%, 5 min = 10.1%, p<0.001). There was a decrease in unsatisfactory rates for Uroes (1 min = 3.3%, 5 min = 3.9%, p<0.022). There were no statistical differences in detection of abnormal cells or in the adequacy rates for Bronchial or Body cavity fluid specimens. Conclusion: Shortening centrifugation times during processing of NGC specimens that undergo ThinPrep slide production increases the detection of abnormal cells, while decreasing the rate of unsatisfactory cases in Uroes. In the majority of specimens however, there is no significant difference in diagnostic rates, and therefore a reduction of the duration of centrifugation expedites processing of samples and conserves laboratory resources, without compromising diagnostic utility.

**P728**

**ENDOSCOPIC ULTRASOUND GUIDED FNA OF POSTERIOR MEDIASTINUM LESIONS: CYTOPATHOLOGY ASPECT.**

S. Zherebtsiuk1, M. Cantor1, P. Baker1, E. Ravinsky1. 1Department of Pathology and 2Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba.

Objective: Tissue sampling with pathologic diagnosis is an important component of the diagnostic work-up of mediastinal lesions. Since 1993 transesophageal endoscopic ultrasound guided fine needle aspiration (EUS FNA) has been used for lesions involving the posterior mediastinum. EUS FNA became available in Manitoba in 2005. Since that time EUS FNA of mediastinal lesions has been used for confirmation and staging of malignancies, predominantly lung cancers. The goal of this study was to assess yield and diagnostic accuracy of EUS FNA as well as its influence on management of patients with posterior mediastinal lesions.

Methods: All EUS FNAs were performed by single physician, using an Olympus curvilinear array echoendoscope (GF-UC140P, Olympus, Canada) equipped by 22 gauge FNA needle (NA-200H-8022, Olympus Canada). Rapid on-site evaluation of the aspirate by a cytopathologist using the Quick-Fast stain was performed. The diagnosis was rendered by a cytopathologist using Quick-Fast and PAP stained smears and H & E stained cell blocks. Special stains and immunohistochemistry were performed on the cell blocks. Patients with primary esophageal lesions were excluded from the study. Surgical and clinical follow up were sought in all cases. Results: 35 out of 47 patients who underwent mediastinal EUS FNA during 2005-2009 were chosen for the study. All of them had suspicious radiologic findings. When performed bronchoscopy or mediastinoscopy had failed to yield diagnostic material. Diagnostic yield of EUS FNAs was high (89%) confirming malignancy in 61%. Squamous cell carcinoma was the most prevalent malignant tumor following by small cell carcinoma and poorly differentiated adenocarcinoma. Where surgical pathology was available, there was 100% concordance with FNA diagnosis. FNA had impact on management in 89% of cases. Conclusion: EUS FNA is effective in the assessment of posterior mediastinal lesions and requires close cooperation of endoscopist and cytopathologist.
CDH1-associated HDGC has not previously been reported in the English literature. **Methods:** A case report of a primary appendiceal carcinoma arising in an individual with CDH1-associated HDGC. **Results:** A 51-year-old woman, identified as a CDH1 mutation carrier, underwent prophylactic gastrectomy, as well as interval appendectomy for a history of acute appendicitis one-month prior to surgery. Pathologic evaluation of the gastrectomy specimen revealed multifocal poorly differentiated diffuse-type adenocarcinoma, confined to the lamina propria (intramucosal). Within the appendix, a high-grade signet ring cell carcinoma with mucinous features was identified. By immunohistochemistry, the gastric carcinoma was CK7+, CK20+, CDX2- and weakly E-cadherin+ (upper gastrointestinal phenotype), and the appendiceal carcinoma was CK7-, CK20+, CDX2+ and E-cadherin+ (colorectal phenotype). **Conclusions:** To the best of our knowledge, this is the first case report of synchronous primary diffuse-type gastric cancer and primary appendiceal carcinoma arising in CDH1-associated HDGC. If symptoms attributable to the lower gastrointestinal system exist in these individuals at risk for malignancy at multiple organ sites, consideration should be given for colonoscopy prior to prophylactic gastrectomy to provide more definitive surgical management.

**P736**

**MICROSATELLITE INSTABILITY STATUS DOES NOT PREDICT ABSOLUTE LYMPH NODE OR NEGATIVE LYMPH NODE RETRIEVAL IN STAGE III COLORECTAL CANCER.**

E. MacQuarrie

T. Arnason

J. Gruchy

S.R. Yan

B. Nassar

A. Drucker

W.Y. Huang

1. Department of Pathology, QEII Health Sciences Center, Halifax, Nova Scotia.

2. Department of Medicine, QEII Health Sciences Center, Halifax, Nova Scotia.

The correlation between a high absolute lymph node (LN) resection number in colorectal cancer (CRC) resection specimens and improved overall survival is well known. A recent prospective study describes an association between a high rate of microsatellite instability (MSI-H) and a high absolute LN count in AJCC stages I and II CRC. The authors suggest that a high numbers of LNs may be predictive of MSI-H status in that cohort. Our objective is to determine whether these associations can be applied to an isolated cohort of AJCC stage III CRC. Reports from 123 stage III CRC resection specimens from January 1995 – January 2006 were reviewed. Expression of the DNA mismatch repair (MMR) proteins was determined by immunohistochemistry on archived tissue and confirmed by polymerase chain reaction. The mean absolute LN count in MSI-H vs. MSS tumors (14.5 vs. 14.6, p=0.976) and the mean number of negative LNs in MSI-H vs. MSS tumors (11.2 vs. 11.4, p=0.928) were not significantly different. Within our cohort of 123 tumors, the median absolute LN harvest was 12 and the median negative LN count was 10. We found no significant difference between MSS and MSI-H absolute LN counts (p=0.605) or negative LN counts (p=0.795) when analyzed with respect to percentage of cases above and below the medians. Our retrospective study of a cohort of stage III CRC does not identify a significant relationship between MSI-H status and a higher absolute number of LNs retrieved. We did not find any association between MSI-H status and number of negative LNs. This raises the possibility that while these associations may be seen in stage I and II CRC, they do not hold true in stage III CRC.

**P737**

**ICILIN ATTENUATES TRI-NITRO-BENZENE SULPHONIC ACID INDUCED COLITIS IN MICE.**

L. Zhao

E. Hyun

M.D. Hollenberg

R. Ramachandran

1. Department of Pathology, University of Calgary, Alberta;
2. Department of Physiology and Pharmacology, University of Calgary, Alberta.

**Aims:** Cold temperatures are commonly used as a local anti-inflammatory treatment. TRPM8 and TRPA1 are the members of the transient receptor potential family of ion channels and play an important role in detecting mild and noxious cold temperatures respectively. TRPA1 is activated by cold temperatures below 18°C and TRPM8 is reported to be activated at temperatures below 25°C. These channels are also activated by chemicals such as menthol and icilin. It is well established that tri-nitro-benzene sulphonic acid (TNBS) can induce colitis in mice, with clinical and histopathological findings resembling those seen in human Crohn’s disease. We hypothesised that the super-cooling agent icilin would diminish TNBS induced colitis in mice by mimicking the protective effects of cold temperatures. **Methods:** Colonic inflammation in C57BL6 mice was induced by treatment with tri-nitro-benzene sulphonic acid (TNBS, 2mg in 100µl 1% of 40% ethanol, intracolonically). Colitis was allowed to develop for 7 days and icilin (5mg/kg in 3% DMSO/saline, intraperitoneally) was administered daily. Control animals received icilin but were not treated with TNBS. Seven days after induction of colitis, macroscopic damage score and bowel thickness were evaluated. **Results:** Mice treated with icilin alone showed no symptoms of colitis as well as no morphological evidence of inflammatory bowel disease. Mice treated with TNBS...
presented with weight loss and bloody diarrhea consistent with development of colitis. Large bowel from these mice revealed marked architectural damage, inflammatory infiltrate and increases in bowel thickness. In contrast, TNBS-induced clinical disease parameters and histological damage scores were significantly reduced in mice that received daily icilin treatment. Conclusion: We conclude that icilin attenuates inflammation associated with the development of colitis in mice. Agents that can activate TRPM6/TRPA1 channels may represent novel therapeutics for colitis. A better understanding of the anti-inflammatory signalling activated by the cold-sensitive channels will uncover novel therapeutic strategies for managing inflammatory bowel disease.

P738
MORPHOLOGICAL SPECTRUM OF BENIGN EPITHELIAL INCLUSIONS IN THE PERIPANCREATIC LYMPH NODES: A REPORT OF TWO CASES SUGGESTING A RELATIONSHIP TO PANCREATIC LYMPHOEPITHELIAL CYSTS.
Z. Zheng1, M. Molinari2, R. Gupta1, H. Sapp1, I. Wanless2 and W.Y. Huang1.
1Department of Pathology, Department of Surgery, Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, Nova Scotia.
Benign epithelial inclusions are rarely found in peripancreatic lymph nodes. We described two cases of benign epithelial inclusions in the peripancreatic lymph nodes with detailed discussion of differential diagnosis. The first case was a 2.2 cm lymph node from a 51-year-old woman with pancreatic ductal adenocarcinoma. The second case was a 4.3 cm lymph node from a 28-year-old man with a cholangiocarcinoma of the distal common bile duct. The epithelial inclusions in the first case consisted of several small squamous cell nests with central duct-like lumina. The lymph node from the second case showed convoluted cystic inclusions lined by a single layer of bland cuboidal epithelium with scattered mucin-producing cells. We conducted a literature review on similar lesions and found that some of lesions were associated with pancreatic heterotopia. It is imperative in clinical practice to distinguish these epithelial inclusions in the lymph nodes from tumor metastasis. A hypothetic connection of these benign epithelial inclusions in the peripancreatic lymph nodes with the enigmatic pancreatic lymphoepithelial cysts was suggested.

P739
LARGE CELL NEUROENDOCRINE CARCINOMA ARISING IN A SESSILE SERRATED ADENOMA: A NOVEL OBSERVATION.
K. Naert1, M.P. Dupre1.
1Department of Pathology and Lab Medicine, Calgary Lab Services and University of Calgary, Calgary, Alberta.
Sessile serrated adenomas (SSAs) have been shown to be precursors to colorectal cancer by the microsatellite instability pathway. Specific cancer morphologies and histologic features have been associated with precursor SSAs. A 68-year-old woman underwent polypectomy of two right-sided colonic polyps identified during routine screening colonoscopy. Both of the lesions were histologically identified as sessile serrated adenomas (SSAs). The larger of the two was found to harbour a 2 mm invasive tumor composed of large cells arranged in nests and cords. Tumor cells were of high nuclear grade. Tumoral mucin was not identified. Tumor cells were positive for synaptophysin, cdx-2, and cytokeratins 7 and 20. Calretinin staining was negative and both the invasive carcinoma and the associated SSA showed decreased expression for hMLH-1 compared to normal control tissues. A diagnosis of large cell neuroendocrine carcinoma arising in an SSA was rendered. Colonoscopic perforation lead to a segmental resection in which no residual tumor or lymph node metastasis could be identified. To date, medullary, mucinous, serrated, and signet ring carcinomas have been reported in association with SSAs. Other features common to these cancers include tumor-infiltrating lymphocytes, Crohn’s-like lymphoid aggregates, location in the right colon, occurrence in older women, and an overall better prognosis than conventional colorectal cancers. Large cell neuroendocrine carcinoma has not yet been reported in association with SSAs, with this case suggesting a rare but potentially novel end-point for the microsatellite instability pathway. It remains to be seen whether tumors of this nature will have the better prognosis associated with SSA-derived cancers, or the poorer prognosis of large cell neuroendocrine carcinomas of the colon.

P740
PROGRESSION IN THE HISTOLOGICAL FINDINGS IN A RAT MODEL OF DIET INDUCED NON ALCOHOLIC FATTY LIVER DISEASE.
A.C. Don-Wauchop1, H. El-Zimaity2, A.C. Holloway1.
1Departments of Pathology and Molecular Medicine and Medicine, McMaster University, Hamilton, Ontario; 2Department of Laboratory Medicine and Pathology, University of Toronto, Toronto, Ontario; 3Department of Obstetrics and Gynaecology, McMaster University, Hamilton, Ontario.
Introduction: Fatty Liver is an increasing health problem as the increasing incidence is associated with the rise of obesity. Fatty liver is now understood to be one of the main contributing factors to cryptogenic cirrhosis of the liver. The understanding of the early development of fatty liver is limited as many animal and human studies have focussed on the progression of fibrosis. We designed a study to investigate the early development of fatty liver from a high fat diet in Wistar Rats. Methods: Nulliparous Wistar rats (N=10) were mated and allowed to deliver normally. Litters were culled to 12 retaining 6 male and 6 female pups. At weaning (postnatal day 21), male and female pups from each litter were randomly assigned to a control diet or high fat diet (3 pups of each gender per diet). At 7, 26 and 39 weeks of age, two male and two female pups from each litter, one from each diet group were randomly selected for necropsy. Histology was assessed by the Brunt scoring system. Results: By 7 weeks of age, rats fed the high fat diet were significantly heavier than their siblings on the control diet. There were differences in fat score, fat type and distribution in the livers of high-fat fed rats; an effect which was evident by 7 weeks of age in female rats but not until 26 weeks of age in male rats. The distribution and nature of fatty change in the liver showed gender specificity at all time frames. There was no significant inflammation detected. Discussion/Conclusion: The early introduction of a high fat diet has resulted in the development of histological changes consistent with fatty liver from 4 weeks after the introduction of the high fat diet. There were significant gender differences in the onset and progression of fatty liver, which require further study to develop understanding of the early changes in fatty liver disease.

P741
EXPRESSION OF E-CADHERIN AND B-CATENIN IN TWO CHOLANGIOCARCINOMA CELL LINES (OZ AND HUCCT1).
Y. Abuetabbi1, S. Persad2, S. Nagamori1, J. Huggins3, R. Al-Bahran1, C. Sergi4.
1Department of Lab. Medicine and Pathology, University of Alberta Hospital, Edmonton, Alberta; 2Department of Pediatrics, University of Alberta Hospital, Edmonton, Alberta; 3Department of Virology II, National Institute of Infectious Diseases, Japan; 4Provincial Lab, Canada.
Background: Cholangiocarcinoma (CC) is the most frequent malignant epithelial tumor of the biliary system. CC has received an increasing interest due to its different etiologic factors, invasiveness, and difficulty of diagnosis at early stage. Calcium-dependent adherence proteins or cadherins are a family of proteins essential to connect the plasma membrane of adjacent cells. Linkage of cadherins with the cytoskeleton occurs through another class of proteins, called catenins. E-cadherin forms a mutually exclusive complex or unit with β-catenin. Loss of E-cadherin - β-catenin adhesion represents an important step in the progression of many epithelial malignancies. Our aim was to investigate the expression and localization of E-cadherin and β-catenin in two CC cell lines. Materials and Methods: OZ and HuCCT1 cells represent homogeneous, functional human biliary epithelial tumor cell lines. Western blot analysis, immunofluorescence and confocal laser microscopy were used to identify the protein expression and their localization of E-cadherin and β-catenin in two CC cell lines. Results: OZ and HuCCT1 cells expressed E-cadherin and β-catenin, but they remarkably showed diferent localization patterns. In HuCCT1, both E-cadherin and β-catenin were localized in the cytoplasm, while in OZ these proteins were localized in the cytoplasmic membrane only. Conclusion: To the best of our knowledge, this is the first time that E-cadherin and β-catenin have been studied in detail in these two cell lines and these data seem to be very promising, because they can add more insights into the cell biology of CC.

P742
DOES SIRT1 HAVE PLEIOTROPIC EFFECTS DURING CANCER DEVELOPMENT OF THE LIVER?
1Department of Lab. Medicine and Pathology, University of Alberta Hospital, Edmonton, Alberta; 2Institute of Pathology, Medical University of Innsbruck, Austria.
Background: Hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC) are the major adult liver cancers. Although some phenotypic overlap is known, both tumors usually have different histology and prognosis. Gene expression and deacetylase activity of the class III histone deacetylase SIRT1 are up-regulated in cancer cells due to oncogene overexpression or loss of function of tumor suppressor genes. SIRT1 may play a critical role in tumor initiation, progression, and drug resistance by blocking senescence and apoptosis, and promoting cell growth and angiogenesis. Pleiotropic effects (anti-proliferation and anti-apoptotic) have been indicated during colorectal cancer development. Our aim was to investigate the expression of SIRT1 in liver malignancies. Materials and Methods: We investigated 18 malignant tumors of the liver, including 12 HCC and 6 CC by
immunohistochemistry using a monoclonal antibody against SIRT1. Results: We found an expression of SIRT 1 in 7 out of 12 HCC and in 4 out of 6 CC. Conclusions: These initial results including clinical pathological correlation seem to be in line with colorectal cancer data showing some SIRT1 overexpression in liver malignancy. SIRT is probably unsuitable for diagnostic purposes, but it may have pleiotropic effects during cancer development in the liver.

P743 TUMOR BUDDING IN STAGE IIA COLORECTAL CARCINOMA: SEMI-QUANTITATIVE ASSESSMENT.
Objective: Tumor budding (TB) in colorectal carcinoma (CRC) refers to single or clusters of tumor cells at the tumor’s invasive front; it is an adverse prognostic factor. Our aim was to develop a reproducible method for assessing TB and to assess its prognostic significance. Methods: 73 cases of stage IIA or less CRC with at least 5 yrs follow up and no recurrence, neoadjuvant therapy, inflammatory bowel disease or polyposis syndromes studied. Overall survival (OS) time, local recurrence, metastasis and adjuvant therapy were recorded. TB defined as a single cell or cluster of ≤4 tumor cells at the invasive front.Slides evaluated by two observers; those with TB seen at 4X were re-evaluated at 20X and categorized as low-grade (<10 buds/field) (LTGB) or high-grade (≥10 buds/field) (HTGB). Absolute TB counts were performed. The semi-quantitative method was compared with absolute counts and between observers. Discrepant cases were re-assessed to achieve consensus. OS analyzed by Cox regression. Results: 69 cases = low grade, 55 cases = T3N0, 17 cases = T2N0, 1 case = T1N0. Three patients had local recurrence; 9 had distant metastases, 23 deaths (8 due to CRC). 68 cases = TB-positive, 5 = TB-negative. 60 cases = LGTB; 8 = HGTB. There was no statistically significant difference in OS between positive and negative cases or between LGTB and HGTB; HGTB cases trended towards a higher risk of death (HR=2.512). There was a good-excellent interobserver agreement at 4X (K=0.53) and 20X (K=0.79), as well as with absolute counts (K=0.92). The semi-quantitative method strongly correlated with the absolute counts (K=0.79). Conclusion: TB assessment using a semi-quantitative method correlates with absolute TB counts with good interobserver agreement at 4X.

P744 PROSTATIC MUCINOUS ADENOCARCINOMA IN A PATIENT WITH HISTORY OF COLONIC MUCINOUS ADENOCARCINOMA: THE HELPFUL CLUES.
D. El Demellawy, S. Taurzi, S. Alowami. Pathology Departments: 1Northern Ontario School of Medicine, Sudbury, Ontario; 2William Osler Health Center, Brampton, Ontario; 3McMaster University, Hamilton, Ontario.
Mucin producing adenocarcinomas of the prostate are rare. We present a 73 year old man presented with elevated PSA and free to total ratio of less than 0.04. His had a significant history of mucinous colonic adenocarcinoma, N0D (pt2, pN0, pM0), treated 5 years prior with right hemicolectomy. Transrectal ultrasound guided biopsy revealed prostatic adenocarcinomas. A radical prostatectomy revealed mucinous adenocarcinomas with dissecting mucin lakes containing floating islands of tubulocarcin glands. The malignant glands and mucin infiltrated fibromuscular stroma and fat. Immunohistochemistry showed PSA expression but absent staining for CK7, CK 20, CEA and hMSH. The regional lymph nodes were negative and clinical investigation showed no evidence of metastasis. The patient received no further therapy and during the follow up period of 4 years, he still alive, with no evidence of metastasis. Because of the history of mucinous colonic adenocarcinomas, the differential diagnosis included primary and secondary tumors. The former included prostatic adenocarcinoma arising from prostate and mucin producing urothelial carcinoma arising from the prostatic urethra. The colon presents one of the most frequent primaries of prostatic metastasis. The clinical findings are crucial to rule out metastasis, particularly endoscopic work up. Despite the absence of adjacent conventional of prostatic adenocarcinoma, the presence of mucinous PIN and the prominent macronucleoli and immunoprofile were features affirming the diagnosis of primary mucinous prostatic adenocarcinoma.

P745 WHAT ARE THE PREDICTORS OF CANCER PROGRESSION IN PAPILLARY RENAL CELL CARCINOMA? A CLINICO PATHOLOGIC STUDY OF 86 PATIENTS.
A.R. Husain, A. Yilmaz, T. Bismar, J. Zhang, D. Heng, K. Trpkov. Department of 1Pathology and Laboratory Medicine, 2Medicine and Oncology, University of Calgary, Calgary, Alberta.

Background: Papillary renal cell carcinoma (PRCC) is the second most common Renal Cell Carcinoma (RCC). Because it is uncertain which are the predictors of PRCC progression and death, we investigated the clinical and pathologic parameters potentially influencing the outcome in PRCC. Material and Method: The study comprised of 86 cases of PRCC, resected from 01/2000 to 07/2007. Tumor size, nuclear grade, stage and type (I, II or mixed), were evaluated. Time to cancer progression or cancer death analysis was evaluated by Kaplan-Meier method and was compared by log-rank test. Results: Patient’s mean age was 60.6 years , male to female ratio was 3:1.1 and left vs right side was 1:1.1. Mean tumor size was 5.1 cm. Type I was found in 41 patients, type II in 31 and 10 were mixed. Tumor stage pT1-2 was found in 73 patients and 13 were pT3-4. Nodal metastases were identified in only 3 patients. Only 3 patients had disease progression and 2 of them died with metastatic PRCC after a mean follow-up of 54 months . Only positive nodes on nephrectomy correlated with cancer progression and/or cancer death. Conclusions: Patients with PRCC had overall a very good prognosis. Only nodal status on nephrectomy correlated with cancer progression and/or cancer death, but limited outcome events precluded more comprehensive survival analysis.

P747 URINARY BLADDER SINUSES – A NOVEL MORPHOLOGICAL LESION WITH CLINICAL AND PATHOLOGICAL SIGNIFICANCE.
Background: Peculiar changes in the urinary bladder, characterized by segmental mucosal invaginations into the submucosa and muscularis propria, were observed in radical cystectomy specimens. We described and termed these lesions as urinary bladder sinuses (UBS). The significance of these lesions has not been studied. Methods: 50 consecutive radical cystectomy specimens (49 - carcinoma with history of BCG / radiation / chemotherapy, 1 - neurogenic bladder), 20 transurethral resections of bladder tumor (TURBT) and 20 biopsies were reviewed. UBS were classified into superficial and deep types. Superficial UBS was defined as invaginations of the mucosa (including urothelium, lamina propria and muscularis mucosa) into the submucosa, while deep UBS was defined as mucosal invaginations into the muscularis propria. Superficial UBS were distinguished from cystitis cystica, and deep UBS differed from intramural ureters by their cleft-like appearance. Results: UBS were often associated with cystitis cystica and proliferation of Von Brunn’s nests. Superficial UBS were identified in 13/20 TURBT specimens. Of the 50 radical cystectomy specimens, superficial UBS were identified in 26 cases, and deep UBS (all with associated superficial UBS) were seen in 13 cases. UBS were found to be more located adjacent to scars or invasive carcinoma than elsewhere in the bladder. Intraepithelial neoplasia involving the mucosa of UBS was observed in 14 cystectomy specimens. Conclusions: Mucosal redundancy and hypertrophy of the muscularis propria associated with UBS can mimic muscle invasive cancer on pelvic examination and imaging. They may pose diagnostic problems with invasive carcinoma. Recognition of UBS is important, both pathologically and clinically, in order to avoid over-staging of bladder malignancies.

P748 A MESOTHELIAL CYST IN AN ADRENAL GLAND THAT IS FUSED WITH THE IPSILATERAL KIDNEY IN A 50-YEAR-OLD WOMAN, AN UNUSUAL CASE.
R.J. Guo MD, PhD, L. Balos, M.D, F. Chen, MD, PhD, J. Sun, MD, PhD. Department of Pathology, State University of New York at Buffalo, Buffalo, New York, USA.
Adrenal cysts are distinctly uncommon and most are endothelial cysts or pseudocysts. Very few true epithelial or mesothelial cysts have been reported. Renal-adrenal fusion is a rare anomaly that involves the upper pole of kidney and is usually identified as an incidental finding in nephrectomy specimens or at autopsy. Here we report an unusual case of a true mesothelial cyst in an adrenal gland that is fused with the ipsilateral kidney. The patient was a 50-year-old woman who presented with right flank and back pain. A CT scan showed a large right adrenal hypodense mass. The resection specimen shows a 6 cm adrenal cyst lined with cuboidal to flattened cells without atypia. The lining cells are positive for pancytokeratin, calretinin and HBME-1, consistent with a mesothelial cyst. Of interest, the adrenal gland is directly adherent to the kidney, with no intervening fibrous capsule or other connective tissue. The adrenal cortex that appears as clusters of clear cells in the kidney parenchyma raises a differential diagnosis of renal clear cell carcinoma. This is excluded by negative CD10 and EMA stains. The adrenal cortical origin is confirmed by positive inhibin stain.
P749

PRIMARY RENAL CARCINOID TUMOR: RARE CASE REPORT.

B. Fahmy,1 S. Taper,2 S. Alowami,2 D. El Demellawy1,4. Pathology Departments: 1Chatham-Kent Health Alliance, Chatham, Ontario; 2McMaster University, Hamilton, Ontario; 3Northern Ontario School of Medicine, Sudbury, Ontario; 4William Osler Health Center, Brampton, Ontario.

Primary renal carcinoid (rc) is an extremely uncommon tumor and little is known about its clinicopathologic features and prognosis. We describe a case of rc in a 57-year-old man presents with loin pain. CT shows a right kidney enhancing 3 cm mass. On resection, a tan tumour displaying microscopic trabecular architecture populated with monotonous cells is noted. Immunohistochemistry shows tumor expression of chromogranin, CD56 and synaptophysin. We report a rare case of rc. Because neuroendocrine cells are not present in normal kidneys, when rc is encountered, it is important to rule out metastatic disease. A primary rc is speculated to arise as a derivation from misplaced neural crest during embryogenesis.

P750

MALIGNANCIES IN THE RENAL TRANSPLANT POPULATION: THE ST. MICHAEL'S HOSPITAL EXPERIENCE.

R. Saleeb1, H. Faragalla2, G.M. Youssef1,2, R. Stewart1, C.J. Streutker1,2, 1Department of Laboratory Medicine, University of Toronto, Toronto, Ontario; Departments of 2Laboratory Medicine and 1Urology and the Li Ka Shing Knowledge Institute, St. Michael's Hospital and the University of Toronto, Toronto, Ontario.

Introduction: Previous publications have shown increased incidence of various malignancies amongst the renal transplant population. The objective of this study was to analyze the rate and types of malignancies occurring in St. Michael's Hospital renal transplant population, and to determine whether the rate, types and outcomes of these malignancies were comparable to those previously published. Methods: The study was approved by the SMH Research Ethics Board. The clinical and pathologic history of all of the patients in the St. Michael’s Hospital Renal Transplant Clinic database was retrospectively reviewed from approximately 1970 to the present. Review of the records and pathology of these 1584 patients was performed using the hospital’s digitalised clinical and pathology data bases. Results: Amongst the 1584 patients with renal transplants, 99 patients with post-transplant malignancies were identified. The highest incidence amid the malignancies were non-melanoma skin malignancies, (SCC, BCC and Kaposi Sarcomas) amounting to a total of 37 patients having 69 separate tumors (2.3% of all the transplant patients, 37% of transplant patients with tumors). Following skin tumours in incidence were gastrointestinal tract (GIT) malignancies (24 patients, 1.5% of patients, 24% of patients with tumors), then urological tumours (kidney and bladder) (13 patients, 0.8% of patients, 13% of patients with tumors), then post-transplant lymphoproliferative disorders (PTLD) (8 patients, 0.5% of patients, 8% of patients with tumors), prostate (7 patients, 0.4% of patients, 7% of patients with tumors), endometrium (6 patients, 0.3% of patients, 6% of patients with tumors), thyroid (2 patients, 0.1% of patients, 2% of patients with tumors), ovary (1 patient, 0.06% of patients, 1% of patients with tumors) and lung carcinomas (1 patient, 0.06% of patients, 1% of patients with tumors). The average patient age when malignancies were discovered was 56. Of the 99 patients, 14 died of malignancy, with the highest mortality being in the GIT malignancies (6 out of the 14 cases). Second in mortality were the PTLD and skin tumour groups, with 3 patients in each dying secondary to the malignancy.

Discussion: Information on the incidence and outcome of various malignancies in renal transplant patients is important in designing guidelines for the follow up of these patients regarding tumor screening and prevention of malignancies. The rate of malignancies in our renal transplant group is comparable to that reported at other centres.

P751

METASTATIC ADENOID CYSTIC CARCINOMA MASQUERADING AS RENAL CELL CARCINOMA IN A PATIENT 10 YEARS AFTER EXTRATION OF TRACHEAL ADENOID CYSTIC CARCINOMA.

N. Aldaoud1, J. Sweet1, N. Fleshner2. 1Department of Pathology and Laboratory Medicine, 2Department of Urology, Toronto General Hospital, Toronto, Ontario.

Adenoid cystic carcinoma is an aggressive, often indolent tumor, with high incidence of distant delayed metastasis. We describe a case of 40 year-old woman who underwent partial nephrectomy for an incidental solitary left solid renal mass during her follow up for a tracheal adenoid cystic carcinoma resected in 2001. The patient received radiotherapy to her neck in 2001 but in 2003 she had lung metastasis which was excised. In 2011, abdominal CT scan found a renal mass which was suspicious for a renal cell carcinoma. The partial nephrectomy specimen showed a well circumscribed white, tan solid mass measuring 2.6 x 2.1 x 1.3 cm. On microscopic examination, the mass had the characteristic cribriform pattern of adenoid cystic carcinoma, with dark compact angular nuclei surrounding pseudoglandular spaces with basement membrane-like material, together with small true glandular lumen. To our knowledge, only 10 cases of adenoid cystic carcinoma metastatic to the kidney have been reported. This case emphasizes the unique slow-growing nature of this tumor and the importance of long follow-up after surgery.
DETECTION OF SERINE-105 PHOSPHORYLATION ON ERß AND ITS CORRELATION WITH THE CLINICAL AND PATHOLOGIC STATUS OF THE PROSTATE CANCER.
L. Siddiqui MD, Y. Liang MD, H.-M. Lam PhD, J. Wang, MD. 1Department of Pathology and Lab Medicine, University of Cincinnati, College of Medicine; 2Department of Environmental Health, University of Cincinnati, College of Medicine.

Estrogen receptor-beta (ERß) plays a crucial role in the development of cancers. Phosphorylation of ERß is evoked by ligands and growth factor mediated rapid pathways has been implicated in stimulation of receptor activation. A novel serine-105 (S105) phosphorylation site was identified in vitro kinase assays using extra cellular signal regulated kinases 1and 2 (ERK1/2) and p38. The purpose of this study was to investigate the expression of ERß and S105 in normal and cancer cells of prostate and correlating the expression with the stage as well as grade of the tumor. We analyzed immunohistochemistry results from 50 cases of prostate cancer archival specimens. pS105 was detected in both the nucleus and cytoplasm of prostate cancer cells and their adjacent benign basal and luminal epithelial cells. In general nuclear staining was higher as compared to cytoplasmic staining (p<0.05). Prostate cancer acini displayed higher nuclear and cytoplasmic staining based on Allred score when compared to adjacent benign acini. In order to understand the role of pS105 on ERß we immunostained each case with an ERß1 specific antibody and we found that nuclear ERß1 staining decreased although not statistically significant (p=0.05) in higher grade cancers as compared to benign epithelium. This is in contrast to the results of S105 staining in higher grade cancers. In conclusion, generally a stronger nuclear staining as compared to cytoplasmic staining was found but no correlation was found between ERß positivity, TNM staging and PS105 staining intensity.

<table>
<thead>
<tr>
<th></th>
<th>benign</th>
<th>cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleus</td>
<td>6.8±/-0.1</td>
<td>7.4±/-0.1</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>4.6±/-0.3</td>
<td>5.3±/-0.2</td>
</tr>
</tbody>
</table>

A. p<0.01 compared to cytoplasmic staining
B. p>0.01 compared to normal tissue.

Quantification of pS105-ERß immunohistochemical staining in prostate specimens. Allred score (0-8) represents the sum of the staining intensity (0-3) and coverage of positive stain (0-5)

MALT LYMPHOMA OF THE PROSTATE – A CASE REPORT.

Primary MALT lymphoma of the prostate is rare. Clinopathologic features are not yet well clarified and more cases are needed to address this deficit. Herein, we report the tenth case of MALT lymphoma of the prostate. Our patient is an elderly, 75 year old male who presented with gross hematuria and an elevated PSA. He underwent TURP for symptoms attributed to a clinical diagnosis of benign prostatic hyperplasia. Pathological examination showed substantial, nodular collections of small, uniform lymphocytes with perineural clearing. The lymphocytes were positive for CD20 and BCL2, equivocal for CD5 (focal and weak) and negative for CD10, CD23 and cyclin D1. Molecular analysis showed clonal proliferation of B lymphocytes. The findings were consistent with a diagnosis of MALT lymphoma. The patient later had a contrast enhanced CT of the chest, abdomen and pelvis that showed a mildly enlarged paratracheal lymph node and notable lymph nodes in the periaortic region and in the cardiophrenic fat pad. Currently, the patient is being investigated and managed by a haem-oncologist. The few previously reported cases suggest that MALT lymphomas arising in this location will have an indolent course with a positive response to chemotherapy.
**P804**

**PRECURSOR LESIONS AND PROGNOSTIC FACTORS IN PRIMARY PERITONEAL SEROUS CARCINOMA.**

S. Lee1, G. Nelson1, A. Klimowicz1, E. Kornaga1, S. Petrillo1, A. Maglioccco1, M. Duggan1. 1Anatomic Pathology, Foothills Medical Center, Calgary, Alberta; 2Gynecologic Oncology, Foothills Medical Center, Calgary, Alberta; 3Molecular Pathology, Foothills Medical Center, Calgary, Alberta.

**Objectives:** Recent investigations suggest that ovarian serous carcinomas may evolve from p53 signatures, a group of 12 consecutive tubal epithelial cells with nuclear p53 accumulation (Am J Surg Path 2007;31:161-169). The objective of this study is to investigate the relationship between p53 signatures, tubal intraepithelial carcinoma (TIC) and primary peritoneal serous carcinoma (PPSC).

**Design:** 22 cases of PPSC processed between 2000 - 2008 were reviewed to identify areas of atypia, TIC, and carcinoma. Sections of omentum, fallopian tubes (FT), and ovaries were stained with p53 to identify p53 signatures. p53 intensity (0 = negative, 1 = weak, 2 = intermediate, 3 = strong) and proportion (0 = none, 1 = 1%, 2 = 10%, 3 = 33%, 4 = 67%, 5 = 100%) were recorded. The highest measurements were added to form a p53 score. Ovarian surface epithelium (OSE) and cortical inclusion cysts (CIC) were scored separately. Results: 4 cases were low grade and 18 were high grade. All cases were stage 3 and 4. Precursor lesions (atypia, p53 sigs, TIC) were present in 45%, located at the fimbriated end of the FT. p53 signatures were identified in 29%. p53 scores for PPSC and FT were similar (average 5.1 and 4.2) and significantly higher than p53 scores for OSE and CIC (average 0.7 and 1.5). Conclusion: p53 scores are significantly higher in PPSC and FT epithelium than OSE and CIC. These preliminary results suggest that recently described precursors in the FT may have a role in the carcinogenesis of PPSC.

**P806**

**ENDOCERVICOSIS OF THE UTERINE CERVIX: A CASE REPORT OF A RARE ENTITY AND COMPARISON TO ITS NEOPLASTIC MIMICS.**

L. Hamilton, M. Khalil. Dept of Pathology and Laboratory Medicine, University of Calgary, Calgary, Alberta.

**Objective:** Endocervicosis, the presence of benign endocervical-type glands in ectopic sites, is unusual and described most frequently in the bladder. Involvement of the outer wall of the uterine cervix is very rare and represents a diagnostic pitfall, as it may resemble some malignant and borderline lesions.

**Methods:** This case study describes the incidental finding of endocervicosis in the outer uterine cervix of a hysterectomy specimen for menorrhagia/leiomyomata. Histologic comparison is made between endocervicosis and its mimics: minimal deviation adenocarcinoma (MAC), and non-invasive uterine implants from a seromucinous borderline ovarian tumor (BOT).

**Results:** All three cases shared an architectural pattern of haphazardly arranged dilated glands within the wall of the uterine cervix; the glands were lined by mucinous columnar/cuboidal cells with mildly atypical nuclei. In contrast to endocervicosis, MAC and the implants had scattered mitoses and focal nuclear stratification. The glands of endocervicosis and the implants were confined to the outer wall, whereas the deeper glands in MAC were continuous with a glandular proliferation in the endocervical mucosa, which focally had a component of poorly differentiated carcinoma. In the case of the seromucinous BOT, the mucinous glandular uterine implants resembled the mucinous component of the ovarian tumor; no serous component was identified in the implants.

**Conclusion:** There are striking morphologic similarities between endocervicosis and its neoplastic mimics. Examining these lesions in isolation may pose a challenging differential diagnosis. Difficulties can be resolved by the careful assessment of the location of the lesion, the overall architecture, and the surrounding stroma. The importance of the clinical context cannot be overemphasized.

**P807**

**CORRELATION OF CERVICAL SMEARS WITH HISTOLOGY AND FREQUENCY OF HUMAN PAPILLOMA VIRUS (HPV).**

M.H. Bukhari1, M. Zainani1, G. Ahmed1, I. Gaderi2, I.M. Bakhshi1. 1Department of Pathology King Edward Medical University, Lahore, Pakistan; 2National University of Science and Technology, Islamabad, Pakistan.

**Background:** The frequency of HPV in cervical carcinoma is rising in our country and conventional cervical smears by Papanicolaou method (Pap smears) are the popular tests for its early detection in Pakistan. The study was conducted to detect the HPV from premalignant and malignant cervical neoplasms by PCR.

**Materials and Methods:** 102 already diagnosed Pap smears for premalignant and malignant cervical neoplasm were compared for histology and PCR for detection of HPV and its subtype. Results: The 46/102 (45%) cases were low grade squamous cell intraepithelial lesions (LSILs), twenty two (21.5%) cases were high grade squamous cell intraepithelial lesions (HSILs), 14 cases (13.7%) were squamous cell carcinomas (SCCs), 6 (5.8%) cases showed features of adenocarcinoma, ten (9.8%) cases showed cytology of atypical squamous cells of undetermined significance (ASCUS) and 4 (3.9%) cases were of atypical glandular cells of undetermined significance (AGUS). Out of 79 malignant cases 67/79 (85%) were positive for HPV and among them 59/67 (89%) cases were of HPV-16 and 7/67 (11%) cases of HPV-18. Out of 12 cases of adenocarcinoma 5 (41%) showed positivity for HPV-16. Conclusion: Premalignant and Malignant cervical lesions are not common in our patients and Pap test is an effective diagnostic modality. HPV is a risk factor for induction of this carcinoma and may be prevented by preventive vaccination. Genotype HPV-18 is more frequent than others.

**P808**

**CLINICO-PATHOLOGICAL DETERMINANTS OF PREMALIGNANT AND MALIGNANT POLYPS OF THE LOWER FEMALE GENITAL TRACT.**

C. Fauch1, A. Franko1, G. Duan1, S. Wood1, M.A. Duggan1. 1Department of Pathology, British Columbia’s Children’s Hospital, Vancouver, British Columbia; Departments of 2Pathology and Laboratory Medicine, and 3Obstetrics and Gynecology, University of Calgary, and 4Clinical Trials Unit, Tom Baker Cancer Centre, Calgary, Alberta.

**Objectives:** To identify clinical and pathological determinants of premalignant and malignant polyps of the lower female genital tract. **Methods:** Using a case control design, clinical and pathological variables of all premalignant and malignant vaginal polyps examined over 6 years at a single institution were compared to a control group of benign cervical and vaginal polyps. Variables were abstracted from patient chart and pathology glass slide reviews and differences were tested for significance using univariate analysis. Significance was set at p<0.05. **Data and results:** Following the pathology review, there were 11 CIN, 2 endometrial hyperplasias and 8 invasive carcinomas. The 21 polyps were randomly matched to 42 benign polyps. The distribution of variables by premalignant-malignant and benign diagnoses fluctuated and statistically significant differences between them was only seen in age at surgery. The frequency of premalignant-malignant polyps in women 40 years and younger was double the frequency of benign polyps (p=0.04). In a separate analysis, polypoid invasive carcinoma was six times more frequent amongst those older than 60 years and this difference approached statistical significance (p=0.09). **Conclusions:** Age at presentation is a significant determinant of premalignant and malignant polyps of the lower female genital tract. Premalignant polyps are more frequent in younger and malignant polyps are more frequent in older women.
Background: Ovarian carcinomas are treated either with debulking surgery and post-operative chemotherapy, or neo-adjuvant chemotherapy followed by interval debulking surgery. Chemotherapy effects on ovarian carcinomas have not been well studied. We sought to 1) assess chemotherapy changes in only ovarian serous adenocarcinomas by comparing pre- and post-chemotherapy samples; and 2) examine grading post-chemotherapy.

Materials and methods: Archival cases of serous adenocarcinomas were reviewed: one group included pre-treatment biopsies (n=7) with comparison to subsequent post-chemotherapy resections; other group included resections prior to chemotherapy (n=14). Cases evaluated for treatment effects (necrosis, bizarre nuclei, epithelial-stromal ratio, old hemorrhage, giant cell reaction, fat necrosis, foamy changes, ballooning and cholesterol clefts); treatment response (none, minimal or marked) and grading (Silverberg).

Results: The epithelial to stromal ratio was increased in all treated cases and correlated with the degree of treatment response. Four cases showed lobular carcinoma-like features. Bizarre nuclei, cholesterol clefts, giant cell reaction, foamy macrophages and intratumoral lymphocytes were nearly exclusively seen in treated cases. Post-compared to pre-chemotherapy grade remained the same or increased in 6/7 cases. Bizarre nuclei were a pitfall for nuclear atypia post-treatment.

Conclusion: Our study highlights specific morphological changes in serous adenocarcinomas treated with chemotherapy, which may be linked to treatment response. Grading post-treatment was similar to pre-treatment (remains high grade 2 or 3).

P811
CLASSIFICATION OF 4, 402 POLYPS OF THE LOWER FEMALE GENITAL TRACT.
C. Faust,1 A. Franko,2 Q. Duan1, S. Wood1, M.A. Duggan1,2,4. 1Department of Pathology, British Columbia’s Children’s Hospital, Vancouver, British Columbia; Departments of 2Pathology and Laboratory Medicine, and 3Obstetrics and Gynecology, University of Calgary, and 4Clinical Trials Unit, Tom Baker Cancer Centre, Calgary, Alberta.

Objective: To establish a pathological classification and calculate the frequencies of polyps arising in the vagina and cervix. Methods: The pathology diagnoses of all cervico-vaginal polyps examined over 6 years at a single institution were classified using standard pathological principles and frequencies calculated. The glass slides of all vaginal and premalignant-malignant polyps were reviewed together by a 3 person panel. Data and Results: Out of 4,402 polyps, 4,340 (98.6%) were cervical and 62 (1.4%) vaginal. There were 4,281 (97.3%) epithelial, 32 (0.7%) mixed epithelia and mesenchymal, 17 (0.4%) mesenchymal and 72 (1.6%) unsatisfactory polyps. Benign epithelial polyp (4,281, 97.3%) was the most frequent category and benign endocervical polyp constituted the most (n=4,137, 98.6%) were cervical and 62 (1.4%) vaginal. There were 4,281 (97.3%) epithelial, tobin 1 and BIN 1 formed the majority. The mixed polyps were all fibroepithelial polyps and the mesenchymal polyps mostly consisted of leiomyomata. The review of the vaginal polyps as benign (n=61) and premalignant (n=1) agreed with the original. Since there was agreement for only 21 (33.9%) of the 62 premalignant-malignant polyps, the overall premalignant-malignant polyp frequency is closer to 0.5%. Most of the disagreement was due to a downgrading of CIN I to benign.

Conclusions: The majority of polyps in the lower female genital tract are cervical and benign endocervical polyps. Vaginal polyps are uncommon and rarely malignant. Premalignant -malignant polyps are uncommon.

P813
CLINICO-PATHOLOGICAL DETERMINANTS OF VAGINAL POLYPS OF THE LOWER FEMALE GENITAL TRACT.
C. Faust,1 A. Franko,2 Q. Duan1, S. Wood1, M.A. Duggan1,2,4. 1Department of Pathology, British Columbia’s Children’s Hospital, Vancouver, British Columbia; Departments of 2Pathology and Laboratory Medicine, and 3Obstetrics and Gynecology, University of Calgary, and 4Clinical Trials Unit, Tom Baker Cancer Centre, Calgary, Alberta.

Objective: To identify clinical and pathological determinants of vaginal polyps. Methods: Using a case control design, clinical and pathological variables of all vaginal polyps examined over 6 years at a single institution were compared to a control group of cervical polyps. Variables were abstracted from patient chart and pathology glass slide reviews and differences were tested for significance using univariate analysis. Significance was set at p<0.05. Data and Results: The 62 vaginal polyps were randomly matched to 126 cervical polyps. Following the pathology review, 61 (98.4%) vaginal polyps were benign and fibroepithelial polyp (n=28, 45.2%) was the most frequent type. Although the distribution of variables by anatomical location fluctuated, statistically significant differences between the 2 locations did occur. Vaginal polyps were three times more frequent amongst women 40 and younger and twice as frequent amongst those 60 plus (p<0.001).

Additionally, vaginal polyps were larger with a mean size of 1.5 cm compared to 1.1 cm for cervical polyps (p=0.001) and the frequency of multiple polyps (n=2) was nearly three times greater (p=0.04). Conclusions: Age at presentation, polyp size and number of polyps are significant clinico-pathological determinants of vaginal polyps. Vaginal polyps occur more frequently in younger and older women, and are more frequently multiple and of larger size.

P814
VAGINAL SPINDLE CELL EPITHELIOMA: A CASE REPORT AND REVIEW OF THE LITERATURE.
E. Mahé BSc, MD,1 M. Bhisha MBCh, PhD, FRCPC,2 D. El Demellawy MBCh, PhD, FRCPC1,4, F. DeNardi, MD, FRCPC,3 S. Alowami MBCh, FCAP, FRCPC.1 1Department of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario; 2Department of General Pathology, Grand River Hospital, Kitchener, Ontario; 3Department of Pathology and Laboratory Medicine, William Osler Health Care, Ontario; 4Northern Ontario School of Medicine, Brampton, Ontario.

Tumours of the female genital tract may demonstrate a range of histogenetic potential. This histogenetic potential is seen in the vaginal spindle cell epithelioma, an entity previously known as the benign mixed tumour of the vagina. We present a case of a 52 year old woman who presented to her primary care practitioner noting a vaginal cyst-like lesion. Primary excision demonstrated a circumscribed lesion with squamoid cells encased by a bland spindle cell component. After an extensive immunohistochemical work-up was undertaken, a diagnosis of vaginal spindle cell epithelioma was rendered. The margins of excision were free of tumour and no subsequent surgical or medical intervention was performed. In addition to the case report, we also present a detailed review of the literature focusing on the epidemiology, histologic and immunophenotypic features and differential diagnosis of this unique lesion.

P815
DOES p53 PREDICT TIME TO FIRST TREATMENT IN MANTELLE CELL LYMPHOMA?
S. Nolan1, T. Aranson1, A. Robertson1, D. MacDonald1, A. Shawa1,1. 2Department of Pathology, 1Department of Medicine (Hematology), Dalhousie University, Halifax, Nova Scotia.

Background: Currently, treatment strategy for mantle cell lymphoma (MCL) varies between centers and is debated worldwide. While some advocate for early aggressive treatment others prefer to “watch and wait” for the development of significant symptoms. A biomarker predictive of early time to first treatment would be useful to make clinical decisions about when to initiate treatment.

Immunohistochemical expression of p53 has been shown to be predictive of overall survival in MCL, but it is unclear if p53 expression is predictive of time to first treatment. Methods: All patients at our institution >17 years old diagnosed with pathologically confirmed MCL from January 1, 1999 to September 28, 2009 were enrolled. Immunohistochemistry for p53 was performed on sections of archived, formalin fixed, paraffin embedded tissue from the time of first diagnosis.

Cases were classified as immunopositive for p53 when >20% of tumor cells showed nuclear staining for p53. Time to treatment was determined by chart review. Results: 35 patients with a confirmed diagnosis of MCL had adequate archived tissue for analysis and clinical records with long term follow up. The mean age at diagnosis was 64 years (range 34-88 years). The median time to treatment was 56 days in the patients with p53 immunopositive tumors and 33 days in patients with p53 immunonegative tumors. Kaplan-Meier analysis showed overlap of the time to treatment curves for the two groups. The log-rank test showed no difference in time to treatment between the two groups (p=0.85).

Discussion: While p53 immunopositivity has been shown to correlate with decreased overall survival in MCL, it was not predictive of time to first treatment in our cohort of 35 patients. Due to small sample size (although typical of single centre MCL studies), our study is not powered to definitely exclude an association between p53 expression and time to treatment.
P816
SEQUENTIAL BONE MARROW ASPIRATE HEMODILUTION AND CALCULATION OF RIMG DIFFERENTIAL COUNT CORRECTION FACTOR.
H. Paulin, D. Werner. Department of Pathology and Laboratory Medicine, QEII Health Sciences Centre and Dalhousie University, Halifax, Nova Scotia.

Introduction and Objectives: Sequential bone marrow aspirates required for diagnosis are presumed to have similar diagnostic characteristics, but studies describe that repeated aspirates may become progressively diluted with peripheral blood. We investigated this phenomenon by analyzing the difference between first and second draw differential cell counts, and devised a correction factor to correctly adjust cell counts in the second draw aspirates.

Methods: May-Grünwald Giemsa stained slides were prepared from first and second draw aspirates from seventeen randomly selected patients. Differential counts were performed by experienced laboratory technologists and reviewed by a hematopathologist. Statistical analysis of the differential counts included computing summary statistics and the Student’s t-Test to assess the differences between first and second draw aspirate counts. We then calculated the Ratio between Immature and Mature Granulocytes (RIMG), defined as the sum of myeloblasts, promyelocytes, myelocytes, metamyelocytes and bands versus neutrophils. The median RIMG ratio between first and second draw aspirates was selected as our correction factor and applied to second draw differentials to decrease counts for cells predominantly seen in the peripheral blood (lymphocytes, monocytes, and neutrophils) and to increase counts for cells predominantly seen in the marrow (all other cells).

Results and Conclusions: There is a significant difference in differential counts between first and second draw aspirates (p<0.05). The median RIMG ratio was 1.25 and accurately adjusted all subpopulations in the second draw aspirates except for the monocyte count, which remained significantly higher after RIMG correction (p<0.05).

P820
ADENOSQUAMOUS CARCINOMA OF THE LARYNX.
S. Mokhtari1 D.M.D, S. Sargolzari2 D.M.D, S. Mokhtar1 D.M.D. ‘Department of Oral and Maxillofacial Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran; 1Faculty of Dentistry, Azad University of Medical Sciences, Tehran, Iran.

Objective of the Study: Adenosquamous carcinoma (ASC) of the head and neck is extremely rare in the larynx, with only 34 cases reported in the literature. Here, we report a case of ASC in the larynx and describe its clinical and histopathological features with an emphasis on its distinct histology in metastatic lymph node. Data and Results: A heavy smoker, 52-year-old man with a 1-year history of hoarseness, systemic therapy. He is alive at six month follow up.

Conclusion: Adenosquamous carcinoma is a recognized pitfall in the diagnosis of extra-gastrointestinal GIST. Most importantly, however, this case illustrates the importance of considering GIST in the differential diagnosis of any persistent, recurrent, or metastatic intra-abdominal spindle cell tumour originally diagnosed in the era before c-kit. Correct classification of these lesions allows for the consideration of tumour-specific systemic therapy.

P821
PULMONARY BENIGN METASTASIZING LEIOMYOMA, REPORT OF UNUSUALLY LONG DELAY IN APPEARANCE, 26 YEARS AFTER RESECTION OF UTERINE LEIOMYOMA.
H. Huang MD, PhD, L. Balos MD, F. Chen MD, PhD. Department of Pathology, State University of New York at Buffalo, Buffalo, New York, USA.

Benign metastasizing leiomyoma (BML) is a rare disease which usually presents as multiple pulmonary nodules, several years (average 15 years) after the resection of uterine leiomyom(s). Only about 100 cases of BML have been reported in English literature. Here we report an unusual case of BML identified 26 years after resection of uterine leiomyoma. The patient is a 44-year-old woman who during workup for a brain lesion that was biopsy-proven astrocytoma, was found to have an incidental lung nodule in the left lower lobe of lung. A lung wedge resection was performed and a solid, well demarcated, 2.5 x 1.5 x 1.5 cm nodule was resected. The lesion comprised bland appearing spindle cells without mitotic activity that were positive for smooth muscle actin, ER and vimentin. CD117, S100, Synaptophysin, HMB-45, CD99, calretnin, pancytokeratin and CD10 were negative. Ki67 staining showed very low proliferative index. In conclusion, the overall morphological and immunohistochemical features, and patient’s remote history of primary uterine leiomyoma supported the diagnosis of pulmonary BML.

P822
METASTATIC GIST TO THE SKULL BASE DIAGNOSED 23 YEARS AFTER PRESENTATION AS A PELVIC SPINDLE CELL TUMOUR.
E. Schollenberg, M.J. Bullock, A.A. Covert. Department of Pathology, Capital District Health Authority & Dalhousie University, Halifax, Nova Scotia.

Background: The definition of gastrointestinal stromal tumour (GIST) as a distinct mesenchymal tumour evolved gradually. It was only in 1998, with the discovery that CD117 (c-kit) is a sensitive marker for GIST, that it became possible to reliably distinguish it from other entities commonly considered in the differential diagnosis. Case: A 73 year-old woman presented with left trigeminal neuropathy and otic effusion. Magnetic resonance imaging demonstrated a 4.7 cm mass centered in the masticator space, between the jaw muscles and the skull base. The patient had a history of a recurrent tumour of the rectovaginal septum, first diagnosed in 1987 as a low-grade leiomyosarcoma. Pathology: A diagnostic core biopsy showed a spindle cell neoplasm with similar morphology to the original pelvic tumour. The tumour was positive for vimentin, CD34, and c-kit, and was negative for S100, actin, and desmin. The archived 1987 material had the same immunoprofile. The core biopsy was ultimately signed out as metastatic GIST and it was suggested that the pelvic tumour be reclassified as GIST in light of the new immunophenotypic information. Discussion: The head and neck area is a very rare site for metastatic GIST, with only four other reports in the literature. Presentation of the primary as a gynecologic tract tumour is also uncommon, but is a recognized pitfall in the diagnosis of extra-gastrointestinal GIST. Most importantly, however, this case illustrates the importance of considering GIST in the differential diagnosis of any persistent, recurrent, or metastatic intra-abdominal spindle cell tumour originally diagnosed in the era before c-kit. Correct classification of these lesions allows for the consideration of tumour-specific systemic therapy.
P823
MUCOEPIDERMOID CARCINOMA OF LARYNX.
S. Mokhtarï1 D.M.D., S. Sargolzaï2 D.M.D. 1Department of Oral and Maxillofacial Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran; 2Faculty of Dentistry, Azad University of Medical Sciences, Tehran, Iran.

Objective of the Study: Mucoepidermoid carcinoma (MEC) is the most common malignant tumor of the salivary glands; however, it is a rare entity in the larynx and few cases have been reported in the literature. In this paper, a literature review relating to laryngeal mucoepidermoid carcinoma has been made and the tumor behavior according to the grade of differentiation is discussed. In addition, diagnostic pitfalls and treatment modalities are presented. Methods: In this paper, a literature review relating to laryngeal mucoepidermoid carcinoma has been made to provide deep insights into pathological and clinical features of laryngeal mucoepidermoid carcinoma; the tumor behavior according to the grade of differentiation is discussed. In addition, diagnostic pitfalls and treatment modalities are presented. Results and Conclusion: Mucoepidermoid carcinomas in the larynx mostly present in the supraglottis and patients usually have progressive hoarseness and dysphagia; however, they often spread submucosally with an intact surface; so primary lesions are not detected by laryngoscopy and most patients are diagnosed in the advanced stages. High-grade tumors, similar to MECs in other sites, have few cystic spaces and more solid areas. Therefore, they are frequently diagnosed as squamous cell carcinoma and as a result laryngeal mucoepidermoid carcinomas are under-reported. These tumors have a wide spectrum of clinical behavior from locally invasive to highly malignant. As the main method for therapy, most agree on wide excision. Since high-grade tumors have more tendencies for recurrence, combination of surgical therapy and radiotherapy is recommended in these cases.

P824
HISTOPATHOLOGICAL EFFECTS OF NEOADJUVANT CHEMO-RADIATION ON THYMIC NEOPLASMS.
G. Allo1, M.S. Tsao1, D.M. Hwang1. University Health Network, University of Toronto, Toronto, Ontario.

Background: Locally-advanced thymic neoplasms may be treated with pre-operative chemo-radiation, to potentially improve surgical resectability and survival. We aim to study the histopathological effects of neoadjuvant chemoradiation (NCR) on thymic tumours. Methods: Retrospective histopathological review of post-NCR thymic tumour cases resected at University Health Network between 2000 and 2010, and comparison with matched thymic tumour cases treated with primary resection. Results: Fourteen post-NCR thymic neoplasms were identified. Tumours were classified as thymoma type A (n=1), AB (n=1), B1 (n=3), and B3 (n=3), metaplastic (n=1), indeterminate (n=1), and thymic carcinoma (n=4). Seven cases showed areas of replacement by proliferation of bland spindle cells expressing cytokeratin, in some cases reminiscent of metaplastic thymoma, comprising up to 70% tumour surface area (Odds Ratio OR=6). In two cases, this resulted in discordant typing between the pre-NCR biopsy and the post-NCR resection specimens. Necrosis was present in 6 cases, comprising up to 20% tumour surface area (OR=2.75). Other features found more commonly in post-NCR tumours include stromal and peri-tumour hyalinization (OR=15), histiocytic infiltration (OR=9.75), myoid stroma (OR=4.5), cholesterol clefts (OR=3.33), edema (OR=3.33), multinucleated giant cells (OR=3.33), hemosiderin-laden histiocytes (OR=3.24) and calcifications (OR=2.75). Conclusion: Significant histologic changes may be present in thymic neoplasms post-NCR, which in some cases may interfere with histologic typing in resection specimens.

P825
ISOLATED METASTATIC MUCOEPIDERMOID CARCINOMA (MEC) TO THE BRAIN: PITFALLS OF CURRENT GRADING SYSTEMS.
D. Ng1, R. Seethala2, M. Khalil3, K. Guggisberg1. 1Dept. of Pathology, University of Calgary, Calgary, Alberta; 2Dept. of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA.

Background: MEC is the most common primary salivary gland malignancy. Current grading systems for MEC include the AFIP grading schema and the Brandwein grading system. Both systems use features including degree of intracyctic component, mitoses, nuclear atypia, perineural invasion and necrosis to stratify MEC into low, intermediate and high grade tumors. However, in addition, the Brandwein system considers infiltrative margins, lymphovascular invasion and bony invasion in their grading schema. The MECT1-MAMLL2 gene rearrangement in MEC has recently emerged as a prognosticator of a less aggressive course and lower mortality risk. Further, the CDKN2A deletion highlights a subset of MECT1-MAMLL2-positive MECs wherein the benefit of translocation is nullified with resultant poorer outcomes. Methods: We describe a case of a 56 y/o female presenting with an isolated right frontal lobe mass 7 years post-parotidectomy for a primary low-grade MEC (as graded by AFIP system). Results: The primary lesion had discordant histologic features with both a prominent cystic component and infiltrative borders. Additional poor prognostic features were absent. Both the primary MEC and subsequent brain metastasis were MECT1-MAMLL2 positive and CDKN2A deletion-negative by fluorescent in-situ hybridisation. Conclusion: To our knowledge, this case represents the first and only reported isolated MEC metastasis to the brain. This case highlights the shortcomings of the current histopathological grading systems and tumor genotyping in predicting an aggressive course in an intermediate grade MEC with presumed favourable features.

P826
HIGH FAT DIET RESULTS IN SIGNIFICANT CHANGES IN VISCERAL ADIPOSE TISSUE IN A RAT MODEL OF DIET INDUCED OBESITY.
I. Narangiñami1, A.C. Don-Wauchop3, A.C. Holloway2, H. El-Zimaity1. 1Department of Pathology and Molecular Medicine and Medicine; 2Dept of Obstetrics and Gynecology, McMaster University, Hamilton, Ontario; 3Dept of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario.

Introduction: Globally obesity has reached epidemic levels. Research evidence shows that obesity is associated with a state of chronic systemic inflammation with adipose tissue as the major site of damage. An increase in adipose tissue macrophages (ATMs) and typical “crowns” of macrophages have been described in obesity. However, much less is known about the extent and relevance of muscle tissue macrophages in an animal model of diet induced obesity. We also wanted to study changes in the cell size of adipocytes in obesity. Methods: Sibling pairs (male and females) from 3 litters were randomized to receive either control or high-fat diet from weaning. At 39 weeks of age, fat (visceral and subcutaneous) and muscle (skeletal and cardiac) were collected for histological review and assessment of macrophage count using immunohistochemical stain ED1 (rat homologue of CD68 macrophage marker). Results: The macrophage count was significantly increased in the visceral fat of animals fed the high fat diet (p value = 0.0043). The macrophage count in subcutaneous fat, skeletal muscle and cardiac muscle did not show any significant association with diet. Adipocyte cell size was significantly increased both in the visceral and subcutaneous fat of animals fed the high fat diet (p = 0.0016 and p = 0.0066 respectively). There is a correlation between ATMs and adipocyte size in visceral fat but not in subcutaneous fat. Conclusion: These findings support a hypothesis that visceral adipose tissue inflammation rather than systemic inflammation is the source of chronic inflammation in obesity.
INCREASING THROUGHPUT BY MULTIPLEXING DRUGS OF ABUSE ANALYSIS.

Introduction: Multiplexing LC systems, and synchronizing to a single MS, generates the high throughput needed by modern laboratories that face increasing sample numbers yet have the expectation to maintain or improve turn around times. An integrated system has been specifically designed to synchronize two LC systems and a mass spectrometer, allowing injections into two LC streams in parallel. Methods: Spiked urine calibrators were prepared using Surine negative control covering 2 to 20000 ng/mL concentration ranges for a panel of drugs of abuse compounds. Sample preparation included a hydrolysis step and analyses of the resulting supernatant by LC/MS/MS. The two-stream integrated multiplex LC/MS/MS system consisted of a mass spectrometer, 2 autosamplers, 2 gradient LC pump systems, a shared loading pump, a column oven, and switching valves for stream selection; controlled via the mass spectrometer software and device driver. Results: Calibration curves consisting of nine standard curve concentrations were constructed for each LC stream, both streams producing comparable results. Limit of Quantification (LOQ) of 2 ng/mL, for PCP and methamphetamine, and 20 ng/mL for all the other analytes were obtained. Most %CVs at the LOQ were below 10%, all within 15%. Accuracy at the LOQ ranged from 87 to 101%. Conclusions: Using the Multiplex LC-MS system in the NIDA-5 analysis, cuts out the time around the peaks of interest allowing this time to be spent performing the injector wash and preloading the next sample. The Multiplex LC-MS system therefore cuts the analysis time of the singleplex LC/MS/MS method in half.

DEMOGRAPHIC AND HAEMATOLOGICAL FEATURES OF APLASTIC ANAEMIA (A TERTIARY CARE CENTRE EXPERIENCE).
S. Naem1*, H. Rafiq. King Edward Medical University, Lahore, Pakistan.

Objective: To complete the data on the demographic and haematological features of patients diagnosed to have aplastic anaemia at a Mayo Hospital over a 5 years period. Methods: Demographic information was collected from patients who presented with features of aplastic anaemia. Their diagnosis was confirmed by performing a complete blood count, absolute reticulocyte count, bone marrow aspirate and trephine biopsy. Data and Results: Over the period of five years i.e January 2005-December 2010 one hundred and sixteen adult patients were diagnosed to have aplastic anaemia at the Pathology department King Edward Medical University. Among them 57 were males and 59 females. Their ages ranged from 15 to 74 years with a mean age of 28 years. Out of these 72 (69%) patients were below the age of 25 years. Fever was the main presenting complain present in 68 (58.6%) patients. Peripheral counts showed thrombocytopenia to be present in 100% of cases, followed by anemia 96%and leucopenia 93% of patients. Severe aplastic anaemia (SAA) was seen in 36%, very severe (VSAA) in 16% and non-severe aplastic anaemia (NSAA) in 48% patients. No obvious cause could be established for 84% of patients. 18% were found to have either hepatitis B virus markers or antibody to hepatitis C at the time of diagnosis of aplastic anaemia. However it was difficult to establish a cause and effect relationship with either drugs or viruses. Conclusion: Aplastic anaemia shows equal sex distribution. NSAA is the most common type of aplastic anaemia. Registry for Aplastic Anemia has been initiated.

STRIKING MIMICRY OF FOLLICULAR LYMPHOMA BY A CASE OF MANTLE CELL LYMPHOMA: A POTENTIAL DIAGNOSTIC PITFALL.
S. Varma, D. LeBrun. Department of Pathology and Molecular Medicine, Kingston General Hospital, Kingston, Ontario.

Mantle cell lymphoma (MCL) is a mature B-cell neoplasm accounting for 5-10% of non-Hodgkin lymphomas. It is an aggressive lymphoma with a median survival of three years and currently no definite treatment options are available. Although the pathological diagnosis of MCL is typically straightforward, it can occasionally mimic other lymphoma types including follicular lymphoma (FL). We describe a case of MCL diagnosed incidentally in a pericolic lymph node removed during hemicolectomy for dysplastic polyps. It showed a striking architectural and cytologic resemblance to grade 1 follicular lymphoma along with abundant expression of Bcl-2 within the follicle centers. Additional immunostains revealed unequivocal expression of CDS and cyclin D1 characteristic of MCL. This case is informative in illustrating the morphological spectrum of MCL. Furthermore, our findings support the practice of performing a judiciously designed panel of immunostains that includes anti-CDS and anti-cyclin D1 even in cases in which the morphological findings appear to justify an unequivocal diagnosis of FL.

SINONASAL SEROMUCINOUS HAMARTOMA WITH FOCAL MYOEPIHELIAL CELLS AND ASSOCIATED RESPIRATORY EPITHELIAL ADENOMATOID HAMARTOMA.
K.E. Fleming1*, B. Perez-Ordonez2, J.G. Nasser1, M.J. Bullock3. 1Departments of Pathology and Surgery, Queen Elizabeth II Health Sciences Center, Halifax, Nova Scotia; 2Department of Pathology, University Health Network, Toronto, Ontario.

Seromucinous hamartomas are benign lesions of the sinonasal tract. They were first described in 1974; since then only a small number of additional cases have been reported. They are composed of proliferations of seromucinous glands and ducts within a variable fibrous stroma. The serous component typically stains positively for S100 (at least focally) and lacks p63 positive abluminal cells. The lack of myoepithelial/basal cells is an important diagnostic feature of seromucinous hamartomas; their absence could be a diagnostic pitfall leading to an incorrect diagnosis of low-grade sinonasal adenocarcinoma. We report the case of a polypoid mass resected from the right posterior nasal cavity and nasopharynx of a 54-year-old woman. The lesion contained a population of small and large glands lined by cuboidal to flattened cells within a hypocellular stroma which varied from dense and sclerotic to myxoid. In addition to the serous glandular proliferation, there was a more superficial focus of ciliated invaginated surface epithelium and glands. Throughout the lesion there was no appreciable cytologic atypia, and there were no morphologic features of malignancy. The histological features were in keeping with seromucinous hamartoma. Immunohistochemistry showed focal S100 positivity of the serous glands. However, in contrast to previously reported cases, both small and large glands focally showed an outer basal layer that was calponin, p63 and actin positive. Our case demonstrates two important points. First, seromucinous hamartomas may have focal p63 staining, and complete absence of p63 should not necessarily be a required feature in the diagnosis. Second, the ciliated larger glands - in keeping with respiratory epithelial adenomatoid hamartomas (REAH) - support the suggestion that seromucinous hamartomas and REAH are a spectrum of lesions, often seen together.
CALRETININ STAINING FACILITATES DIFFERENTIATION OF OLFACTORY NEUROBLASTOMA FROM OTHER SMALL ROUND BLUE CELL TUMORS IN THE SINONASAL TRACT.

J.C. Woolf1, L. Apel-Sarid1, B. Perez-Ordonez2, M.J. Bullock. 1. Department of Pathology, Capital District Health Authority and Dalhousie University, Halifax, Nova Scotia; 2. Department of Anatomical Pathology, University Health Network (UHN), Toronto, Ontario.

Objective: Olfactory neuroblastoma (ONB) has a wide histological differential diagnosis that includes other small round blue cell tumors (SRBCT) of the sinonasal tract. Even with the use of immunohistochemistry (IHC), the correct diagnosis may be difficult, especially in small biopsies. The purpose of this study is to determine the usefulness of calretinin and p63, as an aid to distinguish ONB from other sinonasal SRBCT. Methods: IHC stains for calretinin and p63 were performed on 21 specimens diagnosed as ONB and 42 other sinonasal SRBCT. Specimens were retrieved from the files of the QEII HSC, Halifax and UHN, Toronto. Results: All but one ONB (20/21) showed calretinin staining, with 15/21 showing >75% of the tumor area staining and 16/21 showing moderate to strong staining intensity. Only pituitary adenomas (3/3) and a single case of high grade neuroendocrine carcinoma, NOS (1/2) showed a similar staining pattern. None of the ONBs showed staining for p63. P63 was positive in nasopharyngeal and non-keratinizing carcinomas, but inconsistently stained sinonasal undifferentiated carcinoma (SNUC) and high grade neuroendocrine carcinomas. Conclusion: Calretinin appears to be a useful marker to distinguish ONB from other small round blue cell tumors of the sinonasal tract, particularly when staining is moderate/strong and extensive. P63 is consistently negative in ONB, but its utility is limited due to the inconsistent staining of SNUC and neuroendocrine carcinoma, with which ONB may be confused. The addition of calretinin +/- p63 to an IHC panel may aid in the distinction of ONB from other sinonasal small round blue cell tumors that are poorly differentiated, or in small biopsies.

AN EFFICIENT APPROACH FOR DIAGNOSIS OF ALPHA-1 ANTITRYPSIN DEFICIENCY

P. Tavassoli, G. Ritchie, B. Jung, A. Mattman. Department of Pathology and Laboratory Medicine, St. Paul Hospital, UBC, Vancouver, British Columbia.

Objective: In most cases (>95%), alpha-1 antitrypsin (AAT) deficiency can be reliably detected by quantitative determination of AAT plasma level measured in concert with isoelectric focusing (IEF). IEF, also referred to as phenotyping is yet labor intensive test and prone to difficulties in interpretation. To address these concerns, molecular diagnostic tests have been developed for the common S and Z variants. However, they are not widely available in Canada. At St. Paul Hospital, we have established a cost effective genotyping method using blood cards (DBS) to reliably detect common AAT mutations. DBS requires no special handling or storage conditions, is inexpensive to ship and easy to interpret. Methods: Patient blood samples were collected in EDTA tubes for whole blood DNA extraction using Roche MagNA DNA isolation kit. In parallel, samples were collected on DBS and DNA was extracted using methanol wash followed by distilled water elution at 95°C. Two pairs of PCR primers that amplify the regions spanning codons 264 and 342 respectively, and two set of fluorescent probes that detect either Z or S mutation were used for PCR amplification before melting curve analysis using LightCycler PCR fluorometric analyzer. Results: 31 patients with low serum level of AAT1 and/or difficult interpretable IEF results were enrolled from Aug 2010- Jan 2011. The quality of extracted DNA from DBS was appropriate and yielded PCR amplification comparable to those extracted DNA from whole blood. Furthermore, the genotype results in both methods were 100% consistent. Comparison the IEF and genotype results showed identical results aside from a single F allele that was missed by genotyping. Conclusion and Future Directions: AAT1 genotyping from DNA extracted from DBS appears to be a sensitive, specific and logistically simple alternative to the IEF method for the initial investigation of suspected AAT1 deficiency. The data set is expanding and full results of the comparison study will be reported.

NON-IMMUNE HYDROPS FETALIS IN VANCouver: ARE WE DIFFERENT?


Objective: Analyze the causes of non immune hydrops fetalis (NIHF) in fetal autopsies at the British Colombia Children’s and Women’s Hospital (BCCH) in Vancouver, Canada. Methods: A retrospective review of prenatal autopsies diagnosed with NIHF between 2006-2010 in the department of Pediatric Pathology at BCCW was done to determine identifiable causes for the hydrops. Results: Among 2018 autopsies conducted in BCCW between 2006-2010 we found 87 cases with NIHF (4.3%). The cause for the NIHF was identified in 92% of cases, leaving 7 cases undetermined. The most prevalent cause for the NIHF was fetal chromosomal abnormalities, identified in 51 cases (58.6%). The most common chromosomal abnormalities included Monosomy X (n=26), and Trisomy 21 (n=15). Other chromosomal abnormalities included: 6 cases of Trisomy 18, 3 cases of Trisomy 13 and a single case of del 5p (cri-du-chat syndrome). Cardiovascular abnormalities in otherwise normal karyotype fetuses were identified in 5.7% of cases (n=5). Parvovirus B19 infection was confirmed in 3 cases. Other causes included: Twin-to-twin transfusion syndrome, multiple pterygia, adenomatoid cystic malformation, diaphragmatic hernia, metastatic congenital neuroblastoma, fetal gonadoblastoid dysplasia and inferior vena cava thrombus. Conclusion: Only 8% of cases did not have an identifiable cause for the hydrops, which is lower than what has been reported in previous studies. A chromosomal abnormality was identified in 58.6% of cases, which is higher than what has been previously reported. The most common cause of NIHF in this series was fetal chromosomal abnormalities. The incidence of cardiac malformations in our series is lower than previously published, and is likely related to the much higher rate of chromosomal abnormalities detected.

ATYPICAL CARCINOID TUMOR OF LUNG, CLEAR CELL TYPE.

C. Wang, H. Qiu, G. Qing. Department of Pathology, University of Manitoba, Winnipeg, Manitoba.

Clear cell type of atypical carcinoid tumor is a rare entity that could cause a diagnostic problem in pathological practice. Here we report a case of atypical carcinoid tumor, clear cell type. The patient was a 45 year-old women who presented with a left upper lobe lung nodule on CT scan. Patient underwent a left upper lobe lobectomy. Grossly, the nodule was within the bronchus and was compressing the adjacent vessels. It was a well-circumscribed tan to yellow-red variegated tumor measuring 2.4 x 1.8 x 1.6 cm. Histologically, the tumor showed an organoid arrangement and trabecular pattern with mild cytologic atypia. The majority of the tumor cells show prominent clear cytoplasm. Focal tumor necrosis was noted. Histochemical stainings for mucin with mucicarmine and PAS were negative. By immunohistochemistry, the tumor cells were positive for Pan-CX (AE1/3), CK7, CD56, synaptophysin, chromogranin, and TTF1. They were negative for CK20. Ki67 labelling index was about 10-15%. By electronic microscopy, the tumor cells showed numerous neuroendocrine granules. Based on the morphologic, immunohistochemical and electron microscopic findings, we believe that this is an atypical carcinoid tumor, clear cell type. The differential diagnosis for this clear cell tumor should include squamous cell carcinoma or adenocarcinoma with clear cell features, clear cell tumor of the lung (sugar tumor) and metastatic carcinoma with clear cell differentiation (such as renal clear cell carcinoma and clear cell carcinoma of other organs).

DIPNECH, TUMORLETS, AND A TYPICAL CARCINOID: A SPECTRUM OF NEOPLASIA IN A 48 YEAR OLD FEMALE AND REVIEW OF THE LITERATURE.

A. Stueck MD, Z. Xu MD, FRCP, FCAP, G. Buduhan MD, MSc, FRCS(C)1, 2. Department of Pathology, Dalhousie University, Halifax, Nova Scotia; 3. Department of Thoracic Surgery, QEII Health Sciences Center, Dalhousie University, Halifax, Nova Scotia.

Diffuse idiopathic pulmonary neuroendocrine hyperplasia (DIPNECH) is a rare, pre-neoplastic entity. We present a 48 year-old female with a 15 year history of non-productive cough, dyspnea, and late onset asthma. Pulmonary function tests demonstrated an irreversible, obstructive pattern. High-resolution computed tomography revealed a diffuse, bilateral mosaic pattern of air-trapping, with multiple pulmonary nodules. Wedge biopsies of her lungs were completed. The gross exam of the biopsies revealed a 4.0 x 1.2 x 0.8 cm, yellow-tan, well circumscribed lesion, and a 0.2 cm grey-white nodule. Histologically, there were multiple lesions identified. In addition to a typical carcinoid tumor, there were also proliferations of neuroendocrine cells confined to the bronchiolar and bronchial basement membranes, and others extending beyond the basement membrane, with a maximal dimension of 5 mm. There were minimal mitoses and no necrosis. These cells stained positive for cytokeratin, chromogranin, and synaptophysin, and were focally and weakly positive for TTF-1 and Ki67. The diagnosis is DIPNECH, tumorlets, and a typical carcinoid tumor. We review the literature available on this spectrum of neoplasia, and discuss the clinical course and treatment options.
DISTINGUISHING PVOD FROM IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION (PAH) WAS GRADED ACCORDING TO HEATH-EDWARDS GRADING SYSTEM. METHODS: THE CLINICAL AND PATHOLOGIC DATA OF THREE CASES REPORTED FROM 2003 TO 2010 WITH PULMONARY HYPERTENSION DUE TO PULMONARY VENO-OCCCLUSIVE DISEASE FROM COPATH AND NETCARE WERE REVIEWED. PULMONARY ARTERIAL HYPERTENSION (PAH) WAS GRADED ACCORDING TO HEATH-EDWARDS GRADING SYSTEM. DATA: PATIENTS’ AGES OF 17, 40, AND 59 PRESENTED WITH PULMONARY HYPERTENSION, AND WITH UNDERLYING NOONAN SYNDROME, SCLERODERMA, AND HODGKIN LYMPHOMA TREATED WITH CHEMORADIATION AND SUBSEQUENT BONE MARROW TRANSPLANT RESPECTIVELY. TWO OF THREE SPECIMENS WERE BILATERAL LUNG EXPLANTS AND ONE WEDGE BIOPSY. IN ALL CASES, THE SUBPLEURAL AND INTERLOBULAR SEPTAL VEINS SHOWED XANTHOGRANULOMATOUS INFLTRATION. POST-DIAGNOSIS BONE SCAN DEMONSTRATED SYMMETRICAL OSSEOUS LESIONS IN LONG BONES. THIS IS ONE OF THE RARE ECD CASES WITH ATYPICAL CLINICAL AND RADIOLOGICAL PRESENTATION AND ADEQUATE TISSUE IS REQUIRED TO ESTABLISH SPECIFIC DIAGNOSIS IN SUCH CASES.

PRESENTATION OF A RARE CASE OF ERDHEIM-CHESTER DISEASE.

A 59 YEAR OLD MAN PRESENTED WITH AN EIGHT MONTHS HISTORY OF DRY COUGH, DYSPNEA ON EXERTION AND 30 LBS WEIGHT LOSS. LABORATORY WORKUP SHOWED ANEMIA WITH ABNORMAL LIVER FUNCTION TESTS. WITH A WORKING DIAGNOSIS OF Lymphoma, Multi-detector CT SHOWED ANTERIOR MEDIASTINAL MASS AND ENLARGED RETROPERITONEAL LYMPH NODES. US GUIDED BIOPSIES OF LIVER AND MESENTERIC LYMPH NODES SHOWED NO EVIDENCE OF Lymphoproliferative Disorder WHICH LED TO MINI-THORACOTOMY TO OBTAIN ADEQUATE TISSUE FROM MEDIASTINAL MASS AND CONCURRENT WEDGE BIOPSIES OF RIGHT UPPER AND MIDDLE LOBES. SECTIONS OF ANTERIOR MEDIASTINAL LESION SHOWED ATYPIcular SPINDLE AND TYPICAL XANTHOMATOUS HISTIOCYTIC PROLIFERATION INFRINGING INTO THE MEDIASTINAL ADIPOSE TISSUE WITH SCATTERED TOUTON-TYPE MULTINUCLEATED GIANT CELLS AND LYMPHOMALASMATIC INFILTRATE. THE XANTHOMATOUS HISTIOCYTES STAINED FOR CD68 AND FACTOR XILLIA. LUNG SECTIONS REVEALED DIFFUSE SUBPLEURAL AND INTRALOBAR SEPTAL THICKENING WITH FIBROSIS AND XANTHOMATOUS HISTIOCYTIC INFILTRATION SIMILAR TO THE ANTERIOR MEDIASTINAL MASS AND IDENTICAL IMMUNOPROFILE AIDED TO ESTABLISH A DIAGNOSIS OF ERDHEIM-CHESTER DISEASE. SECTIONS OF RESECTED 2ND RIB AND BONE MARRIOW BIOPSY ALSO SHOWED XANTHOGRANULOMATOUS INFILTRATION. POST-DIAGNOSIS BONE SCAN DEMONSTRATED SYMMETRICAL OSTEOCLASTIC LESIONS IN LONG BONES. THIS IS ONE OF THE RARE ECD CASES WITH ATYPICAL CLINICAL AND RADIOLOGICAL PRESENTATION AND ADEQUATE TISSUE IS REQUIRED TO ESTABLISH SPECIFIC DIAGNOSIS IN SUCH CASES.

PULMONARY VENO-OCCCLUSIVE DISEASE: REPORT OF 3 CASES.

WE REPORT THE CLINICOPATHOLOGIC DATA OF THREE CASES OF THIS RARE PULMONARY VENO-OCCCLUSIVE DISEASE (PVOD) CASE. METHODS: THE CLINICAL AND PATHOLOGIC DATA OF THREE CASES REPORTED FROM 2003 TO 2010 WITH PULMONARY HYPERTENSION DUE TO PULMONARY VENO-OCCCLUSIVE DISEASE FROM COPATH AND NETCARE WERE REVIEWED. PULMONARY ARTERIAL HYPERTENSION (PAH) WAS GRADED ACCORDING TO HEATH-EDWARDS GRADING SYSTEM. DATA: PATIENTS' AGES OF 17, 40, AND 59 PRESENTED WITH PULMONARY HYPERTENSION, AND WITH UNDERLYING NOONAN SYNDROME, SCLERODERMA, AND HODGKIN LYMPHOMA TREATED WITH CHEMORADIATION AND SUBSEQUENT BONE MARROW TRANSPLANT RESPECTIVELY. TWO OF THREE SPECIMENS WERE BILATERAL LUNG EXPLANTS AND ONE WEDGE BIOPSY. IN ALL CASES, THE SUBPLEURAL AND INTERLOBULAR SEPTAL VEINS SHOWED XANTHOGRANULOMATOUS INFILTRATION. POST-DIAGNOSIS BONE SCAN DEMONSTRATED SYMMETRICAL OSTEOCLASTIC LESIONS IN LONG BONES. THIS IS ONE OF THE RARE ECD CASES WITH ATYPICAL CLINICAL AND RADIOLOGICAL PRESENTATION AND ADEQUATE TISSUE IS REQUIRED TO ESTABLISH SPECIFIC DIAGNOSIS IN SUCH CASES.
P844 AUTOMATED IMAGE ANALYSIS OF ENDOGLIN AND MICROVASCULAR DENSITY IN CLEAR CELL RENAL CELL CARCINOMA AND ITS PROGNOSTIC SIGNIFICANCE. W. Dubinski1, M. Gabril2, V. Jakovlev3, Y. Yousef4, K. Kovacs5, S. Mettas6, F. Rotand6, M. Moussa7, C. Streutker8, G. Yousef9. 1. Department of Pathology, St. Michael’s Hospital, University of Toronto, Toronto; 2. Department of Pathology, London Health Sciences Centre, London, Ontario.

Objectives: Endoglin is a novel vascular marker that correlates with prognosis in numerous tumors. In this study, we provide the first automated digital assessment of microvascular density (MVD) in clear cell renal cell carcinoma (ccRCC) using endoglin and compare our findings with clinical outcome data. Methods: Fifty cases of ccRCC were immunostained for endoglin and CD31 to highlight tumor vasculature. Immunostained slides were scanned using an Aperio CS Scanner at 20X magnification, and image analysis was used to count MVD within tumoral and adjacent normal kidney. Clinicopathologic parameters were collected and correlated with IVMD. Results: Increased expression of endoglin was associated with advanced tumor stage (p=0.026). Using a binary cut-off, endoglin-positive patients had significantly lower progression-free survival (p=0.017). When using endoglin as a continuous variable, increased expression correlated with reduced survival (HR:1.87, CI:1.39-2.53, p < 0.001). Conclusion: Automated image analysis of endoglin expression in ccRCC showed that increased MVD is associated with higher tumor stage and decreased survival. The advances in digital assessment of immunohistochemical expression can be helpful in evaluating and establishing the clinical significance of new prognostic markers for renal cell carcinoma.

P845 RENAL AA-AMYLOIDOSIS AND INCIDENTAL RENAL TUMOR. A. Peyman1, L. Geldenhuys1,2, P. Payah1. 1. Department of Pathology, Dalhousie University, Halifax, Nova Scotia; 2. Department of Medicine, Dalhousie University, Halifax, Nova Scotia.

Introduction and Aims: Renal carcinoma may be associated with renal amyloidosis as a paraneplastic phenomenon. Methods: We report a case of a 68-year-old pre-diabetic lady with nephrotic syndrome with 3.5 g/d proteinuria and creatinine of 233 umol/L. Serology for anti-nuclear antibody and hepatitis C virus was positive, but the remainder of serology was negative, and there was no nephritis. Results: Light microscopy showed renal cortex and medulla with a central focus of tumor with features suggestive of renal carcinoma, expressing monokeraatin, CK7 and CD10, but not vimentin. The adjacent non-neoplastic renal tissue showed nodular glomerulosclerosis, and interstitial and vascular eosinophilic material staining positively for Congo red with apple green birefringence on polarization, consistent with amyloid. There was severe chronic tubulointerstitial change and moderate chronic vascular change. Immunofluorescence was negative. Electron microscopy showed randomly arranged fibrils, 10 nm in diameter, consistent with amyloid. Immunoperoxidase staining was positive for AA amyloid. Subsequent diagnostic imaging did not reveal any significant renal masses. Conclusions: It is important to be aware that subclinical renal carcinoma may present with renal amyloidosis as a paraneplastic phenomenon, causing significant renal disease. Sub-typeing of amyloid may be helpful in suggesting this associated lesion.

P846 KIDNEY NERVE SHEATH MYXOMA. A CASE REPORT AND REVIEW OF LITERATURE. M.M. Mashhour, Sunnybrook Health Sciences Centre, Toronto, Ontario.

Background: Nerve sheath myxomas (NSM) are rare benign cutaneous neoplasms that may morphologically mimic other myxoid neoplasms of skin and soft tissue. They are morphologically distinct peripheral nerve sheath tumors with strong predilection for the extremities. These tumors have a relatively high local recurrence rate when managed by simple local excision. Case: This is a 42 years old male patient presenting with frank hematuria of three months duration. CT-scan was done and a huge solid renal mass was detected. Nephrectomy was done and grossly: a well circumscribed yellowish mucoid tumor measuring 11.5x10cm. Microscopically, the lesion was composed of an abundant myxoid matrix, stellate and spindle-shaped cells arranged in lobules separated by fine fibrous septa with mild nuclear pleomorphism and scattered mitoses. Immunohistochemically: the cells were positive for S-100 protein, Vimentin, and focally with GFAP while negative for EMA and CD34 which confirm the diagnosis of NSM. Discussion: In 1969 Harkin and Reed described an unusual myxoid tumour of probable nerve sheath tumour and named it myxoma of nerve sheath. Later in 1980, Gallager and Helwig described similar lesions as Neurothekeoma. Cellular neurothekeoma was described by Barnhill and Mihm in 1990. Nerve sheath myxoma has also been referred to as cutaneous lobular neuro-myxoma, perineurial myxoma, and pacinian neurofibroma. Nerve sheath myxoma is a superficial, multinodulated, predominantly myxoid, spindle cell neoplasm exhibiting Schwann cell differentiation with predilection for females (2:1), peak incidence in 3rd decade and more common in trunk and lower extremities. Many pathologists and dermatologists believe that nerve sheath myxoma is a subtype of neurothekeoma (so-called myxoid, hypocellular variant of neurothekeoma). The clinical appearance of nerve sheath myxoma is indistinguishable from that of a neurothekeoma. Nerve sheath myxoma shows ultrastructural features of Schwann cell differentiation. Neurothekeoma exhibits features of fibroblasts (CD34 positive) or undifferentiated stromal cells. It also shows evidence of smooth muscle differentiation and negative staining for S-100 protein. Cases of (NSM) were reported in Eyelid, oral cavity, paranasal sinuses, Infracranial, spinal, breast and Subungual regions. Ideally excision needs to be complete with a margin of normal tissue to reduce the likelihood of recurrence. Differential diagnosis and a practical approach to mimics will be discussed in this paper. Conclusion: To our knowledge, this is the first reported case of nerve sheath myxoma affecting the kidney in the English literature.

P847 PARVOVIRUS-ASSOCIATED NEPHRITIS. A. Peyman1, L. Geldenhuys1,2, P. Payah1. 1. Department of Pathology, Dalhousie University, Halifax, Nova Scotia; 2. Department of Medicine, Dalhousie University, Halifax, Nova Scotia.

Introduction and Aims: While parvovirus infection is usually associated with a facial rash in children, and less often a purpuric rash of the extremities and arthritis in adults, an aplastic crisis or hydrops foetalis, case reports of renal involvement do exist. We describe a case of parvovirus infection associated with proliferative glomerulonephritis and acute tubulointerstitial nephritis, with the virus identified in the renal tissue on polymerase chain reaction. Methods: The patient was a 63-year-old lady who presented with a three month history of fatigue, and sudden onset of palpable purpura of the trunk, and upper and lower extremities, associated with small joint and ankle arthritis, and abdominal pain. She also had gross hematuria, proteinuria and raised creatinine of 262 umol/L. Serology screen was negative, but parvovirus IgM serology was positive. Results: Light microscopy of a renal biopsy showed mild focal segmental glomerular proliferation with no significant necrosis. There was moderate tubulointerstitial nephritis with red cells in occasional tubules and focal collections of eosinophils. There was also severe chronic vascular change. Immunofluorescence was negative and electron microscopy was unremarkable. Polymerase chain reaction for parvovirus was positive in the renal tissue. Creatinine decreased, and a follow-up renal biopsy showed only mild tubulointerstitial nephritis. Conclusions: It is important to recognize that parvovirus infection may be associated with proliferative glomerulonephritis and acute tubulointerstitial nephritis in adults.

P848 TRICHOEPITHELIOMA WITH MONSTER CELLS. M. Sidinopou 1, W. Hanna2, D.M. Assaad3, and R. Saadi4. 1. Department of Pathobiology and Laboratory Medicine, University of Toronto, Toronto, Ontario; 2. Department of Pathology, Sunnybrook Health Sciences Centre, Toronto, Ontario.

Monster cells imply a strikingly atypical cell with an extremely large and pleomorphic nucleus. Certain lesions have been known to be often associated with monster cells, including dermatofibroma and basal cell carcinoma. Trichoepithelioma is a benign adnexal neoplasm with follicular differentiation. Numerous different forms have been described including solitary, desmoplastic and multiple familial trichoepithelioma. We report a case which had been misinterpreted as a possible sarcoma, of a 62-year-old woman with a trichoepithelioma on her medial left cheek with the unusual histologic feature of monster cells. Clinically, the lesion presented as a subcutaneous lesion of short duration. Histologic examination demonstrated characteristic findings of a trichoepithelioma and a diffuse dermal infiltrate of large, atypical epithelioid cells. Some of these atypical epithelioid cells demonstrated features consistent with monster cells, including large, bizarre, and pleomorphic nuclei, multiple and prominent nucleoli and abundant cyttoplasm. Immunohistochemical staining for CD68 was positive. Melanocytic and dendritic markers were negative. A diagnosis of trichoepithelioma with monster cells was made. To our knowledge, this is the second reported case.
GIANT APOCRINE HIDROCYSTOMA: A BRIEF RARE REPORT OF UNUSUAL PRESENTATION.

Pathology Departments: 1 Northern Ontario School of Medicine, Sudbury, Ontario;
2 William Osler Health Center, Brampton, Ontario; 3 McMaster University, Hamilton, Ontario.

Apocrine hidrocystoma is a benign cystic tumours of the sebaceous portion of apocrine sweat glands, first described by Mehregan [1964]. Occurrence in scalp is rare, with only two cases reported in the English and French literatures. We report a 60 year old male presented with red brown scalp nodule. The lesion was mobile and measured 2.8 x 2.0 cm. The lesion was diagnosed clinically as hematocele and was managed by surgical excision. The excised skin ellipse contained a cyst surrounded by a 0.1 cm. wall. The cyst contained minimal clear fluid and its wall was devoid of hemorrhage. Microscopically it showed a unicellular dermal cystic lesion lined by a double layer of epithelium. The inner layer contained large columnar cells with eosinophilic cytoplasm which has luminal capitation secretion, denoting apocrine differentiation. The outer layer was flat and composed of myoepithelial cells. The lesion was diagnosed as apocrine hidrocystoma of the scalp. We present an unusual hidrocystoma presenting as scalp hematocele. Differential diagnoses considered during the time included hemangioma, lipoma, epidermol apocrine cyst and, dermoid cyst. However the histological findings are pathognomonic of apocrine hidrocystoma. Apocrine cystadenoma should be considered in the differential diagnosis of a large cystic subcutaneous masses of the scalp.

P852
AN EARLY INVASIVE SQUAMOUS CELL CARCINOMA ARISING IN A PROLIFERATING EPIDERMAL CYST.

D. El Demellawy1,2, S. Tauqir3, S. Alowami1. Pathology Departments: 1 Northern Ontario School of Medicine, Sudbury, Ontario; 2 William Osler Health Center, Brampton, Ontario; 3 McMaster University, Hamilton, Ontario.

In contrast to cutaneous epidermal cysts, neoplastic transformation of their epithelium is extremely rare. We report a 48 year old lady presents with a growing skin nodule in her right forearm. The lesion measures 2.8 cm in maximum dimension. The patient has no other relevant medical history. The lesion is excised. Microscopically a rare squamous cell carcinoma arising in the wall of an otherwise conventional epidermal cyst is identified. The cyst showed preserved granular cell layer with few areas of squamous proliferation. No evidence of abrupt keratinisation. The cyst has no evidence of epidermal connection despite examination in total and examination of multiple levels. No evidence of recurrence during the 2 year of follow up period. We present a rare case of early invasive squamous cell carcinoma arising from proliferating epidermal cyst, with emphasis on entities that may overlap morphologically and represent diagnostic pitfalls.

VIRAL-ASSOCIATED TRICHOYDYSPLASIA SPINULOSE: A RARE CUTANEOUS COMPLICATION OF IMMUNOSUPPRESSION.

T. Arnason1, A. Burns2, S. Murray2, R. Fraser2, N. Walsh3. Department of Pathology, 1 Department of Medicine (Dermatology), Dalhousie University, Halifax, Nova Scotia.

A 9 year old girl was seen in dermatology clinic with a mildly pruritic eruption which developed on completion of a course of chemotherapy (6-mercaptopyrinate, methotrexate, vincristine, and dexamethasone) for acute lymphoblastic leukemia. Her hematological malignancy was in remission and she was systemically well. Examination revealed an eruption of follicular crusted papules with keratotic spines on the face, including prominent eyebrow involvement. Her shoulders, arms and legs were also affected. The clinical differential diagnosis included keratosis pilaris, generalized molluscum contagiosum, perforating folliculitis, and atypical infections. A punch biopsy from the back demonstrated an enlarged hair follicle. The bulb was abnormal in that it lacked a papilla. Moreover, the matrical cells were disordered and merged with an expanded inner root sheath with cells containing large trichohyaline granules. The upper segment of the follicle including the infundibulum was distended and plugged with keratin. The histopathological findings, in the context of the clinical setting led to a diagnosis of Viral-associated Trichodyplasia Spinulose (VATS). VATS is a rare virally-induced follicular eruption (20 reported cases) occurring in immunosuppressed patients following solid-organ transplantation or treatment of hematologic malignancies. The clinical and histopathological characteristics of this entity are as described above and ultrastructural demonstration of viral particles in inner root sheath cells is an adjunct to diagnosis. Treatment with topical antiviral agents has yielded favourable results. Recently, a novel human polyoma virus (TSPyV), closely related to the Merkel cell polyoma virus (MCPyV), has been identified as the responsible agent. Anticipating that cross reactivity on immunohistochemistry might exist between (TSPyV) and other polyoma viruses, we stained our case for both SV40 and MCPyV, but both proved negative.

INFILTRATIVE AMELANOTIC/HYPMELANOTIC CELLULAR BLUE NEVUS: AN UNDESCRIBED VARIANT OF BLUE NEVUS.

A. Mishra1, D. Ghazarian2, A. Al Habeeb3, S. Sade1. 1 Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario; 2 Department of Pathology, Toronto General Hospital, University of Toronto, Toronto, Ontario; 3 Department of Pathology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario.

Amelanotic/hypopigmented blue nevi are rare lesions that occur in both sexes, though more commonly in females. These have a wide age distribution with a predilection for young individuals. The histologic diagnosis of amelanotic/hypopigmented blue nevus (loss of melanin pigment in 95% of the lesion) hinges upon the recognition of typical architectural and cytological features of a cellular blue nevus and the exclusion of other tumors. We report two cases of a hitherto unreported variant of hypopigmented blue nevi, the ‘Infiltrative Amelanotic/Hypomelanotic Cellular Blue Nevus.’ These highly infiltrative and diffuse lesions recur after considerable time. The exact biologic potential of these lesions remain undetermined. The lesions could not be completely excised in our patients despite multiple excisions and our patients continue to be closely followed. These recurrent infiltrative hypopigmented/amelanotic cellular blue nevi, affecting young patients can be easily confused with other lesions like: fibromatosis, dermatofibroma, malignant blue nevus (blue nevi like melanoma), desmoplastic melanoma, cellular neurothekoma and clear cell sarcoma. Recognition of this entity is important to foster appropriate diagnosis, and case reporting is essential to determine the exact nature and outcome of these lesions. Herein, we report two cases of Infiltrative Amelanotic/Hypomelanotic Blue Nevi and discuss treatment approaches and follow-up data.

INFILTRATIVE AMELANOTIC/HYPMELANOTIC CELLULAR BLUE NEVUS: AN UNDESCRIBED VARIANT OF BLUE NEVUS.
NEW MOLECULAR GRADING FOR SQUAMOUS CELL CARCINOMA SKIN.

**Background:** The study was conducted to suggest a new molecular grading technique that may predict the risk of disease recurrence as well as potential chemotherapy benefit that may promise in refining clinical decision making.

**Materials and Methods:** Scoring for histology, staging, Ki-67 index and p53 protein expression was performed on 180 samples of squamous cell carcinoma. Data regarding pathologic prognostic factors e.g., lymph node metastasis, local invasion, distant metastasis, recurrence and 5 years survival was also collected for each case.

**Results:** SCC was designated low, intermediate, and high grade grades based on the sum of point values assigned to each 4 scores of histological differentiation, staging, p53 protein expression and Ki-67 index. Expression of p53 was found to be related to the Ki-67 with the scores of histology and stages of SCC. A poor correlation was found between the conventional histological grades (i.e. Spearman correlation=0.928) but a positive correlation was seen in the surgical stages (i.e. Spearman correlation= 0.721). A significant correlation was also seen with disease outcome like local invasion, lymph node involvement, distance metastasis, and recurrence (Kendall’s Tau - b= -0.966, p-value=0.025). **Conclusion:** Molecular grading system indicates a ternary grading scheme for SCC. This practical approach has potential to improve clinical evaluation of SCC in understanding the pathologic and clinical behavior of SCC.

GIANT CELL TEMPORAL ARTERY ARTERITIS ASSOCIATED WITH BASAL CELL CARCINOMA: COINCIDENCE OR CONNECTION?
D. El Demellawy MBBCh, PhD FRCP(C)1,2, A. Bane MBBCh, PhD, FRCPath, E. Mahe BSc, MD3, S. Alowami MBBCh, FCAP, FRCP(C)2. 1Department of Pathology and Laboratory Medicine, William Osler Health Care, Brampton, Ontario; 2Northern Ontario School of Medicine, Sudbury, Ontario; 3Department of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario.

Giant cell arteritis is a granulomatous vasculitis of large and medium sized arteries manifesting as temporal arteritis and/or polymyalgia rheumatica. The histological assessment of temporal artery biopsies is frequently encountered in anatomical pathology and has important diagnostic consequences in patients clinically suspected of having giant cell arteritis. In addition to the morbidity directly attributable to giant cell arteritis, there is ongoing debate in the literature regarding a potential association between giant cell arteritis and various malignancies. We present a case of an 83 year old male presenting with an ulcerating left temporal lesion clinically suspected to be a basal cell carcinoma. Upon histologic interpretation of the primary excision specimen, a focus of giant cell arteritis was identified immediately deep to the basal carcinoma in question. This unique case serves to reinforce the importance of careful histological examination of tissue received by the pathology department in order that an otherwise occult disease process with important clinical consequences is not overlooked. We also present a review of the literature highlighting the continuing debate over the potential association of giant cell arteritis with the development of a malignancy.