RCPA Quality Assurance Programs Pty Ltd Presentations

CORRELATION OF HISTOPATHOLOGY OF PATIENTS WITH NEGATIVE HUMAN PAPILLOMAVIRUS (HPV) AND HIGH-GRADE LIQUID-BASED CYTOLOGY RESULTS FOLLOWING INTRODUCTION OF PRIMARY HPV CERVICAL SCREENING IN AUSTRALIA

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Aim: The study correlates histopathology in patients with negative human papillomavirus (HPV) and high-grade liquid-based cytology (LBC) testing following the introduction of primary HPV screening for cervical cancer in Australia.

Methods: Retrospective audit of cervical samples submitted to Capital Pathology, ACT, between 1 December 2017 and 30 April 2019. HPV testing performed by Roche Cobas 6800 (Roche Diagnostics). HPV and LBC results, patient age and histopathology follow-up within 6 months of cytology was documented. Low grade cytology included low-grade intra-epithelial lesion (LSIL) and possible LSIL. High-grade included all other abnormal cytology results.

Results: A total of 365 cases of HPV-negative, abnormal cytology were identified: 297 of 365 (81.4%) were low-grade and 68 of 385 (18.6%) were high-grade. 14 of 68 (20.5%) cases with HPV-negative and high-grade cytology had histopathology within 6 months: 3 endometrioid adenocarcinoma, 2 endometrial malignancy, 1 adenocarcinoma (endocervical), 2 serous adenocarcinoma, 2 squamous cell carcinoma, 3 high-grade intra-epithelial lesion (HSIL) and 1 adenosquamous carcinoma. The median age was 64 years.

Discussion: This study identified 14 patients with HPV-negative, high-grade cytology confirmed on histopathology. This data may support co-testing of patients in their sixth decade as an alternative to primary HPV testing.

RESOLUTION OF GROSSLY DISCREPANT INTER-ANALYSER BILIRUBIN RESULTS IN PATIENTS ON ELTROMBOPAG THERAPY: A HEPATOTOXIC DRUG THAT AFFECTS BILIRUBIN MEASUREMENT

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Background: Eltrombopag is a thrombopoietin receptor agonist that is increasingly being prescribed for the treatment of chronic thrombocytopenic conditions. Hepatotoxicity occurring in ~15% of patients necessitates regular monitoring of liver function. Depending in which hospital a patient is followed-up, serum bilirubin concentration for a single sample can vary by more than 8-fold, or 64 $\mu\text{mol/L}$, with the true concentration unknown.

Methods: Bilirubin was measured using up to nine assays including the Doumas Reference method and HPLC, for 66 samples from patients on 25–150 mg daily. Plasma/serum eltrombopag concentrations were determined using LC-MS/MS.

Results: There was a positive correlation between inter-analyser total bilirubin difference and plasma eltrombopag concentration ($r=0.679$). Spike-in experiments demonstrated that methods including the Doumas reference method were susceptible to positive interference. HPLC quantified bilirubin after separating eltrombopag, and results show that different analysers are affected to varying degrees by eltrombopag and its metabolites.

Conclusions: We are the first to demonstrate which bilirubin assays can accurately quantitate bilirubin concentration in patients on eltrombopag therapy. We are also the first to provide evidence that metabolites likely contribute to the interference. Resolution of inter-analyser discrepancies may prevent misdiagnosis of hepatotoxicity and improve our understanding of the prevalence of hyperbilirubinaemia in patients on eltrombopag therapy.

AN EIGHT YEAR REVIEW OF INTRAOPERATIVE FROZEN SECTION DIAGNOSES AND ITS LIMITATIONS

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Background: Frozen section consultation (FS) is an integral part of surgical pathology to aid surgical colleagues in making an intraoperative management decision. This audit reviews the performance of FS diagnoses in a tertiary teaching hospital.

Objective: To perform an 8-year retrospective review analysing the concordance rate of FS compared with the final diagnosis on paraffin-embedded sections.

Methods: 2013 cases were received for FS from 1 January 2011 to 31 December 2018, comprising 3503 specimens. The patient's age, sex, specimen type, indication of the FS and the year performed were recorded. The diagnoses between FS and paraffin section were compared, especially for the discrepant cases.

Results: Of the 3503 specimens, 3288 results were concordant (93.86%). The major discordances occurred in 66 incidences (1.88%), the minor discordances in 68 specimens (1.94%) and the diagnoses were deferred in 81 cases (2.31%). Further analyses were performed on the major discordances. The true diagnostic error was seen in 26 specimens. Twenty-one incidences were due to undersampling, 17 specimens as a result of

technical error and 2 specimens were difficult cases requiring specialist referral.

Conclusion: This audit addresses the diagnostic performance of intraoperative consultation and explores ways to minimise error when utilising this method.

OBSERVATIONS FROM A NATIONAL MULTI-SAMPLE EXCHANGE PROGRAM FOR MOLECULAR HAEMATOLOGY TESTING

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Introduction: A national multi-sample exchange (MSE) program for molecular haematology tests without a formal EQAP was established in 2009 and has been co-ordinated by the Peter MacCallum Cancer Centre (PMCC) since 2017. We recently incorporated assessment of the post-analytical reporting phase to the program. We report key analytical and post-analytical phase findings from the program.

Method: Seventeen participating laboratories are enrolled in an annual reciprocal sample exchange roster covering sixteen conventional molecular haematology tests and one next generation sequencing (NGS) module. Participants submit LIS-generated reports which undergo central review at the PMCC Molecular Haematology laboratory. Reports are assessed according to consensus values, NPAAC requirements and relevant international guidelines and a result summary is returned to participating laboratories.

Results: A range of platforms are used for molecular tests. Laboratories show high levels of concordance for qualitative results with discrepancies most frequently due to differences in assay sensitivity. Discordant reporting practices include not incorporating relevant technical information on reports and using non-standard gene nomenclature. NGS reports demonstrated discrepancies in variant nomenclature, classification and interpretation, identifying areas for improvement.

Conclusion: Concordance of molecular haematology testing in the analytical phase is high however opportunities for improvement exist in the post-analytical phase to ensure harmonised reporting and accurate result interpretation.

AN AUDIT OF 10 YEARS' EXPERIENCE OF MMR IMMUNOHISTOCHEMISTRY

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Aim: Canterbury Health Laboratories provides mismatch repair (MMR) immunohistochemical testing nationally for patients investigated by the New Zealand Familial Gastrointestinal Cancer Service for suspected Lynch Syndrome. We will review the rates and types of MMR deficiency in this cohort. Where available we will compare our results to those of the referring laboratory.

Methods: Information was obtained from clinical databases and the NZ Cancer Register.

Results: 534 colorectal adenocarcinoma cases were tested for MMR IHC. 49% were MMR IHC deficient. After excluding those with a BRAF mutation/positive MLH1 promoter hypermethylation status, the total number of dMMR was 67 (13%). Of these, 75% had MLH1/PMS2 loss, 10% had isolated PMS2 loss, and 7% had MSH2/MSH6 loss. 308 separate cases underwent BRAF mutation and/or MLH1 promoter hypermethylation testing only.

There was a high degree of discordance (28/96) in MMR interpretation between our laboratory and referring laboratories if testing had been performed previously. In the majority we interpreted the IHC as combined MLH1/PMS2 loss, while the referring laboratory interpreted their IHC as isolated PMS2 loss. This may be due to misinterpretation of punctate MLH1 staining as retained positivity.

Discussion: In this cohort there was a much higher proportion of MLH1/PMS2 deficient tumours than has been reported elsewhere.¹

Reference

1. Moreira L, Balaguer F, Lindor N, *et al.* Identification of Lynch Syndrome among patients with colorectal cancer. *JAMA* 2012; 308: 1555–65.

EVALUATING THE UTILITY OF DETECTION OF GBS BACTERIURIA IN ADDITION TO STANDARD SCREENING IN PREGNANT WOMEN

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Group B streptococcus (GBS) causes maternal and neonatal morbidity and mortality.¹ GBS bacteriuria during pregnancy likely reflects heavy genital colonisation, and intrapartum prophylaxis is indicated. Screening recommendations vary, especially regarding GBS bacteriuria.

At Royal Prince Alfred Hospital, we perform routine screening culture on combined low vaginal-perineal/rectal swabs. In addition, beta-haemolytic streptococci are identified and GBS reported (irrespective of colony count) in all urine specimens from women of reproductive age.

We performed a retrospective audit of women aged 15–49 years who had urine and GBS screens collected during pregnancy (January 2010–June 2019), to determine whether identification of GBS carriage through screening of urines at any time during pregnancy increases the sensitivity of detection of GBS colonisation, compared to screening swabs alone.

The mean age of study women was 31 years. GBS was detected in screening swabs in 18.4% (95%CI 17.9–18.8%). 499 women who had GBS in urine also had GBS (*n*=182) and genital (*n*=491) swabs collected. In this group, there were 81 patients (16.2%) in whom GBS was identified in urine only. Sensitivity of swabs alone was 83.8% (95%CI 80.2–86.9%).

Detection of GBS colonisation during pregnancy is increased by addition of urine culture to screening swabs.

Reference

1. Braye K, Foureau M, de Waal K, *et al.* Group B streptococcal screening, intrapartum antibiotic prophylaxis, and neonatal early-onset infection rates in an Australian local health district 2006–2016. *PLoS One* 2019; 14: e0214295.