# The Annual Scientific Meeting of College of Pathologists, Academy of Medicine of Malaysia: Opportunities and Challenges in Laboratory Medicine, was held at Riverside Majestic Hotel, Kuching, Sarawak on 27-28 June 2019. Abstracts of K. Prathap Memorial Lecture, plenary, symposium and paper (poster) presented are as follows:

*K Prathap Memorial Lecture:*
**Opportunities and challenges for laboratory professional in patient safety**

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Pathology has been the engine of healthcare system in understanding diseases and in the last few decades in monitoring therapy. However, the approach and technique we use remain very much the same. As we move into the future of the digital age and artificial intelligence, the challenge is should we continue doing the same or do we need to change and reinvent the discipline and the service we provide. To remain relevant, we have to embrace the change and move with the times. The digitization of pathology laboratories makes the specialty more efficient, specimen more reproducible and the work of pathologists less cumbersome. New technologies that produce biomedical "big data" (next generation sequencing, multiparameter / multiplex flow cytometry, high-throughput proteomics and metabolomics, systems biology analysis) have also caused us to rethink the best approach to diagnostics. While these opportunities and challenges seem daunting, we still have to grapple with old challenges of funding and leadership.

*Plenary 1:*
**Challenges in diagnosis of monoclonal gammopathy**

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The monoclonal gammopathies (MG) are a group of disorders characterised by the proliferation of clonal plasma cells to produce resulting in a detectable abnormality called monoclonal component or M-protein or paraprotein. Direct measurement of the M-protein spike by electrophoresis and immunochemical measurements of specific isotypes or free light chains pairs has provided useful information about the quantity of M-protein. Nonetheless, quantitation of M-protein by electrophoretic method gives suboptimal measurements on small M-proteins. In addition, measurements by electrophoresis of M-proteins migrating in the β- and α-regions are difficult due to the presence of normal serum proteins in those regions. The nephelometric quantitation of immunoglobulins (Igs) is a simple automated method that uses anti-human Ig antigen binding fragments (Fabs) that target the constant region of Ig. The method measures both monoclonal and polyclonal immunoglobulins, and therefore, its diagnostic use for identification of monoclonal proteins is not recommended and is also of no value for biclonal and triclonal gammopathies. Use of the serum free light chain (FLC) immunoassay, has led to improvements in the diagnosis and monitoring of patients with plasma cell dyscrasia and other monoclonal gammopathies. Not all MG secrete excess FLC. Abnormal serum FLC ratios have only been detected in 90–95% of intact Ig multiple myeloma and 40% of MGUS. Since these two patient groups can be easily diagnosed by serum M-proteins by protein electrophoresis, a combination of tests is needed to detect all MGs. Nephelometric methods using antisera specific for Ig heavy and light chain epitopes separately quantitate IgG kappa and IgG lambda, IgA kappa and IgA lambda, and IgM kappa and IgM lambda and may be useful for monitoring monoclonal proteins migrating in the beta fraction. The heavy-light, isotype-specific kappa to lambda ratio has been proposed as a potential monitoring method for IgA or IgM M-proteins migrating in the beta fraction. Although the assay is not sensitive enough to use as a routine screening method for MM, a 97% sensitivity observed in IgA MM and IgA MGUS indicates that almost all IgA MM patients can be monitored by HLC for both detection of the disease clone and quantitation using the IgA HLC assay. A 24-hour urine collection allows the quantitation of both the albumin and M-protein that has been rapidly cleared by the kidneys. The potential broad use of mass spectrometry for MG has been recently demonstrated by the application of matrix assisted laser desorption ionization – time of flight instruments (MALDI-TOF) for detecting monoclonal proteins. The Mayo Clinic group performed a large retrospective study in which patients with an assortment of plasma cell proliferative diseases had SPE, IFE, and FLC as well as urine protein electrophoresis and IFE performed at the time of diagnosis. The study shows patients would have had M-proteins detected by the various tests singly or in combination and if urine assays are removed from the diagnostic panel, there is no decrease in sensitivity. This and other studies have led the IMWG to recommend a panel of serum protein electrophoresis, immunofixation electrophoresis and FLC to screen for a MG; the inclusion of diagnostic urine testing is only recommended if amyloidosis is suspected, which simplifies collection for the patient and workflow for the laboratory and reduces costs as well.

**HM-27.  A randomized control trial comparing peginterferon-α-2a versus observation after stopping tyrosine kinase inhibitor in chronic myeloid leukaemia patients with deep molecular response for at least two years: Interim analysis**

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*Introduction:* Treatment free remission (TFR) is a fairly new treatment concept in chronic myeloid leukaemia (CML) that develops after two frontier studies from French and Australia published in 2010.  About 40% of CML patients, who have achieved deep molecular response (DMR) with tyrosine kinase inhibitor (TKI), are able to remain in TFR after stopping their TKI.  Studies are going to search means to increase TFR rate.  Consolidative therapy using interferon (IFN), the standard treatment of CML before era of TKI, is a logical possibility because of data suggesting IFN-induced immunity towards the leukemic clone.  We conducted the first randomized controlled trial comparing the use of pegIFN versus observation in CML patients attempting TFR. *Materials & Methods:* Adult CML patients from multi-centre in Malaysia with stable DMR for 2 years or more and at least two readings of MR4.5, were stopped TKI and randomized into two arms: (1) subcutaneous pegIFN-α-2a starting at $180\mu$g weekly for a year, followed by observation, or (2) observation.  Outcome is relapse, defined as either (i) one reading of loss of major molecular response ($>0.1\%^{IS}$), or (ii) positivity of *BCR-ABL1* transcripts, as confirmed by a second analysis point, indicating the increase ($\geq 1$ log) in relation to the first analysis point at two successive assessments. *Results & Discussion:* A total of 30 patients started intervention from July 2015 to October 2018 (pegIFN n=15, observation n=15).  Analysis was taken on 13th Mar 2019.  A total of 9 patients relapsed (pegIFN n=4, observation n=5).  The median time of relapse was 13.1 months (range 9.2 to 25.5) and 1.8 (1.2 to 12.0) after stopping TKI in pegIFN and observation arm, respectively.  Dose of tolerable pegIFN was age dependent. Commonest adverse event of pegIFN was transaminitis. Quality of life assessment using EORTC QLO-C30 showed similar result between the two arms. *Conclusion:* PegIFN is a potential consolidative therapy to increase TFR.

**HM-28.  Prevalence of normal population harbouring *BCR-ABL1* fusion gene in Southern Sarawak, Borneo Island**

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*Introduction:* Level of *BCR-ABL1* fusion gene, the driver mutation in chronic myeloid leukaemia (CML), is monitored using quantitative polymerase chain reaction (PCR) (qPCR) reported in International Scale (IS) to guide disease treatment.  *BCR-ABL1* was also found in asymptomatic normal subject without blood/marrow feature of CML.  Previous studies used convenient sampling and qualitative PCR or qPCR but not IS to study normal subjects harbouring *BCR-ABL1*.  Hence, the result could neither infer to normal population nor impact treatment of CML.  *Materials & Methods:* We conducted the first normal population study to determine population prevalence of normal subject harbouring *BCR-ABL1* using qPCR$^{IS}$.  It was a cross sectional community-based study studying southern Sarawak population aged $\geq 18$ and using two-stage sampling (stratified followed by cluster) based on Malaysia Department of Statistics population survey procedure.  The sampling frame was divided into enumeration block (EB) and subdivided into living quarter (LQ). qPCR$^{IS}$ *BCR-ABL1* was done using validated commercial kit. *Results & Discussion:* A total of eight EBs, total of 88 LQs and total subject of 190 were studied and analysed.  23 (12.1%) out of 190 samples had poor quality with sum of control gene, *ABL1*, less than 10,000 copy number, while 102 (53.7%) had good quality with sum of *ABL1* more than 100,00.  Quality of each run of qPCR$^{IS}$ *BCR-ABL1* was satisfactory fulfilling the evaluation criteria. One subject was found positive, *i.e.* 0.0023%$^{IS}$.  Repeat qPCR$^{IS}$ was 0.0032%$^{IS}$.  Sequencing confirmed e13a2 transcript. *Conclusions:* Prevalence of normal population harbouring *BCR-ABL1* in southern Sarawak was 0.5% to 1%. Sum of control gene *ABL1* copies number in two replicates should be adequate ($>100,000$) to enable efficient screening.

**HM-29.  Genomic landscape of *BCR-ABL* kinase domain mutation in chronic myeloid leukemia patients with imatinib resistance**

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*Introduction:* Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder involving the pluripotent haemopoietic stem cell compartment. It is caused by a reciprocal translocation between chromosomes 9 and 22, t(9;22) (q34;q11) which encodes for the *BCR-ABL* fusion protein. Discovery of imatinib mesylate (IM) as targeted *BCR-ABL* protein kinase inhibitor