

Brunei Darussalam

19 - 21

**January 2018** 

Journal of Health

# rd NATIÔNAL SCIENTIFIC Symposium

"INNOVATING PRECISION MEDICINE FOR PATIENT CARE"

STERILE R



# 2018 Volume 08

# 3<sup>rd</sup> National Scientific Symposium Special Issue

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# 2018 Volume 08 3<sup>rd</sup> National Scientific Symposium Special Issue

This special issue of BDJH is based upon proceedings of the 3rd National Scientific Symposium in Brunei Darussalam from 19<sup>th</sup> to 21<sup>st</sup> January 2018.

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# About BAMLS

Brunei Darussalam Association of Medical Laboratory Scientists (BAMLS) was first launched on Sunday, 21 June 1998. The launching was followed by BAMLS first General Meeting in which the first Executive Committee were elected. Today, 286 members (including fellow and associate memberships) have registered with BAMLS.



### **KEYNOTE ADDRESS**

# The Regulation of p53 in Human Cancer

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Keywords: p53 mutations, therapy

Whole genome sequencing of human cancers has confirmed that mutations in the p53 gene are the most common specific genetic events in human cancer. The strength of the database is now such that we can be sure that this is a final answer. What then does p53 mutation do that is so important and how might we exploit this knowledge for the improved diagnosis and treatment of cancer?

The p53 protein is a highly regulated master transcription factor that is induced by stress and in particular by DNA damage. It induces a complex pattern of transcription that activates cellular repair pathways, as well as cell cycle arrest and apoptotic processes all of which act to prevent cancer formation. Mutations in p53 result in loss of these tumor suppressor functions, but some point mutations additionally convert p53 into a driver oncogene. For this gain of function to be realised, the mutant protein must be expressed at high levels.

Using mice homozygous for mutant p53 and mice treated with proteosome inhibitors to stabilize p53, we have carried out an extensive investigation of the regulation of p53 expression in normal and pre-neoplastic mouse tissue. Interestingly, the p53 gene is only transcribed in proliferating cells and the gene is rapidly turned off as cells differentiate and exit the cell cycle. Protein expression levels are very modest and high levels of expression are only reached in tumor cells and in some pre-neoplastic conditions.



### **KEYNOTE ADDRESS**

# Transforming Medicine: Genomics, Bioinformatics & Global Health

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The 4th Industrial Revolution is the current trend of automation and data exchange in manufacturing technologies. It includes cyber-physical systems, the Internet of things (IoT), and cloud computing controlled by smart algorithms or artificial intelligent (AI). Three ways the 4th Industrial Revolution can transform healthcare; one of them is genomic medicine.

### 1. Embedding disease management in our daily lives

Devices could become more seamlessly interconnected through IoT to enhance patient monitoring, potentially allowing individuals and their physicians to better manage conditions like non-communicable diseases (NCDs). Sensors connected to the IoT have the potential to engage NCD patients in their disease management, which could help reduce the incidence of adverse events and associated costs. Patients with a respiratory condition, for example, could have "invisible" sensors embedded in objects in their homes and cars that may be able to determine when their breathing could become labored, and remind them to intervene with therapies like an inhaler before hospitalization is necessary.

### 2. Caring for the aging population

The population over age 60 is expected to reach nearly 2 billion by 2050. In the U.S., for example, the cost of providing healthcare for one person aged 65 or older is three to five times higher than the cost for someone younger than 65. Combined with AI, robotics could potentially provide some caregiving services to older individuals such as continuous monitoring and assisting with tasks like keeping track of medicines.

### 3. Precision medicine based on genomic medicine

New technology, such as next generation sequencing, has made it possible to sequence a person's genome within 24 hours for \$1,000, resulting in an explosion of genomic data that helps patients take preventative measures, and physicians and scientists develop more personalized treatments. Although there are important ethical dilemmas to consider, the high demand for genomic counsellors and the emerging field of gene editing may offer new hope for untreatable genetic conditions, or diseases like Alzheimer's. Genome editing technology could allow us to precisely delete, repair or replace the genes that cause certain diseases.



Diseases such as HIV and hepatitis C were not even discovered until the 1980s, and today we now have medicines that treat HIV-infected patients, and curing HCV-infected patients, patients suffering from these once life-threatening conditions.

Center of Medical Genomics, Ramathibodi Hospital, Mahidol University has been recently established due to the Thailand 4.0 policy. Many success applications of genomic medicine have been implemented into clinical practices. For example, in the fields of infectious diseases, reproductive health, pharmacogenomics, next-generation sequencing for diagnosis of rare or undiagnosed diseases, metagenomics, and cancer genomics.



### FOCUS: CANCER DIAGNOSTIC AND CARE IN BRUNEI DARUSSALAM

# Radiotherapy - It's Here

Dr Jamsari Khalid The Brunei Cancer Centre, Jerudong, Brunei Darussalam BG3122

The talk will start from the beginning of oncology Services from 2009 to the current date. Our mission is to enhance lives through quality cancer services and our vision is to increase capabilities to treat patient locally. The Brunei Cancer Centre (TBCC) is equipped with the latest linear accelerators (The EDGE and TRUEBEAM), high dose rate (HDR) brachytherapy equipment, 3D Planning System capable of intensity modulated radiotherapy (IMRT), volumetric arc therapy (VMAT), stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT). We also have a computed tomography (CT) simulator, a positron emission tomography-computed tomography (PET-CT) scanner, a cyclotron and radio-iodine isolation room. We have facilities for consultation rooms and 63 inpatients, day care facilities, and 64 chemotherapy infusion chairs/beds.

A summary of how radiotherapy works will be given along with a general overview of the cancer cases through the department since its commencement for both men and women. Old radiotherapy and newer high precision radiotherapy are explained with a brief mention on gynae-brachytherapy and prostate services which we will have in the future.

There will be videos on the movements of the linear accelerators, and if time permits, a video on the "mask" making with thermoplastic devices.



### FOCUS: CANCER DIAGNOSTIC AND CARE IN BRUNEI DARUSSALAM

# Molecular Genomics in Malignant Mesothelioma

Dr Lu Shir Kiong

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Cancers result from an accumulation of genetic aberrations that are either acquired or inborn. Technologies have been developed to determine the molecular profile of cancer that may have implications for clinical care. Advances in sequencing technologies such as next generation sequencing and array-based approaches have revealed the genetic landscape, including driver genes in a wide range of cancers. These have already translated into better understanding of the biological behaviour of several cancer types to improve diagnosis, prognosis and treatment. Malignant pleural mesothelioma (MPM) is a rare and aggressive type of cancer related to asbestos exposure. The treatment options are limited and response to standard chemotherapy regime is poor. Current understanding of the genetic makeup of this deadly disease is still lacking. Thus, the aim of my research was to gain further insights into the pathogenesis of MPM by exploring the tumour mutational and transcriptional profiles. The results showed MPM is a complex disease with heterogeneous molecular aberrations. By combining findings from both transcriptome and exome analyses, we identified alterations in genes involved in common signalling pathways, such as WNT and MAPK. These may have important roles in driving MPM carcinogenesis with therapeutic implications and require further explorations.



### FOCUS: SOLID CANCERS

# Solid Tumour Diagnostics - The Evolving Landscape

### Dr Edwin Lim Chyi Chyuan

Brunei Ministry of Health National Hospitals, Health Centres and Clinics

Cancers of the same histopathological category differ in their molecular anomalies and thus even the most frequent cancer types are a collection of "rare" diseases from a molecular standpoint. Each cancer has multiple gene alterations that affect the function of several signalling pathways, which may be peculiar to a cancer type or similar among different tumour types.

This molecular heterogeneity is an ongoing process that is responsible for the clonal evolution of cancers in both primary sites and metastasis, resulting in resistance to treatment. Thus, an accurate assessment of tumour heterogeneity is essential for the development of more effective personalized therapies.

Advancements in technologies such as next generation sequencing would allow for the identification and quantification of molecular heterogeneity, sequencing multiple genes simultaneously from routine materials, such as small biopsies and cytological samples.

Further down the line, it may be possible for the routine use of liquid biopsies to evaluate tumour load and monitor response to therapy, as well as whole genome/transcriptome sequencing to assess the molecular landscape of individual cancers.



### FOCUS: SOLID CANCERS

# Potential Role for Spleen Tyrosine Kinase (SYK) in Breast Cancer

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**Keywords:** breast cancer, drug induction, SYK, apoptosis, caspases

### INTRODUCTION

Spleen Tyrosine Kinase (SYK) is a non-receptor tyrosine kinase produced mainly by hematopoietic cells reflecting their important role in B-cell progenitor development. While the roles of many tyrosine kinases in cancer cell development are well-documented, the ability of others like SYK to modulate the growth ability of cancer cells is less well-understood. SYK has been described to act as a tumour promoter or suppressor of cancer development depending on the stimulating environment. We were interested to study if SYK was involved in apoptosis in breast cancer cells.

### METHODS

Stable transfection of the *SYK* gene into breast cancer cells was performed using FuGENE<sup>R</sup>. Stable cell line was induced to undergo ell death using staurosporine. LC50 of staurosporine was determined using Vybrant MTT cell proliferation assay. Apoptosis was investigated by qPCR and Western blotting to show gene and protein expressions of the cell cycle genes, caspases and inhibitors and promoters of apoptosis respectively.

### RESULTS

Our results showed a substantial cell death of breast cancer cells carrying the *SYK* gene when induced with staurosporine. LC50 was determined to be 10 $\mu$ m. Cell cycle genes *CDK6* and *cyclin D* mRNAs were reduced during cell growth and apoptosis was indicated and characterised by the expression of mRNAs for caspases 8 and 9 and the proteins Bax and Bcl-2 respectively.

### CONCLUSIONS

*SYK* gene was stably-expressed in breast cancer cells. Upon staurosporine-induction, SYK appeared to cause a downregulation of the cell cycle genes and upregulation of apoptosis genes indicating a tumour suppression role in breast cancer development.



### FOCUS: HAEMATOLOGICAL MALIGNANCIES

# Minimal Residual Disease in Leukaemia

### Dr Noorainun Hj Md Yusof

Brunei Ministry of Health National Hospitals, Health Centres and Clinics

Monitoring of minimal residual disease (MRD) has revolutionized the management of acute leukaemia. Currently almost all paediatric patients and a large part of adult acute leukaemia cases are being monitored with MRD techniques. The purpose of MRD monitoring is to assess treatment effectiveness and assign patients to MRD-based risk groups.



### FOCUS: HAEMATOLOGICAL MALIGNANCIES

# **Clinical Proteomics**

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Clinical proteomics aims to apply the large-scale characterization of protein profiles performed on patient samples (cells, tissues and fluids) for prediction, diagnosis, prognosis, and therapeutic management & monitoring of treatments. Coupling the vast knowledge obtained by mapping both the human genome and proteome with technological breakthroughs in CRISPR/Cas9 genome editing have fuelled the anticipation of a personalized, individualized, precision medicine in the near future. The spectacular advances in sample preparation using liquid biopsy and the improvements in sensitivity and robustness of instrumentation based on mass spectrometry (MS), together with the development of the powerful tools in dataset analysis have established the foundation for adoption of recent discoveries into the clinical setting. The capability to quantify more accurately and precisely the profile of entire proteoforms (all proteins including their modified forms) from clinical specimens provide a source of multi-parametric data that can give insights into the underlying mechanisms of a disease for informative translation into patient care. To apply proteomics discoveries in the clinic requires proper experimental study design, standardization of proteomic platforms, improvement of biospecimen collection & processing, and provision of systematic data analysis tools to convert data sets into easily interpreted information that answers the most important clinical questions. To harness the power of clinical proteomics, it is necessary to set up a clinical system comprising of a more automated, sensitive, robust, accurate, reliable, easy-to-operate and cost-effective MS-based platforms that will become an integrated part of the clinical laboratory. The medical revolution goal is to characterize every human disease one patient at a time, yielding a novel-targeted medicine for smarter decisions and investment of resources.



## SYMPOSIUM 2 – LIFESTYLE DISEASES

### FOCUS: RISK FACTORS

# Is Sitting the New Smoking?

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Sedentary behaviour (SB) is any behaviour that requires very low energy expenditure of less than 1.5 metabolic equivalents (METs). The main SB postures are sitting or lying down. It includes activities such as sleeping, sitting, watching television, writing, deskwork, typing, playing seated computer games and sitting during commuting. The terms 'sitting time' and 'sedentary time' are often used interchangeably, but both refer to SB. SB increases with age and is higher among those living in high income countries.

In large scale epidemiological studies, SB has been linked to excess risk for cardiovascular disease (CVD) (HR 1.14), cancer (HR 1.13) and Type 2 diabetes (HR 1.91). There is also associated higher mortality from CVD (HR 1.18), cancer (HR 1.17) and all causes (HR 1.24). It has also been suggested that SB may be related to adverse effects on physical musculoskeletal capability, quality of life, mental health and cognitive performance.

The mechanism of action of physical inactivity in causing adverse health outcomes is believed to be via cardiometabolic pathways. These include alterations in genetic expression of energy metabolism, reduction in insulin sensitivity, increase in triglycerides and LDL cholesterol, decrease in net calorie expenditure, and increased abdominal & visceral adiposity. An emerging hypothesis is that the physiological mechanisms underlying health benefits of physical activity may be distinct from mechanisms causing deleterious health consequences by SB. The elevated mortality associated with prolonged, uninterrupted sedentary bouts suggest the potential importance of skeletal muscle inactivity on cardiometabolic pathway mechanisms.

To be physically active is not enough to prevent the adverse health effects caused by SB. Experts also recommend that we should avoid SB, especially prolonged bouts of SB. The current recommended guidelines for adults are for 150 minutes of moderate to vigorous physical activity per week. In addition to this, it is recommended that short breaks should be taken after every 30 minutes of SB.



## SYMPOSIUM 2 – LIFESTYLE DISEASES

### FOCUS: OBESITY

# Cholesterol - Who, What, When and How to Screen

### Dr Fung En Ching

Department of Laboratory Services, Ministry of Health, Brunei Darussalam

This talk summarises the rationale and accompanying evidence underpinning the current recommendations for cholesterol screening in the population. Specific issues addressed include non-fasting lipids, non-HDL, cholesterol/HDL ratio, familial causes of dyslipidaemia, biological source of variation and frequency of testing.



# SYMPOSIUM 2 – LIFESTYLE DISEASES

### FOCUS: OBESITY

# Obesity in Brunei Darussalam

Dr Alice Yong Moi Ling

Brunei Ministry of Health National Hospitals, Health Centres and Clinics

Obesity epidemic continues to worsen worldwide and threatens to be the commonest noncommunicable disease. In Brunei Darussalam, we have seen a huge rise in the prevalence of obesity from 12% in 1997 to 27.2% in 2011. It poses a huge economic burden: in the UK, the direct costs of obesity and its comorbidities are in the order of £6 billion per year (Health and Social Care Information Centre, 2014). Despite this, the provision of weight management and obesity services is not readily available or highly developed in most countries. In 2006, we started Obesity Clinic at RIPAS Hospital and strive to provide a comprehensive, broad based multidisciplinary weight management, nutrition and metabolic service which encompass positive mental and physical health. This lecture will cover the multi-pronged approach to weight management that is individualized to each participant.



# SYMPOSIUM 2 – LIFESTYLE DISEASES FOCUS: CARDIOVASCULAR DISEASES

# Troponin Assays for Diagnosis of Myocardial Infarction - Still the Gold Standard?

Dr Pg Sofian DP Dr Hj Johar Department of Laboratory Services, Ministry of Health, Brunei Darussalam

The introduction of troponin assays has significantly improved the detection and diagnosis of myocardial infarction. The development of high sensitivity troponin assays has made it possible to detect myocardial injury at an earlier stage which is important when rapid diagnosis is essential. However, troponin measurements still have their limitations and other biomarkers are under investigation for clinical use. One in particular, co-peptin, has been proposed for use as an adjunct to troponin measurements. This talk will review the use of troponins for the diagnosis of myocardial infarction, discuss limitations and look at potential new biomarkers.



# SYMPOSIUM 2 – LIFESTYLE DISEASES FOCUS: CARDIOVASCULAR DISEASES

# The Simulation Theatre: A Mean to Enhance Learning and Improve Patient Safety

Md Khairulamin Abdullah Sungkai

PAPRSB Institute of Health Sciences, Universiti Brunei Darussalam, Tungku Link Road, Bandar Seri Begawan, Brunei Darussalam BE1410

The emergence of simulation based learning using high fidelity simulators has become a fast moving trend in healthcare education and has gained a strong reputation as a valuable investment to enhance learning, practice and patient safety. It is a teaching-learning strategy that emulate the realism of clinical practice in a controlled environment. The PAPRSB Institute of Health Science SimCentre is also keeping abreast with this learning paradigm, and has progressively improve since its official opening in June 2014. To date, more than 30 clinical case scenarios have been developed with different degrees of complexity to cater the need of various level of learners. Besides that, SimResus course training, ECG simulation training, inter-professional education and simulation drill are also implemented through this simulation learning approach. This presentation will give the snapshot of the faculty journey in maximizing its utilisation and feedback from the learners.



## FOCUS: EMERGING PATHOGENS

# Emerging Infectious Diseases: The Third Epidemiologic Transition

Dr Justin Wong Yun Yaw Brunei Ministry of Health National Hospitals, Health Centres and Clinics

The epidemiological transition model describes the changing relationship between human populations, their environment, and diseases which affect them. The first transition occurred with the shift to agriculture resulting in a pattern of infectious and nutritional diseases still evident today. In the last century, some populations have undergone a second transition, characterized by a decline in infectious disease and rise in chronic, degenerative disease. This presentation analyses the proposal that we are now undergoing a third epidemiological transition, in which a resurgence of familiar infections is accompanied by an array of novel diseases, all of which have the potential to spread rapidly due to globalization. It outlines the opportunities for innovative approaches to mitigate these risks.



## FOCUS: EMERGING PATHOGENS

# *Stapylococcus aureus* Bacteraemia: What is the Clinical Significance?

Dr Hjh Riamiza Natalie Hj Momin Brunei Ministry of Health National Hospitals, Health Centres and Clinics

*Staphylococcus aureus* (*S. aureus*) is a worldwide leading cause of bacteraemias or bloodstream infections. It is a common skin commensal and has the innate propensity to cause invasive infections with metastatic complications in multiple body sites such as endocarditis, septic arthritis, psoas abscesses and spondylodiscitis. Infection may be sourced from both community and healthcare settings.

Susceptibility to methicillin is a common discerning pathogen characteristic, with Methicillin-Resistant *Staphylococcus aureus* (MRSA) bacteraemias prognostically leading to poorer outcomes than Methicillin-Sensitive *Staphylococcus aureus* (MSSA) bacteraemias. Adequacy of treatment in terms of timing, optimal choice and duration of antimicrobial treatment, as well as stratification of those at risk of complicated infection also have bearing on overall prognosis. Available evidence has shown that infectious diseases consultation contributes to improved outcomes. In essence, beta-lactam treatment remains the optimal choice for MSSA bacteraemias, and this should be coupled with adequate source control where relevant. Persistent bacteremia is a risk factor for complicated disease and should trigger an earnest search for a distant focus. MSSA in the urine may herald an associated bacteremia hence, awareness should also be raised of its significance.

The clinical case shared illustrates the sequelae of suboptimally-treated *S. aureus* bacteraemia and tying these to the rationale behind management principles can optimize clinical management of *S. aureus* bacteraemia. Special mention is also made of the importance of adequate infection control measures in the mitigation of nosocomial spread of MRSA, especially with regards to hand hygiene and appropriate transmission based precautions.



### FOCUS: ANTIBIOTIC RESISTANCE AND CROSS CONTAMINATION

# Can the Antibiotic Stewardship PKPD Strategies and New Drugs Win the Power of Antimicrobial Resistance?

Dr Terrence Rohan Chinniah Department of Laboratory Services, Ministry of Health, Brunei Darussalam

Rising tide of antimicrobial resistance among Gram-positive and Gram-negative pathogens has become a major clinical challenge in the treatment of infectious diseases. Development of new agents is one part of the needed response; yet global drug pipeline is thin due to difficulty of discovery of new safe agents to counter the rapid progression of emerging resistance and due to the difficulty in the economics of antibiotics. Hence proper use of existing antimicrobials is essential. The primary goal of an antimicrobial stewardship program is to improve clinical outcomes while minimizing unintended consequences and collateral damage of antimicrobial use, namely emergence of antimicrobial resistance. Scientific and practical strategies of pharmacokinetics, pharmacodynamics, and dosing of available anti-microbial agents will further optimize clinical outcomes. These along with modification of behavior in prescription and robust infection control practices will help to overcome antimicrobial resistance in both clinical and public health settings.



### FOCUS: ANTIBIOTIC RESISTANCE AND CROSS CONTAMINATION

# Plasmid-Mediated Colistin Resistance in Brunei Darussalam: A Cause for Concern?

Md Haziq Fikry Hj Abd Momin Department of Laboratory Services, Ministry of Health, Brunei Darussalam

The use and misuse of antibiotic in humans and animals has contributed to an advancing crisis in antibiotic resistance. A major problem is when the treatment of common infections is now compromised. This has led to the repurposing of old antibiotics particularly for Gramnegative infections. Colistin is one such drug considered as a treatment of last resort the treatment for multidrug resistant (MDR) bacterial infections. Recent reports from China have identified the emergence of a new plasmid-mediated mechanism of colistin resistance (MCR-1) circulating in food animals, humans and the environment. Regrettably, *mcr* genes and plasmids have rapidly disseminated worldwide and extensively in South East Asian countries (Cambodia, Laos, Malaysia, Singapore, Thailand and Vietnam). We have recently shown this also in Brunei Darussalam.

Phenotypic and molecular analysis of clinical human and veterinary strains of *Escherichia coli* present in Brunei Darussalam showed a very high prevalence of existing *mcr-1* genes and novel variants. Of great concern is the horizontal transmission of the gene to other bacteria with additional mechanisms of multidrug resistance genes. Although reports have shown that food producing animals may act as significant reservoirs and a gateway to the human food chain. Rather than attributing blame, interventions should be focused on improved understanding of the transmission dynamics and a unified collective reduction in total antibiotic use.

With the increasing threat of resistant bacteria in the farming, healthcare, environmental and cultural activities in Brunei Darussalam, implementing the 'One Health Approach' would surely be valuable. The One Health Approach recognizes that the health of humans, animals and the environment are closely linked and the overall goal to reduce the consumption of antibiotics in each will be beneficial. This requires national and global action plan that incorporate enhanced surveillance, development of rapid diagnostics, effective antimicrobial stewardship programs and restricted use of agents such as colistin in human, veterinary and agricultural practices.



### FOCUS: LATEST TECHNOLOGIES IN DIAGNOSTICS

# Molecular Genetics Microarrays in Disease Diagnostics

Loh Yung Kiang EUROIMMUN (SEA) Pte Ltd

Molecular genetic analysis is gaining new momentum in diagnostics as the genetic components behind many diseases such as coeliac disease, thrombosis, Alzheimer's diseases, ankylosing spondylitis and others have been characterized. This paved the way for the development of specialized diagnostics microarrays such as EUROArray to analyze the genetic susceptibility through highly sensitive and specific detection of disease-associated alleles. The EUROArray system is designed to greatly improve molecular genetic analysis in diagnostic laboratories: (i) innovative microarray technology employing sophisticated EUROArray constellations with integration of multiple controls systems to ensure unambiguous identification of relevant alleles and subtypes; (ii) direct procedure for DNA extraction which eliminates the DNA isolation step that drastically reduces hands-on time and material costs; and (iii) the repertoire of diagnostic assays (e.g., HLA-B27, HLA-DQ2/DQ8, FV/ FII+/ MTHFR, heomochromatosis, APOE, HPV, sexually transmitted diseases, and so on).

Sexually transmitted infectious (STI) agents are spread predominantly by sexual contact through vaginal, anal and oral sex. More than 1 million STIs are acquired everyday worldwide. Timely detection of these pathogens and subsequent treatment can prevent consequential damage, which can lead to severe chronic diseases or infertility. In addition to the direct consequences for the patient, infection with most of the above pathogens during pregnancy can lead to intrauterine death, premature birth or damage to the fetus. Many pathogens can also be transmitted to the newborn during birth, causing severe postnatal infections. PCR-based direct detection is useful for detection of STI pathogens that are difficult or impossible to cultivate. Low titre pathogens can also be reliably identified during the amplification of the pathogen DNA. A combined multi-parameter detection of several pathogens is especially useful in cases such as clarifying ambiguous clinical findings, identifying asymptomatic infections as part of pregnancy healthcare, and identifying multiple infections.



### FOCUS: LATEST TECHNOLOGIES IN DIAGNOSTICS

# *Mycobacterium tuberculosis* 'Dormancy' Antigens: Novel TB Diagnostic Biomarkers

Dr Nor Azian Hj Hafneh Department of Laboratory Services, Ministry of Health, Brunei Darussalam

The success of *Mycobacterium tuberculosis* (*M. tuberculosis*) as a highly adaptable human pathogen relies upon its ability to switch to dormancy or non-replicating persistence (NRP) and establish an infection despite the assaults of host's immune system and hostile living microenvironment. The survival strategies employed by the pathogen depend on transcriptional reprogramming, metabolic alteration and development of phenotypic resistance to antimicrobial agents. Dormant mycobacteria are of particular interest; since they are believed to be associated with latent tuberculosis infection (LTBI) and persisting infections. One of the research priorities includes identifying the panoply of genes or pathways involved in dormancy that will progress our understanding on LTBI and also potentiate as candidate vaccines and biomarkers for diagnosis of *M. tuberculosis* infection.



# Evaluation of Serum Protein Electrophoresis Reports in Clinical Chemistry Laboratory

Dk Siti Yusrima Caesarina Pg Hj Md Yussof

Clinical Chemistry Laboratory, Clinical Laboratory Services, Department of Laboratory Services, Ministry of Health, Brunei Darussalam

### INTRODUCTION

Serum protein electrophoresis (SPE) is a technique used to separate and quantify monoclonal paraproteins in clinical laboratories. Clinicians use SPE results to identify patients with protein disorders, particularly for diagnosis and monitoring of multiple myeloma.

### OBJECTIVE

To audit the serum protein electrophoresis results in clinical chemistry laboratory.

### MATERIALS AND METHODS

Sebia Capillarys 2 electrophoresis is an automated system used in clinical chemistry laboratory, RIPAS Hospital. Depending on the bands seen, a follow-up tests of capillary and gel immunofixation electrophoresis (IFE) will be performed for confirmation. The capillary immunofixation is performed using the same system, whereas the gel immunofixation is performed using Sebia Hydrasys 2 system. The patient information, SPE and IFE reports are then tabulated in an excel sheet.

### RESULTS

A total number of 268 samples were requested for SPE from January to October 2017. 191 (71.3%) samples were analysed for immunofixation electrophoresis. 120 (62.8%) samples were analysed using gel electrophoresis, 64 (33.5%) samples using capillary electrophoresis and 7 samples (3.7%) went on to both gel and capillary electrophoresis. Hematology unit has the highest request (n=113, 42.2%) with a positive results of 67.9%. Immunoglobulins IgG lambda and IgG kappa are the most common result with 28.6% and 25.9% respectively.

### CONCLUSIONS

The automated Sebia Capillary 2 electrophoresis system is a fast technique for SPE study with minimal operator skill required. However, a dual system with the Sebia Hydrasys 2 system for gel immunofixation electrophoresis is the best and effective practice for the identification and confirmation of bands, especially from the hematology unit, which has the highest request and some undefined bands.



# Tumour Marker Requests in 2016

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### OBJECTIVE

Tumour markers are used for screening, diagnosis, prognosis, monitoring and detection of early disease recurrence. There has been an increasing number of tumor marker requests over the years. This study will look into the patterns of the sample requests for the year 2016.

### MATERIALS AND METHODS

Data extraction from BruHIMS was performed for the period 1/1/2016 to 31/12/2016 on samples analysed in RIPAS Clinical Chemistry laboratory. We examined the following tests in serum: AFP, CEA, CA125, CA199, total PSA (TPSA), free PSA (FPSA), and hCG. Patient details are de-identified and anonymised; only gender, age, ordering location and numeric results were used for this study. Data analysis was done using Microsoft Excel and SPSS Statistics.

### RESULTS

The highest tumour marker requested is AFP (18.9%). This is followed by CEA (15.1%), hCG (14.6%), CA199 (11.8%), TPSA (11.1%), FPSA (10.8%), CA125 (10.5%) and CA153 (7.3%). Most of the tumour marker requests came from wards and clinics in RIPAS hospital at 73.6%. This is followed by PMMPMHAMB Hospital (8.0%), Health Centres (6.6%), SSBH Hospital 6.5%), PIHM Hospital (4.4%) and Rimba Dialysis Centre (0.9%).

### CONCLUSIONS

For the most requested tumor marker AFP, the top three requesting locations are gastroenterology & hepatology (52.1%), unspecified locations (5.8%) and gynaecology (3.3%). This is expected as AFP is used in the monitoring of hepatocellular carcinoma in hepatic conditions such as chronic hepatitis B.



# Maintaining Quality in Clinical Chemistry Laboratory

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### OBJECTIVE

As part of the laboratory's effort to continuously provide accurate and reliable patient results, a quality monitoring system has been adapted into the work process. This is important in ensuring patient safety. The two monitoring systems are Internal Quality Control (IQC) and External Quality Assurance (EQA) or Proficiency Testing (PT). In addition, a method validation is required to verify that a specific assay is suitable for its intended use. One of the method validation protocols is linearity. This study aims at looking into the steps involved in these processes in ensuring that the quality in Clinical Chemistry Laboratory is maintained.

### MATERIALS AND METHODS

RIPAS Hospital Clinical Chemistry laboratory's standard operating procedures (SOPs) are used in this study. Supporting data is extracted from the laboratory's quality control data management software, Unity Real Time<sup>®</sup> (Bio-Rad Laboratories). Documents from SAC-SINGLAS ISO15189:2012, CLSI and Westgard guidelines are additionally used as references.

### RESULTS

There are a total of 121 tests performed in Clinical Chemistry Laboratory. There are 25 IQC materials, 14 EQA programs subscribed and 10 linearity kits in use. 52% of the IQC materials are run daily and the others are run as required in batch tests. For EQA materials, 64% are run monthly. 29% are run biyearly and 7% are run in every 4 months.

### CONCLUSIONS

We highlight the steps necessary to maintain the quality of patient results and this is in accordance to recognized practice worldwide. In total, there are 216 IQC determinations. There are 1, 621 EQA reports that need to be reviewed per year.



# Treating to Target Blood Pressure: Audit of Blood Pressure Management in Diabetic Patients at RIPAS Hospital

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### INTRODUCTION

The mainstay of blood pressure (BP) treatment in diabetic patients is with angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs). The National Diabetes Guideline (NDG) of Brunei Darussalam recommends a target BP of  $\leq$ 130/80mmHg irrespective of existing microvascular or macrovascular complications. However, the NICE (CG127) guideline recommends target BP of  $\leq$ 140/90mmHg in patients without microvascular or macrovascular complications, and a tighter target BP of  $\leq$ 130/80mHg in those with microvascular or macrovascular complications.

### OBJECTIVES

This audit aims to determine the: (i) percentage of patients who meet the NDG's target BP of  $\leq 130/80$  or the new NICE guideline's target BP of  $\leq 140/90$ ; (ii) number of BP lowering agents required to achieve target BP; and (iii) percentage of patients who are on the recommended classes of BP lowering agents

### METHOD

The sample population consisted of all diabetic patients that attended the Diabetes Centre, RIPAS Hospital over the Ramadhan month of May 2017. Diabetic patients who were not on any BP treatment were excluded.

### RESULTS

149 patients were included in the audit where 63(37.7%) and 95(56.9%) met the target BP of  $\leq$ 130/80 and  $\leq$ 140/90, respectively. An average of two agents were needed to achieve target BP. More than 80% of the patients were treated with either an ACE inhibitor or ARB.

### CONCLUSION

Just over a third of patients met the target BP as suggested by the NDG and over 80% are on an ACE inhibitors or ARB.



# Gynaecologic Cytologic Histologic Correlation - A Three Year Study

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### INTRODUCTION

Pap smear testing and cervical screening programmes brought a dramatic decrease in morbidity and mortality of cervical cancer. Cytologic-histologic correlation is a laboratory based comparison of all Pap test reports interpreted as high grade squamous intraepithelial lesion (HSIL) and above. It helps to monitor the performance of the laboratory to improve overall quality. The study was conducted for the first time to perform the correlation for a three year period (2014-2016).

### OBJECTIVE

This study aims to evaluate the pattern of cervical cytology and its correlation with biopsy findings.

### MATERIAL AND METHODS

This is a 3 year retrospective and prospective study. All Pap test reports from 1/1/2014-31/12/2016 were retrieved from lab information system. Results were analysed on Excel. Only cases with a cervical biopsy were included for correlation. Statistical analysis was done by MedCalc statistical software. Sensitivity and positive predictive value (PPV) of the Pap smear test were calculated using cervical biopsy as the gold standard.

### RESULTS

29,946 Pap smears were analysed. The results show 95.7 % were negative for intraepithelial lesion or malignancy (NILM), 2.08 % ASCUS and 0.2 % were unsatisfactory. 0.98 % LSIL, 0.50 % HSIL and 0.30% malignancy (0.08% squamous cell carcinoma, 0.19% adenocarcinoma and 0.03% adenosquamous carcinoma). In our study, sensitivity and positive predictive value of pap smear in diagnosing epithelial lesion and malignancy were 84.81% and 87.01%, respectively.

### CONCLUSIONS

Cytologic-histologoic correlation is a powerful cytopathology quality assurance tool. Our Pap results and cytohistologic correlation was at par with the rest of the international studies.



# Phylogenetic Analysis of Dengue Virus Isolated in Brunei from June 2015 to July 2016

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### BACKGROUND

Dengue is an emerging mosquito-borne viral infection with well-known endemicity in Southeast Asia, including Brunei Darussalam. There are four serotypes of dengue virus (DENV-1 to DENV-4), each of which is further subdivided into distinct genotypes. There is a lack of available information regarding the genotypes of dengue virus strains circulating in Brunei. Therefore, we conducted an investigation of dengue infections throughout Brunei using samples collected from June 2015 to July 2016 in order to describe the genotype pattern of dengue viruses in Brunei.

### MATERIALS AND METHODS

A total of 115 serum samples confirmed as NS1 dengue positive through serology testing were selected. Real time-polymerase chain reaction was performed on extracted viral RNA of the samples to obtain the serotypes. Additionally, these serum samples were sent to Environmental Health Institute, National Environment Agency, Singapore for genotype analysis and data shared on UNITEDengue platform.

### RESULTS

Serotyping showed that all four serotypes were present during this time period with DENV-1 as the dominant serotype. A total of 35 sequences were obtained from the sample population (28 of DENV-1, 2 of DENV-2 and 5 of DENV-3). The DENV-1 isolates were grouped into Genotype I and II, DENV-2 into Cosmopolitan clade I and DENV-3 into Genotype I and III with DENV-1 Genotype I as the most predominant strain.

### CONCLUSION

Phylogenetic analysis revealed that the DENV-1 isolates were most closely related to viruses isolated in Singapore and Malaysia since 2013 and associated with the 2005 Singapore outbreak.



# Brunei Dengue Virus Characterisation Study from August 2016 to June 2017

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### BACKGROUND

Dengue infection has always been a major public health threat globally including Brunei Darussalam. The re-emergence of dengue is increasingly associated with a shift in epidemiology. Dengue fever can be caused by any of four (DENV-1 to DENV-4) genetically related but antigenically distinct dengue virus (DENV) serotypes. Dengue virus characterization has been shown to be very important in determining the origin, evolution and geographic distribution of the dengue virus serotyping and genotyping study. In this study, we characterise the dengue virus isolated in Brunei from the period of August 2016 to June 2017.

### **MATERIALS & METHODS**

A total of 100 serum samples from suspected dengue patients (NS1 antigen or IgM positive) were collected from August 2016 to June 2017. Molecular analysis of dengue virus serotype and dengue virus nucleotide sequences, followed by sequence alignment and phylogenetic analysis of the dengue virus envelope (E) protein were performed and data submitted to UNITEDengue.

### RESULTS

The serotype pattern fluctuated between October 2016 and February 2017. DENV-1 continued to drive the dengue transmission in subsequent months and accounted for 74.3% of the total serotyped cases (March to May 2017). Within DENV-1 population, genotype Ia continues as the dominant strain (77.3%). Identical sequences (at E gene level) were observed in different districts - Muara, Temburong & Belait. DENV-1 genotype Ia in Brunei is genetically distinguishable from genotype Ia strains reported in Malaysia and Singapore.

### CONCLUSION

DENV-1 continued as the dominant strain within the population during the first half of 2017 in the country.



# Sensitisation to Aero/Food Allergens and Association with Allergic Diseases in Brunei in 2015/2016

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### OBJECTIVES

The aims of the study were to identify the demographic pattern of allergy patients, determine the spectrum of allergen sensitisation, determine association between different allergen sensitisations with allergic diseases, determine the association between total IgE and specific IgE, and visualize the pattern of specific IgE titre across different allergic diseases.

### MATERIALS AND METHODS

This retrospective cohort study includes all patients who were subjected to blood specific IgE testing from January 2015 to December 2016 in the Department of Laboratory Services, RIPAS hospital, Brunei Darussalam. Data collected includes the specific IgE titre, total IgE titre, demographics and patient histories.

### RESULTS

A total of 223 patients were recorded with 170 patients sensitized to one or more allergen. Levels of house dust mite sensitisation were the highest in this population (n=113). The most prevalent aeroallergen was *Dermatophagoides pteronyssinus* (d1; n=98 positive results), followed by *Dermatophagoides farinae* (d2; n=88) and *Blomia tropicalis*, (d201; n=62). Shrimp (f24; n=68) was the most common food allergen, followed by peanut (f13; n=47) and egg white (f1; n=43). There was a strong significant correlation between atopic dermatitis and top 5 allergens (d1 *D. Pteronyssinus*, P<0.001; d2 *D. farina*, P<0.001; d201 *B. tropicalis*, P=0.001; f13 peanut, P<0.001; and f24 shrimp, P=0.001). Total IgE has a very strong significant correlation with specific IgE (P<0.001).

### CONCLUSIONS

There was a dominance in sensitisation to house dust/storage mite allergens in Brunei coinciding with the regional trend. Atopic dermatitis was the only allergic disease significantly associated with sensitisation to any of 5 the most common allergens.



# Towards Breast Cancer Profiling - Exploring the Potential Roles of Candidate Genes in Breast Cancer

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### OBJECTIVE

The discovery of comprehensive somatic genomic abnormalities has led to the molecular profiling of many cancer types and contributed to the development of targeted therapies. This study aims to develop the Brunei Cancer Genome Atlas, which is an atlas of genomic mutations in specific cancers of the Bruneian population, particularly in breast cancer.

### MATERIAL AND METHODS

To date, this study has evaluated the patient characteristics, performed RNA extraction from breast tumours by laser capture microdissection (LCM), as well as investigated the mRNA and protein expressions of Syk, Btk, and the hippo pathway components YAP and Mst1 in breast cancer by real-time quantitative polymerase chain reaction (qRT-PCR) and immunohistochemistry.

### RESULTS

Patients diagnosed with breast cancer were all female at a mean of 54 years old (SD: 43-65) with high expression of estrogen and progesterone receptors (ER/PR) in majority of them. Microdissected cells yielded a sufficient amount of RNA allowing for downstream experiments. The expression levels of Btk and YAP were markedly increased, whereas the Syk and Mst1 expression levels were reduced in invasive breast tumours.

### CONCLUSION

A genetic pattern in Bruneian breast cancer patients is likely to emerge which warrants further systematic genomic investigation in a larger number of breast cancer cases.



# *BRCA1* and *BRCA2* Mutation Analysis in Breast Cancer Patients in Brunei Darussalam

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### OBJECTIVE

This study investigates mutational analysis of *BRCA1* and *BRCA2* genes in breast cancer patients in Brunei Darussalam.

### MATERIAL AND METHODS

Blood samples are taken from consented breast cancer patients from The Brunei Cancer Centre (TBCC) diagnosed from 2001 to 2015. Mutational analyses of *BRCA1* and *BRCA2* coding region are conducted using polymerase chain reaction (PCR) and Sanger dideoxy sequencing using forward and reverse primers on an 8 capillary 3500 Genetic Analyzer (Applied Biosystems). Variant Reporter Version 1.0 is used to perform variant analysis. Experiments are conducted twice as a validation method.

### RESULTS

Preliminary analysis of thirty index cases shows the majority of breast cancer patients in Brunei Darussalam were Malays (n=23, 76.7%), Chinese (n=3, 10%) and others (n=4, 13.3%), reflecting the population. The mean age of diagnosis was 48.5±9.00 years. Ten index cases (33.3%) had family history of breast or ovarian or other cancers in first-degree relatives, and six (20%) had them in second-degree relatives. Ten deleterious insertion/deletion (indel) mutations in *BRCA2* gene were detected in ten different cases (0.33%). Various missense, synonymous and variants of unknown significance (VUS) were identified in all the cases. Nine of the indel mutations have not been validated yet.

### CONCLUSIONS

Ten deleterious indel mutations in *BRCA2* were detected in ten breast cancer cases. Large rearrangement analysis and mutational analyses of *TP53* and *PALB2* genes would provide more comprehensive mutational findings in the studied index cases. Strong family history is an indicator for breast cancer risk.



# Actin Rearrangement of Brain Endothelial Cells and Its Effect on Tight Junction Proteins during a Dengue Infection

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**Keywords:** dengue virus, brain endothelial cells, actin cytoskeleton, tight junction proteins

### INTRODUCTION AND AIM

During early infection, viruses such as dengue virus (DENV) and Japanese encephalitis virus can interact and manipulate actin cytoskeleton of host cells, leading to a variety of cellular and molecular alterations. These alterations may affect the molecular structure and morphology of endothelial cells, resulting in blood-brain barrier hyper-permeability and disruption. Our study was aimed to investigate the role of actin in early dengue infection of brain endothelial cells and the effects on tight junction (TJ) proteins, specifically occludin and claudin-5, as the infection progresses.

### MATERIAL AND METHODS

A mouse brain endothelial cell (bEnd.3) monolayer was infected with DENV type 1 or 2 at 1.5 multiplicity of infection (MOI) in a time-dependent manner. Cells were incubated with virus for 2, 4, 6, 18 & 24 hours, and 4 & 24 hours for actin and TJ proteins alteration study, respectively. The actin and TJ proteins were then detected using immunofluorescence assay.

### RESULTS

Actin thickening was observed as early as 2 hours post-infection (p.i.) with subsequent nuclear localization of actin as the infection progressed. At 4 hours p.i., cytoplasmic diffusion of occludin was observed, but not claudin-5. Significant degradation of claudin-5 was observed at 24 hours p.i. (p<0.0001) when cell rounding occurred.

### CONCLUSIONS

DENV interacts with actin during early infection and may utilize them as a transport system to the replication site. The retraction of actin resulted in the diffusion of occludin into cytoplasm, and together with claudin-5 degradation, leads to compromised integrity of brain endothelial cells.



# Liquid-Based Cytology of Villoglandular Adenocarcinoma of Endocervix - A Case Report

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### OBJECTIVES

Adenocarcinomas are the second most common type of cervical cancers in women comprising 10-20% of the cases. Villoglandular adenocarcinoma of cervix accounts for 3.7-4.8% of the cases. It is a rare histological subtype of invasive adenocarcinoma which usually afflicts young women and carries an excellent prognosis. The tumour is slow growing and conservative management is usually advised. The sub-classification of the tumour is important, as it may dictate the type of treatment to be provided and the prognosis of the cancer. Screening with Pap smear helps in early detection of pre-cancers and cancers. The prognosis of cervical villoglandular carcinoma depends upon a set of several factors, including the stage of the tumour, age of the individual, the size of the tumour, and many other factors. The aim of this report is to share a case of villoglandular adenocarcinoma diagnosed on liquid based cervical cytology. Histopathology correlation is provided.

### MATERIALS AND METHODS

Clinical data and patient details were retrieved from laboratory computer system BruHIMs (Brunei Health Information System). The case slides were reviewed and discussed with the cytotechnologist and pathologists.

### **RESULTS AND CONCLUSION**

Cytologic features of villoglandular adenocarcinoma will be shown and differential diagnosis will be discussed. Proper diagnosis of this subtype assists in conservative management of patients with villoglandular adenocarcinoma.



# Clear Cell Carcinoma in Cervical Cytology in Brunei

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### OBJECTIVE

Clear cell carcinoma (CCC) of the endometrium is a rare tumour. Clear cell is caused by intrauterine exposure to diethylstilbestrol (DES). It can also occur in postmenopausal women without exposure to DES. The aim of this report is to share about cervical clear cell carcinoma in Brunei Darussalam with the cytopathology society.

### MATERIALS AND METHODS

Data from the laboratory information system was searched from 2011 to 2015 for clear cell carcinoma in cervical cytology, and also its follow up biopsy report(s). Data of other histology reports with clear cell carcinoma was also retrieved. The slides were reviewed with the pathologist and diagnosis reconfirmed.

#### RESULTS

Clear cell carcinoma in cervical cytology and a few histology reports were found.

### CONCLUSIONS

Cases of clear cell carcinoma were found in cytology reporting. Data of clear cell carcinoma was also found in histology reporting. Therefore, the study of this rare case is shared.



# Increasing Trend of Antibiotic Resistance in Pantai Jerudong Specialist Centre, Gleneagles-JPMC and Jerudong Park Medical Centre

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### OBJECTIVE

In recent years, the rise of antibiotic resistance has become a medical concern in Brunei Darussalam which makes treatment more challenging. This leads to lengthier hospital stays and increase in the cost of healthcare. Several factors such as prolonged or inappropriate use of antibiotics, poor infection control and inadequate sanitary conditions could be the cause of antibiotic resistance. This study aims at observing the emergence and rise of antibiotic resistance in Pantai Jerudong Specialist Centre (PJSC), Gleneagles-JPMC (GJPMC) and Jerudong Park Medical Centre (JPMC).

### MATERIALS AND METHODS

Data were collected between January 2013 and September 2017. Isolates [methicillinresistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Escherichia coli*] were analysed according to location. Antibiotic susceptibility of drug-resistant bacteria were also closely monitored. Isolates are from clinical specimens, identified and tested as per standard methods. Data were obtained using WHONET software.

### RESULTS

Drug-resistant *A. baumannii*, primarily found in BNSRC and GJPMC, accounts for 95% of the total number of *Acinetobacter* infections in year 2017. These findings correlate with the data from Centres for Disease Control and Prevention. Higher number of MRSA cases are seen in Brunei Neuroscience Stroke & Rehabilitation Centre (BNSRC). These may be due to cross-infection between hospitalised patients. Linezolid is still comparable to vancomycin in the effectiveness against MRSA. Colistin sulphate remains as the last resort antibiotic treatment for MDR/XDR *P.aeruginosa* and *A.baumannii*.

### CONCLUSION

This data calls for the need of the implementation of national surveillance and stricter infection control protocols, as well as ensuring compliance to antibiotic stewardship programmes.



# An Audit on Gout Disease and Its Associated Lifestyle Diseases

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### BACKGROUND

Gout is a common form of inflammatory arthritis. It is considered a lifestyle disease. It was reported that there is an increase in its prevalence, and there is a strong relationship between diet and lifestyle with the development of gout. Gout is associated with age, males, obesity, hypertension and high purine diet. As a metabolic disorder, gout is often responsive to changes in diet, lifestyle, and medication usage.

### OBJECTIVES

The objective of this audit is to determine the demographics of patient with gout disease at Rheumatology Clinic, RIPAS Hospital, and to determine the correlation of gout patient with other lifestyle diseases.

### METHODS

This is a retrospective study using the data collected from BruHIMs. Any patients seen in Rheumatology's Clinic, RIPAS hospital from 1st January until 30th June 2017 were included in this audit. A total of 104 patients were used for this audit. Demographics data collected include age, sex, obesity, comorbidities (i.e. hypertension, type 2 diabetes mellitus, and dyslipidaemia), uric acid level and consumption of high purine diet.

### RESULTS

From this audit, gout patients in this clinic are predominantly of male sex (91.3%). Most of the patients are in the age group from 31 to 60 years old, which account for 79.8%. Patients with gout also associated with obesity (50%), hypertension (65.3%), type 2 diabetes mellitus (20.2%), dyslipidaemia (30.8%) and high purine diet (43.3%)

### CONCLUSIONS

In Rheumatology Clinic, it was noted that obesity, hypertension and high purine are associated with gout. This was also reported in other literatures which support this finding. This suggests that by lifestyles changes and the use of medication, it will help to treat the gout. In addition, by treating this metabolic syndrome, it will prevent other lifestyle diseases.



Audit of Antimicrobial Prescribing and Adherence to Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital Critical Care Medicine Guidelines in Patients Admitted to Adult Intensive Care Units in RIPAS Hospital, Brunei Darussalam

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### OBJECTIVES

Antibiotic therapy is used extensively in intensive care units, where up to 20% of nosocomial infections are acquired. Their unnecessary use contribute to resistant microbes. However, if inadequate, they are associated with significant mortality. This audit assessed antibiotic prescribing in adult intensive care units (ICUs) in RIPAS Hospital, Brunei Darussalam, and prescribing adherence to RIPAS Hospital Critical Care Medicine (CCM) guidelines.

### MATERIAL AND METHODS

Thirty-two patients admitted to medical and surgical adult ICUs at RIPAS hospital were randomly selected over a 3-month period (April to June 2017). Antibiotics must be prescribed by critical care medicine (CCM) doctors. Excluded criteria were patients electively admitted to surgical ICU for post-operative observation and patients who did not receive antibiotics. Data collection included the first five antibiotic drugs prescribed by CCM doctors and whether prescribing was empirical or definitive. CCM guidelines adherence were determined by appropriateness of antibiotic prescribing, de-escalation, stopping within time limit and antimicrobial sensitivity.

### RESULTS

108 antibiotics prescribed to thirty two patients were audited. Prescribing was empirical in 63% and definitive in 37%. They were mostly prescribed for ventilator-associated pneumonia (26%), followed by community-acquired lung infections (25%). Cultures were positive in 71% of antibiotic prescribed, with 63% isolated from endotracheal tube or sputum and 31% from bloodstream. Almost all (98%) antibiotic prescribed were sensitive to isolated microbes. However, two definitive cases of multi-drug sensitive *Acinetobacter baumanii* were treated with Colistin antibiotic, which is reserved for multi-drug resistant pathogens. Adherence to CCM guidelines were varied. Antibiotic therapy was appropriate in 89 out of 108 (82%) cases. Most of them (78 cases or 72%) were discontinued within time limit (five to seven days). Only 5% (5 out of 108 antibiotics) were de-escalated, even with antimicrobial sensitivities available.



Tailoring antibiotic choice to antimicrobial sensitivity and treatment duration are important to avoid growth of resistant pathogens. Prescribing must be judicious, especially where pathogens are classically multi-drug resistant, including *Acinetobacter baumanii*. Thus, antimicrobial prescribing adherent to CCM guidelines must be further improved.



# Comparison of LBC Pap Test with Nucleic Acid Probe Test (BD Affirm VPIII) for the Detection of *Trichomonas vaginalis* Infection

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### INTRODUCTION

Trichomoniasis is a sexually transmitted infection (STD) caused by *Trichomonas vaginalis* protozoa. It is commonly associated with other STDs and is a marker of high risk sexual behaviours. It is associated with premature rupture of membranes and post-partum endometritis. It is also a high risk factor for acquiring and transmission of human immunodeficiency virus (HIV) infection including newborns. Diagnosis, treatment and control of *T. vaginalis* infection is essential. In the hands of trained cytotechnologists, sensitivity and specificity of LBC Pap test for *Trichomonas* is 60% and 95%, respectively. Affirm VPIII (BD) is a non-amplified nucleic acid probe hybridisation test developed for the detection of *T. vaginalis* in symptomatic women. This study was designed to compare LBC Pap test with the BD Affirm VPIII for the detection of *T. vaginalis* infection.

### OBJECTIVE

To assess the sensitivity and specificity of detection of *Trichomonas vaginalis* by liquid based Pap smear cytology compared with BD Affirm test.

### **MATERIAL & METHODS**

The retrospective and prospective studies are being conducted on Pap test received from 01/01/2017 till 31/12/2017 showing *Trichomonas* infection. Only those patients with both Pap test and pre-treatment molecular testing done will be included in the study. Positive and negative predictive values, sensitivity and specificity of both the tests will be compared. The study is still in progress.

### **RESULTS AND CONCLUSION**

An average incidence of *Trichomonas* in Pap smear is about 1.1%. The study is still ongoing till the end of 2017, and the results will be presented.



# The Role of Point of Care Testing (POCT) Section at Clinical Laboratory Services, Brunei Darussalam

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### INTRODUCTION

Point of Care Testing, which is also known as bedside testing, is a clinical laboratory test in the clinic or intensive care unit where patient is receiving care, rather than at the central or main laboratory. It is designed to provide rapid test results, thus shortening turnaround time. Examples of POCT offered are: urinalysis, pregnancy test, glucose test using glucometer, *Helicobacter pylori* breath test, ketone test and blood gas analysis. Where these POCT have been around in Brunei government hospitals and health clinics, the quality management system to ensure accurate and reliable test results produced by operators is not monitored by the laboratory, hence impacting doctor's clinical decision and patient's safety.

### OBJECTIVE

The objective is to implement POCT quality assurance program in Brunei Darussalam in a stage by stage manner for health centres and hospitals in Brunei, with the establishment of POCT Section under Clinical Laboratory Services, Ministry of Health, Brunei Darussalam.

### **MATERIALS AND METHODS**

Due to Joint Commission International requirement of POCT, the POCT committee is formed, which later came to the decision of creating a new section called POCT. The policy on POCT quality assurance and procedures on specific tests are created, which aid the performing facilities to make their own programs and procedures. With these policies and procedures, POCT section scope of work is implemented.

### RESULTS

POCT quality assurance program has been fully implemented and established in Pengkalan Batu Health Centre. Other government hospitals and health centres will soon be included for the implementation of the POCT program.

### CONCLUSION

POCT program is an essential part of patient's safety to ensure the results produced are accurate and reliable.