SQU Med J, May 2011, Vol. 11, Iss. 2, pp. 304-310, Epub. 15th May 11

Oman International Conference on Laboratory Medicine – Part II

Sultan Qaboos University

9 – 11th November 2010

المؤتمر العالمي العُماني لطب المختبرات – القسم الثاني

جامعة السلطان قابوس

9–11 نوفمبر 2010

Abstracts Histopathology and Microbiology Sessions

ABSTRACTS HISTOPATHOLOGY SESSIONS

Fine Needle Aspiration Cytology of Pancreaticobiliary Tract

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Fine needle aspiration (FNA) is the method of choice for the diagnosis of pancreatic mass/cystic lesions. FNA may be performed percutaneously or under endoscopic ultrasound (EUS) guidance. Clinical and radiological examinations are not reliable methods to distinguish benign/inflammatory pancreatic disease from a carcinoma. FNA provides an accurate preoperative diagnosis for optimal and timely patient management. Most solid neoplasms are at an advanced stage at the time of detection and are mostly high grade adenocarcinomas which are readily diagnosed on cytology. Even if the tumour is unresectable, a tissue diagnosis is essential for the initiation of an appropriate treatment protocol. Low grade carcinomas can prove to be a challenge and are often differentiated from reactive ducts by certain features. Benign acinar cells can be differentiated similarly. Pancreatic endocrine neoplasms can likewise be distinguished by features peculiar to them. Cysts of the pancreas include congenital, developmental, inflammatory and neoplastic lesions. The cytology of pseudocysts are well characterised. Cystic neoplasms include serous cystadenomas, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms, solid pseudopapillary neoplasms and cystic neuroendocrine tumours. Accurate preoperative diagnosis is critical, since this will determine the type of intervention needed, but clinical and imaging criteria are not consistently reliable. The use of FNA with cyst fluid analysis for amylase and tumour markers such as carcinoembryonic antigen (CEA), has improved the preoperative diagnosis of these lesions. The main diagnostic dilemmas in cytology specimens are distinguishing nonneoplastic from neoplastic lesions (particularly mucinous lesions) and benign neoplasms from borderline or malignant neoplasms. Cytology alone can distinguish mucinous from nonmucinous lesions and diagnose specific entities, such as solid-pseudo papillary tumours, cystic pancreatic endocrine tumours and carcinomas when the cell sample is sufficient, but lacks sensitivity due to sampling problems.

Molecular Pathology Targeted Therapeutics Leading the Paradigm Shift for Pathology

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The availability of an expanding armamentarium of antibodies and small molecule inhibitors has transformed the way we practice oncology. By targeting key oncogenic genes and pathways, many solid tumours can now be therapeutically addressed in a more focused and clinically efficient manner. This revolution in oncology treatment has also deeply transformed the way we practice pathology. Indeed, correct stratification of patients often depends on the immunophenotype or genotype profile of a single tissue-based biomarker. In our experience, the introduction of molecular testing in a traditional molecular histopathology operation multiplies the overall volume of tests by several fold, leading to substantial revenue gains. This also has a repercussion in the overall volume of testing in pathology departments. In our setting, the volume of molecular diagnostics after the validation of tests for targeted therapeutics amounts to an additional 10–20% increase in the overall testing volume. Targeted therapeutics is invariable changing the way we look at the taxonomy of cancer. We are currently witnessing the dawn of what appears to be a targeted therapeutics-oriented diagnostic paradigm in tumour pathology. The presentation provides several examples to this effect, showing both current and future trends that have a significant impact in the classification and characterisation of diseases. The main consequence of this new approach, however,

has to do with the specific weight of pathology in overall diagnostic and therapeutic decision-making and, as a consequence, the way pathology and pathologists are perceived by the medical community, by our patients and by the industry. From the 1960s to perhaps the end of the 20th century, surgical pathology established itself as a central and fundamental discipline in clinical medicine. However, from a phenotypic-clinical framework of diagnosis, we are shifting into a phenotypic-molecular-clinical dimension. As a result of this shift, the process leading from morphological surgical pathology to therapeutic decision-making includes an area of expanding molecular diagnostic complexity. Increasingly so, surgical pathology departments understand that maintaining professional relevance requires not only passive knowledge of these techniques (i.e., when or how to order them), but active molecular diagnostic skills for molecular assay validation and interpretation to maintain key diagnostic relevance. Interestingly, the development of therapeutic pathology is also broadening the scope of pathology practice and, in particular, the role of pathologists in the pharmaceutical and the diagnostic industry. Therefore, it is the time for surgical pathology to embrace molecular pathology by integrating it, when indicated, into daily clinical practice at sign out. To do so, we should revisit and ensure its teaching in our residency programs—all of this building on the role of molecular pathologists certified by professional organisations as invaluable bridges between pathologists' roles as responsible diagnosticians and as clinical scientists. In essence, the systematic embracement of molecular pathology will allow pathology departments to regain a central role at the core of the diagnostic and therapeutic endeavour.

Molecular Pathology–ErbB2 Testing: FISH (flourescence in situ hybridisation), CISH (chromagen in situ hybridisation), SISH (silver in situ hybridisation) and HIC (immunohistochemistry) - What is their relevance?

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A better understanding of "molecular markers" in recent years has allowed the characterisation of a group of drugs, primarily antibodies and small molecule inhibitors, developed against a specific target based on its important function in cancer. These treatments are "personalised", i.e. the target analysis will indicate the patient's likely chance of response (Personalised Medicine 2009; 6:465–8). Of these, the use of the antibody trastuzumab or the small molecule inhibitor lapatinib, targeting Her-2 for the treatment of breast cancer, is arguably the best established example to date. Which is the most accurate manner of analysing Her-2 status prior to treatment is still a matter of some controversy. A few years ago, we and others proposed a cost-effective manner of analysing Her-2 using IHC and complemented by FISH in selected cases (Modern Pathology 2003; 16:79–85 and Human Pathology 2003; 34:362–8). More recently, the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) Guidelines have tried to present a homogeneous approach to Her-2 testing (Journal of Clinical Oncology 2007; 118–45), although authoritative opinions against this approach have been voiced (Journal of Clinical Oncology 2009; 1323–33). We shall review this body of evidence, which will be complemented with other more recent technical approaches that may be relevant in years to come. Finally, the increasingly important issue of Her-2 testing in gastric cancer will also be reviewed.

Molecular Pathology: A hospital-based platform for translation research

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Formalin fixed and paraffin embedded tissue (FFPE) collections in pathology departments are the largest resource for retrospective biomedical research studies. Based on the literature analysis of FFPE related research, as well as our own technical validation, we present the Translational Research Arrays (TRARESA), a tissue microarray centered, hospital based, translational research conceptual framework for both validation and/or discovery of novel biomarkers. TRARESA incorporates the analysis of protein, DNA and RNA in the same samples, correlating with clinical and pathological parameters from each case, and allowing a) the confirmation of new biomarkers, disease hypotheses and drug targets, and b) the postulation of novel hypotheses on disease mechanisms and drug targets based on known biomarkers. While presenting TRARESA, we illustrate the use of such a comprehensive approach. The conceptualisation of the role of FFPE-based studies in translational research allows the utilisation of this commodity, and adds to the hypothesis-generating armamentarium of existing high throughput technologies.

Immunohistochemistry: Basic aspects

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The process of implementing immuno-histochemical tests in the diagnostic laboratory has been greatly simplified by the availability of standardised re-agents, instruments, and assay protocol from commercial manufacturers. However, researchers and diagnosticians who wish to develop new immuno-histochemical assays, or explore new applications for existing tests, must carefully consider the methods of tissue preparation and the reaction conditions for each assay step in order to obtain clear, specific antigen signals and to minimise non-specific reactions.

Fine Needle Aspiration Cytology of the Thyroid

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Fine needle aspiration (FNA) is an important widely used investigative procedure for both palpable and ultrasonographically detected thyroid nodules. FNA is a reliable triage method for identifying patients requiring surgery. The direct smear technique is highly sensitive and specific. A trained cytopathologist is skilled in recognising the different types of non-neoplastic and neoplastic cells in these FNAs. The main diagnostic categories of fine needle aspiration of the thyroid are benign and functional and include the thyrotoxic goitre, nodular goitre, hyperplastic nodules, thyroiditis, acute suppurative thyroiditis, subacute thyroiditis (de Quervain's disease) and chronic lymphocytic thyroiditis (Hashimotos disease). Tumours of the thyroid such as follicular adenoma/carcinoma, papillary carcinoma, medullary carcinoma and lymphoma infiltrating the thyroid and metastatic tumour also can be diagnosed by FNA. The potential Tiered Classification Scheme proposed in the 2007 National Cancer Institute (NCI) Thyroid Fine Needle Aspiration, State of the Science, Conference clearly stratifies the means of identifying the different grades and types of malignancies in the thyoid gland and the benign lesions, such as those lesions with a low risk of malignancy listed below. This category includes but is not limited to following terms: nodular goitre, chronic lymphocytic thyroiditis and hyperplastic/adenomatoid nodule in goitre. Patients with a benign nodule are followed by clinical and periodic radiological examination and some patients may undergo repeat FNA due to an increase in the size of nodule. Follicular lesion of undetermined significance/ atypia of undetermined significance are also classified. This is a heterogeneous category that includes cases that cannot be classified as either benign or follicular neoplasm. Follicular-neoplasm/ suspicious for follicular neoplasm is also defined. Most patients with this diagnosis undergo lobectomy/hemithyroidectomy and a definite diagnosis of adenomatoid nodule versus adenoma versus carcinoma is rendered on surgical pathology examination. Another category is that termed suspicious for malignancy for papillary, medullary carcinomas, lymphomas, metastatic cancers and anaplastic cancers with marked necrosis. The clearly malignant category and the non-diagnostic categories are the last two to be classified as lesions which can be diagnosed on FNA. The non-diagnostic cytopathological features of lesions are also well known and must be learned by cytopathologists. Ancillary studies on thyroid aspirates are indicated in cases of suspected medullary carcinoma, anaplastic carcinoma, metastatic carcinoma, lymphoma, parathyroid lesion and indeterminate or suspicious aspirates. Specific ancillary studies to be performed for each indication and sample preparation for each study have been documented by the NCI thyroid Fine Needle Aspiration State of Science Conference.

ABSTRACTS MICROBIOLOGY SESSIONS

Antimicrobial Resistance - A global perspective

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The development and spread of antimicrobial resistance has been recognised since shortly after antibiotics were used in clinical practice. In recent years, antimicrobial resistance has been become more of a problem due to 'macro' reasons (the widespread use of antibiotics, complexity of health care, patient movement and global travel). In addition, 'micro' reasons for this problem occur, such as genetic linkage and mechanisms for horizontal transfer of resistance genes between organisms. The relevance of 'macro' and 'micro' influences on antibiotic resistance will be discussed using current and historical examples. Finally, there is only slow development of new antimicrobials in relation to the speed of resistance development and spread. Measures to tackle antibiotic resistance require action at international/national and local level to be successful. These measures will be discussed.

NDM-1 Producing Klebsiella Pneumonia in Oman

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The rapid international spread of Klebsiella peumoniae strains that are carbapenem resistant is a major concern. Treatment options are severely limited and are a great challenge for infection control. Recently two cases of NDM-1 K. pneumoniae have been identified in Oman; this mandates urgent actions/measures to limit the spread of this strain and any other resistant bacteria.

Emergence of Resistance among Gram Negative Pathogens

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Antimicrobial resistance is one of the world's most pressing public health problems of today. Multiresistant Gram-negative infections are not only the cause of infections for hospitalised patients, but also for people in the community. Mechanisms of resistance are variable and options for treatment are limited. Clinical diagnostic laboratories are of variable capabilities and may not always be able to identify isolates with novel mechanisms of resistance which may lead to delays in diagnosis. The versatility with which these pathogens are able to produce resistance is quite impressive and extremely intimidating and challenging to the medical community. The emergence of extended-spectrum beta-lactamases (ESBLs) as a mode of resistance and their presence on transferrable plasmids has increased their presence within the Enterobacteraceae species and allowed for easy transfer between patients and between patients and health care workers. Over 800 ESBLs have been identified in the Lahey database todate and many unidentified genes still exist. The explanation of the emergence of this resistance is not clearly identified; however, the wide misuse of antimicrobials in medicine and agriculture have most likely resulted in pressure selection of bacteria resistant to the microbiologic activity of these agents. In addition, poor compliance of health care workers with infection control measures may also play a role in the spread of these pathogens in the health care setting.

These resistant bacteria fail to respond to treatment, resulting in prolonged hospitalisations, increased cost and increased risk of death.

Multiplex Polymerase Chain Reaction in Diagnosis of Viral Infections: The Qatar experience

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Multiple polymerase chain reaction (PCR) is a variant of PCR which enables simultaneous amplification of many targets of interest in one reaction by using more than one pair of primers. In diagnostic microbiology, multiplex PCRs are designed for detection of multiple microbial agents in a clinical sample. Our laboratory has recently introduced four commercially available multiplex PCRs for the diagnosis of viral infections. In the respiratory assay, 10 viruses (influenza A, influenza B, parainfluenza virus types 1 to 4, coronaviruses, human metapneumovirus, rhinovirus, respiratory syncytial virus, adenovirus, enterovirus and bocavirus) are detectable in respiratory samples. Multiplex PCR for acute infections of the central nervous system detects the herpes simplex virus types 1 and 2, varicella zoster virus, enterovirus and mumps virus mainly in cerebrospinal fluid. The other two multiplex PCRs are for the diagnosis of viral infections in immunocompromised patients (the cytomegalovirus, Epstein-Barr virus and adenovirus) and the detection of viruses which cause fever and skin rash (measles, enterovirus, human herpes viruses 6 and 7, and parvovirus B19). Preliminary data on the frequency of these viruses in clinical samples submitted to our laboratory will be presented. There is evidence to show that this approach in diagnostic molecular virology is both economical and reduces turnaround time when compared to single PCR assays of the same viruses.

Molecular Characterisation of Rotavirus Strains Circulating in Oman 2005–2009: Disease and economic burden

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Globally, rotavirus remains a major cause of morbidity and mortality and is associated with approximately 400,000 to 600,000 deaths annually in infants and young children under five years of age. Limited genotyping data is available for rotavirus strains in the Middle East. The current study was undertaken to investigate the disease burden and molecular epidemiology of human rotavirus strains circulating in Oman from 2005 to 2008 so as to help policy makers to arrive at informed decisions about the introduction of a rotavirus vaccine in Oman. A total number of 5,462 stool samples were collected between 2005 and 2008 from young children <5 years admitted to hospitals and outpatients clinics with mild, moderate or severe diarrhoea, and analysed on an annual basis. The rotavirus antigen was detected by ELISA (Dako Inc.). Antigen positive samples were set for polyacrylamide gel electrophoresis (PAGE) and later genotyped by multiplex PCR. Out of the 5,462 collected samples, 2,539 (47%) were ELISA positive, predominantly in the age group 6–12 months. Polyacrylamide gel electrophoretic patterns demonstrated long RNA electropherotypes with 8 distinct electrophoretic patterns identified. PCR results revealed fluctuating genotypes across Oman year wise. Genotypes G1P[8], G2P[4], G2P[4], and G1P[8] were found to be predominant in 2005, 2006, 2007 and 2008, respectively. A few cases of G3P[8] were also detected. Several strains exhibited unusual combinations of G and P genotype and RNA electropherotype indicating the likelihood of natural reassortment events occurring with high frequency. In addition, the unusual P[10] genotype was identified among the rotavirus strains, in combination with G1. Since 2008, we have observed an increase in P[11], predominantly a bovine genotype. The results of this study provide strong support for the continuation of hospital based rotavirus surveillance that would give greater insight into the magnitude of rotavirus infection on the health of Omani children. The outcome of the study will also be used in advocacy regarding the impact of the future introduction of a rotavirus vaccine in Oman.

Primary Immunodeficiency in Oman - Experience at Sultan Qaboos University Hospital

Dr. Salim Al-Tamimi
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Primary immunodeficiency diseases (PID) are considered to be rare but they are expected to be more common in Middle Eastern countries. The prevalence and characteristics of PIDs are unknown in Oman. Sultan Qaboos University Hospital is the national referral center for PIDs in Oman. Patients are referred for evaluation and management when suspected to have underlying immunodeficiency. They are diagnosed and classified according to the clinical and laboratory criteria of PID reported by the International Union of Immunological Societies (IUIS) Primary Immunodeficiency Diseases Classification Committee. Between July 2005 and July 2010 there were a total of 90 patients, 55 males and 35 females who were diagnosed to have PID with an estimated prevalence of 1:30,000 in the country. The most common form of immunodeficiency was phagocytic disorders (42%) followed by predominantly antibody disorders (18%), other well defined PID syndromes (13%), combined immunodeficiency (12%), complement deficiencies (6%), unclassified PIDs (6%), and immune dysregulation syndromes (3%). The age of onset of symptoms varied from the first month of life up to 12 years of age with a mean of 20.1 months and a median of 9 months. The age of diagnosis ranged from the first week of life up tp 16 years of age with a mean of 35.5 months and a median of 24 months. Consanguinity was present in 81% of patients. A family history of PID was present in 42.2% of the patients. A history of death of a previous child was present in 48.8% of cases. The most common infectious presentation was pneumonia (42.2%) followed by deep abscess (26.7%) and BCGosis (12.2%). Furthermore 12.2% patients were diagnosed by screening because of a family history. A total of 57.6% patients required regular prophylactic anti-microbial therapy; 25% patients required intravenous immunoglobulin (IVIG) treatment, 4% patients required gamma interferon therapy, and 11% underwent bone marrow transplants (BMT). A total of 90% of all PID patients are alive and 10% died. Strategies to reduce or eliminate PIDs are needed. Awareness among parents and physicians would improve the survival of these patients.

Laboratory Diagnosis and Genetic Characterisation of Measles Virus

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Measles is one of the most easily transmitted diseases. Transmission is primarily through large droplet spreads or direct contact with nasal or throat secretions from an infected person. Measles is a vaccine preventable disease, but it remains a major cause of death in infants in developing countries. The WHO Eastern Mediterranean region (EMRO) is in the elimination phase of the measles virus. In this phase, it is well established that surveillance based on only clinical recognition of cases is inaccurate. Laboratory confirmation of each and every suspected case is critical for effective surveillance. Detection of measles specific IgM is the standard test for the rapid laboratory diagnosis for measles. Isolation of the measles virus involves a high quality specimen collected in the window 0–5 days after rash onset. Vero/hSLAM cell lines have been approved for the isolation of measles virus in the Global Laboratory Network. However, expansion of measles surveillance to include the molecular characterisation of the measles virus will help facilitate measles control during this global phase of measles eradication. In 2007, the Omani Central Public Health Laboratories, which is a designated WHO Regional Reference Laboratory, established molecular characterisation of the measles virus by sequencing. Molecular characterisation of measles viruses is an important component of measles surveillance as it provides a method for identifying the geographical origin and tracing the transmission pathways of a virus. It also provides a valuable tool for measuring the effectiveness of measles control and elimination programmes, and also provides information that can be used to document the interruption of transmission of endemic measles. The sequence of the 450 nucleotides that code for the COOH-terminal 150 amino acids of the nucleoprotein (N) is the minimum amount of data required for determining the genotype of a measles virus. Sequence data can be obtained from a viral isolate or by amplification of measles sequences directly from ribonucleic acid (RNA) extracted from a clinical specimen. The circulating measles genotypes in Oman and neighbouring EMRO countries will be discussed. Currently, there are 8 clades (A–H) and 23 genotypes within these clades of the measles virus.

Cytomegalovirus Infection and Disease after Solid Organ and Bone Marrow Transplantation: An overview

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Cytomegalovirus (CMV) is a well known cause of morbidity and mortality in immunocompromised patients. It is the most important pathogen affecting transplant recipients, which causes both direct effects, including tissue injury and clinical disease, and a variety of indirect effects. The impact of these CMV-induced effects on the organ transplant itself is great. There is a strong relationship between CMV and organ rejection and this relationship appears to be bidirectional. The prevention of CMV infection is of great importance either using the prophylaxis or the pre-emptive treatment approach. Treatment of clinical CMV disease usually requires administration of intravenous ganciclovir for two to four weeks. Clearance of viraemia should be documented before intravenous therapy is ceased.

Methicillin-Resistant Staphylococcus Aureus (MRSA) Management in Health Care Settings: Current guidelines

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The current approach to managing MRSA in healthcare settings in many countries has resulted from a combination of history, scientific evidence and patient/political pressure. This talk will compare and review the basis for existing guidelines that are used in different health care settings. It will review the success of approaches to MRSA control and provide some insights into how organisational influences might help achieve successful control.

Management of Health Care Workers Infected with HIV, HCV, HBV

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In July 1990, the Centre for Disease Control and Prevention (CDC) reported the first case of possible transmission of HIV to a patient from an infected health care worker (HCW). Fear of transmission was rampant and several recommendations were published. The latest updated recommendations were from the Society of Healthcare Epidemiology of America (SHEA) regarding the management of health care providers infected with HIV, hepatitis B and C (HBVand HCV) were published early 2010. The society recommends that the HCW should not be prohibited from health care practice on the basis of a blood borne pathogen infection. The types of procedures done by HCW are divided into 3 categories according to the risk of transmission. For each pathogen, the recommendations are graduated according to the relative viral load level of the infected provider. However it is emphasised that because of the complexity of these cases each case will be slightly different and cases should be considered independently. The guidelines also reflect the importance of patient safety as well as provider privacy and medical confidentiality, all of which are absolutely essential. The presentation will cover the details on overall management of HCWs infected with blood borne viruses based on SHEA guidelines.

Measles Outbreak in Dhofar March–April 2009: Cross-border importation

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The index case of the current outbreak was a 24 year-old woman (non-Omani) who reported, on 23rd March 2009, to Harwib Health

Centre in the Dhofar region of Southern Oman with high-grade fever. She was immediately referred to Sultan Qaboos Hospital in Salalah, the capital city of the region. She was admitted and kept in isolation with a provisional diagnosis of viral fever. She gave history of visiting Al-Hauf village in Yemen from 12–19 March. She developed a rash after admission which was then classified as a drug-induced rash and hence neither was a blood sample taken nor was the case notified as required under the Fever & Rash surveillance order. Field Investigation: Action taken: Genotype identification and classification of the cases. Recommendation: Active case-finding: House-to-house survey will be conducted in the neighbouring villages in the border area after assessing feasibility. Mop-up immunisation campaign: The need for the immunisation of the population in the border area is being assessed

Infective Endocarditis in the Era of Multi-Drug Resistant (MDR) Organisms

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The prevalence rate of infective endocarditis is increasing as a result of aging, intravenous (IV) drug users and increased rate of line related bacteraemia. In January 2010, the American Heart Association declared that the rate of implantable device infections was increasing which increased the risk of in-hospital death by more than two-fold. Currently Staphylococci are the most common aetiological organism responsible for these infections and these organisms are becoming more resistant. The WHO has identified antimicrobial resistance as one of the three greatest threats to human health. At the same time, infectious disease experts have announced that multi-drug resistant organisms (MDRo) are responsible for >25% of serious infections in developing countries, with some of these bacteria not being susceptible to any licensed antibacterial agent. Some antimicrobial resistance mechanisms are difficult to detect with routine microbiological testing leading to inappropriate treatment. Biofilm formation by MDRo (mainly Staphylococci, Acinetobacter and Pseudomonas) increases the difficulty of management of infective endocarditis. Clear understanding of biofilm development, antibiotic pharmacokinetics, antimicrobial resistance mechanisms, institution of infection control measures and antibiotic stewardship are the mainstay of controlling this growing problem.

Diagnostic Approach to Primary Immunodeficiency

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Host immune defense is accomplished by innate immunity and adaptive immunity; both of these are essential in order to fight infections and prevent autoimmune diseases. Innate immunity includes naturally occurring barriers, mucociliary clearance, peristalsis, secretions, cells and protein enzymes that do not involve the production of immunologic memory for their function. Adaptive immune responses are both humoral and cellular and depend on immunologic memory for antigen recognition. Patients who are immunodeficient present mainly with recurrent or severe infections. Immunodeficiency can be separated into primary and secondary states and the type of infection suggests the particular component of the system involved. Examples that can cause secondary immunodeficiency are HIV, drugs (e.g. cytotoxic agents, steroids) protein losing states. Primary immunodeficiency results from absence or malfunction of bone marrow precursor stem cells, various blood cells, and soluble molecules that make up the immune system which can lead to compromise of the host defense system. Over the last two decades, many genes have been discovered that are responsible for disease status in the immune system. These genes either fail to produce specific proteins (immunoglobulins in X-linked agammaglobulinaemia) or produce altered proteins (truncated common gamma chain of the interleukin-2 receptor in X-linked severe combined immunodeficiency), and enzyme deficiency, as seen in adenosine deaminase deficiency. Conventionally, immunodeficiency is classified into four major host defense mechanisms (B-cell immunity, T-cell immunity, phagocytic cells, and complement pathways). Immunodeficiency usually presents with unusual severe or recurrent infections, the following are the most warning signs of primary immunodeficiency: 1) a family history of immunodeficiency disease; 2) two new ear infections within 1 year; 3) two serious sinus infections within 1 year; 4) two months on antibiotics with little effect; 5) two pneumonias within 1 year; 6) two deep-seated infections, such as meningitis, sepsis or osteomylitis; 7) need for IV antibiotics to clear infections; 8) recurrent deep skin or organ abscesses; 9) failure to thrive; 10) persistent thrush in mouth or fungal infection on skin. When an immunodeficiency is suspected, the following screening tests should be performed and may be tailored according to the clinical information with respect to the immune system arm likely to be involved: antibody mediated immunity; quantitative immunoglobulins (IgG, A, M, E); isohaemagglutinins; functional antibodies e.g. diphtheria/tetanus titers, T-cell immunity; total lymphocyte count; T and B cells numbers; lymphocyte proliferation assay; lateral chest X-ray; HIV, neutrophil, cell count and differential nitro blue tetrazolium test (NBT); dihydrorhodamine 1,2,3 test; complement, total haemolytic complement test, C3 and C4 concentration. Further specialised functional immunological tests may be required to establish an accurate diagnosis; these tests are not available in all laboratories, for example phagocytic assays and cytotoxic assays. Genetic studies are more commonly used now.

Update on Zygomycosis

Dr. Saleh Al-Azri
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Zygomycosis is one of the most rapidly progressing forms of mould infections, which usually begins in the nose and paranasal sinuses. This infection produces angioinvasive disease with tissue necrosis and is prone to dissemination. Diabetes and immuno-suppression are major risk factors. Recent reports showed an increased incidence of zygomycosis. The presentation and diagnosis are usually challenging and the treatment is even more so. Zygomyces are resistant to most commonly used antifungal medications, but high dose liposomal amphotericin followed by posaconazole are considered in most cases. The clinical outcome is closely related to the patient's overall health and control of the underlying diseases.

Prosthetic Joint Infections

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Since its development in the late 1960s, total hip and knee replacement has increased from an infrequent procedure to one that is commonly performed. The success of these procedures is hampered in part by the development of joint infections. The rate of infection in most centres ranges between 0.5 to 1.0 % for hip replacements, 0.5 to 2 % for knee replacements, and less than 1 % for shoulder replacements. Prosthetic joint infections can be classified according to the time of onset (early, delayed and late) or the pathogenic mechanism causing infection. Any microorganism can cause prosthetic joint infection and the distribution of organisms varies with the time from implantation and source of infection. Diagnosis of prosthetic joint infections always requires obtaining samples of joint fluid or tissue. Treatment usually involves both medical and surgical measures. The type and timing of such therapies is dependent upon the cause and timing of the infection and the condition of the host.

Molecular Epidemiology of Tuberculosis in Oman

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Tuberculosis continues to be a major cause of morbidity and mortality throughout the world with 8.8 million new cases and 1.6 million deaths in 2005 (WHO fact sheet, 2007). Rapid detection, adequate treatment, and contact tracing to arrest further transmission are the key factors in the control of this infectious disease. Various developments in DNA technology and molecular biology have led to methods to trace tuberculosis transmission routes by the differentiation of clinical isolates based on polymorphism in genomic DNA of Mycobacterium tuberculosis. This presentation gives a brief introduction to molecular epidemiology and its applications, and then focuses on the molecular characterisation of Omani M. tuberculosis isolates by spoligotyping, a study performed by our laboratory. We identified 265 different spoligotypes among the 786 M. tuberculosis isolates. The designation of the spoligotype was attributed by comparison of the pattern to those contained in a SpolDB4 database. Out of these, 124 spoligotypes (containing 573 isolates) showed matching with SpolDB4 database, while 141 spoligotypes (containing 213 isolates) were not found in SpolDB4 database and an ST number could not be assigned for them. Most unidentified spoligotypes were orphan (n = 109), however, 104 clustered spoligotypes (without ST numbers) were roughly assembled into the Unknown group 1 to 32. Over all clustering was observed in 77.2% (n = 607) isolates, whereas 22.8% (n = 179) clinical isolates harboured unique profiles. This study gives an outline of the M. tuberculosis strains circulating in Oman, and describes the distribution of the major phylogenetic families. It contributes towards a better understanding of the current trend of TB epidemiology in a low-incidence Middle Eastern country.