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Revalidation: What does it offer a national health service?

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The purpose of revalidation is to provide greater assurance that licensed doctors are up-to-date and fit to practise. The introduction of medical revalidation throughout the UK means doctors who wish to retain their licences to practice in the UK will need to demonstrate they fit these criteria. Revalidation is a new way of regulating the medical profession, providing a focus for doctors' efforts to maintain and improve their practice; facilitate medical organisations in supporting doctors in keeping their practice up to date, and encourage patients and the public to provide feedback about the medical care they receive from doctors. In these ways, revalidation will contribute to the ongoing improvement in the quality of medical care delivered to patients throughout the UK. The successful introduction of revalidation is a shared responsibility involving the General Medical Council, the health departments in England, Northern Ireland, Scotland and Wales, the medical Royal Colleges, the medical profession and the revalidation support team (RST) working with the National Health Service and other employers in the UK. This group of interested parties should work together to develop, test, and implement a system of revalidation throughout the UK that is feasible, flexible, proportionate, cost effective, and provides the necessary level of assurance to the public. Revalidation will be based on a local evaluation of doctors' performance through appraisal, which will be conducted annually in the workplace. The responsible officer, informed by the appraisal and appraiser, will make a recommendation to the GMC concerning the doctor's fitness to practise. This presentations by the medical director for the Department of Health England Revalidation Support, will give an overview of the design and implementation of this programme, with particular reference to the implications for and improvements offered to integrated clinical governance.

Thyrotoxicosis

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Thyrotoxicosis affects ~3% of the population and thus represents a significant workload to endocrinologists, general physicians, and primary care clinicians alike. Clinical presentation is often stereotyped, but in the elderly there may be an atypical presentation as apathetic thyrotoxicosis. Autoimmune and nodular hyperthyroidism represent the vast majority of causes of thyrotoxicosis; however, it is important to have a clear understanding of rarer causes, such as post-infectious/post-partum thyroiditis or amiodarone-induced thyrotoxicosis as the clinical management differs in such cases. Approaches to definitive treatment differ across the world. Anti-thyroid drugs are used to render patients euthyroid prior to radioiodine treatment or thyroid surgery and, in some instances, longer term anti-thyroid drugs are used in an attempt to induce a long-term remission in patients with Graves' disease. There are clinical markers to help predict which patients are likely to do well/poorly with such approaches. This presentation will highlight the optimum management of patients with different forms of thyrotoxicosis, with particular emphasis on markers for success, adverse effects of treatment and long-term outcomes following treatment of thyrotoxicosis.

Epigenetics of Cancer

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Epigenetics is a fascinating and rapidly expanding field in medical research. It has wide applications in early diagnosis, prognosis, and therapeutic interventions, particularly in cancer. In this presentation, the basic mechanisms of post translational epigenetic alterations will be discussed with particular emphasis on the role of deoxyribonucleic acid (DNA) methylation, histone modifications and chromatin remodelling, and micro-ribonucleic acid (MiRNA) transcription regulation in carcinogenesis. The second part will be devoted to translational epigenomics with presentation of some available data on the significance of epigenetics in determining cancer risk predispositions and its value as early diagnostic, predictive and prognostic tool. Furthermore, the therapeutic interventions utilising DNA methylation, in particular, will be presented.

Obesity in Pregnancy

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Obesity is increasingly recognised as harmful to the mother, affecting fertility and causing higher incidence of gestational diabetes, pre-eclampsia, caesarian section and postoperative infection. It is also potentially harmful to the foetus through higher incidence of macrosomia, congenital anomalies, premature or stillbirth, and epigenetic effects leading to obesity and metabolic syndrome. Guidelines from the Institute of Medicine suggest that overweight women should gain only 7–12 kg, and obese women 5–9 kg during pregnancy. While few women receive adequate counselling or weight management, and over half exceed these recommended weight gains, a recent systematic review concluded that even 'intense' interventions did not prevent weight gain during pregnancy. Can better interventions be devised, in the context that so far no pharmacological aids have been shown to be safe or effective? The acceptability of bariatric surgery has resulted in increasing numbers of obese women of child bearing age receiving surgery, sometimes as a prelude to infertility treatment. Increasing numbers of women who have had bariatric surgery present later with pregnancies from which arise specific concerns and weight management problems. Although evidence syntheses of pregnancy outcomes find poor quality evidence, surgery seems to improve maternal health, markedly decreases the incidence of gestational diabetes mellitus, and probably also decreases incidences of hypertension and eclampsia. Fetal outcomes are improved in respect of decreased macrosomia, without adverse effects on prematurity, low birth weight or perinatal mortality.

Cutaneous Sarcoidosis: Diagnosis and management

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Sarcoidosis is a multi-organ immune-mediated disease of unknown aetiology with varying clinical presentations. The skin can be involved in close to one-third of patients. The cutaneous manifestations are protean and often masquerade as several other skin diseases; hence, the diagnosis is often missed or delayed. Dermatologists are often the first to diagnosis sarcoidosis. The treatment is challenging and there are no randomised clinical trials on any treatment modality. Options include topical or systemic steroids, anti-malarials, immunosuppressive drugs, novel therapies and, more recently, the anti-tumour necrosis factor biologic therapies. The latter has been a significant advancement in therapy. This talk will discuss the clinical spectrum and differential diagnosis of cutaneous sarcoidosis. Traditional and recent advances in the management of this challenging disease drawing on experience from a tertiary referral centre will be discussed.

The Management of Severe Hypoxaemic Respiratory Failure in Critical Care

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The recent H1N1 pandemic has once again brought focus on the management of severe acute hypoxaemic respiratory failure. A significant number of young and previously fit individuals suffered severe respiratory failure. These patients received both conventional and experimental forms of respiratory support. Conventional ventilatory support is based on the findings of the multi-centre ARDSnet trial (2000). This found that ventilation with lower tidal volumes reduced mortality in patients with severe acute lung injury (ALI). This was despite the fact that, at early stages, the lower tidal volume patients were on average more hypoxaemic and hypercapnic as a result of the lower volumes/pressures used in that group. Positive end expiratory pressure (PEEP) is also part of a standard approach to ALI and can improve oxygenation. However, a number of studies have not found a significant improvement in mortality when PEEP levels have been compared. Although this conventional approach was effective in many patients, a number developed intractable hypoxaemia following H1N1 infection. This group received a number of interventions including steroids, prone positioning, tight fluid control, airway recruitment manoeuvres, high frequency oscillation, and extra corporeal membrane oxygenation (ECMO). All these approaches have been subjected to various studies with often promising results in small initial studies, but lack of confirmation of efficacy in larger, randomised trials. For example a recent RCT of ECMO reported improved outcomes in the intervention group. However, the study design was complex and the interpretation of the results remains controversial. Further studies of other treatments are on-going. Case series from a number of large centres during the H1N1 outbreak indicate a good outcome in many patients despite the lack of a strong evidence base for rescue treatment. One explanation may be the efficacy of these techniques in the most severely ill group of patients.

Relatively few of these are included in individual RCTs but a meta-analysis of the effect of prone positioning suggested better outcomes in the most hypoxaemic patients.

The Role of PET/CT in Cancer Diagnosis

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Positron emission tomography/computed tomography (PET /CT) imaging uses radiolabelled molecules to take images of molecular interactions of biological processes in vivo. It enables inspection of glucose metabolism in all organ systems in a single examination. This hybrid imaging system utilises short-lived radiotracers that are cyclotron products with a short half-life ranging between 2 and 110 minutes. Cancer cells have higher metabolic activity and use more glucose. The hexokinase activity levels increase and the phospho-related glucose moves to the glycolysis pathway. Fludeoxyglucose (FDG) is a glucose analogue; hence, there is an increased uptake in cancer cells due to an increase in glucose transporter activity and hexokinase levels, leading to elevated levels of phosphorelated FDG. On the other hand, G-6-phosphatase levels are low in the cancer cells; therefore, the phosphorelated glucose cannot diffuse out of the cells. Unlike glucose, FDG is not metabolised further and remains trapped in the cancer cells. It is well-documented in the literature that there is a dramatic improvement in the diagnostic accuracy of PET/CT for lung, colorectal, breast, head and neck, and thyroid cancers, and lymphoma. PET/CT is important in improving the detection and staging of cancer, selecting therapies, assessing therapeutic response, and in restating in cases of disease recurrence. In addition, it is more accurate in evaluating residual lesions and in differentiating fibrosis versus active disease. PET/CT is cost effective when used for evaluating therapy response. It can be used following 1–3 chemotherapy cycles to assess therapy response. Effective treatment sharply reduces metabolic tumour activity and helps guide physicians in effective use of expensive chemotherapy medications. PET/CT is a cost effective, essential imaging tool for evaluating various tumours. It is essential for staging, therapy response, and residual tumour evaluation, and to gauge effective use of chemotherapy.

Acute Non-Invasive Ventilation

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Non-invasive ventilation (NIV) now has a major role in the management of patients presenting with respiratory failure on the acute medical take. It has a number of potential advantages compared with invasive mechanical ventilation (IMV). The obvious attraction is the avoidance of intubation and its attendant complications. Its use opens up new opportunities in the management of patients with ventilatory failure, particularly with regard to location and the timing of intervention. With NIV, paralysis and sedation are not needed and ventilation outside the intensive care unit (ICU) is an option; given the considerable pressure on ICU beds in some countries, the high costs, and the potentially distressing experience of ICU, this is an attractive option. Ventilatory support can be introduced at an earlier stage in the evolution of ventilatory failure. Additionally, it is possible with NIV to give very short periods of ventilatory support, which in some cases may be sufficient to reverse the downward spiral into life-threatening ventilatory failure. Patients can co-operate with physiotherapy and eat normally. Intermittent support is possible, and patients can start mobilising at an early stage. They remain able to communicate with medical and nursing staff, and with their families; this is likely to reduce feelings of powerlessness and anxiety associated with ventilatory support. A reduction in complications, particularly infections, is a consistent and important finding. However, NIV does have limitations; concerns have been voiced that it may delay endotracheal intubation (ETI) and mechanical ventilation, resulting in a worse outcome. NIV may be time consuming for medical and nursing staff, though in part this may represent a learning effect. The use of NIV for patients with acute exacerbations of chronic obstructive pulmonary disease (COPD), cardiogenic pulmonary oedema, and acute on chronic hypercapnic respiratory failure due to other causes will be discussed.

Targeted Treatment in Haematological Cancers

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Developing targeted treatment for haematological cancers is a key aim of current research. These stratified cancer medicine strategies are being developed in colon cancer and sarcoma, and offer improvements in patient outcomes and the value of novel therapies. The key concept underlying this approach is to identify a specific molecular lesion found within the tumour cells which can be switched off using a targeted treatment. The access to tumour tissue in haematological cancers has allowed the generation of many years of clinical data which. These data provide insights into how these approaches can work in the clinic. The disease that has exemplified the role of targeted treatment best is chronic myeloid leukaemia. This disease is characterised by a chromosomal translocation BCR/ABL, which leads to the over-expression of a tyrosine kinase. This tyrosine kinase can be targeted using imatinib, a specific inhibitor. This use of this drug in the clinic results in patients achieving complete remissions. This tolerable treatment strategy has lead to a rapid decline in allogeneic transplantation, which was previously the key clinical treatment for this disease. A surprising result of the treatment has been the emergence of treatment resistance mediated via tumour specific mutations, affecting the ability of the targeted treatment to inhibit its target. This emerging treatment resistance has led to the development of a range of different kinase inhibitors which have different characteristics and abilities to overcome resistance. Targeted treatment is also relevant to other haematological diseases, including B-cell lymphomas and acute leukaemias. Overall, we have made big strides in the application of targeted treatments strategies in haematological cancers and it is expected this will form the basis of improved outcomes in other haematological conditions over the next years.

Emergency Oxygen Therapy

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Oxygen is one of the most common treatments in emergencies, with many patients given supplementary oxygen. However, oxygen supplementation is not without risk, and there are occasional deaths due to under or over-use of oxygen. Audits of oxygen use have consistently shown poor performance, but there are few randomised controlled trials to guide practice, which is largely guided by precedent. Tissue hypoxia and cell death can occur, especially in the brain, after just a few minutes of profound hypoxaemia, such as occurs during cardiac arrest. Sudden exposure to oxygen saturations below about 80% can cause altered consciousness, even in healthy subjects. However, the degree of hypoxia that will cause cellular damage is not well-established. Dogma is that a high FIO2 is protective and gives a margin of safety; therefore, practitioners should err on the side of generous oxygen supplementation. However, some patients may be placed at risk by the use of high dose oxygen therapy. Oxygen is a drug and should be prescribed with the same rigour and monitoring of effect as pharmaceutical preparations. In most situations, a target of 94 to 98% is appropriate, but there are a few situations in which a lower target range should be used. Most commonly, this will be for patients whose level of oxygenation when "well" is known, and in whom adverse effects of oxygen have been previously been documented or can reasonably be expected. Additionally, bleomycin-induced pulmonary fibrosis, paraquat ingestion, and probably acid aspiration should be treated with a lower target saturation. Supraphysiological oxygen is seldom warranted, except in cases of carbon monoxide poisoning and occasionally pneumothorax. All clinicians should be trained to recognise and treat hypoxia; this must include understanding of the role and limitations of pulse oximetry and interpretation of blood gas samples.

The Cutaneous Manifestations of HIV

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HIV continues to be a medical problem worldwide, and almost all HIV patients develop skin disease. Skin disease is often the presenting sign and certain skin conditions are markers for diagnosing HIV. Conditions have either a typical appearance, or exaggerated and unusual manifestations occur. The therapy for HIV with highly active antiretroviral therapy (HAART) has resulted in unusual manifestations as a result of immune reconstitution. Having previously worked in South Africa, which is the epicentre for HIV, and now working at the largest HIV dermatology unit in Europe, tremendous experience on HIV and skin has been acquired. This talk will describe the diverse cutaneous manifestations, complications from medication, and clinical clues to diagnosis, and provide an update on the management of HIV-associated skin disease.

Targeted Therapy in Cancer Management

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Agents that target a multitude of both haematopoietic and solid malignant tumours are state-of-the-art available therapy. They have become an integral part of cancer management when used alone or in combination with cytotoxic agents. The target therapy, since its inception in the modern era with trastuzumab and crizotinib, is an ever expending area and a success story. Newer targets are identified on a regular basis and should be exploited therapeutically by the identification of newer molecules.

Primary Hyperparathyroidism – Surgery or conservative management?

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Primary hyperparathyroidism (PHPT) is a common, usually coincidentally discovered diagnosis made on 'routine' blood testing. Most patients with PHPT are, therefore, asymptomatic at presentation. Therein lies the dilemma of whether to treat surgically or manage by conservative follow up although the risks of overt PHPT are well-established in terms of end organ damage (e.g. fractures and nephrolithiasis). There is far less evidence that mild, asymptomatic disease has such effects and that parathyroidectomy (PTx) can reverse any adverse risks. That said, surgery for PHPT has become very refined and is often performed by a minimally invasive approach that is associated with low morbidity. In experienced hands, first time cure rates following PTx are greater than 95% and, in light of associations between cardiovascular dysfunction and possibly increased risk of malignancy even in mild asymptomatic PHPT, the threshold for surgical intervention has fallen. This presentation will cover a contemporary overview of the evidence base for management of PHPT and address thresholds for intervention and potential roles for calcimimetic agents in the management of PHPT.

Advances in the diagnosis and treatment of interstitial lung disease

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The interstitial lung diseases (ILDs) are a varied group of over 200 separate disorders that account for up to 15% of the work load encountered in a general respiratory clinic. Recent diagnostic advances, particularly in thoracic imaging, have greatly improved our

ability to diagnose individual ILDs and have therefore been important in refining treatment approaches for this diverse group of conditions. Furthermore, the last decade has seen the evolution of large, multi-centre trials for the commonest of the ILDs, idiopathic pulmonary fibrosis. These developments mean that there can no longer be a "one-size fits all" approach to the management of ILD. This talk will therefore explore current diagnostic and therapeutic strategies for the commonest of the ILDs, including idiopathic pulmonary fibrosis (IPF).

Venous Thromboembolism: A patient safety priority

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It is estimated that venous thromboembolism (VTE) causes around 25,000 potentially avoidable deaths in hospital in England each year, many more than all causes of hospital- acquired infection. VTE is often a silent condition, and the acute and chronic complications have serious consequences for some patients. We have known for decades how to safely prevent this condition, but awareness and understanding remain patchy, both within the health professions, and in the community at large. The presentation will focus on the successful national VTE prevention programme in England, described as a " world first" by the previous chief medical officer, Sir Liam Donaldson, who initiated the design and development of this patient safety programme, which transferred at the implementation stage to the NHS Medical Directorate under Sir Bruce Keogh. The speaker led the programme for 5 years, latterly as the National Clinical Director for VTE Prevention for the Department of Health, England. The unique development of the VTE Exemplar Programme will be described, as well as the system drivers and levers influenced to drive improvement. Key elements of the programme design, challenges and opportunities will be discussed, together with an update on current preventative and therapeutic questions relating to both acute and chronic VTE as a clinical condition.

Management of Severe Sepsis

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Septic shock is a major cause of death in hospitalised patients throughout the world. It presents as a clinical syndrome characterised by the presence of hypotension and the rapid development of multiple organ dysfunction and failure. Fever is common, although not invariably present. Sepsis is initiated by a wide range of pathogens, some of which are highly virulent and others which only cause problems in the immunosuppressed. Mortality remains high—around 40% in most observational studies. Twenty years of research into the basic science of sepsis has led to a detailed understanding at the cellular and molecular level of the innate immune response to invading pathogens. A type of 'standard model' of the initiation of the septic state has been developed which emphasises the induction of an intense, acute inflammatory response caused by the activation of cellular and soluble mediators, driven by specific pathogen/receptor interactions. This understanding has led to the development of a range of anti-inflammatory agents, which have been subsequently tested in large scale clinical trials in patients with severe sepsis. Unfortunately, none of these agents were found to have consistent or replicable beneficial effects on mortality. Due to this translational failure, recent research has focused again on the management of the haemodynamic or shock aspect or the syndrome. In particular, early goal-directed resuscitation of the septic patient may be effective. Currently a number of large, multi-centre clinical trials, including the ProMISe (Protocolised Management In Sepsis) study in the UK, are being conducted to examine this hypothesis. Despite the lack of positive RCTs to guide the treatment of human sepsis, there is strong evidence that the outcome of septic shock has improved in the last two decades. The reason remains uncertain but is likely to be due to better awareness of the condition in combination with improvements in the organisation and delivery of acute and critical care.

Multiple Myeloma

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Myeloma has a unique set of features which makes an excellent model in which to study the impact of interplay between a malignant cell, its supporting microenvironment, and the immune system. Many of the molecular features of myeloma modify and hijack these interactions, favouring the growth of the malignant clone within the specialised bone marrow niche. During the progression of the disease, the acquisition of further genetic hits leads to the clone becoming fully independent of stromal interactions, and to the development of a treatment-resistant leukaemic phase. Its transition to plasma cell leukaemia represents a model system in which the molecular evolution and intraclonal dynamics of myeloma can be studied. The basic premise underlying the initiation and progression of myeloma is that multiple mutations in different pathways regulate the intrinsic biology of the plasma cell, changing it in ways that generate the features of myeloma. Many of the genes and pathways important in this transformation process have now been characterised. However, the results of recent sequencing data make it clear that there is no single molecular abnormality leading to multiple myeloma, but that multiple mutations occur and deregulate a limited number of pathways relevant to the biology of the plasma cell, leading to their malignant transformation. We are starting to develop an insight into the aetiological factors that lead to myeloma. While normal immune responses are important in protecting against infections, the responses can also be deranged, leading to other chromosomal translocations that cause myeloma later in life. It is perhaps, therefore, not surprising that monoclonal gammopathy of undetermined significance (MGUS), a pre-malignant condition of multiple myeloma, is present in 3% of people over sixty. We are also now starting to understand how the multiple mutations that lead to myeloma interact to give rise to multiple myeloma. The challenge

that we face in myeloma now is to turn these genetic insights into clinical strategies that benefit patients.

Peak Bone Mineral Density Levels in Omanis Compared to those of Caucasians and Asians

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To establish normal peak bone mineral density (PBMD) values in a cohort of healthy young Omanis aged between 25 to 34 years, Omani employees at Sultan Qaboos University Hospital (SQUH) were randomly chosen and invited to participate in a study of comparison. The study's aim was to compare the PBMD of Omanis with those of Caucasians and Asians. Fifty males and females were studied after having excluded those who did not fulfill established selection criteria. Their fully informed consent was obtained to establish PBMD values using dual energy X-ray absorptiometry (DXA). Blood was also taken to determine bone and electrolyte profiles, serum parathyroid hormone (PTH) levels, and a complete blood count (CBC). Statistical analysis was done based on Hologic Delphi reference values on a reference curve generation using z-scores and the fitting a polynomial curve of third order. These data were interpolated, sampled, and tested to verify the initial results. Our results show that normal Omani PBMD values of L1-L4 are substantially lower than those of a normal Caucasian population by 25% in men and 24% in women. Bone profiles and serum PTH levels were within the normal range in all subjects. In SQUH and possibly other centres the diagnosis of osteopenia and osteoporosis (using DXA) is made using normal Caucasian reference values. Our findings indicate that we are over-diagnosing these disorders and that some patients might be receiving inappropriate antiresorptive and/or bone forming medications. Our findings highlight the need to use data from a normal local population. At the moment we suggest using normal reference Asian values in Omanis not of obvious African stock.

Management of Obesity and Its Complications

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Few organ systems are unaffected by obesity and the list of disorders linked to excess weight continues to grow. However, evidence for benefits from obesity management is largely restricted to cardiovascular and metabolic outcomes, as well as quality of life and health economic improvement. The development of a new obesity classification based on body mass index (BMI) and disease status, the Edmonton Obesity Staging Scheme, helps promote a better understanding of the patient's needs and the potential for improving health by obesity management. Life-style interventions with diet and exercise are successful at producing modest weight loss maintenance, and should still be at the heart of medical interventions. The dearth of new and safe pharmaceutical agents, together with the increasing prevalence and incidence of severe obesity, has led to an explosion in bariatric surgery, which shows increasingly dramatic health gains and economic value for money. Procedure-specific variations in efficacy and risks exist and require further study to clarify the specific indications for, and advantages of, different surgical procedures. However, there is already abundant evidence that surgery is effective at improving quality of life, inducing diabetes remission, and reducing mortality from cardiovascular disease and cancer. Effective obesity management requires multi-disciplinary teams and application of the appropriate interventions at the appropriate stage of the disease in appropriate individuals.