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MOVEMENT DISORDERS 101: BEAUTY IS IN THE EYE OF THE BEHOLDER

Jawad A. Bajwa, MD

*Assistant professor of Neurology, University of Florida, FL, USA
Consultant Neurologist, National Neuroscience Institute, King Fahd
Medical City, Riyadh, Saudi Arabia*

Movement Disorders have seen tremendous growth in basic, clinical and translational research over the last 50 years. It brings together the most interdisciplinary team model in Neurosciences to deliver clinical care and scientific growth. But still it remains a very clinically oriented and challenging specialty where the diagnosis is essentially made through careful bedside history and examination. The field still has reminiscences from the days of Dr. IbnSina but has evolved into a dynamic subspecialty where it is leading efforts in the science of neuro-modulation. The presentation will illustrate through video cases some of the most common Movement Disorders and their diagnostic tricks.

MANAGEMENT OF MIGRAINES - AN UPDATE

*Aziz Badruddin Sonawalla, MD (India), DM Neurology (India)
Senior Lecturer, Section of Neurology, Aga Khan University Hospital,
Karachi, Pakistan*

Migraines are a leading cause of disability and functional impairment worldwide. Although not a serious disorder, it is responsible for significant morbidity. Fortunately, the majority of patients can be relieved of their symptoms if treated appropriately. The aim of management is to achieve the most optimum pain control possible, and to prevent recurrence of attacks. However, there is no cure. Pharmacological management consists of treatment of the acute attack as well as therapy for prophylaxis. Acute treatment should be introduced with the mildest of analgesics, preferably ibuprofen or naproxen, although even medications like paracetamol can suffice. Medications need to be started in the early stages of the migraine headache to maximize response. Ergot alkaloids are very useful anti migraine medications, though their use is restricted due to the high incidence of side effects. The triptans are now the most widely used amongst the medications for migraine relief. These are highly selective 5HT_{1B} / 5HT_{1D} receptor agonists with lesser side effects as compared to ergotamines. Only sumatriptan and zolmatriptan are available in

Pakistan. Combination of a triptan along with naproxen offers greater pain relief than either one alone. Medications for migraine prophylaxis consist of a broad range of medications, mainly from the anti convulsant, anti hypertensive and anti depressant groups. A appropriate use and dosage is able to reduce the frequency and intensity of migraines in the majority. A duration of 3 to 6 months' therapy is appropriate if found effective. Supplements like riboflavin, Coenzyme Q, etc have been claimed to be effective, though controlled studies are lacking. Exercises, relaxation training, stress management etc are useful ancillary treatment modes that may be useful in the individual patient. For the patient with chronic migraines, the use of Botox, greater occipital nerve blocks etc are now being increasingly used with good results. The advent of newer medications - based on a better understanding of the migraine pathophysiology - is likely to see the introduction of newer and better drugs to tackle headache and the other symptoms of migraine.

WOMEN WITH MIGRAINE-SPECIAL ISSUES

Dr. Naila N. Shahbaz,

*Associate Professor, Department of Neurology, Dow University of
Health Sciences, Karachi*

Approximately 75% of all persons who experience migraines are women. Before puberty, the prevalence and incidence of migraine are higher in boys than in girls. After age 12 years, the prevalence increases in females. The female-to-male ratio is 2.5:1. The highest incidence of migraine in women occurs between the ages of 25 and 55, the most productive years of their lives. Furthermore, women in their 30s tend to have an increase in the severity as well as the frequency of attacks. Women are also more likely than men to suffer severe functional disability from migraine. All these evidences point towards a strong association between normal physiological hormonal landmarks in a women's life and migraine etiology. These events include menarche, menstrual cycle, use of oral contraceptives, pregnancy, lactation and menopause. Hormonal events that may trigger migraine include menarche, menstrual cycle, estrogen administration in OCT and HRT and immediate post-partum period. Hormonal events that may arrest migraine include second and third trimesters

of pregnancy and physiological menopause. This talk encompasses management issues associated with these specific periods in a woman's life

BOTOX IN CHRONIC MIGRAINE

Fayyaz Ahmed

Consultant Neurologist, Hull & East Yorkshire Hospitals NHS Trust, Yorkshire, United Kingdom

Headache is the most prevalent symptom in the general population and an estimated 1 in 6 people suffer from migraine. Around 2-4% of the general population suffers from daily headache disorders (Chronic Daily Headache) of which the majority have chronic migraine. This is the most disabling form of the headache disorder. In addition around 1% of the general population in the western world suffers from headaches due to analgesic overuse and the figure may be higher in the 3rd world countries where self-medication is more common due to the availability of pain killers of various types over the counter. Combining medication overuse and chronic migraine makes up the most disabling but potentially treatable headache disorders that are responsible for direct costs to healthcare and indirect cost to the economy in general. The headache symposium is meant to highlight on these disorders, particularly their recognition and ways to tackle them with new and emerging treatments. The arrival of Botulinum toxin in 2010 was a major breakthrough after the triptan discovery in early 90's. Neurostimulation both invasive and non-invasive is appearing to be promising for the future. The future of headache treatment is changing and most innovative and novel approach would be available to tackle a disorder that virtually affects everyone in the general population.

ENDOVASCULAR TREATMENT OF CEREBROVASCULAR DISEASE

Adnan H Siddiqui; Dr. Ashish Sonig

Associate Professor of Neurosurgery and Radiology, University at Buffalo, SUNY, Buffalo, NY, USA

Neurointervention has evolved since the days when cerebral angiogram was conceptualized by Haschek, Lindenthal, and Moniz. It has now mellowed into a rarified and complex field, with a set of techniques and a knowledge base that are distinct from other fields within medicine. At the same time, clinicians from an assortment of disciplines have come to practice neurointervention, with backgrounds ranging from neurosurgery to radiology, neurology, cardiology, and vascular surgery. The last two decades have witnessed a growing application of endovascular techniques for the treatment of cerebral aneurysms, arteriovenous malformations, acute stroke, intra and extracranial atherosclerotic disease. The greatest advances have

come in the management of cerebral aneurysms, carotid stenosis and acute stroke. We have moved from the era of "only coiling" to "flow diverters". While pipeline embolization device is the commonest flow diversion used in USA, the SILK flow diverter (SFD; Balt Extrusion, Montmorency, France) is the most used in Europe and South America. The Carotid Revascularization Endarterectomy Versus Stenting Trial established the safety and efficacy of Carotid artery stenting and now we have the options of varied embolic protection devices, ranging from distal filters to proximal protection and flow diversion. The prowess of endovascular neurosurgery could be judged from the fact that it is the only available option for the treatment of acute stroke, once intervention is planned. Acute stroke intervention has undergone phenomenal technological metamorphosis since the days of early conception. We have moved from the Merci Retriever (Stryker; Kalamazoo, MI, USA) to stent retrievers like the Solitaire Flow Restoration (FR) device (ev3/Covidien Vascular Therapies, Irvine, California) and Third-Generation Endovascular Stroke Treatment Device trevo-2. Improvement in technology and operator experience and the encouraging results of clinical trials have led to broader acceptance of the use of these devices in acute stroke management. Continued innovation and refinement of endovascular devices and techniques will inevitably improve technical success rates, reduce procedure-related complications, and broaden the endovascular therapeutic spectrum for cerebrovascular disease.

ADVANCES IN INTERVENTIONAL PAIN MANAGEMENT

Hasnain Haider Shah

Interventional Radiologist, Sheikh Khalifa Medical City/ Cleveland Clinic, Abu Dhabi, UAE.

Pain management and Interventional pain management are quickly growing fields in subspecialty neurology. Emerging science and treatment options for patient care are growing rapidly and it is important for clinicians specializing in this field of medicine to know, understand and evaluate available options to be able to continue to provide the best treatment options and quality of care for patients. Image-guided pain interventions are used for both diagnostic and very precise therapeutic capabilities. This presentation will review basic principles of the advanced image-guided diagnostic techniques. It will also include discussion of pain diagnosis, simple and then more advanced modes of therapy, including spinal cord stimulation and intrathecal therapy, providing Neuro physicians with an understanding of the primary indications and utilization for these therapeutic modalities.

UPDATE ON STROKE PREVENTION

Naveed Akhter

Consultant Neurologist, Hamad Medical Corporation, Doha, State of Qatar.

Stroke is preventable yet is increasing globally. The same few major risk factors account for much of the leading health problems of the world but remain uncontrolled in the majority of affected individuals. Stroke survivors are at an increased risk for recurrent stroke and other ischemic vascular events and face significant cross-risk for atherothrombotic conditions affecting the coronary and peripheral vascular beds. Hence adequate primary and secondary prevention strategies are mandatory. By getting everything right, patients can reduce the risk of stroke by 80% or more; however, getting everything right is a tall order. Primary prevention is an individually based clinical approach to disease prevention, directed toward preventing the initial occurrence of a disorder in otherwise healthy individuals. This includes lifestyle and risk factor management, hypertension screening, dyslipidemia screening, diabetes management, management of atrial fibrillation, and asymptomatic carotid stenosis. Secondary prevention is directed to those risk factors most relevant to stroke, including lifestyle (diet, sodium intake, exercise, weight, smoking, and alcohol intake), hypertension, dyslipidemia, previous stroke or transient ischemic attack, atrial fibrillation and stroke, and carotid stenosis. Recommendations for secondary prevention of stroke should be implemented throughout the recovery phase, including during inpatient and outpatient rehabilitation, reintegration into the community and ongoing follow-up by primary care practitioners. Secondary prevention should be addressed at all appropriate healthcare encounters on an ongoing basis following a stroke or transient ischemic attack. Economic studies that are updated with more recent clinical findings and studies that seek to identify the cost-effective combinations of different types of treatments are warranted.

NEW ORAL ANTICOAGULANTS (NOACS) IN ATRIAL FIBRILLATION

Naeem Dean, MD, FRCP

Professor of Medicine, University of Alberta, Edmonton, Canada

Approximately 20% of ischemic strokes have a cardio-embolic source and about 45-50% of these are due to atrial fibrillation. In individuals with atrial fibrillation the relative risk reduction of ischemic stroke with Aspirin is about 21%. Overall risk reduction with long-term anticoagulation with warfarin is about 68%. In spite of this huge benefit, prolonged treatment with warfarin has its limitations e.g. unpredictable patient response, requirement of constant monitoring and dose

adjustment, slow onset of action, narrow therapeutic window, dietary restrictions and drug interactions. An improved understanding of how the blood clotting cascade works has led to evolution of new oral anticoagulants. These NOACs offer an alternative to warfarin therapy. In recent years randomized clinical trials have shown that some of the new anticoagulants are non-inferior and in certain cases superior to warfarin in preventing ischemic strokes / thrombo-embolism in patients with non-valvular atrial fibrillation. Currently the new anticoagulants, which have been approved and are being used for this indication, are Dabigatran (Direct thrombin inhibitor), Rivaroxaban (Factor Xa inhibitor) and Apixaban (Direct factor Xa inhibitor). These novel oral agents have predictable dose responses, thus eliminating the need of routine monitoring; are prescribed as a fixed dose; have few, if any food and drug interactions, and in comparison to warfarin have less risk of intra-cranial bleeding. The main drawback of these new drugs is that we still do not have antidotes to reverse the anticoagulant effect in case of major bleeding. But overall the NOACs are simpler and convenient alternatives to warfarin in management of patients with atrial fibrillation.

STROKE IN YOUNG

Khurshid Khan

Associate Professor of Neurology, University of Alberta, Edmonton, Canada

Stroke is responsible for significant disability and mortality worldwide. More than 16 million people suffer from stroke every year. Majority of these occur in the developing countries. The risk of stroke doubles with every decade after age 55. While the overall prevalence remains high due to extended life expectancy, the incidence of stroke in the elderly appears to have declined especially in the developed countries. However, the rate of stroke in the young seems to be on the rise. Approximately 15 % all ischemic stroke affect young adults and adolescents. In the young the distribution of ischemic and hemorrhagic strokes (subarachnoid and intra cerebral hemorrhage) is approximately equal. Timely diagnosis of stroke in the young may be challenging due to lack of awareness, heterogeneity of risk factors and initial consideration of non vascular etiologies as cause of focal neurological symptoms. A young stroke victim is relatively more adversely impacted due to early loss of productivity with the resultant devastating effects on the patient, family and society at large. The etiology of young stroke is diverse ranging from the traditional risk factors commonly seen in the elderly to non atherosclerotic arteriopathies e.g. dissection, vasculitis, infections and various cardiac and hematological disorders. Non atherosclerotic causes

account for most stroke in young adults and adolescents. However, the traditional risk factors may co exist and increase with age. High index of suspicion for early diagnosis is important. The spectrum of diagnostic work up is much broader in young stroke victims. Acute and preventative treatment is similar to older patients.

STROKE IN PREGNANCY AND PUERPERIUM

Prof. Muhammad Wasay, MD, FRCP, FAAN

Professor of Neurology, Aga Khan University Hospital, Karachi, Pakistan

Pregnancy and puerperium have long been associated with an increased risk of strokes. The absolute risk increases only slightly but there is a marked increase in the relative risk of both stroke subtypes during pregnancy. The precise pathophysiology which accounts for this increased risk in pregnancy is not entirely clear. However, the physiological changes which accompany the state of pregnancy may largely account for this elevated risk. The peripartum period carries the highest risk and most studies have reported an increased incidence of strokes, particularly hemorrhages in this period. According to estimates, 50% of strokes are seen in the puerperial period and another 40% occur close to delivery. The risk factors for stroke observed during pregnancy can be divided into pregnancy related and unrelated causes. The pregnancy unrelated causes are the same risk factors seen in non pregnant patients including hypertension, tobacco use, arterial diseases, coagulopathies etc. Risk factors for pregnancy related intracerebral hemorrhage have been reported from the US population by Bateman. Advanced maternal age, African American race, pregnancy related and pre-existing hypertension, preeclampsia/eclampsia, Coagulopathy and the use of tobacco were independently associated with an increased risk of ICH in pregnancy. General principles of management are the same as for non-pregnant individuals with special focus on strict control of blood pressure so as to balance the risk of bleeding and the risk of cerebral and placental hypoperfusion. Aneurysms and AVMs need to be definitively managed to prevent bleeding, which may be achieved through surgical or endovascular procedures.

Vaginal delivery is preferred unless a cesarean is indicated for obstetric reasons. Risk of subsequent bleeding exists irrespective of whether the patient becomes pregnant again or not unless the lesions are obliterated.

VASCULAR INSULT TO INJURY: STROKE AND CANCER

Dr. Muzafar Siddiqui

Assistant Professor, Grey Nuns Hospital, University of Alberta, Edmonton, Canada

Cancer related causes of death and Stroke remain the most common causes of death in the industrialized

world. Despite advances in both Cancer and Stroke treatment; important questions regarding the risk, treatment and rehabilitation of Stroke amongst Cancer patients remain. In this series of cases, we hope to highlight the diagnostic and treatment related challenges and dilemmas that emerge in this setting. We will also review the existing literature in order to offer guidance for such clinical scenarios while suggesting areas for further investigation.

INVESTIGATIONS IN STROKE-A PRACTICAL APPROACH

Numan Amir, MD

Consultant Neurologist, SKMC, Abu Dhabi, UAE

Stroke is a devastating illness. The impact of stroke on individual and society is enormous. Therapeutic interventions rely heavily upon determination of the underlying pathophysiologic mechanisms that result in stroke. It is imperative to understand the underlying cause of stroke in an individual to tailor the treatment accordingly. Divided in two groups, ischemic and hemorrhagic, stroke investigations differ for the two types. Individuals presenting to an emergency room with symptoms of acute stroke are investigated differently from those who are encountered in a stroke prevention clinic. In acute setting, evaluation of a stroke victim requires a plain CT rather than an MRI brain to rule out intracranial hemorrhage. Additionally, if thrombolysis is considered, further work up including blood glucose level, PT/ INR and CBC determination is mandatory. Each patient presenting with acute stroke needs to have EKG and for selected patients, if clinically warranted, cardiac enzyme assessment should be considered. In sub-acute setting, further investigations are tailored according to the stroke type. Brain MRI is far superior to CT in outlining the extent of brain damage due to stroke. CT or Catheter angiography is used to evaluate extra and intracranial circulation for suspected arterial stenosis or dissections, aneurysms or vasculitic changes. Cardiac evaluations including echocardiography and holter monitoring are used to determine structural and functional cardiac health. Specialized blood tests for abnormal clotting of blood are reserved for individuals who are younger and are not found to have the traditional stroke risk factors namely hypertension, diabetes, hypercholesterolemia, obesity and smoking.

STROKE UNITS IN PAKISTAN - WHY AND HOW?

Dr. Ismail Khatri, MD

Consultant Neurologist, King Abdul-Aziz Medical City, National Guard Health Affairs, Riyadh, Saudi Arabia

Stroke is one of the leading causes of death and disability around the world. The burden of stroke is likely to rise over next several decades, particularly in low to middle income countries. Care for patients with

stroke is expensive and cumbersome. Stroke patients who receive organized inpatient care in a stroke unit are more likely to be alive, independent, and living at home one year after the stroke. The benefits of stroke unit care are most apparent when the stroke unit is based in a dedicated discrete ward. Although most stroke centers provide thrombolytic therapy in acute stroke, the benefits of stroke units are not exclusively dependent on thrombolytic therapy. The fact that intravenous or intraarterial thrombolytic therapy is not routinely available in Pakistan does not preclude the establishment of stroke units in Pakistan. Success of stroke units depends on dedicated, organized, multidisciplinary care according to standardized, evidence based protocols. The multidisciplinary team includes dedicated stroke physicians, stroke nurses, physical therapists, occupational therapists, speech and language pathologists, clinical nutritionists, and social workers. Emergency room physician and staff, neurosurgeon, radiologist, pharmacist, and rehabilitation specialist further add to the successful team. Stroke team coordinator and quality improvement specialist are two other members of the stroke team in the institution of author. All private and government hospitals in all major cities of Pakistan can establish stroke units by modest restructuring and restaffing. It is obvious that there are not enough neurologists in the country to run stroke unit in every big hospital of Pakistan; medical specialists can be trained in fundamentals of stroke care to lead the stroke units. Ancillary staff can be trained through short courses and focused seminars or conferences. Protocols can be modified for local use under the guidance and supervision of Pakistan Stroke Society. A massive burden of stroke is impending on the health care system of Pakistan and all low and middle income economies. If appropriate steps are taken now, significant reductions in death and disability can be achieved. Small investments now, will lead to huge savings in future. It is high time for medical community and policy makers to invest in establishment of stroke units across Pakistan. A stitch in time saves nine.

SUBARACHNOID HEMORRHAGE

*Dr. Muhammad Umar Farooq, MD, FACP, FAHA
Assistant Professor, Michigan State University, Grand Rapids, Michigan,
USA*

Subarachnoid hemorrhage (SAH) is a neurological emergency, often resulting in severe neurologic disability or death. A SAH can be categorized as traumatic or nontraumatic. Traumatic SAH is much more common than spontaneous or nontraumatic SAH, and it is not associated with the same complications. The majority of nontraumatic SAHs are due to the rupture of an intracranial aneurysm. The most common presenting

complaint is that of a severe or worst headache of life, which occurs in 85% to 95% of patients. Misdiagnosis of SAH is thought to be as high as 12% especially in good-grade patients with mild symptoms. The most common diagnostic error is failure to obtain a non-contrast brain CT scan. Lumbar puncture must be performed if the history is suspicious for SAH but the brain CT is negative. Failure to diagnose SAH is associated with 4-fold increase in death or severe disability. My talk will further cover different treatment options and Clinical Trials on Subarachnoid Hemorrhage.

RECENT ADVANCES IN MANAGEMENT OF CEREBROVASCULAR DISEASE

*Prof. Ashfaq Shuaib, MD, FRCPC, FAHA
Professor of Medicine, University of Alberta, Edmonton, Canada*

2013 was a busy year for outcome studies in cerebrovascular disease. Major advances were made in prevention of stroke in high risk TIA patients, improvements in endovascular therapy with the addition of exciting new tools and the early management of intracranial hemorrhage. Patients with transient ischemic attacks are at an extremely high risk of recurrence of stroke within the first 2-3 days after the event. The CHANCE study from China evaluated more than 5500 patients in whom treatment was initiated within 24 hours of onset of symptoms. The combination of clopidogrel (75 mg/day) and ASA (75 mg/day) were compared to ASA (75 mg/day) for 21 days, and outcome compared at 90 days. The investigators showed that the subsequent risk in 90 days was decreased from over 11% to approximately 8%. This highly significant reduction in stroke did not come at an increased risk of major bleeds. Minor bleeds, however, were more than double in the dual antiplatelet therapy compared to aspirin alone. These findings will hopefully be replicated in the POINT study currently underway in North America and funded by the NIH. A study is current planned for the Middle East where 10 days of dual antiplatelet therapy will be compared with 30 days, and investigators of the MENA (Middle East and North Africa stroke prevention and TIA trial) are currently in the process of submission of the protocol to the ethics committee. The treatment of acute stroke has significantly improved with the introduction of new, highly effective stent retrievers. The 'Solitaire and TREVO devices' are relatively easy to use and can achieve reperfusion in over 80-90% of patients with proximal MCA or distal carotid occlusions. The preliminary uncontrolled studies show very promising results that are being confirmed in several clinical trials currently underway in North America, Europe and Asia. In addition to endovascular technology, advances in imaging allow for better identification of patients in

whom collaterals are extensive and active and in whom reperfusion strategies at 9-12 hours or even longer after onset of symptoms may reverse the effects of cerebral ischemia. While the technology/treatments are currently offered at highly selective, very organized stroke programs, completion of the currently undergoing trials may allow for more widespread use, leading to continued improvement in the quality of life after this devastating disease. The INTERACT trial on the use of antihypertensive agents acutely in the treatment of intracranial hemorrhage was presented at the European Stroke Conference in London in May of this year. The data was published simultaneously in the New England Medical Journal. Antihypertensive therapy when used early in the setting of intracranial hemorrhage is safe and may hold the promise of better outcome. Other treatment modalities include the use of intraventricular tPA and intravenous activated Factor VII to improve outcomes. My presentation will review recent advances in the evaluation and management of transient ischemic attacks in acute stroke. I will also summarize briefly the impact of blood pressure control in hypertensive intracranial hemorrhages

GENETICS OF PAKISTANI POPULATIONS

Dr. Aisha Mohyuddin, PhD

Associate Professor Biochemistry, Shifa College of Medicine, Shifa Tameer-e-Millat University, Islamabad, Pakistan

DNA based markers have been widely used for the study of human evolution and genetic diversity of the human race. Pakistan lies on the postulated coastal route out of Africa to Australia and it has been suggested that humans arrived here about 60,000 years ago. Over the centuries, this region has witnessed multiple migrations and invasions including the nomadic Indo-Europeans tribes from central and west Asia, Alexander's army, Arabs, Afghans and Mongols. All have contributed to the ethnic variety of the extant Pakistani populations. The present day population of Pakistan is represented by many ethnic and linguistic groups including the Pathan, Punjabi, Hazara, Burusho, Kashmiri and Balti in the North and the Sindhi, Balochi, Brahui and Makrani in the South, among others. The majority of Pakistani ethnic groups speak Indo-European languages with the exception of the Burusho whose language Burushaski is a language isolate, the Balti who speak a Sino-Tibetan language and the Brahui who speak a Dravidian language. The genetic origins of various Pakistani ethnic groups have been investigated using autosomal short tandem repeat (STR) markers, biallelic markers and STRs on the Y chromosome as well as the polymorphic HLA system. The results of these studies indicate genetic relationships within the Pakistani ethnic groups are dictated primarily by geographic proximity rather

than linguistics. Most of the Pakistani ethnic groups, with the exception of the Hazara, show admixture with European populations, most probably the result of the invasion of nomadic Indo-European settlers from the pastoral highlands of West and Central Asia

MOLECULAR GENETICS OF PRIMARY MICROCEPHALY AND JAWAD SYNDROME

Dr. Mohammad Jawad Hassan, PhD

Assistant Professor Biochemistry, Shifa College of Medicine, Shifa Tameer-e-Millat University, Islamabad, Pakistan

Aim of present talk is to address some basic detail about the disease and to propose some suggestions for establishment of diagnostic facilities for these disorders. Autosomal Recessive Primary Microcephaly (MCPH-MIM 251200) is a rare disorder of neurogenic mitosis characterized by reduced head circumference at birth with variable degree of mental retardation. In MCPH patients, brain size reduced to almost one-third of its original volume due to reduced number of generated cerebral cortical neurons during embryonic neurogenesis. So far, ten genetic loci (MCPH1-12) for this condition have been mapped with all ten corresponding genes identified from different World populations. Contribution of ASPM (MCPH5) and WDR62 (MCPH2) genes mutations in MCPH is more than 50%. Jawad syndrome (MIM 251255) is a recessively inherited disorder characterized by Congenital Microcephaly with skeletal and skin abnormalities. Clinical features of affected individuals include congenital microcephaly with sharply sloping forehead, moderate to severe mental retardation, onychia congenita, and digital malformations (polydactyly and syndactyly). Some spots of unknown etiology are also present on the skin. By screening human genome this condition was mapped to a 15.33 cM interval between markers D18S1150 and D18S997 on chromosome 18p11-q11. An exonic frameshift mutation (1868delTA) was found in this family. High incidence of Congenital Microcephaly (syndromic or isolated) in Pakistani population reflects the most probable involvement of consanguinity. In fact, presence of different ethnic/linguistic backgrounds within Pakistani population and high levels of consanguinity among these groups give us an opportunity to establish ethnic group based mutation database. This will certainly help in diagnostics and will reduce the cost. On the other hand, genetic heterogeneity of the disorder (12 genes so far and many other coming) is a barrier for establishment of diagnostic facilities for affected families in particular and for general population in common. Genetic counseling and clinical management through carrier detection/prenatal diagnosis in affected families should be the focus of research in this field as this can help reducing the incidence of these autosomal

recessive disorders.

GENETICS OF INFLAMMATORY MYOSITIS

Mohammad Saeed Mehmood, MD

Assistant Professor Rheumatology, Liaquat National Hospital and Medical College, Karachi, Pakistan

Inflammatory myopathies are rare autoimmune disorders with onset in adulthood and cause severe morbidity due to their debilitating effect on the musculoskeletal system. This presentation will provide an overview of the clinical aspects of these diseases including their epidemiology, pathology, diagnosis and treatment. It will also review the underlying genetic and molecular causes of some specific subtypes so far elucidated. This will include a general overview of the genetics of myositis detailing the various genes and regions involved along with the molecular etiologies of MDA-5 and statin myopathies.

VASCULAR DEMENTIA

Kaysar Mamun, MD

Assistant Professor of Medicine, Duke University and National University of Singapore Graduate Medical School, Singapore

Dementia can be defined as an acquired and persistent impairment in intellectual function with problems in at least three of these areas: Memory, Language, Visuospatial skills, Emotions and personality, Complex cognition. The impairment is sufficient to interfere with usual social and occupational activities. Dementia is not always progressive or irreversible. Vascular dementia is the second most common form of dementia (10-25%) after Alzheimer's disease. Vascular dementia is classified as: Multi-infarct dementia, Strategic infarct dementia, Subcortical ischemic dementia, Hypoperfusion dementia, Mixed (usually with Alzheimer's). The severity of dementia may depend on the severity of the vascular disease, area of the brain affected and amount of brain involved. Diagnostic criteria, strategy of early detection and management will be discussed in details along with a review of the latest treatment strategy as noted in Cochrane database. Speaker will also highlight on effective preventive strategies and importance of raising public awareness about dementia and will share Singapore experience on these two issues

ROLE OF MOLECULAR IMAGING IN DEMENTIA

Asif Moinuddin, MD

Consultant Nuclear Medicine and PET Imaging, King Fahad Specialist Hospital, Dammam, Kingdom of Saudi Arabia

Imaging modalities whether anatomical or functional have developed significantly in the past several decades. In addition to the clinical manifestations and laboratory evaluations, imaging has now taken an integral role in patient's disease management. Biopsy specimen analysis

is by far the gold standard in the evaluation of a pathology however it is an invasive process and bears its consequences. Imaging on the other hand is non-invasive and not only it can provide most of the information needed for patient's management but can also guide tissue sampling. This in dementia is very important where brain biopsy is not routinely performed and clinical, laboratory and imaging is the cornerstone for patient's treatment. Molecular imaging using Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) agents are more sensitive from anatomical imaging (Computed Tomography and Magnetic Resonance Imaging) in showing disease changes earlier. These agents can also compliment anatomical imaging in further characterizing different subtypes of dementias. This differentiation is very important as management of dementia differs for reversible versus irreversible causes. Recent advancement in PET tracers using Fluorine-18 (F18) and Carbon-11 (C-11) isotopes are now more commonly used than SPECT agents. Among PET agents Fluorodeoxyglucose (FDG) and Pittsburgh Compound B (PiB) has shown promising results and are now incorporated in dementia evaluation.

NEUROLOGICAL MANIFESTATIONS OF DENGUE

Dr. Mohammad Athar Javed, MRCP, FRCP

Associate professor Neurology, King Edward Medical University, Lahore, Pakistan

Dengue is the most common arthropod-borne viral (Arboviral) illness in humans. Each year, an estimated 50-100 million cases of dengue fever and 500,000 cases of dengue hemorrhagic fever occur worldwide, with 22,000 deaths. Dengue fever (DF) is endemic in Pakistan with annual seasonal outbreaks observed every year. The country witnessed a major outbreak of dengue fever in 2011. Punjab was the worst affected province with over 250,000 suspected cases including 217 deaths reported from this outbreak in 2011. Our study is the largest on neurological manifestations of dengue fever from Pakistan. It showed that dengue fever may be complicated by a variety of central and peripheral neurological manifestations. However, the most frequent neurological manifestations were encephalitis followed by acute polyradiculoneuropathy (AIDP), myositis, transverse myelitis & acute disseminated encephalomyelitis (ADEM). Overall mortality is low and most of the manifestations are reversible. Some of the manifestations like cranial nerve palsies and anterior horn cell disease have not been reported in the literature before. The current priority for the country should be to respond to the situation adequately and appropriately. Standardization of case management using a nationally adopted protocol would be the key to minimize deaths

in the health facilities.

EPILEPSY CARE IN PAKISTAN - EVIDENCE-BASED CAPACITY BUILDING

Zarine Mogal, MD
Consultant Neurologist, Sindh Government Hospital

Epilepsy is a commonly prevalent neurological disorder worldwide. The 1986-87 population-based epidemiologic and knowledge, attitude and practice study revealed prevalence of epilepsy in Pakistan to be 0.98% and only 2% rural and 28% urban patients to be taking medicines. Lack of awareness about its treatability, misconceptions, erroneous socio-cultural beliefs and practices, stigma and poverty were the main reasons for a large number not taking any medicines. To bridge this huge treatment gap capacity building for epilepsy care in Pakistan was undertaken by a newly established NGO, Neurology Research and Patient Welfare Fund in 1989 which evolved stepwise from an institutional/organizational level to the national level. Following assessment of ground realities, targets were identified, strategic planning and implementation of indigenous interventional projects to achieve the goals was done that continues to date. The NGO's Comprehensive Epilepsy Control Programme of Pakistan formally launched in 2001 incorporated old and new projects for intense and sustained public awareness. The NGO-run National Epilepsy Centre in Karachi has been providing holistic management of patients with epilepsy since 2007. Success or failure of this ongoing project since a quarter of a century has been assessed through direct and indirect methods. The entire project has been possible through the gracious donations of individuals and organizations.

VIDEO EEG- THE AKUH EXPERIENCE

Fowzia Siddiqui, Sabirud Din
Aga Khan University Hospital, Karachi, Pakistan

Our understanding of Epilepsy has been greatly advanced by video EEG monitoring which allows prolonged simultaneous recording of patients' behavior and EEG. This allows precise correlation between seizure semiology and correlating activity in the brain. Video-EEG recordings can be done on hospitalized inpatients or on outpatients, AKU has only inpatient recording facilities, which is preferred as technologists are available to adjust electrodes and diminish outside artifacts. Video-EEG can be vital in the diagnosis of epilepsy and epileptic seizures. It allows the doctor to determine:

1. whether events with unusual features are epileptic seizures
2. Type of epileptic seizures
3. Region of the brain from which the seizures arise

this last step is critical in assessing a patient for possible epilepsy surgery (phase I and II).

The Aga Khan University Hospital (AKU) is a private university hospital pioneering VEEG in Pakistan since 2001, its use increased as the comprehensive epilepsy center was set up in 2006 and from an average of about 20 per year increased to over 60 per year. In our experience 42.8% of total VEEG show Non epileptic events with normal EEGs 30.9% clearly ictal events with a Focus corresponding to MRI. 16.6% had non convulsive status and frequent inter ictals 4% both NES and epileptic events. This shows the immense number of non epileptic patients on unnecessary AEDs as refractory seizers and also the ability to further epilepsy surgery in patients with clear focus.

Molecular and Cellular Biology as the Third Dimension of Neurodegeneration: study of ALS and ALS/dementia

Teepu Siddique, MD
Les Turner Foundation/Herbert C. Wenske Foundation Professor,
Davee Department of Neurology and Department of Cell and Molecular Biology, Northwestern Feinberg School of Medicine, Chicago, USA

The phenotype, the neural connections and the molecular cellular biology constitute the three convenient levels for the study of amyotrophic lateral sclerosis (ALS) and related neurodegenerations. ALS is at least three things, a clinical condition with multiple etiologies, an isolation of the motor pathway connectome, both of these are caused by a third, a disorder of cellular/molecular pathways. Our thirty year experience with this group of disorders has resulted in two major paradigm shifts in the molecular/cellular understanding of this disorder. The first strike against ALS was in the application of molecular genetics techniques to study the familial form of the disorder in the period of 1985-1993, and the second paradigm occurred with the discovery of direct evidence for the involvement of protein quality control pathways in ALS and ALS/dementia in the period 2000-2011. This second strike was the discovery of mutations in SQSTM1 (p-62) and UBQLN2. These recent findings suggest that two common protein recycling pathways, the ubiquitin-proteasome system (UPS) and the autophagosome-lysosome pathways, are directly involved in neurodegeneration and are rational targets for prevention and treatment of ALS and ALS/dementia and related disorders.