2010 PROGRAM

The program will consist of a series of oral and poster presentations highlighting basic and clinical research performed by School of Medicine students, residents and fellows. Please use pages 12 through 15, to locate presenters, their abstracts, presentation times and location of presentation. The complete agenda is available at http://www.musom.marshall.edu.

Intended Audience

The 22nd Annual Research Day is designed for physicians, residents, basic scientists, medical students, graduate students, and other interested health professionals.

GOALS

- To involve faculty, medical and graduate students in the process required to formally present their research in either oral or poster presentations.
- 2) To inform and involve the community in ongoing research at Marshall University Joan C. Edwards School of Medicine.
- To encourage the attitude among faculty, residents, and students for Continuing Medical Education in the area of clinical research.

GLOBAL LEARNING OBJECTIVES

By the end of these lectures the participant will be able to:

- 1) Compare different approaches to medical investigation.
- 2) Compare and contrast the importance of basic research and cellular mechanisms as it relates to human disease.
- 3) Discuss and review research related to current and future improvements in the clinical management of patients.
- 4) Interpret and analyze data for medical investigation to potentially determine the effectiveness towards improving patient care.
- 5) Stress the importance of translational research benefits to the basic scientist in support of the practicing physician.
- Discuss the quality of research in medical education and its application to educational practice in undergraduate and graduate medical education.

CREDIT STATEMENT

Marshall University Joan C. Edwards School of Medicine designates these educational activities for a maximum of 4.5 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. (Session Registration and Evaluation are required).

EVALUATION FORM Completion

Please follow specific instructions for completing the bar coded evaluation form. Keep your "X's" in the bubbles and your written comments in the designated boxes. Your input is needed for planning future events.

ASSISTED SERVICES

If special arrangements are required for an individual with a disability to attend these events, please contact Continuing Medical Education at (304) 691-1770 no later than 1 week before the event date or See a CME Representative at the Registration Area on the day of the event.

PLANNING COMMITTEE - NO DISCLOSURE

David N. Bailey, MBA Todd Gress, MD Linda Holmes, MA Beverly McCoy, MA Charles McKown, MD, Dean Richard Niles, PhD, Chair Darshana Shah, PhD

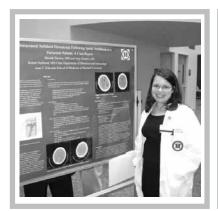
STAFF COORDINATORS - NO DISCLOSURE

Anita Mathis - BMS Coordination & Registration Patricia "Trish" Martin - Registration Judy Ross - Web Publications

RESEARCH DAY 2008













PAST INVITED LECTURERS

2008 – Gregory Alan Hale, MD

Associate Professor of Pediatrics

University of Tennessee

- 1) Transplantation and Cellular Therapies: Current Research and Future Opportunities
- **2)** An introduction to Hematopoietic Cell Transplantation

2007 – Daniel D. Bikle, M.D., Ph.D.

Professor of Medicine and Dermatology

In residence University of California

- The skin game: Calcium and vitamin D regulated cellular differentiation
- 2) Vitamin D: how much do we need and why

2006 - Mark E. Shirtliff, Ph.D.

Assistant Professor, Department of Biomedical Sciences Dental School, University of Maryland-Baltimore Baltimore, Maryland

1) Staphylococcus aureus biofilms: in vitro and in vivo studies

2006 - J. William Costerton, Ph.D.

Director & Professor, Center for Biofilms, School of Dentistry University of Southern California Los Angeles, California

1) Biofilms in Device-related and other Chronic Bacterial Diseases

2005 – William F. Balistreri, MD

Director, Gastroenterology

Cincinnati Children's Hospital Medical Center

- 1) Inborn Errors of Bile Acid Biosynthesis
- 2) Viral Hepatitis 2005

2004 - Joseph S. McLaughlin, MD

Professor Emeritus of Surgery University of Maryland

- 1) Traumatic Ruptured Aorta
- 2) Strange Tumor I Have Known

2003 – W. Jackson Pledger, Ph.D.

Professor, Interdisciplinary Oncology

University of South Florida College of Medicine Tampa, Florida

- 1) Regulation of proliferation by cyclin dependent kinase
- 2) Functional genomics and cancer therapy

2002 - Alan H. Jobe, M.D., Ph.D.

Professor of Pediatrics

Cincinnati Children's Hospital Medical Center Cincinnati, Ohio

1) Mechanisms of lung injury in the preterm

2) Translational research on lung maturation based on clinical observations

2001 - Arnold Starr, M.D.

Director, Alzheimers' Research Center

Institute Brain Research of California, Irvine

- 1) Hearing but not understanding: auditory nerve dysfunction in the presence of preserved cochlear receptors
- 2) Patients 'stories and their seminal importance for research

2000-Fredrick L. Brancati, M.D., M.H.S.

Associate Professor, Medicine and Epidemiology

John Hopkins Medical Institute

- 1) Novel risk factors for type 2 diabetes mellitus and their implications for treatment
- 2) Prevention and clinical epidemeology in the new milleniuum

1999 – Robert B. Belshe, MD

Director and Professor, Div. of Infectious Diseases and Immunology St. Louis University

- 1) Live attenuated influenza vaccine: using genetics to defeat the flu
- 2) Vaccines for the 21st century

1998 – Jerome S. Brody, MD

Vice-Chairman of Medicine for Research, Professor of Medicine Director, Pulmonary Center

Boston University School of Medicine

- 1) Lung development: lesson from flies connections to cancer
- 2) Molecular approaches to the diagnosis of lung cancer

1997 – Rochelle Hirschhorn, MD

Professor of Medicine, Department of Medicine NYU School of Medicine

- 1) Advances in defects in host defense
- 2) Reflection on the changing face of medicine

1996 - Stuart F. Schlossman, MD

Baruj Benacerraf Professor of Medicine

Harvard Medical School

Chief, Division of Tumor Immunology

Dana-Barber Cancer Institute, Boston

- 1) Human T-cell activation
- **2)** What's in a name -cd nomenclature

1995 – Frank M. Torti, MPH, MD, FACP

Director, Comprehensive Cancer Center

Professor Charles L. Spurr Professor of Medicine

Section Head for Hematology/Oncology, Wake Forest University

Chairman, Department of Cancer Biology

- Bowman Gray School of Medicine

 1) New pathways for the regulation of iron
- 2) Popeye spinach and iron: the politics

1994 - Abner Louis Notkins, MDB

Director, Intramural Research Program Chief, Laboratory of Oral Medicine National Institute of Dental Research, National Institutes of Health, Bethesda, MD

1) Polyreactive antibody molecules and matter

2) The Bethesda experiment

1993 - Erling Norrby, MD, PhD

Dean of Research and Professor of Virology Karolinska Institute, Department of Virology Sweden

1) Immunization against HIV-2/SIV in monkeys

2) The selection of Nobel Prize winners

1992 - Simon Karpatkin, MD

Professor of Medicine

New York University School of Medicine

1) Role of thromin, integrins and oncogenes

2) How scientific discoveries are made

1991 - Robert M. Chanock, MD

Chief, Laboratory of Infectious Diseases National Institute of Allergy & Infectious Diseases National Institutes of Health, Bethesda, MD

1) Epiedemiology, pathogenesis, therapy

2) New approaches to development of treatment plans

1990 – Dewitt S. Goodman, MD

Director, Institute of Human Nutrition
Director, Arteriosclerosis Research Center
Tiden-Weger-Bieler Professor of Preventative Medicine
Professor of Medicine, Columbia University,

College of Physicians and Surgeons Director, Division of Metabolism and Nutrition Department of Medicine Columbia-Presbyterian Medical Center, New York

Retinoid and retinoid-binding proteins

1989 – Michael A. Zasloff, MD, PhD

Charles E.H. Upham, Profess of Pediatrics University of Pennsylvania School of Medicine Chief, Division of Human Genetics & Molecular Biology The Children's Hospital of Philadelphia

1) The flow of genetic information

2) Magainin peptides

21ST ANNUAL 2008 RESEARCH DAY WINNERS

March 18, 2008



Thelma V. Owen Memorial Clinical Vignette Poster Winner Jay Lakhani

"Renal atrophy as a complication of umbilical arterial catheterization"



Roland H. Burns Memorial Clinical Science Poster Winner Waseem Ostwani

"Habitual constipation in children: it's all in the family!!"

and Roland H. Burns Memorial Clinical Science Oral Winner

"A retrospective study comparing beractant and poractant treatment in very low birth weight infants with respiratory distress syndrome"



Anagene B. Heiner Memorial Basic Science Poster Winner Jennifer Napper

"Epigenetic modulation through HSP90 serves as a mechanism of induced phenotypic plasticity"



Thelma V. Owen Memorial Clinical Vignette Oral Winner Tracy Hendershot

"A report of a rare 'slit fracture' through two adjacent cervical vertebrae"



Anagene B. Heiner Memorial Basic Science Oral Winner Amy Nash

"Effects of decreased SKI on invasive properties of testicular cancer cells"

RICHARD J. STEVENS, MD MEMORIAL LECTURE MARCH 31, 2010, 11:45 AM INVITED LECTURER



Gregory Germino, MD (No Disclosure or Conflicts)

Deputy Director of the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) at the National Institutes of Health (NIH)

"Dia-besity: converging problems, emerging science."

Learning Objectives:

- 1. Review the mission of NIH and the role of NIDDK in pursuing fundamental knowledge about the nature and behavior of the endocrine system and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.
- 2. Explain how NIDDK is approaching the dual problems of diabetes and obesity.
- 3. Learn new insights into the biology of beta-cells and adipocytes and how this knowledge will help improve our treatment of the related disorders diabetes and obesity.
- 4. Review findings of recent clinical studies and their implications for patient care.
- 5. Learn about our public education efforts and how these can be utilized in practice.
- 6. Discuss the role of our trainees in helping to solve this problem.

ABOUT THE RICHARD J. STEVENS, MD MEMORIAL LECTURE

The Richard J. Stevens, MD Memorial Lecture is supported annually by the family of Dr. Stevens. Dr. Stevens was an outstanding medical practitioner characterized by Dean Charles H. McKown, Jr., of the Marshall University Joan C. Edwards School of Medicine as a pioneer "who was never in a hurry but always on the move."

Born in Portsmouth, Ohio, Dr. Stevens received his undergraduate degree from Marshall University, attended West Virginia School of Medicine for two years, then went on to earn his medical degree from Rush Medical School in Chicago.

Dr. Stevens returned to Huntington in 1941 as one of the first board certified practitioners in internal medicine in the area. He was a member of the Alpha Omega Alpha, the medical honorary, as well as gastroenterology and research societies.

Dr. Stevens was one of three physicians who first researched prothrombin testing for guidance in administering anticoagulants to patients with coronary occlusion.

Remembered as genuinely committed to his profession, his community and those around him, he had the unique ability to bring about a meeting of the minds among colleagues, patients and families.

The memorial lecture is presented each year at the Marshall University Joan C. Edwards School of Medicine's Research Day. It was established by Dr. Steven's wife, Dr. Sarah Louise Cockrell Stevens, and their seven children: Chari Louise Stevens Singleton, Mary Alice Stevens, Richard J. Stevens II, Johanna Stevens Holswade, Robert C. Stevens, and Randall C. Stevens.

ACADEMY PAGE



PROMOTING EXCELLENCE IN MEDICAL EDUCATION

Since its inception, the Academy of Medical Educators has provided some of our school's most outstanding faculty and residents with a breadth and depth of teaching resources that are taking our educational program to a new level of excellence. As we conclude the fifth successful year for this innovative program, at the JCESOM, Academy takes on even greater importance when the members pursue scholarship in teaching and learning. The scholarly activity generated by the members themselves continues to bring honor and recognition to Marshall.

Nomination for the academy will be accepted in August 2010

PRESENTING AT THE 2010 RESEARCH DAY

Yousef Darrat Waseem Ostwani William Nitardy Shadi Obeidat

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Registration & Breakfast		7:00AM
ORAL SESSION I - Page	e 17 INTRODUCTION	8:20AM
1 Abdrhman Hamo	Look to the right, and you may pass out	8:30AM
2 J. Adam Hall	A role for the chromatin-remodeling CHDI	8:42AM
3 Susan Flesher	in a mouse model of Sjogren's Syndrome Improved growth and development in premature	8:54AM
5 Susan Piesnei	infants managed with nasal continuous positive	0.34AW
	airway pressure	
4 Dana Eilen	A 15 year old male with acute coronary thrombosis	9:06AM
	secondary to acute myleogenous leukemia	
5 Melinda Asbury	The Specific Mechanism by which Dopamine-induced	9:18AM
	MApK p38 Activation Serves as a Molecular Switch	
	Between Cellular Protection and Destruction in a Mod	el
	of Methamphtamine Neurotoxicity	
BREAK	POSTER SESSION I - ATRIUM - Page 41 9:45	-10:30AM
ORAL SESSION II - P	age 23	
6 Saif Mashaqi	Utility of CT angiography of the chest for evaluation	10:30AM
o buil musikqi	of pulmonary embolism in an emergency room	10.5011.11
7 Andrea Lauffer	A MSM with VDRL-negative neurosyphilis	10:42AM
	co-infected with previously undiagnosed AIDS	
8 Brian Price	Diabetes Alters Vascular Mechanotransduction:	10:54AM
	pressure-induced regulation of phosphatase and	
	Tensin Homologue (PTEn) in the Rat Infereior Vena Cava	
9 Mustafa H. Awili	Imatinib Induced Serositis	11:06AM
10 Rohit Aswani	Acanthosis nigricans as clinical marker for insulin	11:18AM
10 10 m 10 m m	resistance in obese children	11.1011.11
Dr. McKown intro Dr. Jo	seph M. Farrell Professorship Announcement	11:30AM
	Germino, MD, Deputy Director of the National Institu	te of
	nd Kidney Disease (NIDDK) at the National Institute	
Health (NIH)	and a second control of the second control o	, 01
"Die hesity: convergin	g problems, emerging science."	11:45AM
Dia-besity: convergin	g problems, emerging science.	11.43AM
BOX LUNCH		12:40PM
ORAL SESSION III -	Page 31	
11.70.124		1.150) (
11 Rohit Aswani 12 Linda Eastham	Seasonal trend of eosinophilic esophagitis in children	1:15PM
12 Liliua Eastilaili	AKAP12 Expression and Regulation in Mouse and Human Melanocytes and Melanoma Cells	1:27PM
13 L. Emily Morris	Presentation and outcome of a pregnant patient with	1:39PM
Dilling 11201110	acute on chronic pancreatitis due to	1.071.11
	hypertriglyceridemia	
14 Lauren Richards-Waugh	The Role of CyP3A5 Genetic Polymorphisms in	1:51PM
	Unexpected Methadone Death	
15 Samia Kanooz	Self reported risk factors for bone loss: utility	2:03PM
	of a patient questionnaire completed at time of	
	bone mineral density testing	

ORAL AND POSTER PRESENTATIONS

BREAK	POSTER SESSION II- ATRIUM - Page 7	1 2:30PM 3:15PM
ORAL Session IV - Pa	ge 37	
16 Jasjeet Bhullar	YB-1 Expression in Early Hematopoiesis and Leukemic Cells	d 3:15PM
17 Yousef Darrat	Do erroneous reports of computer interpreted electrocardiogram influence analysis by medical trainees?	1- 3:27PM
	EVALUATION TURN IN	3:39PM
Research Day AWARDS Academy of Medical Educ	PRESENTATION-Harless Auditorium ators Scholar Recognition	4:00PM
POSTER PRESENTATION	ONS SESSION I, ATRIUM - Page 41	9:45AM-10:30AM
PRESENTER	TITLE	TIME*
1 M. Lea Morton-Fishman	Variable Response to First Line Treatments for PTSD: An Associated Finding	9:45AM-10:30AM
2 Aileen Marcelo	The Potential Role of Vascular Endothelial Growth Factor (VEGF) in the Diabetic Brain Microvasculature	9:45AM-10:30AM
3 Kathleen C. Brown	Anti-neoplastic activity of capsaicin in human small cell lung cancer	9:45AM-10:30AM
4 Lacey Mae Vence	P-Gluyocoprotein UP-Regulation by 2,3,7,8- Tetrachlorodibenzodioxin is Ameliorated by Epigallocatechin 3-Gallate	9:45AM-10:30AM
5 J. Michael Brown	Acetaminophen Alterations of Antioxidant Enzyme Function Negated by SAMc	9:45AM-10:30AM
6 Megan Valentine	Role of Chmp1 Protein in Drosophila	9:45AM-10:30AM
7 Rounak Nande	Eradication of Therapy-Resistant Human Prostate Tumors Using Ultrasound Guided Site-Specific Cancer Terminator Virus Delivery Approach	9:45AM-10:30AM
8 Sarah Kelly	Omega-3 and -6 Fatty Acids Select, Proliferate and Sensitize Colorectal Cancer Stem-like Cells to Chemotherapy	9:45AM-10:30AM
9 Dilip Nair	Perspectives of Family Medicine Residents on Residency Curriculum Regarding Worldv Thinking in Patient Care	9:45AM-10:30AM iew
10 Waseem Ostwani	Pilot Pediatric Electrocardiogram Curriculum for First Year Pediatric Residents	n 9:45AM-10:30AM
11 William Nitardy	Enhancing Educational Effectiveness of Bedside Rounds	9:45AM-10:30AM
12 Shadi Obeidat	Evaluation of Teaching Methods and Chest X-Ray Interpretation Skills of Senior Medical Students	9:45AM-10:30AM
13 Daniel Felbaum	Pediatric ependymal spinal tumor: case report and literature search	9:45AM-10:30AM
14 Naveen Bellam	Assessing the utility of heat CTs in patients presenting with altered mental status or Sync	9:45AM-10:30AM

POSTER PRESENTATIONS		
15 Mateen Hotiana	Hypercalcemia in a patient with co-existent primary hyperparathyroidism and sarcoidosis	9:45AM-10:30AM
16 Mateen Hotiana	Association of Retinol Binding Protein-4 and Obesity in Children	9:45AM-10:30AM
17 Eyad Hamoudeh	Cardiomyopathy and Multiple Organ Failure in Patient with Neurofibromatosis	9:45AM-10:30AM
18 Minty Shah	Wernicke's encephalopathy after bariatric surgery	9:45AM-10:30AM
19 Rohit Aswani	Left Atrial Appendage Thrombus in a Preterm Neonate in Sinus Rhythm with Septic Shock	9:45AM-10:30AM
20 Rohit Aswani	An Unusual Case of Community Acquired Extended Spectrum β Lactamase Producing E-Coli Urinary Tract Infection in an Infant	9:45AM-10:30AM
21 Ihtisham Choudhry	Big Trouble with Bartonella: A Complicated Case of Endocarditis in a Healthy, Non-homeless Man	9:45AM-10:30AM
22 Saba Faiz	Etiology of Endogenous Hyperthyroidism in two patients with long standing hypothyroidism	
23 Saba Faiz	A Case Report of Unusual Presentation of Colon Cancer as Multi Nodular Goiter	9:45AM-10:30AM
24 Tae Hoon Lee	Ranitidine-induced hepatitis: a rare case of hepatotoxicity	9:45AM-10:30AM
25 Samantha L. Cook	Pediatric Demographics Associated with Methicillin Resistant Staphylococcal Aureus (MRSA) Infections	9:45AM-10:30AM
26 Misty R. Shoemaker	Feasibility of Telemedicine Fetal Echocardiography in the Perinatal Center in Appalachia	9:45AM-10:30AM
POSTER PRESENTATION	ONS SESSION II, ATRIUM - Page 71	2:30PM-3:15PM
PRESENTER	TITLE	TIME*
27 Rohit Aswani	Left Atrial Appendage Thrombus in a Preterm Neonate in Sinus Rhythm with Septic Shock	2:30PM
28 Joshua Dillon	Methicillin-Resistant Staphylococcus Aureus Osteomyelitis Leading to Septic Thrombophlebitis in Two Adolescent Males	2:30PM
29 Amanda Pauley	Management of Pregnancy, Labor, and Delive in a Patient with Hypertrophic Obstructive Cardiomyopathy	2:30PM
30 Gregory Thomas Burg	Neisseria meningitidis type C pneumonia and septicemia misidentified as Neisseria sicca in a woman with the Acquired Immunodeficienc	
31 Firas Almahasneh	Acetaminophen diminishes age-associated inc in Cardiac Oxidative Stress in the Male Fisher344XBrown Norway Rats	
32 Robert Cross	Subacute Ventricular Free Wall Rupture: A Ca	
33 Peter DiMartino	Accessory mitral valve leaflet associated with aortic coarctation, bicuspid aortic valve, and s regurgitation	severe mitral
34 Feras El-Bash	Vagally mediated atrial fibrillation	2:30PM
35 Aaron Kaibas	"Inverted" Takatosbo Cardiomyopathy	2:30PM

F	POSTER PRESENTATIONS	
36 Mehrette Maru	Effect of iron chelation on cardiac function in the iron-overloaded Mongolian gerbil	2:30PM
37 Raja Nawaz	Unique case of atrial fibrillation induced by	2:30PM
7 Raja Nawaz	pronation of the right arm	2.301 WI
38 Nizar Noureddine	Osler's Trial Complicated by Prosthetic	2:30PM
o i vizar i voaredame	Aortic Valve Abscess	2.501 111
39 Prasanna Santhanam	The Diagnostic Predicament of Secondary	2:30PM
,	Adrenal Insufficiency	_,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
10 Padma Venkatraman	An Unusual Presentation of Pheochromocytoma	2:30PM
	as Stress Induced Cardiomyopathy	
41 Saif Arsan Mashaqi	Gender Difference and the Severity of	2:30PM
1	Nocturnal Oxygen Desaturation in Obese Patients	
12 Audra Pritt	Fighting obesity: Should medical intervention start earlier?	2:30PM
13 Kevin Johnson	Sex Differences in Epicardial Fat Micro RNAs	2:30PM
	in Patients with Coronary Artery Disease	
14 Chris Adams	Sex differences in Epicardial Fat Biomarkers	2:30PM
	in Patients Undergoing coronary Bypass Graft	
	Surgery-West Virginia Appalachian Heart Study	
5 Ryan Kerr	Mycobacterium Fortuitum Soft-Tissue Infection	2:30PM
	after Bilateral Mastectomy	
l6 Samia Kanooz	An unusual presentation of Germinoma with	2:30PM
	negative initial neuro-imaging	
7 Sarah Miles	Effect of quercetin and antioxidants on the	2:30PM
	growth of human melanoma	
18 Sasha A. Zill	Sensing force of a muscle that actively engages	2:30PM
	the substrate: testing sensory responses of tarsal	
	campaniform sensilla using a "bionic" preparation	
19 W. Elaine Hardman	Omega 3 fatty acids to slow progression of indolent	2:30PM
	B-cell malignancies	2 20D) (
50 Anne M. Silvis	Differentiation induction with all-trans retinoic	2:30PM
	acid (ATRA) parallels reactive oxygen species	
1 C 1 V-11-	(ROS) generation in SK-N-SH neuroblastoma cells	2.20DM
51 Sunil Kakarla	Chronic acetaminophen attenuates age-associated	2:30PM
	increases in cardiac ROS and apoptosis in the Fischer brown Norway rat	
2 Jennifer M. Napper	17-AGG treatment induces a diverse response in	2:30PM
2 Johnson W. Nappel	human AML cells	2.301 W
3 Sandeep S. Joshi	Hypoxia inducible factor-1a regulates	2:30PM
5 Surdeep 5. Josiii	Microphthalmia-associated transcription	2.501 W
	factor expression in huyman melanoma	
54 Matthew Harlow	Nuclear-mediated function of CHmp1A in the	2:30PM
Tiviatile () Tiulio ()	regulation of ATM signaling for the control of	2.5 01 111
	human pancreatic tumor cell growth	
55 Ryan Mackie	Chmp1A mediated chromatin modification	2:30PM
,	and cell cycle regulation in HEK 293T and PanC-1 cells	
66 Reem H. Kheetan	Thyroid Maltoma	2:30PM
77 Beatrice Grasu	Partial epicondylectomy with digital palpation of	2:30PM
, Dualito Giusa	the ulnar nerve: a new surgical technique	2.501 141
I D AWADDO	PRESENTATION-Harless Auditorium	4:00 PM





LOOK TO THE RIGHT, AND YOU MIGHT PASS OUT. Abdrhman Hamo MD, Esam Baryun MD, Mehiar El-Hamdani MD, and Paulette Wehner MD. Marshall University Joan C. Edwards School of Medicine, Department of Cardiovascular Services. Huntington, WV.

Introduction: Practicing medicine in 2009 revolves more commonly around the use of technology and interpretation of study results. We present here a diagnosis made by completing a careful history and physical and avoidance of an unnecessary procedure, i.e. permanent pacemaker placement.

Case Presentation: A 63-year old hypertensive gentleman presented with episodes of light headedness, chest tightness, and generalized weakness for the past year which became more frequent in the last few weeks. He recently noticed that his heart rate (HR) was getting obviously slower when he exercises on the treadmill. He is taking Atenolol for hypertension and the dose was decreased a month ago without benefit. On physical examination, a right-sided asymmetric goiter was noted. The EKG showed sinus bradycardia with HR of 55 bpm. Laboratory analysis revealed intact thyroid function tests, cardiac enzymes, and electrolytes. Carotid massage was negative for hypersensitivity syndrome (no pause or hypotension). A treadmill stress test and 2D-Echo were unremarkable. Atenolol was discontinued and he was discharged home with an event monitor. A few days later, the patient had recurrent symptoms. The event monitor showed no evidence of bradycardia but at the time of symptoms, he had a sudden decrease in his HR from 110 to 70, which was inappropriate as it occurred while walking upstairs. Upon further questioning, it was found that turning his head to the right side always precipitated the patient's symptoms. The episodes occurred during his vacation looking out the window to the right. Another event occurred at home while running up the stairs and making a sharp right turn. Therefore a high suspicion of a neck mass compressing the carotid sinus causing a reflex bradycardia developed. **Discussion:** In a patient who presents with bradycardia or syncope of unknown origin, a thorough history and physical examination can sometimes provide clues suggesting unusual causes of bradycardia like our patient. Reversible causes of bradycardia include: medications, increased intra-cranial pressure, carotid sinus pressure, hypothyroidism, hypoxia, and obstructive sleep apnea. Symptomatic bradycardia is a Class I indication for permanent pacemaker implantation. It is very important to rule out completely reversible causes of bradycardia before a permanent pacemaker is indicated. Our patient was successfully treated with thyroidectomy.

A ROLE FOR THE CHROMATIN-REMODELER CHD1 IN A MOUSE MODEL FOR SJÖGREN'S SYNDROME J. Adam Hall, Nicholas L. Adkins, and Philippe T. Georgel. Cell Differentiation and Development Center, Marshall University, Huntington, WV.

Sjögren's Syndrome is characterized by an autoimmune attack on multiple organs, most notably the salivary glands. Its effects can be debilitating, resulting in difficulty in phonation and deglutition, mucosal ulcerations, and dental caries. These pathologies result from hyposecretion of mucins, glycoprotein constituents of saliva, by the sublingual gland (SLG). A model for Sjögren's Syndrome, NFS-sld mice, exhibit nonfunctional SLGs as neonates. Interestingly, through quantitative PCR and immunoblotting methods, we found these mucin-deficient NFS-sld neonates to express and produce 3-fold more of the chromatin-remodeler Chd1 compared to their wild-type counterparts (NFS-N mice). With Chd1 being an epigenetic factor, we sought to assess its role in the regulation of SLG marker genes in mucin-deficient (NFS-sld) and mucin-producing (NFS-N) mice. As expected, expression of SLG marker genes was affected in NFS-sld neonates compared to the NFS-N strain. Utilizing assays for chromatin remodeling (nucleosome repeat length analysis) and *in vivo* protein-DNA interaction (chromatin immunoprecipitation or ChIP), we found these changes in expression to be highly correlated with both changes in Chd1 occupancy of SLG marker regulatory loci and alterations in nucleosome spacing at the same genetic regions. Initial NFS-sld and NFS-N SLG marker co-localization studies (ChIP) on Chd1 and two of its binding partners, GCN5 and NCoR, indicate a switch from Chd1-repressor to Chd1-activator interactions consistent with states of gene activity and functionality of the SLG. Overall, our results seem to indicate that a dosedependent amount of Chd1 is required for proper mucin production and SLG functionality. Overproduction of Chd1, as seen in mucin-deficient NFS-sld neonates, can lead to aberrant localization, activity, and interactions at key genetic loci. Subsequently, the potential for Chd1 as a therapeutic target for salivary pathologies such as Sjögren's Syndrome seems ripe for investigation.

IMPROVED GROWTH AND DEVELOPMENT IN PREMATURE INFANTS MANAGED WITH NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (NCPAP). Susan Flesher and Renee Domanico. Department of Pediatrics, Joan C. Edwards School of Medicine, Huntington, WV 25701.

Objective: The purpose of our study is to assess the association between the use of NCPAP vs. conventional mechanical ventilation (CMV) in premature infants and their physical growth and developmental outcomes.

Methods: A retrospective chart review of two groups of NICU babies was conducted. The first group (n=140) was from 1/1999 – 12/2000 and was managed primarily by NCPAP. The second group (n=168) was from 1/2003-12/2004 and was managed primarily by NCPAP. To evaluate the similarity of the groups demographic and intervention variables of gender, gestational age, birth weight, length, and head circumference, APGAR scores, size for gestational age, maternal chorioamnionitis, nosocomial infections, antenatal steroids, transport status, early intervention, and use of high calorie formula were compared. Outcome variables included mean weight at 2 weeks, 1 month, discharge, 4-6 months, 9-12 months, 15-18 months, and 2 years. Mean head circumference and length were evaluated at these intervals except 2 weeks and 1 month. Mean Bayley Infant Neurodevelopmental Screening (BINS) scores at the same post discharge intervals were calculated. Categorical variables were analyzed using Pearson Chi Square. Mean numerical values were analyzed with the student t-test.

Results: There were no statistically significant differences in demographic or intervention variables. Mean weight at one month was 1340 in the CMV group and 1449 in the NCPAP group (p=.02). The NCPAP group continued to show improved growth in weight at 9-12 months (p=.009) and 15-18 months (p=.002), in length at 4-6 months (p=.02), 9-12 months (p=.03), 15-18 months (p=.002), and 2 years (p=.05). BINS scores were higher in the NCPAP group at 9-12 months (p=.00) and 15-18 months (p=.006).

Conclusions: NCPAP therapy when compared with CMV increased weight at 1 month which was sustained at 9-12 and 15-18 months, increased length at all follow up visits, and increased BINS score at 9-12 and 15-18 months.

A 15 YEAR OLD MALE WITH ACUTE CORONARY THROMBOSIS SECONDARY TO ACUTE MYELOGENOUS LEUKEMIA. Dana Eilen MD, Yazan Haddadin MD, Robert Cross MD, Everett Wray MD. Marshall University Joan C. Edwards School of Medicine. Huntington, WV

Introduction: Acute Myelogenous Leukemia is a hematologic malignancy most commonly found in adults. Acute Mocardial Infarction's are rarely associated with this condition, but when it is found it is typically secondary to a highly elevated white blood cell count causing leukostasis.

Case Report: We present a 15 year old previously healthy male presented to a local community medical center with complaints of chest pain found to be secondary to an acute anterolateral ST elevation myocardial infarction. His labwork showed pancytopneia including platelets of 11,000/µL, elevated cardiac enzymes, elevated liver enzymes, and elevated lactate dehydrogenase. He was transferred to our regional medical center for further workup. Upon arrival, his CP had resolved and his EKG showed extensive Q waves anterolaterally. Transthoracic echocardiography showed moderate to severe mitral regurgitation with severe anterior hypokinesis and ejection fraction of 35%. Peripheral blood smear showed extensive blasts with Auer rods very suggestive of Acute Myelogenous Leukemia (AML). Hematology initiated a transfer to a tertiary referral center for specialized chemotherapy. Just prior to the transfer, the patient began complaining of peri-infarct angina so he was emergently transferred and immediate coronary angiography was performed showing a thrombosed Left Anterior Descending Artery. Thrombectomy and stent placement was then performed as well.

Discussion: This is the first reported case of coronary thrombosis secondary to AML in a child that we are aware of. Possible etiologies include hyperhomocysteinemia due to the leukemia itself, hyperexpression of tissue factor, or other unspecified hypercoaguability.

THE SPECIFIC MECHANISM BY WHICH DOPAMINE-INDUCES MAPK P38 ACTIVATION SERVES AS A MOLECULAR SWITCH BETWEEN CELLULAR PROTECTION AND DESTRUCTION IN A MODEL OF METHAMPHETAMINE NEUROTOXICITY. Melinda L. Asbury, Mariela I. Tassone, Richard D. Egleton, and K. Kelley Kiningham. Department of Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Huntington, WV.

Methamphetamine (MA) neurotoxicity is particularly evident in the striatum where MA causes extensive dopamine (DA) release resulting in neurodegeneration. To identify specific signaling pathways and macromolecules involved in DA-induced striatal toxicity; we used a SK-N-MC cell model that mimics post-synaptic D1 receptor-expressing striatal neurons. We previously reported 25-50 µM DA resulted in elevated RO/NS, increases in caspase 9 and 3 cleavage, and PARP fragmentation. To study the mechanism by which this occurs, we pretreated with a D1 antagonist, SCH23390. PARP cleavage was attenuated when compared to DA, but yielded significant fragmentation compared to control suggesting a redox-sensitive apoptotic component of DA. Antagonism did not significantly reduce p38 phosphorylation indicating that p38 activation was redox-sensitive. Co-incubation with SCH23390 and a p38 inhibitor, SB203580, abolished caspase 3 and PARP cleavage suggesting an apoptotic role for redox activated p38, whereas cells co-treated with SB203580 and the D1 agonist SKF38393 showed increased PARP cleavage indicating a protective role for D1-stimulated p38. We then assessed AP-1 activity as it is a downstream target of p38 and a regulator of cell-life and -death. AP-1 transfected cells pretreated with SCH23390 had similar luciferase activity as DA, while SKF38393 did not enhance reporter activity. Pretreatment with SB203580 reduced activity and AFos-, a cFos dominant negative, transfected cells eradicated PARP cleavage indicating DA-induced AP-1 is a redoxsensitive, p38-mediated, cFos-dependent apoptotic pathway. Despite elevated MnSOD protein there was not increased activity. Examination revealed that MnSOD was nitrated following DA treatment. Pretreatment with PEG-SOD, a SOD mimetic, abrogated PARP cleavage. We hypothesize that DA increases RO/NS and alters redox-sensitive signaling mechanisms which result in apoptosis; and by 1) blocking D1- and p38-activation 2) inactivating AP-1 or 3) providing antioxidants we can prevent DA-mediated apoptosis that is stereotypical of MA-induced neurodegeneration.





UTILITY OF CT ANGIOGRAPHY OF THE CHEST FOR EVALUATION OF PULMONARY EMBOLISM IN AN EMERGENCY ROOM Saif Mashaqi, Abdullah Altayeh, Todd Gress and Imran Khawaja. Marshall University School of Medicine, Huntington, WV

PURPOSE: Acute pulmonary embolism (PE) is a common and potentially fatal disease. CT angiogram (CTA) of the chest is considered the gold standard diagnostic test for diagnosis of PE. The purpose of this study is to evaluate the appropriate use of an established CTA chest-based diagnostic algorithm in patients with suspected PE presenting to the emergency room (ER) setting. **METHODS:** We performed a retrospective review of 258 consecutive patients admitted to our University-affiliated ER who underwent CTA of the chest to rule out PE from January to May 2006. We collected information on demographics, clinical presentation, laboratory and radiographic findings. The pretest clinical probability for PE was calculated using the modified Wells criteria. Data was analyzed using chi square and Fisher's exact for categorical variables and the Student's t test for continuous variables.

RESULTS: Of 258 patients, nine (3.5%) had confirmed acute PE on CTA of the chest. The modified Wells score classified the pretest probability for 231 patients as 'unlikely' (4 with PE by CTA) and for 27 as 'likely' (5 with PE by CTA). Of patients with an 'unlikely' pretest probability, one patient with PE and 107 patients without PE did not undergo D-dimer testing. Thirty nine patients (15.0%) with an 'unlikely' pretest probability and a negative D-dimer still underwent CTA chest. Based on our rate of 31.7% likelihood of a negative D-dimer in patients with 'unlikely' pretest probability and no PE by CTA chest, 33 additional patients would have avoided CTA chest had D-dimer testing been obtained.

CONCLUSION: Patients presenting for diagnostic evaluation of PE undergoing CTA chest with pretest probability stratified by the modified Wells criteria were often not evaluated according to an established CTA-based diagnostic algorithm. D-dimer testing was grossly underutilized.

CLINICAL IMPLICATIONS: Physicians need to be more aware of the diagnostic algorithm for CTA-based evaluation of PE, which if similar to our study, would result in a significant reduction in testing by CTA chest, reducing the cost of patient care and radiation exposure to patients.

A MSM WITH VDRL-NEGATIVE NEUROSYPHILIS CO-INFECTED WITH PREVIOUSLY UNDIAGNOSED AIDS. Andrea Lauffer and Thomas C. Rushton: Department of Internal Medicine, Section of Infectious Diseases, Joan C. Edwards School of Medicine, Huntington, WV.

Introduction: The incidence of syphilis continues to increase in specific populations such as males having sex with males (MSM). While syphilis and HIV co-infections occur with regular frequency, the determination of neurological involvement may be problematic as the Venereal Disease Research Laboratory (VDRL) assay may not be positive. We report a case of VDRL-negative neurosyphilis with previously undiagnosed acquired immune deficiency syndrome (AIDS).

Case: A 27 year old bisexual male presented with a diffuse macular-papular rash including the palms and soles for 3 months. He was originally diagnosed with giant mite infestation acquired from a dog. A local clinic referred him to the health department as his rapid plasma reagin (RPR) test was defined to be > 1:64. He had a low grade fever, headache, bone pain, and rash. His cerebrospinal fluid (CSF) showed pleocytosis with 495 white blood cells, 95% lymphocytes, elevated protein, and a glucose of 29. Opening pressure was 17.5 cm H₂O. The CSF VDRL was negative. The ELISA/WB HIV assay was positive and confirmed by an HIV RNA viral load (159 K). His CD4 count was 111 cells/mm³. He was treated with high dose intravenous penicillin G. His rash resolved rapidly and somatic symptoms improved.

Conclusion: Clinicians should have high suspicion of syphilis in MSM patients. Secondly, there should be high suspicion of HIV in patients with syphilis. Thirdly, high RPR ratios should be evaluated with lumbar puncture and cerebrospinal fluid analysis. Finally, in patients co-infected with HIV, negative cerebrospinal fluid VDRL does not rule out the diagnosis of neurosyphilis. An elevated WBC with pleocytosis, elevated protein and hypoglycorrhachia, with no other attributable cause, is sufficient evidence to diagnose and treat as neurosyphilis.

DIABETES ALTERS VASCULAR MECHANOTRANSDUCTION: PRESSURE-INDUCED REGULATION OF PHOSPHATASE AND TENSIN HOMOLOGUE (PTEN) IN THE RAT INFERIOR VENA CAVA. Brian Price²,Kevin M. Rice ¹, Sunil K. Kakarla ³, Anjaiah Katta ³, Deborah L. Preston ³, Paulette Wehner ² and Eric R. Blough ^{1,31} Department of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, ² Department of Cardiology, Joan C. Edwards School of Medicine, ³ Department of Biological Sciences, Marshall University

Background: Diabetes mellitus is an important risk factor for increased vein graft failure after bypass surgery. The molecular mechanism(s) underlying graft failure in this population remain largely unexplored. Recent data has suggested that pathological remodeling of vein grafts may be mediated by alterations in the activity of phosphatase and tensin homologue (PTEN) and the effects PTEN on the activation of the PI3K-AKT/PKB-mTOR-p70S6k signaling axis. On the basis of these data and previous work examining the effect of insulin resistance on vascular structure, we hypothesized that diabetes may be associated with alterations in how veins "sense" and "respond" to altered mechanical loading. **Methods:** Inferior venae cavae (IVC) from the non-diabetic lean (LNZ) and the diabetic obese (OSXZ) Zucker rats were isolated and incubated *ex vivo* under basal or pressurized conditions (120 mmHg). Protein expression, basal activation and the ability of increased pressure to activate mTOR signaling was evaluated by immunoblot analysis.

Results: Immunoblotting indicated a differential expression and activation of PTEN, AKT, mTOR, and p70s6k in the IVC of diabetic rats as compared to non-diabetic rats. An acute increase in IVC intraluminal pressure failed to change the phosphorylation of PTEN in the non-diabetic IVC, however increase intraluminal pressure decreased PTEN phosphorylation in the diabetic IVC. IVC loading led to equivalent responses in phosphorylation of mTOR, AKT, and p70s6k in both non-diabetic and diabetic IVC.

Conclusion: These data suggest that diabetes is associated with significant alterations in the manner that the IVC regulates PTEN activity and related signaling. Whether these changes are responsible for the increases in vein graft failure seen in the diabetic population will require further investigation.

IMATINIB INDUCED SEROSITIS. Fuad Zeid, Fadi W.Alkhankan, Mustafa H. Awili. Department of Internal Medicine, Joan C. Edwards School of Medicine, Huntington, WV.

Serositis in an inflammation of serous membranes of different etiologies. Imatinib induced serositis is an infrequent cause. This infrequency with which it is encountered makes Imatinib induced serositis a formidable diagnostic challenge.

A 90- year- old women consulted her doctor because of progressive shortness of breath associated with non productive cough one week in duration. She was diagnosed with chronic myelogenous leukemia (CML) three months ago .She was started on Imtinib, a tyrosine kinase inhibitor (TKI), four weeks ago. Chest X-ray and CAT scan on presentation showed new large pleural effusion and pericardial effusion. Echocardiogram showed normal left ventricular function and moderate pericardial effusion with no evidence of tamponade .Diagnostic thoracenthesis revealed an exudative effusion. Common causes of exudative effusion were excluded. At this point, Imtinib was discontinued .Two weeks later; patient had a recurrence of her pleural effusion. Therapeutic thoracenthesis was done. Patient symptoms improved .Follow up chest X-ray and CAT scan did not show recurrence of her pleural and pericardial effusion.

This case illustrates the potential for serositis with use of Imatinib, the time of onset is variable, and management frequently requires repeat invasive procedures. There are occasional reports of Imatinib related pleural effusion in the literature, frequently associated with Pericardial effusion and most commonly involved patient treated with higher doses of Imatinib .Recognition of this side effect is critical and close clinical monitoring for the emergence of symptoms of effusion is warranted.

ACANTHOSIS NIGRICANS AS A CLINICAL MARKER FOR INSULIN RESISTANCE IN OBESE CHILDREN. Rohit Aswani, Amy Lochow and Yoram Elitsur. Department of Pediatrics, Section of Gastroenterology, Joan C. Edwards School of Medicine, Huntington, WV

Insulin resistant diabetes mellitus type -2 (IR-DM2) in obese children is a major risk factor for developing diabetes mellitus and cardiovascular complications. Increased skin pigmentation around the neck and /or at the armpits (Acanthosis Nigricans) is a common finding observed in obese children.

Aim: To investigate the accuracy of Acanthosis Nigricans (AN) to detect IR-DM2 in obese children

Methods: Obese children who attended the gastroenterology and the outpatient general clinics were prospectively recruited to the study. Demographic data, BMI value, and fasting serum levels of glucose, insulin, lipid profile, and liver enzymes were obtained at first visit in all children. The presence or absence of AN was also recorded. Insulin resistant was calculated (HOMA equation) in each child and was compared to the AN rate.

Results: A total of 54 children participated. The mean age was 13.01 ± 3.5 and the Male: Female ratio was 1.6:1.0. The mean BMI was 32.85 ± 5.54 . The mean cholesterol level, TG, HDL, and LDL were 162 ± 32 , 130 ± 77 , 40 ± 9 , and 96 ± 25 , respectively. Acanthosis nigricans was documented in 33 (61%) children, and IR-DM2 was found in 28 (51.8%) children. AN detected IR-DM2 in obese children with a Sen. Of 72.4%, Spec. -52%, PPV- 63.6%, NPV- 61.9%, and the accuracy rate was 63.6%. Significant correlation was found between BMI and IRDM2 (r=0.482).

Conclusion: Acanthosis Nigricans is an adequate clinical marker to detect IR in obese children. AN and BMI are associated with the development of IR-DM2 in obese children





SEASONAL TREND OF EOSINOPHILIC ESOPHAGITIS IN CHILDREN. Rohit Aswani, Dementieva Yulia, Vicki A Lund, and Yoram Elitsur Department of Pediatrics, Section of Gastroenterology and Department of Mathematics, Joan C. Edwards School of Medicine, Huntington, WV.

Eosinophilic esophagitis (EE) is a newly discovered disease associated with various allergic related diseases. Asthma, eczema, food and environmental allergens are detected in over 70% of children with EE.

Previous data in adults and children suggested that EE has a seasonal trend

Aim: To investigate whether children in WV who are diagnosed with EE, have a seasonal trend.

Methods: A retrospective review of all endoscopic charts of new patients diagnosed with EE between 2003-2009 was done. In addition, a retrospective chart review of all upper endoscopies performed in 2007 and 2008 was performed, and the patients with histological diagnosis of GERD or normal findings were considered for control groups. Demographic, clinical information and endoscopy data collected from the charts.

Results: A total of 261 patients' charts reviewed of which 97 had GERD, 122- normal, and 42- had EE. The seasonal distribution showed a significant increase during the winter season compared to all other groups (standardized r=2.055; alpha=0.05).

Conclusion: A significantly higher number of newly diagnosed children with EE occurred during the winter season compared to other seasons of the year (spring, autumn, & summer). Patients who were diagnosed with GERD by histology and/or children with normal histology showed no season preference. We hypothesize that the winter season is the most common period for the development of EE in children from WV.

AKAP12 EXPRESSION AND REGULATION IN MOUSE AND HUMAN MELANOCYTES AND MELANOMA CELLS. Linda L. Eastham and Richard M. Niles. Department of Biochemistry and Microbiology, Marshall University – Joan C. Edwards School of Medicine, Huntington, WV.

Retinoic Acid (*at*RA) is the most metabolically active form of Vitamin A and has been shown to inhibit growth of mouse and human melanoma cells. Profiling of *at*RA induced genes in melanoma identified AKAP12, a scaffolding protein that is involved in assembling multi-protein signaling complexes, as the most highly induced gene. The focus of our study was to characterize *at*RA regulation of AKAP12 expression in B16 mouse melanoma cells, as well as normal human melanocytes and six different human melanoma cell lines (SbCl2, WM3211, WM3248, WM1366, WM9 and WM239).

Results show that B16 mouse melanoma cells, as well as human melanocytes and all six human melanoma cell lines express AKAP12 protein and/or RNA and its expression can be further induced by atRA. These results also show a good correlation between atRA induced increases in AKAP12 levels in melanoma cells, and the ability of atRA to inhibit cell proliferation. However, an exception is WM3248 cells, which produce the highest levels of AKAP12 in response to atRA treatment, but only exhibit a modest decrease in proliferation. The reason for this discrepancy is currently being investigated. *In* silico analysis of the promoter region of the AKAP12 gene revealed 3 activator protein (AP)-1 transcription factor binding sites. Our lab has previously shown that atRA stimulates AP-1 activity in B16 melanoma cells. Reporter gene assays showed that atRA treatment not only increased AP-1 activity in B16 mouse melanoma cells, but also in WM3248 and WM239 human melanoma cells. Co-transfection of these melanoma cells with the AP-1 reporter plasmid and with a plasmid encoding A-fos, a dominant-negative version of c-fos, resulted in inhibition of atRA induced AP-1 activity. Transfection of the A-fos into the human melanoma cells also inhibited the ability of atRA to stimulate expression of AKAP12. Our laboratory is the first to report that human melanocytes and melanoma cells express AKAP12, and that its expression is regulated by AP-1. In addition, this is the first report that AP-1 activity regulates AKAP12 expression.

PRESENTATION AND OUTCOME OF A PREGANT PATIENT WITH ACUTE ON CHRONIC PANCREATITIS DUE TO HYPERTRIGLYCERIDEMIA. L. Emily Morris and David C. Chaffin Department of Obstetrics and Gynecology. Joan C. Edwards School of Medicine. Huntington, WV.

Background: Hypertriglyceridemia induced pancreatitis in pregnancy is extremely rare and usually only occurs in women with preexisting abnormalities in lipid metabolism. The physiologic increase in triglycerides during the third trimester of pregnancy predisposes these patients to an acute exacerbation. This disease can be life threatening for the pregnant patient and fetal mortality is high.

Case: A 22 year old pregnant female with known history of chronic pancreatitis due to hypertriglyceridemia and type I diabetes mellitus presents with acute exacerbation of pancreatitis and hypertriglyceridemia at 18 weeks gestation. The patient was treated aggressively, discharged home, and readmitted with a repeat exacerbation at 24 weeks gestation which was complicated by hemorrhagic pancreatitis. Her pregnancy was then complicated by preterm premature rupture of membranes and she delivered a viable infant by cesarean section at 26 weeks and 3 days for chorioamnionitis.

Conclusion: Patients with chronic pancreatitis due to hypertriglyceridemia often experience acute exacerbations during pregnancy due to the physiologic increase in triglycerides. These patients often have a poor outcome due to hypovolemia, hypoxia, and acidosis. Tight pharmacologic control of triglycerides should be attempted to prevent acute exacerbations. During an acute exacerbation these patients should be treated with aggressively with fluid replacement, IV insulin for triglyceride control, and pain management as needed. They should be cared for in an intensive care unit and monitored for complications such as necrotizing pancreatitis, pseudocyst formation, and hemorrhagic pancreatitis.

THE ROLE OF CYP3A4 GENETIC POLYMORPHISMM IN UNEXPECTED METHADONE DEATH. Lauren L. Richards-Waugh1,2, Donald A. Primerano3, Yulia Dementieva4, James C. Kraner1, and Gary O. Rankin2.1West Virginia Office of the Chief Medical Examiner, Charleston, WV. 2Departments of Pharmacology, Physiology, and Toxicology, 3Biochemistry and Microbiology, and 4Mathematics and Integrated Science, Marshall University, Huntington, WV.

Methadone users are at an increased risk for unexpected overdose due to extreme variability in interindividual pharmacokinetics. The rate of conversion of methadone to its principal metabolite (EDDP) can be expressed as [methadone]/[EDDP] ratio. In a retrospective study from the West Virginia Office of the Chief Medical Examiner (WV OCME) from 2003 to 2008, the methadone/EDDP ratio was found to be 18.3 for "methadone-only" deaths compared to a ratio of 5.3 for individuals successfully undergoing methadone maintenance treatment. The higher ratio may be associated with one or more single nucleotide polymorphisms (SNPs) on the CYP3A4 gene that affect the function of the P450 protein, a key cytochrome P450 in methadone metabolism. The hypothesis of this study is that one or more genetic polymorphisms within the CYP3A4 gene could lead to decreased methadone metabolism, allowing an individual to achieve a fatal concentration of methadone at normal dosing levels. Individuals from West Virginia and Kentucky who died due to a methadone-only overdose were genotyped at five different SNP loci (rs2246709, rs3735451, rs4646437, rs2242480, and rs2740574) within the CYP3A4 gene. SNP genotyping was performed by Tagman Allelic Discrimination Analysis using genomic DNA isolated from dried blood spots obtained at autopsy. The average methadone concentration for the deceased individuals was 0.601 mg/L (within therapeutic range). Although, methadone/ EDDP ratios were not available for the Kentucky cases, results from SNP genotyping in this group could help determine the role of CYP3A4 variants in methadone overdose. Observed genotypic frequencies were significantly different from the frequencies for the general population (p<0.01) for three of the SNPs (rs2246709, rs2242480, and rs2740574). These initial findings indicate an enrichment of rare polymorphisms within the CYP3A4 gene may contribute to unexpected methadone death.

SELF-REPORTED RISK FACTORS FOR BONE LOSS: UTILITY OF A PATIENT QUESTIONNAIRE COMPLETED AT TIME OF BONE MINERAL DENSITY TESTING. Samia Kanooz, Kanooz-ul-Qadir, Todd W. Gress, and Abid Yaqub. Department of Medicine, JCESOM, Marshall University, Huntington, WV.

Objective: We examined the prevalence and association of self-reported risk factors for bone loss with the bone mineral density (BMD) values in a cohort of patients undergoing DXA scanning in our clinical center.

Methods: 201 consecutive patients (post-menopausal females and men>50 years of age) underwent BMD testing and were included in our study. Each patient completed a standardized questionnaire developed by the Canadian Panel of International Society of Clinical Densitometry (ISCD). The DXA scans of patients were reviewed to evaluate BMD and the respective T and Z scores. Information on serum vitamin D was obtained from the patient's record when available.

Results: Patients were predominantly female (87%) and white (87%) with a mean age of 65 years. Patients reported the following: frequent falls (13%), steroid use (20%), chemotherapy(5%), smoking (15%), family history of hip fracture (9%), fragility fracture (42%), and use of epilepsy medications (7%). Inadequate 25-hydroxy vitamin D levels were found in 47 percent (N=61 of 132 available). We found no association between a diagnosis of osteopneia or osteoporosis by DXA and any of the self reported risk factors. We found current smokers had significantly lower BMD (10% lower BMD; p<0.001) and Z scores (33% lower score; p=0.02), but there was no significant association with T scores. These results were unaffected by adjustment for age, gender, and race using multiple linear regression.

Conclusion: We found that most of the ISCD self-reported risk factors for bone loss in our patient population were not associated with lower BMD or the respective T and Z scores. Perhaps this lack of association is related to a lower accuracy of the survey in our patient population. Nevertheless, these risk factors were previously established based on the outcome of osteoporotic fracture, which was not measured in our study. Further study of the ISCD questionnaire is needed to determine if it can be utilized in diverse patient populations.



YB-1 EXPRESSION IN EARLY HEMATOPOIESIS AND LEUKEMIC

CELLS Jasjeet Bhullar and Vincent E. Sollars Department of Biochemistry and Microbiology, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

Hematopoietic Transcription factors play a critical role in directing the commitment and differentiation of hematopoietic stem cells (HSC) along a particular lineage. Y box protein (YB-1), a cold shock family protein is a transcription factor which is widely expressed throughout development and has been implicated as a cell survival factor that regulates transcription and translation. YB-1 is involved in erythroid cell development by interacting with Globin Transcription Factor (GATA); this study aims to investigate YB-1 expression in normal hematopoietic differentiation and leukemia. EML-clone 1 cells, a murine hematopoietic stem cell line, was used as a model for looking at the expression of YB-1 during myeloid differentiation by western blotting and quantitative RT-PCR. Fluorescence activated cell sorting was conducted to isolate lineage⁻/IL-7R⁻/c-kit⁺/Sca1⁺ (LKS) hematopoietic stem, lineage⁻/ IL-7R⁻/c-kit⁺/Sca1⁻ myeloid progenitor cells and granulocytes from mouse bone marrow to assess the YB-1 expression in vivo. YB-1 protein levels were analyzed in a panel of myeloid leukemic cell lines by immunoblotting. YB-1 mRNA and protein levels were high in the EML cells but the expression goes down in RA/IL-3 treated EML-clone 1 cells (myeloid progenitors) and was even more dramatically down-regulated in GM-CSF treated EML cells during the course of myeloid differentiation. Interestingly, LKS (enriched fraction of hematopoietic stem cells) and myeloid progenitor cells showed high level of YB-1 expression as compared to the differentiated cells like granulocytes. Further, we observed that YB-1 protein was expressed in several myeloid leukemic cell lines blocked at different stages of myeloid development. Thus, our data suggest that YB-1 is down-regulated during myeloid differentiation and it might be involved in hematopoietic differentiation. Aberrant YB-1 expression could be a contributing factor in the development of leukemia thus making it an excellent molecular target for therapy in myeloproliferative disorders and leukemia.

DO ERRONEOUS REPORTS OF COMPUTER INTERPRETED-ELECTROCARDIOGRAM INFLUENCE ANALYSIS BY MEDICAL TRAINEES? Yousef Darrat , Darshana Shah , Nessren Benhamed , Todd Gress, Mehiar Elhamdani. Joan C Edwards School of Medicine, Marshall University, Huntington, West Virginia.

Introduction: Computerized electrocardiogram (EKG) analysis has been one of the most rapidly and widely adopted computer applications in medicine. Evolving algorithms for the interpretation of cardiac rhythm have improved over time but remain imperfect and at times automated diagnostic statements mislead the interpreter. Many teaching hospitals in the United States use automated electrocardiographs with computer based rhythm interpretation. Therefore, medical trainees are faced with such electrocardiograms regardless of the accuracy of the analysis.

<u>Objective:</u> Our study is descriptive; it investigates whether the presence of computer analyzed EKGs in teaching hospitals will interfere with the ability of basic interpretation as well as the learning process of medical students, residents and cardiology fellows.

<u>Methods:</u> The 58 research subjects were gathered in different sessions and provided with the same EKGs. The printed EKG set, which is a total of 20 EKGs, is a mix of automatically machine reported, intentionally false reported and no report EKGs in order to examine the subject's responses. Data was collected and analyzed by quantitative and qualitative methods.

Results: Statistical analysis showed 48.5% of medical students, 63.5% of medical residents and about 78% of cardiology fellows made correct interpretations. This reflects the fact that EKG reading skills correlate with the level of training. On the other hand, the percentage of medical trainees who have been mislead by erroneous reports is very close among the 3 different groups and is as follows; medical students (19.6%), medical residents (11.75%) and cardiology fellows (17.5%).

<u>Conclusion:</u> EKG reading skills improve in a chronological manner, but the effect of false EKG statements is similar regardless of the level of training. These findings suggest the exposure of medical trainees to EKGs with computer-generated readings in a teaching setting may exert a negative impact on their educational process.





VARIABLE RESPONSE TO FIRST-LINE TREATMENTS FOR PTSD: AN ASSOCIATED FINDING? M. Lea Morton-Fishman and Richard D. Egleton. Department of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, Huntington, WV.

Post-traumatic stress disorder (PTSD) is a debilitating psychiatric condition that develops following exposure to a traumatic event which causes or threatens serious harm to self or others and elicits an intense fear response and perception of helplessness. The characteristic symptoms of PTSD, such as hypervigilance, avoidance of associated stimuli, recurrent intrusive recollections of the event and blunting of emotional responses are managed primarily via the use of psychotherapy and anxiolytic medications, most commonly selective-serotonin reuptake inhibitors (SSRIs). Although some individuals respond quite favorably to SSRIs and ultimately recover from their condition, many others experience only mild-to-moderate alleviation of their symptoms or are completely refractory to first-line treatment. Currently, PTSD has an estimated 8% lifetime prevalence in the United States with a projected increase to 13% within the next twenty years. The potential for a PTSD-related healthcare crisis has prompted many recent studies in order to assess possible underlying etiologies for the condition and the efficacy of alternative treatment modalities. A literature review of recent research findings provides strong evidence of a multifactorial etiology for PTSD, including a variety of studies which implicate genetics and abnormal fetal development as key predisposing factors for the condition by creating alterations in the neurobiological systems necessary for regulating the production and response to cortisol and other neurotransmitters. Further studies are warranted to determine if poor response to first-line treatments might also be the result of preexisting alterations in these systems. If so, the potential for novel treatments such as gene therapy might provide an element of prevention in addition to symptomatic treatment.

THE POTENTIAL ROLE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN THE DIABETIC BRAIN MICROVASCULATURE.

Aileen Marcelo and Richard Egleton, Department of Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Huntington, WV.

Diabetic patients are at risk for stroke, vascular dementia, and other cardiovascular events. Clinical studies have shown that the blood brain barrier (BBB) of diabetic patients is "leaky" (Starr, 2003). Experimental studies report that this leakiness is due to a loss of tight junction protein expression resulting in increased permeability (Hawkins, 2007). Other studies have shown similar results in the blood-retinal barrier, which may be due to increased expression of vascular endothelial growth factor (VEGF), and that VEGF plays a role in vascular changes and altered angiogenesis (Antonetti, 1998). In the present study, we investigate the potential role of VEGF and its receptor system on the BBB in both streptozocin (STZ) and Zucker obese models of diabetes. Male Sprague Dawley rats were injected with 65 mg/kg of STZ or equal volume of 0.9% sterile saline. After 14 days, microvessel preps of RNA and protein were collected. Real-time PCR studies revealed that there were increases in the microvessel expression of VEGF and its receptors, Flt-1, Flk-1, neuropilin-1 (NP), and NP-2, as well as the VEGF co-regulator semaphorin 3A (SEMA 3A) in STZ-treated rats. Western analysis showed that there was no appreciable change in VEGF protein levels in the STZ model of diabetes, but VEGF levels increased in the Zucker obese model. Additionally, there were increases in the up-regulation in the protein expression of the VEGF receptors and SEMA 3A in the STZ model of diabetes. Similar increases were observed in the Zucker obese model except for NP-1. These data suggest that there are significant changes in VEGF signaling at the BBB of both models diabetic rats. VEGF is a potent regulator of both angiogenesis and barrier permeability, and it is likely that these changes contribute to the previously reported permeability changes. Further this data also suggests that there could be a change in angiogenic potential in the diabetic brain, potentially modulated via different VEGF receptors in animal models of type 1 and 2 diabetes. These reported changes in VEGF signaling may play an important role in the development and progression of diabetes-related diseases, and thus provide a potential target for therapeutic interventions.

ANTI-NEOPLASTIC ACTIVITY OF CAPSAICIN IN HUMAN SMALL CELL LUNG CANCER Kathleen C Brown, Ted R. Witte, W.E. Hardman and Piyali Dasgupta; Joan C. Edwards School of Medicine, Marshall University, Huntington, WV 25504

KEYWORDS: SCLC, capsaicin, growth-inhibitory, apoptosis, cisplatin, TRPV6,

ABSTRACT

Small cell lung cancer (SCLC) is characterized by rapid progression, early metastasis and a dismal survival rate. Chemotherapy remains the cornerstone of treatment for SCLC. However, insensitivity to chemotherapy and subsequent relapse are responsible for the poor treatment outcomes in SCLC patients. Recent studies have shown that capsaicin (the spicy ingredient of chilli peppers) can inhibit the growth of human gliomas, non small cell lung cancers, colon cancers and prostate cancers. The growth-inhibitory abilities of capsaicin have not been studied in human SCLCs. Here we will show that capsaicin displays potent growth-inhibitory activity on multiple human cancer cell lines. TUNEL and caspase-3 cleavage assays show that capsaicin induced 5-6 fold increase in apoptosis in human SCLC cells. Most interestingly, the apoptotic activity of capsaicin was only displayed in SCLC cells and not in normal human lung epithelial cells. The dietary administration of capsaicin suppressed the growth of human SCLC cells xenotransplanted in nude mice. Furthermore, low concentrations of capsaicin were able to sensitize human SCLC cells to the growth-inhibitory effects of cisplatin, one of the drugs used to treat SCLC. The growth-inhibitory activity of capsaicin requires the TRPV6 receptor and depletion of TRPV6 by siRNA ablated the growth-inhibitory activity of capsaicin. These studies suggest that capsaicin may have potential applications as a novel nutrition-based therapeutic agent for the treatment of human SCLCs.

P-GLYCOPROTEIN UP-REGULATION BY
2,3,7,8-TETRACHLORODIBENZODIOXIN IS AMELIORATED
BY EPIGALLOCATECHIN 3-GALLATE. L.M. Vence, N. Proper, T.B.
Salisbury and R.D. Egleton. Department of Pharmacology, Physiology and
Toxicology, Joan C. Edwards School of Medicine, Huntington, WV.

P-glycoprotein (P-gp) a member of the ABC family of drug efflux transporters plays a major role in limiting the transport of drugs across the blood brain barrier (BBB) into the CNS. Changes in both the expression and activity of P-gp have been linked to the reduced efficacy of a number of clinically relevant CNS targeted drugs including opioids and anti-epileptics. The aryl hydrocarbon receptor (AhR) is a transcription factor that modulates P-gp expression, recent studies have shown that AhR is highly expressed in the endothelial cells that make up the BBB. In this study we investigated the effect of 2,3,7,8-tetrachlorodibenzodioxin (TCDD), an AhR substrate, on P-gp activity in a mouse BBB cell line (bEND.3). We also tested the effects of coincubation with epigallocatechin 3-gallate (EGCG) a green tea catechin AhR inhibitor. bEND.3 were grown to confluence in 24 well plates. At confluence, cells were incubated for 48 hours with TCDD, EGCG or a combination (1nM or 10nM TCDD with or without 100µM EGCG. After the 48 hr incubation P-gp activity was assessed using a R123 uptake assay. Uptake of R123 was calculated per mg of protein and compared using one way ANOVA followed by Newman-Keuls post Hoc test using Sigma plot 11.

TCDD lead to a significant dose dependent reduction in R123 uptake by bEND.3 cells ($\downarrow 38\%$ for 1nM and $\downarrow 74\%$ for 10nM), indicating an increased activity of P-gp limiting R123 entry into the cells. This increased activity was significantly ameliorated by the addition of EGCG.

In conclusion this study shows that P-gp at the BBB can be regulated by the AhR. Agonists such as TCDD will lead to an increased activity which can be in part ameliorated via the action of EGCG a polyphenol with antagonist activity at the AhR. Drug delivery to the CNS is hampered in part via drug induced up-regulation of P-gp. These studies indicate that EGCG may be a useful agent for reducing the up-regulation of P-gp that is observed in chronic therapy with a number of CNS targeted agents.

ACETAMINOPHEN AL TERA TIONS OF ANTIOXIDANT ENZYME FUNCTION NEGATED BY SAMe. J. Michael Brown, John G. Ball, and Monica A. Valentovic. Department of Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine Huntington, WV 25755

Acetaminophen (AP AP) is the leading cause of drug induced liver disease in the United States resulting in over 500 deaths annually. AP AP toxicity is caused by the formation of the reactive metabolite N-acetyl-phenzoquinone imine (NAPQI), which adducts proteins and causes mitochondrial damage. The mitochondrial damage in addition to the reactive nature of NAPQI leads to the generation of reactive oxygen species (ROS) causing severe hepatic centrilobular necrosis. AP AP has previously been demonstrated to decrease antioxidant enzyme function with overdose. Prior research by our lab reported that SAMe protects as well as Nacetylcysteine (NAC), the current treatment for AP AP overdose. The current study sought to test the hypothesis that S-adenosyl-L-methionine (SAMe) prevents the loss of antioxidant function induced by AP AP overdose. C57B1I6 mice were randomly allocated into groups (n=5/group) and injected intraperitoneal with Vehicle (Veh; water 15ml/ kg), SAMe (1.25 mmo l/kg), AP AP (250 mg/k:g), and SAMe administered 1 hour following APAP. Livers were collected 4 and 6 hr following APAP administration and the activity glutathione peroxidase (GPx), catalase, glutathione reductase, and superoxide dismutase (SOD). GPx function was significantly reduced (p<0.05) 4 and 6 hr following AP AP administration compared with Veh. SAMe significantly increased (p<0.05) activity 0 GPx when given 1 hour following AP AP, but not back to control levels. Catalase and glutathione reductase activites were decreased (p<0.05) 4 hr following AP AP administration. SAMe was able to completely abate the loss in function in these enzymes returning activity to Veh levels. In conclusion, we report here for the fust time the ability of SAMe to protect antioxidant enzyme function in the liver following AP AP overdose.

ROLE OF CHMP1 PROTEIN IN *DROSOPHILA* Valentine, M., Park, M. and Collier, S. Department of Biomedical Sciences, Marshall University, Huntington, WV.

Chmp1A is a component of the ESCRT III (Endosomal Sorting Complex Required for Transport), a complex required for recycling and degradation of receptor proteins. Chmp1A has recently been linked to pancreatic cancer in humans, as pancreatic tumors have lowered Chmp1A expression. Recent work in zebrafish suggests *Chmp1A* as a tumor suppressor, as knockdown results in tumor formation. Chmp1A has also been shown to interact with Strabismus (Stbm), a component of the Frizzled (Fz) Planar Cell Polarity (PCP) signaling pathway. *Chmp1A* knockdown in zebrafish results in convergent extension phenotypes similar to loss of Fz PCP signaling, suggesting that Chmp1A regulates PCP through Stbm. *Drosophila* has one Chmp1 protein [encoded by the *Chmp1* gene (CG4108)] with homology to vertebrate Chmp1A.

Using a VDRC RNAi line, we have found that ubiquitous reduction of *Chmp1* activity in the wing results in oversized wing veins. This vein phenotype is significantly suppressed by reduced activity of Epidermal Growth Factor (EGF) pathway activators, Vein and Rhomboid, suggesting that *Chmp1* normally suppresses EGF signaling. We have also found that localized *Chmp1* knockdown can affect PCP, and our results suggest that *Chmp1* regulates wing PCP through an interaction with Stbm as it does in vertebrates. We recently acquired an independent *Chmp1* RNAi line from TRiP stocks and obtained very similar *Chmp1* knockdown phenotypes, validating that our results were in fact due to *Chmp1* knockdown.

Twenty transgenic fly lines were created and used to investigate effects of *Chmp1* over-expression in the wing. We found that ubiquitous over-expression of *Chmp1* in the wing results in a phenotype that suggests misregulation of Notch-Delta signaling. To date, each line has provided consistent results, and wing phenotypes are mainly restricted to the wing veins. One over-expression line however, gives a similar phenotype to *Chmp1* knockdown suggesting it has acquired dominant negative activity, and is currently being characterized. EGF and Notch-Delta signaling are extremely important for wing vein formation, and our studies of how Chmp1 may be regulating these pathways to execute proper wing vein formation are still in progress.

ERADICATION OF THERAPY-RESISTANT HUMAN PROSTATE TUMORS USING AN ULTRASOUND GUIDED SITE-SPECIFIC CANCER TERMINATOR VIRUS DELIVERY APPROACH Rounak Nande¹, Mary Allison Teter¹, Candace Howard^{1,2}, and Pier Paolo Claudio^{1,3} 1 Department of Biochemistry and Microbiology, Department of Orthopedic Surgery, and 2 Department of Surgery, Marshall University, Huntington, WV.

Prostate cancer is the most common cancer and the second leading cause of cancer-related deaths in men in the United States. At present, no effective therapy is available for metastatic prostate cancer (PC). Advanced PC is refractory to conventional anticancer treatments because of frequent overexpression of antiapoptotic proteins Bcl-2 and/or Bcl- x_L .

A major challenge for effective gene therapy is the ability to specifically deliver nucleic acids and potentially toxic gene products directly into diseased tissues. The quest for novel, safe and more efficient systemic gene delivery systems has recently highlighted ultrasound (US) contrast agents (microbubbles) as a potential candidate for enhancing delivery of molecules to target tissue.

We have previously demonstrated the feasibility of site-specific gene delivery mediated by diagnostic US using Adeno-GFP encapsulated in commercially available US contrast agents *in vitro* and *in vivo*.

Goal of our current investigation was to determine if *mda*-7/IL-24, a gene that has shown significant potentials as a selective and effective anticancer agent in Phase I, II and III intratumoral gene therapy trials in patients with advanced solid cancers, could effectively treat Bcl-x_L overexpressing prostate tumors (refractory to conventional therapies), which were implanted in mice. We showed that microbubble/Ad.*mda*-7 complexes targeted to PC cells using US dramatically reduced tumor burden in xenografted nude mice. Additionally, US guided microbubble/Ad.*mda*-7 delivery completely eradicated not only targeted DU-145/Bcl-x_L-therapy resistant tumors, but also non-targeted distant tumors (established in the opposite flank), thereby implementing a cure. The latter results are due to the intrinsic properties of Mda-7, which being a secreted protein (IL-24), travels through the blood stream and act upon the secondary tumoral localizations. These findings highlight potential therapeutic applications of this novel image-guided gene therapy technology for advanced prostate cancer patients with metastatic disease.

OMEGA-3 AND -6 FATTY ACIDS SELECT, PROLIFERATE AND SENSITIZE COLORECTAL CANCER STEM-LIKE CELLS TO CHEMOTHERAPY

Sarah E. Kelly¹, Miranda Carper¹, Colleen Conlen^{1,2}, Jagan Valluri², and Pier Paolo Claudio^{1,3}

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Diets high in fat and cholesterol (especially from animal sources) are emerging as one of the major causes of colon cancer. Vice versa, it has been found a decreased incidence of colon cancer in populations consuming a diet rich in omega-3 fatty acids (FAs). Additionally, controlled *in vitro* and *in vivo* experiments linked omega-3 FAs to attenuated colon cancer proliferation and carcinogenesis. Interestingly, recent published data from clinical trials of the use of omega-3 fatty acids supplementation on rectal mucosal proliferation in 20 patients with sporadic adenomatous colorectal polyps showed altered proliferation rate of cells in the colonic crypt. In normal crypts, stem cells (SC) at the crypt bottom generate rapidly proliferating cells, which undergo differentiation while migrating up the crypt.

A growing body of evidence is lending support to the idea that human cancer can be considered a stem cell disease. Recently, we have shown in our laboratory that various cancer cell lines, including colon cancer cell lines, contain a sizeable sub-population of CSCs. We have also recently shown that treatments of various cancer cell lines with omega-3 and omega-6 supplements selected and proliferated CSCs, which are usually resting in nature and therefore resistant to conventional chemo and radiation therapy regimens.

We hypothesized that omega-3 and -6 fatty acids may increase the sensitivity of colon cancer stem cells to chemotherapy regimens.

To test this hypothesis we have challenged numerous colon cancer cell lines with conventional chemotherapy agents used against colon cancer such as fluorouracil, irinotecan (CPT-11), and oxaliplatin and have assessed their sensitivity to the drugs by evaluating cell viability and number using a trypan blue exclusion cell count method, flow cytometry, and MTT assay. We have observed that the efficacy of the cancer chemotherapy drugs was greatly increased after omega-3 and -6 treatment in the colon cancer cell lines tested, opening up the road to the development of less toxic treatments for colon cancer patients.

PERSPECTIVES OF FAMILY MEDICINE RESIDENTS ON RESIDENCY CURRICULUM REGARDING WORLDVIEW THINKING IN PATIENT CARE. Dilip Nair. Department of Family and Community Health, Joan C. Edwards School of Medicine, Huntington, WV.

To engage in worldview thinking in patient care is for the physician to take into account that both physician and patient bring basic assumptions about reality to their relationship. This activity can promote professionalism in caring for diverse patient populations. A learner-centered approach to curriculum development is considered beneficial. The objective of this report is to describe the perspectives of family medicine residents at Marshall University concerning worldview thinking in patient care and concerning curricula designed to promote such thinking.

Residents were invited to participate on a voluntary and confidential basis. Personal interviews were conducted by the investigator with 8 out of the 14 PG 1 and 2 residents in the program. Input from two additional residents was obtained later. The semi-structured interviews were recorded digitally and stored in audio file format. They were transcribed and analyzed by the investigator using the editing method of qualitative analysis. The study participants' perspectives were found to be consistent. The analysis of the data was verified with them.

The residents viewed worldview thinking in patient care as relevant in responding to differences between themselves and their patients by respecting the patient's preferences while negotiating a compromise to optimize patient care. They understood the value they placed on worldview thinking in patient care as a result of personal life experiences in which they were confronted with ideas and values different from their own. Their reactions to mandatory medical education curriculum in this area were generally negative. They strongly preferred that any new curricula involve personal, real-life patient interactions. Developing learner-centered curriculum requires listening carefully to resident-learners. Optimal curricula will confront resident-learners with patients of a different worldview in "real-life" situations. Finally, important questions are raised about whether it is feasible or even suitable to attempt to foster a high value for worldview thinking in patient care among all residents, by means of mandatory residency program curricula.

PILOT PEDIATRIC ELECTROCARDIOGRAM CURRICULUM FOR FIRST YEAR PEDIATRIC RESIDENTS. Waseem Ostwani, Bob Miller, and Darshana Shah. Department of Pediatrics, Joan C. Edwards School of Medicine, Huntington, WV

The electrocardiogram (ECG) is frequently used to screen for cardiac abnormalities. Careful ECG interpretation by the ordering physician influences the course of patients' management. No prior studies have looked at developing an ECG curriculum for the pediatric residents. The purpose of this study was to design, develop and implement a pilot pediatric ECG curriculum for First Year Pediatric Residents.

Pilot ECG curriculum: Four focused one hour teaching sessions in a group format were planned over a four-month period which included five first year pediatric residents. Sessions were evaluated with an open ended question regarding the best way of learning pediatric ECG interpretation; this was followed by group discussion led by the chief resident. The principles of reading a normal pediatric EKG were discussed during the first session. Seventy different pediatric ECG interpretations were completed and discussed in the other three sessions.

Formative and Summative Evaluation: Both verbal and written feedback at the mid-curriculum evaluation suggested continuing the curriculum in the same fashion, with an emphasis on the value of small group discussions for residents at the same level. The pilot program was evaluated by pre and post questionnaires on ten distinct and clearly different pediatric ECGs. Test takers were asked to define the rhythm, the axis, and the impression for each of the ten ECGs.

Results: Feedback during the post teaching session indicated that the residents felt more comfortable reading pediatric ECGs with an improvement to a mean of 7 from 3.6 on a 10-point scale. In verbal feedback, residents also expressed that overall the course is valuable. The correct answers for the basic questions provided (Rhythm, Axis) were improved in the post test (94% vs. 80%, 50% vs. 40%, respectively) compared to the pre-test. The residents' impression of the possible diagnosis also improved from 16% to 36% in the post curriculum test. **Closure:** We recommend having a pediatric ECG curriculum for the first year pediatric residents which is started early in the academic year, focused group learning sessions, which if possible, would include relevant cases, including ECGs as part of morning report. The cases should be modified to matching each residency programs resources and needs.

ENHANCING EDUCATIONAL EFFECTIVENESS OF BEDSIDE ROUNDS. William Nitardy, Bob Miller, Darshana Shah, Academy of Medical Educators Joan C. Edwards School of Medicine at Marshall University

Background: The traditional structure of Medical Education in the United States consists of Bedside Teaching. Attendings, Senior Residents, Interns and Students participate in examination, reviewing the history and developing a plan of care for the hospitalized patient. This venue has functioned as both a method of completing daily work and as serving as an opportunity for teaching medical professionals. This structure however is at risk of becoming solely a work related function. Resident work hour restraints, increased administrative requirements, and rapid turnover in admissions and discharges forces ward teams to spend more team on paperwork than on education.

Objective: Ascertain Residents perspectives to see if Bedside Rounds are effective.

Methods: Questionnaires were provided to Residents at an Academic hospital in West Virginia. Respondents were asked a variety of questions from the amount of time spent teaching to whether or not they have input to what teaching transpires. They were given five questions that asked them to rank the level of satisfaction they had with the current composition of Bedside Rounds. Lastly, they were given the opportunity to provide comments on how they might improve the education that occurs during rounds. The survey was sent to all residents in all specialties. The survey was anonymous.

Results: There were 42 respondents of 102 potential residents. Residents overall were satisfied with the education that was provided during rounds. However, greater than 50% of the respondents thought that the amount of time discussing recent literature and treatment options was inadequate. Furthermore, they felt they had too little input on the topics of discussion. An equal number of residents felt that they had adequate input on the structure of rounds.

Conclusions: Residents at our institution are generally satisfied with the education they receive on daily rounds. Opportunities exist to enhance learning by improving literature discussions and by allowing the residents more say in the topics of discussion.

A committee is being created currently at the Internal Medicine Department to look into how best to structure the inpatient teams and attending to not only facilitate patient care but to increase learning.

EVALUATION OF TEACHING METHODS AND CHEST X-RAY INTERPRETATION SKILLS OF SENIOR MEDICAL STUDENTS,

Shadi Obeidat, Nancy Munn, Fadi Alkhankan and Darshana Shah. Academy of Medical Educators, Joan C. Edwards School of Medicine, Huntington, WV.

Objectives: To evaluate medical students' degree of comfort and confidence reading chest X-rays (CXRs) and try to determine the best teaching method through which the students learned CXR interpretation.

Methods: An anonymous survey focused on teaching and interpreting CXRs was sent electronically to all fourth-year medical students at Marshall University JCESOM (n=52) two months prior to graduation.

Results: 37 students responded to the survey (71%). In general, only 37.8% of students felt fairly or very comfortable interpreting CXRs, while 62.2% felt only little or not comfortable interpreting CXRs. Students who completed a radiology elective felt more comfortable than those who did not (66.7% Vs 28.5%), but this was not statistically significant (P value 0.056). "Small group teaching by an attending" was voted as the most useful CXR teaching method (41.2) while "Basic lecture" was voted as the least useful method (50%). 62.1% said they review their patients' CXRs, while 37.9% said they review them rarely or look up the report only. 45.9% said they try to interpret CXRs before looking up the official report, while the other 54.1% said they rarely try to interpret CXRs or they only look up the report. Students complained of having no access to the radiology viewing computer system.

Conclusions: A high percentage of fourth-year medical students close to graduation do not feel comfortable interpreting CXRs. Although students who have had radiology elective felt more confident of their CXR-reading skills, this did not prove to be statistically significant (likely due to small sample size); nonetheless, the difference appears to be practically significant. The study identified a need to develop a more consistent and uniform CXR-teaching curriculum to enhance graduating students' competence and confidence in their CXR interpretation skills. A strong improvement for CXR teaching in this specific study group would be to grant students access to the radiology viewing computer system.

PEDIATRIC EPENDYMAL SPINAL TUMOR: A CASE REPORT AND LITERATURE SEARCH Daniel Felbaum and Richard Coulon. Department of Neuroscience. Joan C. Edwards School of Medicine. Huntington, WV

In the United States, the incidence of central nervous system tumors in the pediatric population is 4.5 cases per 100,000. The incidence of true spinal cord tumors is even rarer at an incidence of 1 per 1 million children. Furthermore, ependymomas are the second most common CNS tumor in children, with only 10% of all ependymomas occurring in the spinal cord. The objective of the study is to present a case of a pediatric spinal ependymal tumor and to review the current therapeutic strategies for managing it. In our case, a 2-year old female with a chronic history of cervical pain was referred to the neurosurgery service. Upon examination, the patient exhibited signs of cervical area tenderness, decreased biceps reflex, and had bilateral positive Babinski. An MRI of her spine showed an intramedullary cervical spinal cord tumor in the C2-C6 range. A resection was performed the next day and histological evidence confirmed an ependymoma. The patient responded well to the surgery and has resumed normal activities. In conclusion, although primary CNS tumors are rare, they should always remain in the differential for chronic cervical pain in the pediatric population. Our study includes a literature review of current management and treatment.

ASSESSING THE UTILITY OF HEAD CTs IN PATIENTS PRESENTING WITH ALTERED MENTAL STATUS OR SYNCOPE. Naveen Bellam, Rachel Shemtov, and Michael N. Cantor. Dept of Internal Medicine, Joan C. Edwards School of Medicine, Huntington, WV. Dept. of Internal Medicine, New York University School of Medicine, New York, NY.

Background: Syncope and altered mental status (AMS) are common presenting problems, and a head CT is often part of the routine workup for either condition. For patients without other presenting neurological signs, however, head CTs are often low yield.

Methods: Using retrospective, de-identified data from the Electronic Medical Record (EMR) system at Bellevue Hospital, this study evaluated the rate of acute, clinically relevant findings on head CTs ordered between 2005-2006. Using the indication field in the electronic radiology order, all head CTs were filtered to those where the indication was either syncope or AMS. The full radiology reports were then extracted from the system, and 2 physicians read and evaluated the reports for acute findings, coming to a consensus for each final result. Patient problem lists were also evaluated to determine if sets of specific problems correlated with acute findings on head CT.

Results: During the study time period, 843 head CTs were ordered to evaluate AMS (684) or Syncope (159). Of the syncope patients, 5 (3.1%) had acute findings on head CT, 3 had equivocal findings, and the remainder had negative studies. All of the patients with acute findings had had other presenting neurological signs or risk factors such as HIV. Eighty-five (12.4%) patients with AMS had acute findings, and 15 had equivocal studies. About half of the patients with acute findings had evidence of some form of stroke on CT. There was no significant correlation between patients with acute findings and their medical history as obtained from their electronic problem lists.

Conclusions: In patients with AMS or syncope and no other accompanying neurological signs, head CT's have a relatively low clinical yield. Obtaining the data from this study from an EMR system allowed for quick turnaround and query modification. Translating the findings from this study into practice will require both validation as well as major changes to physician behaviors and incentives.

HYPERCALCEMIA IN A PATIENT WITH CO-EXISTENT PRIMARY HYPERPARATHYROIDISM AND SARCOIDOSIS Mateen Hotiana, Oscar F. Ballester and Abid Yaqub Section of Endocrinology and Oncology, JCESOM

Introduction

Hypercalcemia is a well documented endocrine manifestation of sarcoidosis. Primary hyperparathyroidism is one of the most common causes of hypercalcemia seen in the outpatient setting. Hypercalcemia can rarely be caused due to the co-existence of these two conditions in the same patients.

Case Report

A 71-year-old white female was admitted to the hospital with lethargy, nausea, vomiting and had a calcium level of 13.6 mg/dl (nl: 8.5-10.1) with intact PTH of 97 pg/ml (nl: 8-74). She underwent right inferior parathyroid adenoma removal with successful resolution of hypercalcemia and normalization of parathyroid hormone levels.

About 2 months later, she was found to have an elevated calcium level of 11.2mg/dl with low PTH of at 7pg/ml. A work-up for non-PTH related causes of hypercalcemia revealed normal results. Her complete blood count showed normocytic anemia with leucopenia Pt subsequently underwent a bone marrow biopsy for anemia and was found to have multiple non-caseating granulomas consistent with sarcoidosis.

Discussion

Hypercalcemia in a patient due to coexistent hyperparathyroidism and sarcoidosis is a rare occurrence. The mechanism of hypercalcemia in sarcoidosis is increased activity of 1 α -hydroxylase in the macrophages with increased production of 1, 25 (OH) 2 D. When the two conditions co-exist the mechanism of hypercalcemia is not clear.

Conclusion

Hypercalcemia can rarely be due to co-existent PTH and non-PTH mediated causes. It should be suspected in patients in whom the calcium levels do not improve after parathyroidectomy. In patients with sarcoidosis, if the calcium levels do not improve with steroid therapy, coexistent primary hyperparathyroidism should be ruled out.

Association of Retinol Binding Protein-4 and obesity in children Mateen M. Hotiana, Abid Yaqub, Jennifer Wheaton, Ronald Stanek, Todd Gress and Yoram Elitsur Department of Medicine and Pediatrics, JCESOM

Objective:

The objective of our study was to compare the levels of RBP-4 (an adipokine secreted by adipose tissue) in obese and non-obese children and to determine the relationship between RBP-4 and BMI, waist circumference, and other markers of insulin resistance in a cohort of obese children in Huntington, WV.

Materials and Methods:

This was a case control study. Subjects were children aged 8-18 years (n=45) recruited at the MU pediatric clinic. The cases (n=28) were children with BMI above 95th percentile on CDC growth curve where as controls (n=17) were children with BMI of less than 95th percentile. Both groups were matched for age, gender and pubertal status. RBP-4 was measured by ELISA technique (ALPCO diagnostics). We studied the relationship between plasma RBP-4 levels and BMI, BMI SDS, waist circumference, triglyceride level and other markers of insulin resistance.

Summary of results:

Study and control groups were well matched for age, gender and pubertal status. The plasma RBP-4 level in obese group was 16.3 ± 5.02 and in the non-obese group 12.4 ± 4.26 . p value of 0.0048. Using Spearman's rank correlation, there was a significant correlation between RBP-4 levels and BMI ϱ (rho) 0.53, p value <0.001, BMI SDS ϱ (rho) 0.55, p value <0.001and waist circumference ϱ (rho) 0.9, p value <0.001.There was no significant correlation between RBP-4 levels and serum triglycerides, insulin resistance, insulin sensitivity, age or gender.

Conclusion:

Plasma RBP-4 levels were higher in obese children when compared with nonobese children of the same age, gender and pubertal status in our study cohort. There was a significant correlation between RBP-4 levels and BMI, BMI SDS and Waist circumference. Plasma RBP-4 level did not correlate however with triglyceride levels, HOMA IR, insulin sensitivity, age and gender CARDIOMYOPTHY AND MULTIPLE ORGAN FAILURE IN A PATIENT WITH NEUROFIBROMATOSIS. Eyad Hamoudeh, Department of Endocrinology, Joan C. Edwards School of Medicine, Huntington, WV

Introduction: Pheochromocytomas are rare, catecholamine secreting tumors derived from chromaffin cells that lead to excessive catecholamine release, occurring in 0.05-0.2% of hypertensive individuals. The incidence of pheochromocytoma in neurofibromatosis type 1 is 0.1-5.7%. A massive catecholamine secretion due to a pheochromocytoma can lead to a cardiogenic shock and multiple organ failure which is a rare but a life threatening event that can be potentially treatable if recognized early.

Case description: A 49 year old Caucasian female with a history of neurofibromatosis type 1 and hypertension presents to the emergency department with acute onset of severe chest pain and abdominal discomfort. The patient was intubated for acute respiratory failure and placed on mechanical ventilation. An emergent bedside echocardiogram revealed severe global hypokinesia and severe left ventricular function with ejection fraction of 10%. Laboratory analyses revealed elevated serum creatinine, lactic acidosis, elevated pancreatic, liver and cardiac enzymes. A chest x-ray confirmed bilateral pulmonary edema. Her initial blood pressure reading was 220/110 mmHg that was treated with nitroglycerin infusion for hypertensive emergency but then included the use of volume and catecholamine administration controlled by a pulmonary artery catheter for subsequent shock. the suspected diagnosis of pheochromocytoma which was confirmed by elevated catecholamine levels in the urine and computer tomography scanning of the abdomen revealing a right suprarenal mass measuring 4.7 x 3.8 cm with a central area of necrosis. After stabilization and subsequent administration of phenoxybenzamine and phentolamine the echocardiographic findings, electrocardiogram and all cardiac markers had returned to normal within a few days as well as other pancreatic, renal and liver parameters.

<u>Discussion:</u> Physicians should be aware that although rare; pheochromocytoma can present as cardiovascular collapse and multiple organ injury rather than just hypertension. A high index of suspicion is essential to reduce morbidity and mortality in these patients through early diagnosis and aggressive management.

References:

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- Tancic-Gajic M; Vujovic S; Tatic S; Stojanovic M; Ivovic M; Drezgic M. Adrenal incidentaloma in neurofibromatosis type 1. Srp Arh Celok Lek 2008 May-Jun; 136(5-6):295-8.

CASE STUDY: WERNICKE'S ENCEPHALOPATHY AFTER BARIATRIC SURGERY Minty Shah, Tae Hoon Lee, Eva Patton-Tackett, Department of Internal Medicine, Joan C. Edwards School of Medicine, Huntington, WV

Introduction Wernicke's encephalopathy is a disease from thiamine deficiency. It is an acute disease requiring emergent intervention to prevent permanent neurologic deficit. This is a case of Wernicke's encephalopathy after bariatric surgery.

Case 60 year old male with significant past medical history of hypothyroidism, obstructive sleep apnea, irritable bowel syndrome and, obesity status post bariatric surgery about 2 months ago from outside facility. Patient presented to emergency room because of falling down, poor oral intake (tolerating only 20 to 40 ounces per day), double vision, dizziness, short term memory difficulty and ataxia. He denied alcohol drinking. His medications include levothyroxine, multivitamin, vitamin B12 and vitamin C. He was not able to tolerate these medications recently because of stomach fullness. On physical examination, patient was oriented to place, person, month and year, but not exact date. Neurological examination showed limited horizontal eye movement, especially to the right side. Patient has vertical nystagmus to upward gaze. No ptosis. Pupils were equal to light and accommodation. Ataxia was not examined because of the weakness. Other physical examination was within normal limit. Laboratory test showed thiamine level of 1.1 (normal range 4-20 ug/L). Under the impression of Wernicke's encephalopathy, patient was treated with intravenous thiamine 100mg for 2 doses and folic acid. Dextrose 5% fluid was started after thiamine. Patient's symptoms improved slightly just after treatment and he was transferred to outside facility on patient's request.

Discussion Classic triad of Wernicke's encephalopathy includes encephalopathy, oculomotor dysfunction and gait ataxia. It can occur due to chronic alcoholism, poor nutrition, malabsorption, or Bariatric surgery. There is no lab testing or imaging study for Wernicke's encephalopathy. A serum thiamine level can be measured but sensitivity or specificity of these blood tests in symptomatic patients is not clear. The result of testing is not required to treat a patient. If a diagnosis of Wernicke's encephalopathy is suspected, thiamine replacement precedes lab testing.

Wernicke's encephalopathy may be precipitated by administering intravenous glucose solution in patient with thiamine deficiency. Hence glucose administration should be preceded or accompanied with intravenous thiamine. Thiamine supplementation along with other multivitamin supplementation is essential for patient with high risk of thiamine deficiency.

POSTER SESSION I • 9:45 A.M. - 10:30 A.M.

Conclusion Wernicke's encephalopathy is primarily clinical diagnosis and can be easily missed due to low index of suspicion, especially in this case. Institution of treatment is a priority than diagnosis. Response to therapy may actually be diagnostic in most clinical scenarios

LEFT ATRIAL APPENDAGE THROMBUS IN A PRETERM NEONATE IN SINUS RHYTHM WITH SEPTIC SHOCK Rohit Aswani, Joseph Werthammer, Prabhat Shrestha, Mahmood Heydarian. Department of Pediatrics and division of Pediatric Cardiology ,Joan C. Edwards School of Medicine, Huntington, WV.

Left Atrial appendage (LAA) thrombus is rare in the neonate. Only one case of LAA thrombus has been reported in a term neonate after an episode of sustained supraventricular tachycardia. We describe a preterm infant born to a diabetic mother with a large thrombus in the left atrial appendage detected by echocardiography after a septic shock. To our knowledge this is the first case of LAA thrombus in a preterm neonate, and the first case in a neonate in sinus rhythm. The thrombus resolved following treatment with lowmolecular-weight-heparin without complications.



Echocardiographic Subcostal 4-chamber view: Large thrombus in the left atrial appendage

AN UNUSUAL CASE OF COMMUNITY ACQUIRED EXTENDED SPECTRUM B LACTAMASE PRODUCING E-COLI URINARY TRACT INFECTION IN AN INFANT. Rohit Aswani, Eva Patton-Tackett, Department of Pediatrics, Joan C. Edwards School of Medicine, Huntington, WV.

Community acquired extended spectrum β lactamase (ESBL) producing Gram negative infections are uncommon and occur mainly in adult patients. Prolonged antibiotic use and increased length of hospital stay are clear risk factors for acquisition and infection by ESBL producing bacteria. Its isolation in pediatric cases is even more unusual. We report a rare case of community acquired urinary tract infection caused by ESBL-producing and multidrug resistant E.Coli in a previously healthy 9-week old female infant who had no prior hospital exposure. The infant was successfully treated with IV antibiotics. Repeat urine examination with culture and sensitivity results revealed no growth. This report serves as a reminder that the incidence of community acquired multidrug resistant infection such as bacteremia or urinary tract infection caused by ESBL- producing E.Coli has been increasing and should be taken into account in young infants.

BIG TROUBLE WITH BARTONELLA: A COMPLICATED CASE OF ENDOCARDITIS IN A HEALTHY, NON-HOMELESS MAN. Intisham Choudhry and Jose Mario Fontanilla. Departments of Internal Medicine and Infectious Diseases. Joan C. Edwards School of Medicine. Huntington, WV.

Bartonella endocarditis commonly presents as a culture-negative, subacute illness which results in significant valvular damage in the homeless, patients with advanced HIV disease or those with exposure to body lice (B. quintana) or cats (B. henselae). We present a complicated case of Bartonella endocarditis in a 35 year-old immunocompetent male with no known risk factors for the disease. JLS is a 35 years old previously healthy carpenter who presented to the ER with a 4-month history of fatigue, weight loss and acute R leg pain. He was found to have a superficial femoral artery embolus. 2D Echo revealed a large aortic valve vegetation. 5 sets of blood cultures obtained off antibiotics were negative after prolonged incubation. However, Bartonella IgG titers were positive at 1:2560. On hospital day 8, the patient developed congestive heart failure requiring emergent aortic valve replacement. PCR of the aortic valve was positive for Bartonella sp. On hospital day 15, he complained of burring of vision, which was due to a mycotic aneurysm in the M4 branch of the middle cerebral artery. Patient was treated with a 6-month course of doxycycline with a 2 week-course of IV gentamicin. Follow-up angiogram 3 months into therapy showed resolution of aneurysm. Patient is well and has regained normal function 1 year after valve replacement.

ETIOLOGY OF ENDOGENOUS HYPERTHYROIDISM IN TWO PATIENTS WITH LONG STANDING HYPOTHYROIDISM. Saba Faiz, Tipu Saleem, Abid Yaqub, Prasanna Santhanam. Division of Endocrinology, Department of Medicine, Joan C Edwards School of Medicine, Huntington, WV.

Objective: To describe etiology and diagnostic work up of endogenous hyperthyroidism in two patients who have long standing hypothyroidism. **Methods**

Case1: A 48 year old lady admitted to psychiatry ward with suicidal ideation. She has hypothyroidism for 20 years. She was taking synthroid 250 mcg/day for many years with normal TFTs one year ago. She has a recent contrast enhanced CT scan of spine for surveillance of spinal cord tumor. Physical examination revealed pulse 101, temp 98.1, blood pressure 116/76 and non-tender enlarged goiter with a nodule on left side. TFTs showed TSH .015(.3-4.4) and FT4 5.38 (.75-2.0). Synthroid was stopped, repeat TFTs in a week showed TSH<.004, FT4 1.44 and FT3 2.28(1.8-4.2). TFTs in 2 months showed TSH .016, FT4 1.95 and thyroglobulin 13. Anti TPO AB, anti thyroglobulin AB, thyroid stimulating AB and thyrotropin receptor AB were negative. She has low I-123 uptake of 2.3 % at 24 hours while 24 hour urine iodine 786 ug/spec (100-460) was high .Neck US showed multinodular goiter. Toxicity of multinodular goiter was attributed to recent iodine loading in form of contrast material used in recent CT scan. FNAC of left sided 3 cm nodule was categorized as atypical cells and pt had total thyroidectmy. Histopathology showed benign nodular hyperplasia. Case2: A 86 year old lady presented with CHF and atrial fibrillation. She has long standing hypothyroidism. She was on a stable dose of synthroid 50 mcg/ day. She denies any symptoms of hypothyroidism or hyperthyroidism. She has temp 97.9, HR 90, BP 120/60 and palpable thyroid gland without any discrete nodule or bruit. TFT's showed TSH .025 and FT4 2.02. Synthroid was stopped for a week and repeat testing showed TSH .067, FT4 1.70, FT3 2.53 and thyroglobulin 195. Thyroglobulin AB and Anti TPO AB were negative. Thyroid stimulating AB 412 (0-129) and thyrotropin recptor AB 2.80 (0-1.75). Graves' disease causing hyperthyroidism was diagnosed.

Conclusion: Endogenous hyperthyroidism can develop in patients with long standing hypothyroidism due to various etiologies. Non-suppressed thyroglobulin can differentiate endogenous hyperthyroidism from exogenous hyperthyroidism due to over dose of levothyroxine. Non functional thyroid nodules may become functional over time and cause endogenous hyperthyroidism especially in setting of Iodine loading. In autoimmune thyroid disease lymphocytes can switch from producing thyroid receptor blocking to stimulating antibodies over time and can cause endogenous hyperthyroidism after long standing hypothyroidism.

A CASE REPORT OF UNUSUAL PRESENTATION OF COLON CANCER AS MULTI NODULAR GOITER. Saba Faiz, Tipu F M Saleem, Mateen Hotiana, Prasanna Santhanam. Division of Endocrinology, Department of Medicine, John C Edwards School of Medicine, Huntington, WV.

Introduction:Metastasis of non-thyroidal cancers to thyroid gland is very rare. We are presenting an unusual case of colon cancer which presented initially as multinodular goiter.

Methods: Case Report: A 50 year old lady presented with neck swelling which was found to be a goiter on physical examination. US of neck confirmed multi nodular goiter with multiple solid nodules, largest nodules were 2.6 cm in right lobe and 1.8 cm in left lobe respectively. She was euthyroid. US guided fine needle aspiration cytology (FNAC) of right nodule, showed atypical follicular cell clusters, suspicious for neoplasm. Surgical consultation was recommended. Her neck mass grew more than expected in short time. Pre-operative CT neck and chest showed enlarged heterogeneous goiter, enlarged right supraclavicular (1.8 cm), right lateral cervical and sub carinal lymph nodes and bilateral small lung nodules. CT guided core biopsy of right supraclavicular lymph node showed small focus of suspicious epithelial cells without a definitive diagnosis.

Follicular thyroid cancer with lymph node metastasis was suspected and Patient underwent total thyroidectomy and central neck dissection, invasion of goiter into neck structures was noted intra operatively. Preliminary histopathology report from our institution favored multifocal (largest focus 5 cm) tall cell papillary thyroid cancer with angiolymphatic, extra capsular and cervical lymph node metastasis. However due to aggressive presentation and atypical microscopic features, specimen was sent to Mayo Clinic for immunoperoxidase staining for definitive diagnosis.

Immunoperoxidase staining showed, tumor cells were positive for CDX2 and keratin 20, focal staining for keratin 7, negative for TTF-1, chromogranin and HBME-1. Histological features were reviewed at Mayo Clinic and found to be consistent with moderately differentiated adenocarcinoma. Histological and immunoperoxidase picture together was suggestive of colon or ovarian Cancer. PET scan showed intense hyper metabolic activity in wall of rectosigmoid junction, with metastatic disease to bilateral cervical and mediastinal lymph nodes, lungs and liver. Colonoscopic biopsy of sigmoid mass confirmed colon Cancer. Up till now Pt has survived for one year on chemotherapy.

Conclusions:If FNAC of a large thyroid nodule shows suspicious atypical cells, metastatic non thyroidal cancer can be considered in differential diagnosis. Pre-operative Neck US or CT scan for screening metastatic lymph nodes can modify the extent of surgery for large thyroid nodules with suspicious FNAC. Imunoperoxidase studies should be conducted in setting of invasive and unusual histopathological features of thyroid nodules to differentiate thyroid cancer from rare metastatic non-thyroidal cancers.

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RANITIDINE-INDUCED HEPATITIS: A RARE CAUSE OF HEPATOTOXICITY Tae Hoon Lee, Kenneth J. Vega, Joe Gerges El-Khoury Department of Internal Medicine, Joan C. Edwards School of Medicine, Huntington, WV.

Introduction: Ranitidine and other H2 Recepter Antagonist are considered extremely safe, resulting in use without prescription. Despite this, it rarely can be associated with severe hepatotoxicity.

Case: A 27 year old male, without significant past medical history, presented to emergency room with jaundice and mild RUQ discomfort for three days. Medication use upon presentation was over the counter ranitidine for intermittent epigastric pain and heartburn only. Active alcohol or drug use was not reported by the patient. Physical examination was significant for clinical jaundice, icteric sclera and mild RUQ tenderness. No heaptomegaly or splenomegaly was noted. Labaratory data revealed a WBC count of 4.3 K/cmm, AST of 1385 U/L, ALT 2544 U/L, total bilirubin of 10.7 g/dl, direct bilirubin of 7.5 g/dL. Alk Phos was 199 U/L, Ferritin >1650 ng/ml and iron saturation of 62.1 %. PT was 14.5 seconds, and INR 1.47. Acute hepatitis panel for HAV, HBV and HCV was negative. CMV and EBV serologies were negative. Anti mitochondrial, anti nuclear and anti smooth muscle antibodies were negative. Alpha 1 antitrypsin and ceruloplasmin serum levels were normal. HFE gene mutation was negative. CT of the abdomen was significant for a 6 mm gallstone. ERCP was performed and revealed a normal cholangiogram without ductal dilation, choledocholithiasis or sludge. Liver biopsy showed mild portal inflammation, predominantly composed of small lymphocytes and a few eosinophils with mild lobular inflammation. There was intra hepatic cholestasis, but no viral cytopathic effects or evidence of iron overload. Trichrome stain demonstrated minimal portal fibrosis. These findings correlated with a drug induced hepatitis, likely due to ranitidine, the sole medication used by patient. The latter was discontinued at the time of admission. LFTs, ferrtin and iron saturation levels improved over following 7 weeks back to the normal range.

Discussion: Ranitidine-associated acute hepatitis has been estimated to occur in less than 1 per 100,000 patients. In most reported cases, the association was not clear due to confounders including other potential hepatotoxic medications at the time of illness, recent vaccination, or the presence of preexisting liver disease. Other cases had an incomplete evaluation, including the absence of liver biopsy, autoimmune or viral serologies as well as no endoscopic or radiologic evaluation of the biliary tree. This case highlights the seriousness of drug-induced hepatitis caused by a widely used over the counter medication. Our patient had no other concurrent medical conditions, was not using any other medications at the time of illness and had a complete assessment including a liver biopsy.

PEDIATRIC DEMOGRAPHICS ASSOCIATED WITH METHICILLIN RESISTANT STAPHYLOCOCCALAUREUS (MRSA) INFECTIONS S.

Cook, C. Sorge, and J. Shields. Department of Pediatrics, Joan C. Edwards School of Medicine, Huntington, WV.

MRSA is a major cause of skin and soft tissues infections and the AAP has recommended that physicians develop awareness of MRSA rates and sensitivity data in their pediatric communities in order to guide empiric antibiotic therapy. Such data has not been reported for our community. Thus, the objective of this study was to study local pediatric MRSA infections and identify any associated demographics for such infections.

A retrospective, inpatient chart review for any diagnosis containing the terms "cellulitis" or "abscess" between '06 and '09 was done. Patient demographics, location of infection, length of stay, culture results, and need for incision and drainage were all recorded.

A total of 200 patients were reviewed, of whom 109 had MRSA, 15 had MSSA, and 76 fell into the "other" category, representing other infections, negative cultures, and any patients who did not have a culture performed. 14 of the 15 MSSA cultures were sensitive to clindamycin, as were 96 of the 109 MRSA cultures. Susceptibility to Bactrim was 100% in both groups. The mean age of patients with MRSA were lower and trended toward statistical significance (Anova T test p value = 0.055). These patients were also significantly more likely to need incision and drainage (chi squared p value = 0.001). Other demographics including gender and LOS were not significantly different between the groups.

Therefore, pediatric MRSA infections are more likely to require incision and drainage and may occur in younger children. Bactrim may be a better empiric antibiotic choice, especially in repeat offenders. Pediatric MRSA infections have different antibiotic sensitivities than those reported by the hospital for both adults and children.

FEASIBILITY OF TELEMEDICINE FETAL ECHOCARDIOGRAPHY IN THE PERINATAL CENTER IN APPALACHIA. Misty Shoemaker, Eric Michelfelder, David Chaffin, Robin Reeves, Debby Brooks, Shailini Singh. In association with the following institutions: Marshall University Joan C. Edwards School of Medicine, Department of Obstetrics and Gynecology, Huntington, WV. Children's Hospital of Cincinnati Fetal Heart Center, Cincinnati, Ohio; Cabell Huntington Hospital, Perinatal Center, Huntington, West Virginia.

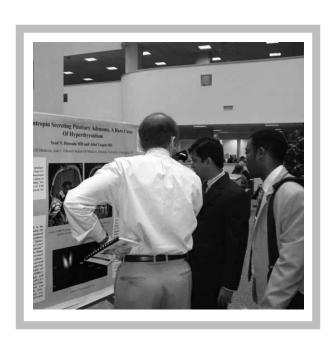
OBJECTIVE: Appalachia has the privilege of a never before telemedicine program offering fetal echo cardiography. We are proud to offer the Cabell Huntington Hospital Perinatal Center in Huntington, WV and serve approximately 38,000 deliveries thus far/per year (Southern WV, Eastern Kentucky and Southern Ohio.). Many of our patients require fetal echo screening ultrasound. Unfortunately greater than 50% of our patient population is unable to travel to Cincinnati for a referral of this nature. Thus the Telemedicine Fetal Echo Cardiography by Ultrasound Program was implemented.

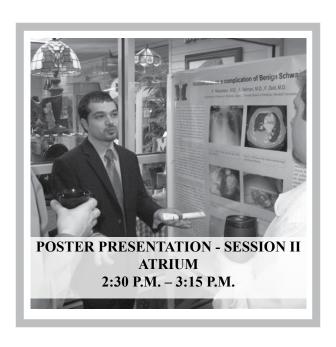
Method:

The Telemedicine Program was established in July of 2006. This retrospective observational cohort was conducted from July 2006 - June 30, 2008. A T1 line was established and the telemedicine fetal echo cardiography was initiated. Trained sonographers were sent to Cincinnati, OH to Pediatric Cardiologist Eric Michelfelder, M.D., for review in order to ensure reproducibility of fetal echocardiography technique. Dr. Michelfelder was subsequently licensed and credentialed appropriately to engage in research at Cabell Huntington Hospital. The projected volume for adequate research pool required a single telemedicine fetal echocardiography session per month. Two – four patients were scheduled per monthly session. A total of 57 subjects were scanned in 24 months. Indications for fetal echocardiography included; Intracardiac Echogenic Focus, Insulin Dependent Diabetes Mellitus, Two-Vessel Umbilical Cord, Systemic Lupus Erythematous, Increase Nuchal translucency (> 95%), or Fetal Arrhythmia. Critical views to the fetal echo cardiography inclusive scan include; Four-Chamber View of Fetal Heart (apical and transverse views) (with and without color doppler), Aortic Arch (AO), Ductal Arch, Right Ventricular Outflow Tract (RVOT), Left Ventricular Outflow Tract (LVOT), Superior Vena Cava (SVC), Inferior Vena Cava (IVC), Three-Vessel View (RVOT, AO & SVC).

RESULTS: 57 patients' fetal echocardiography scans were reviewed. Of these, 42 patients (73%) were considered to have a negative fetal echocardiography, while 11 patients (19%) were found to have positive findings on fetal echocardiography and 4 patients (7%) were lost to follow up. Details of abnormalities will be presented.

CONCLUSION: Implementation of the Telemedicine Fetal Echo Cardiography by Ultrasound Program was proven successful utilizing trained Sonographers. Once the program was establiahed no patient required referral to Cincinnati for further follow up. Successful implementation of the Telemedicine Fetal Echo Cardiography by Ultrasound Program allowed patients with nearly impossible access specialized medical care exposure to subject-matter-expert opinion without undue hardship. This exposure provided invaluable information and provided means to create appropriate and informed treatment plans to the benefit of our patients and their families.





LEFT ATRIAL APPENDAGE THROMBUS IN A PRETERM NEONATE IN SINUS RHYTHM WITH SEPTIC SHOCK Rohit Aswani, Joseph Werthammer, Prabhat Shrestha, Mahmood Heydarian. Department of Pediatrics and division of Pediatric Cardiology ,Joan C. Edwards School of Medicine, Huntington, WV.

Left Atrial appendage (LAA) thrombus is rare in the neonate. Only one case of LAA thrombus has been reported in a term neonate after an episode of sustained supraventricular tachycardia. We describe a preterm infant born to a diabetic mother with a large thrombus in the left atrial appendage detected by echocardiography after a septic shock. To our knowledge this is the first case of LAA thrombus in a preterm neonate, and the first case in a neonate in sinus rhythm. The thrombus resolved following treatment with lowmolecular-weight-heparin without complications.



Echocardiographic Subcostal 4-chamber view: Large thrombus in the left atrial appendage

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS OSTEOMYELITIS LEADING TO SEPTIC THROMBOPHLEBITIS IN TWO ADOLESCENT MALES. Joshua L. Dillon and J. Michael Waldeck. Department of Pediatrics, Marshall University Joan C. Edwards School of Medicine, Huntington, WV.

Community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infections are increasingly more common, and rare complications of these infections are becoming more common as well. Two patients who both presented with deep venous thrombophlebitis were subsequently diagnosed with MRSA bacteremia and osteomyelitis. In addition, one patient developed tachypnea and an increased oxygen requirement due to multiple pulmonary emboli. Both patients received a prolonged course of intravenous antibiotics and anticoagulant therapy. A well-established triad has been reported consisting of MRSA osteomyelitis, deep venous thrombophlebitis, and septic pulmonary emboli associated with extremely high mortality. The presence of MRSA bacteremia and any component of this triad should prompt evaluation for the other components, as early, aggressive management can be life-saving.

MANAGEMENT OF PREGNANCY, LABOR, AND DELIVERY IN A PATIENT WITH HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY. Amanda N. Pauley and David C. Chaffin. Department of Obstetrics and Gynecology. Joan C Edwards School of Medicine. Huntington, WV.

Background: Hypertrophic Obstructive Cardiomyopathy is a genetic disease of the cardiac sarcomere that leads to cardiac hypertrophy and narrowing of the left ventricular outflow tract. The disease can be life threatening in pregnant patients secondary to the enhanced physiologic demands of pregnancy.

Case: A 30 year old pregnant female with concentric ventricular hypertrophy, LVOT obstruction, systolic anterior wall motion, mild pulmonary hypertension and pleural and pericardial effusions presents with ventricular tachycardia and dyspnea at 28 weeks gestation. The patient was treated aggressively and was free of hospitalization until spontaneous rupture of membranes at 35 weeks. The patient was delivered in an intensive care unit with both a central line and arterial line in place for hemodynamic monitoring. She was monitored for 72 hours after delivery without any complications.

Conclusion: Patients with hypertrophic obstructive cardiomyopathy generally respond to the enhanced physiologic needs of pregnancy. However, if symptomatic, these patients should be treated aggressively with beta blockers, calcium channel blockers, and diuretics as needed. These patient require intensive monitoring during both the peripartum and postpartum periods due to the increased cardiac output

NEISSERIA MENINGITIDIS TYPE C PNEUMONIAAND SEPTICEMIA MISIDENTIFIED AS NEISSERIA SICCA IN A WOMAN WITH THE ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS). Gregory T. Burg and Thomas C. Rushton. Section of Infectious Diseases, Department of Medicine, Joan C. Edwards School of Medicine, Huntington, WV.

Introduction: We report a case of an AIDS patient who had pneumonia and septicemia due to an organism originally identified as *N. sicca* but later confirmed to be *N. meningitides* type C using the Abbott IBIS mass spectrometer/PCR array. This case raises not only the issues of public health, the atypical presentation of infection in an immunocompromised patient but also the role of genotypic analysis of ambiguous microbiological results.

Case report: A 32 year old female AIDS patient presented to the emergency department with two weeks of fever, shortness of breath, productive cough and hemoptysis. The chest x-ray showed a right middle lobe infiltrate. The patient was treated with levofloxacin. A blood culture grew a gram negative diplococcus. A reference laboratory identified the isolate as *N. sicca*. Using a molecular diagnostic assay, it was determined that the patient had been infected with *N. meningitides* type C. She recovered quickly, and comprehensive antiretroviral therapy was initiated; incidental AIDS-related nephropathy also improved. There were no other cases of *N. meningitides*, even in close family contacts.

Discussion and Conclusion: Either *Neisseria* species might have caused infection in this patient. Antibiotic therapy was the same for both, but N. *meningitides* is a public health threat. As here, where there is ambiguity, novel molecular diagnostic techniques may provide not only a definitive diagnosis but also critical epidemiological information.

ACETAMINOPHEN DIMINISHES AGE-ASSOCIATED INCREASES IN CARDIAC OXIDATIVE STRESS IN THE MALE FISCHER344XBROWN NORWAY RATS. Firas Almahasneh, Sunil Kakarla, Sumit Narula, Jacqueline Decker, Anjaiah Katta, Kevin M. Rice, Ernest M. Walker Jr., Paulette Wehner, and Eric R. Blough, Department of Pharmacology, Physiology and Toxicology, Department of Biological Sciences, Marshall University, Department of Pathology, Department of Cardiovascular Services, Joan C. Edwards School of Medicine, Marshall University

Background: Cardiovascular disease remains the foremost cause of death and disability in the rapidly increasing aged population. Age-associated elevation of reactive oxygen species (ROS) levels is strongly correlated with cardiovascular disease. Recent studies have suggested that acetaminophen possesses antioxidant properties and it may serve as a cardioprotective agent.

Purpose: We examined whether chronic treatment with a therapeutic dose of acetaminophen can diminish age-associated myocardial oxidative stress in male Fischer344XBrown Norway (F344XBN) rats.

Methods: Aging male F344XBN rats (27 month old: n=6) were treated with acetaminophen (30mg/kg/day p.o.) for six months. Age-matched control rats and young (6-months) rats did not receive any drug treatment. Immunohistochemical analyses for markers of oxidative stress were employed to assess effects of chronic acetaminophen treatment on the myocardial ROS accumulation.

Results: Immunohistochemical analyses showed that indices of oxidative (superoxide anion [O2òû], 4-hydroxy-2-nonenal [4-HNE]) and nitrosative (protein nitrosylation) stress were markedly higher in 33-month control rat hearts compared to 6-month control and 33-month treated animals.

Conclusion: Taken together, these data suggest that chronic acetaminophen ingestion may diminish the age-associated increases in the cardiac oxidative stress in the male F344XBN rat.

SUBACUTE VENTRICULAR FREE WALL RUPTURE. A CASE REPORT. Cross RC, Sayyed R, Studeny M, El-Hamdani M, Wehner P.; Marshall University Department of Cardiology, Huntington, West Virginia.

INTRODUCTION: Mechanical complications as a result of myocardial infarction can be devastating. The actual incidence is unknown due to discrepancy in the literature. Etiologies include rupture of the free wall, papillary muscle or interventricular septum. Evaluation includes clinical exam, echocardiography, and pericardiocentesis. We present the following case. CASE REPORT: A 58 year old male patient was sent to the ED on a Monday morning by work colleagues secondary to chest pain and dyspnea. Data confirmed the patient suffered his myocardial infarction approximately 60 hours earlier. ECG demonstrated inferior ST elevation in the inferior leads with Q waves and the first Troponin I was 70. The patient was still in moderate pain and respiratory distress. His face and upper torso were slightly cyanotic. His blood pressure was labile. The patient was taken for cardiac catheterization. The patient had 2 bare metal stents placed in the distal right coronary artery without dissection or perforation. An intra-aortic balloon pump was placed due to hypotension and an ejection fraction of approximately 30% with severe inferior wall hypokinesis. The peripheral angiograms demonstrated no flow in the right external iliac artery which was successfully opened by angioplasty and the left common femoral artery which could not be opened. Cardiovascular surgery was consulted. In the OR exploration of the left common femoral artery revealed only spasm. Stat TTE and TEE were performed which showed a hemopericardium. A pericardial incision was made and clot and fluid were removed relieving the tamponade. The patient was admitted to the CCU and had an uneventful recovery.

DISCUSSION: Ventricular free wall rupture can range from a catastrophic immediate death to a subacute presentation such as ours. Clinical features show more events occur in elderly, women and hypertensive patients. The left ventricle, anterior or lateral walls, thin walls, and the junction of infarct and normal muscle are usually affected. It most commonly occurs in 1 to 4 days. Diagnosis is made on clinical suspicion, echocardiography and pericardiocentesis. Treatment involves hemodynamic support and surgical therapy.

ACCESSORY MITRAL VALVE LEAFLET ASSOCIATED WITH AORTIC COARCTATION, BICUSPID AORITC VALVE, AND SEVERE MITRAL REGURGITATION. Peter DiMartino, M.D., Wray B. Everett, M.D.; Department of Cardiovascular Services, Joan C. Edwards School of Medicine, Huntington, WV.

INTRODUCTION: Accessory mitral valve tissue is a rare congenital cardiac anomaly. It can be an isolated or found with other congenital cardiac anomalies. Patients may present with symptoms of subaortic obstruction or be totally asymptomatic. CASE REPORT: A 27-year-old white female whose cardiac history dates back to infancy when she was found to have coarctation of the aorta and a bicuspid aortic valve. She underwent surgical correction of her coarctation at age 15 months. She was reevaluated in 2005 when a heart murmur was detected during pregnancy. Echocardiography (Echo) at that time showed mild subaortic stenosis due to the presence of apparent accessory mitral valve tissue. A bicuspid aortic valve was again identified and mild mitral regurgitation (MR) was noted. A transesophageal echocardiogram (TEE) was recommended but never done. In 2009 during a routine visit, a very loud heart murmur was detected, but she was essentially asymptomatic. PHYSICAL **EXAMINATION**: Blood pressure was 148/80 in the right arm and 130/90 in the left arm. Palpation at the precordium revealed sustained apical impulse but not displaced. There was a harsh grade 3/6 ejection murmur maximal in the aortic area, and along the left sternal border, a soft early diastolic blowing murmur was heard. At the apex, a grade 4/6 holosystolic murmur was noted which radiated into the axilla and back. A third heart sound was audible as well. A repeat echo again showed accessory mitral valve tissue within the LV outflow track resulting in relatively mild subaortic stenosis and evidence of a bicuspid aortic valve. This echo showed prolapse of the anterior mitral leaflet associated with severe MR confirmed by TEE. Despite being asymptomatic, it was felt she was a candidate for mitral valve repair and resection of the accessory mitral valve tissue. Given the complexity, a referral was made to a specialty clinic for possible mitral valve surgery. **DISCUSSION**: The patient has also developed severe MR secondary to prolapse possibly from ruptured chordae tendineae. With few published case studies, this is an example of an asymptomatic patient with accessory mitral valve tissue associated with coarctation and bicuspid aortic valve.

VAGALLY MEDIATED ATRIAL FIBRILLATION. Feras Elbash MD, Hany Guirgis, MD, Mark Studeny, MD and Paulette Wehner, MD., Marshall University Joan C. Edwards School of Medicine, Department of Cardiovascular Services, Huntington, WV

Introduction: Atrial fibrillation (AF) could be a result of Sympathetic or Parasympathetic over stimulation. The sympathetic type is usually related to exertion, alcohol, caffeine and emotional stress. This is common in middle-aged and elderly patients with underlying heart disease. In the young patients, vagal influences are more likely to predominate. Recognition of vagally mediated AF in young adults could be challenging yet important for the diagnostic and therapeutic implications, which are entirely different from the sympathetic driven arrhythmia. Case Report: A 60-year-old, with a history of severe CAD, presented to the hospital complaining of severe palpitations while eating or drinking cold beverages. His palpitations usually last for several minutes after finishing his drinking. He has no complaints of palpitation with any exertion. His palpitations have also been noted at night while he is relaxed and going to sleep. His EKG was done while drinking cold water and demonstrated the initial part with NSR, then AF started with a ventricular response of 180bpm. His rhythm converted back to NSR spontaneously within a few minutes. Conclusion: Cases of vagally mediated AF have been documented in the literature, but have always been noted in young healthy hearts. Our patient with the underlying severe CAD represents a unique setting for the vagally mediated AF. The most common timing for cardioversion to NSR is early in the morning while the sympathetic drive is highest and the most common timing for initiation of AF is late at night or during eating or drinking cold beverages, while vagal stimulation is highest. Medications that are highly effective in sympathetically mediated AF, are not indicated for vagally mediated AF, and may even prolong the dysrhythmia. Either electrical cardioversion or pharmacologic cardioversion with antiarrhythmics such as procainamide or ibutilide are appropriate for termination of the acute event. Flecainide may be more effective since it has more significant vagolytic actions. Atrial pacing or ablative therapy may be used as a last resort.

"INVERTED" TAKOTSUBO CARDIOMYOPATHY IN A POST-OPERATIVE PATIENT. Aaron Kaibas, Ellen Thompson; Department of Cardiovascular Services, Marshall University Joan C. Edwards School of Medicine, Huntington, WV.

Introduction: Stress-induced cardiomyopathy is an increasingly recognized condition causing transient LV dilation and dysfunction or "ballooning." The pathophysiology is not yet clear, but commonly thought to be a catecholamineinduced process. This has been called "tako-tsubo" cardiomyopathy, which in Japanese means and resembles an "octopus trap." The most common location of the transient dysfunction is the apex with sparing of the basal segments of the left ventricle. Recently, another form of stress-induced cardiomyopathy has been described involving dysfunction of the mid and basal segments and sparing the apex. This has been described as "inverted takotsubo" cardiomyopathy, transient apical-sparing cardiomyopathy, amount others. We present a case of inverted takotsubo cardiomyopathy in a post-operative patient. Case Presentation: A 78 year old female with a history of nonobstructive coronary artery disease, hypertension, and hyperlipidemia presented for an elective abdominal surgery under general anesthesia. Pre-operatively, and echocardiogram was performed and revealed normal left ventricular function. Post-operatively, she was extubated without difficulty. Shortly thereafter, she became dyspneic and tachycardic. Worsening respiratory status prompted re-intubation. ECG revealed sinus tachycardia with ST changes suggestive of ischemia. Cardiac enzymes were elevated; chest x-ray showed pulmonary edema. Echocardiography was repeated, demonstrating akinesis of the mid and basal segments of the LV and normal function of the apex. Non-ST elevation myocardial infarction was diagnosed and medical therapy was started with antiplatelet agents, ACEI, and diuretics. She improved uneventfully. Cardiac catheterization revealed normal coronary arteries without significant stenoses. On left ventriculography, the left ventricular function had completely recovered with no wall motion abnormality. The diagnosis of inverted takostubo cardiomyopathy was confirmed. Discussion: This case demonstrates inverted takotsubo cardiomyopathy in a post-operative setting. The catecholamine surge peri-operatively is postulated to be the cause in this patient. LV function returned to normal as expected with this syndrome. Currently, there are no randomized trials of this rare disorder. Medical therapy for actue heart failure has been used in case reports. Consideration for causes of catecholamine excess should include significant emotional and physical stress.

EFFECT OF IRON CHELATION ON CARDIAC FUNCTION IN THE IRON-OVERLOADED MONGOLIAN GERBIL Mehrette Maru⁸, Lucy Dornon⁸, Rabaa M. AL-Rousan^{1,6}, Kamran Manzoor ⁷, Joseph P. Laurino⁴, Ernest M. Walker³, and Eric R. Blough^{1,2,5,6}

¹ Department of Pharmacology, Physiology and Toxicology, Marshall,

Background: Iron-induced cardiovascular disease is the leading cause of death in iron-overloaded patients. Deferasirox is a novel tridentate oral chelator that exhibits a half-life suitable for once-daily dosing. However, little is known regarding the effectiveness of this agent in preventing iron-induced cardiovascular dysfunction. Methods: Adult male Mongolian Gerbils were randomly divided into three groups: control (C), iron overload (IO), and iron overload + deferasirox (DFX) (n = 8 / group). Iron overload animals received iron dextran 100mg/kg i.p /5d for 10 wks while deferasirox was given 100mg/ kg/d p.o. Cardiac iron levels were determined by inductively coupled plasma atomic emission spectrometry (ICP-AES). Gerbil EKG (standard leads I, II, & III) and echocardiograms (Philips Sonos 5500) were obtained in anesthetized animals at regular intervals. Results: Deferasirox treatment reduced cardiac iron by 23.5% (C: 0.08 ± 0.002 mg/g, IO: 0.68 ± 0.08 *mg/g, DFX: 0.519 ± 0.027 *† mg/g (P<0.05)), the ratio of cardiac mass/ body wt by 24% (C:0.39 \pm 0.01, IO: $0.52\pm.02^{*}$, DFX: $0.4\pm.01^{\dagger}$ (P<0.05)) and restored iron-induced changes in the QRS (C: 0.09 ± 0.002 ms, IO: 0.12 ± 0.002 *ms, DFX: 0.09 ± 0.001 †ms; P<0.05) and PR interval (C: 0.053 ± 0.001 ms, IO: 0.058 ± 0.001 * ms, DFX: 0.052 ± 0.001 ms, P<0.05). Iron overloaded gerbils were found to exhibit frequent PVC's 67%, SVT 17%, recurrent sustained and non sustained VT 33%, and increased incidence of death (2/8) with the latter occurring most likely due to fatal arrhythmias. Echocardiographic assessment demonstrated iron-induced increases in LVM (13%; P<0.05), and LVPWd (39%; P<0.05), while EF decreased (29%; P<0.05). Deferasirox treatment following iron overload either prevented or significantly decreased all iron-induced changes in cardiac structure LVM (11%, P<0.05), LVPWd (21%, P<0.05) and EF (26%, P<0.05) and function. Conclusion: Once daily oral deferasirox treatment appears to be very effective in preventing or reducing iron-induced cardiac dysfun

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UNIQUE CASE OF ATRIAL FIBRILLATION INDUCED BY PRONATION OF THE RIGHT ARM Raja Nawaz MD, Mark Studeny MD and Paulette Wehner, MD. Department of Cardiovascular Services, Marshall University Joan C. Edwards School of Medicine, Huntington, WV.

Introduction: Atrial fibrillation is the most common cardiac rhythm disturbance. It is often associated with structural heart disease, although many patients with atrial fibrillation have no detectable heart disease. This report describes a unique case of atrial fibrillation that was associated with pronation of the right arm.

Case Report: A 68 year old white female was admitted in the hospital with chest discomfort and palpitations. She was ruled out for acute coronary syndrome and was found to be in atrial fibrillation with rapid ventricular response. She had no significant past medical history except for paroxysmal atrial fibrillation. Adenosine stress test was not suggestive of ischemia. Echocardiogram did not reveal any structural heart disease. Her thyroid functions were normal and no underlying cause of the atrial fibrillation was found. She was initially treated with beta blockers along with anticoagulation. Lately she has noticed that these episodes were triggered by the pronation of her right arm. In this hospitalization her symptoms and the atrial fibrillation was reproduced on telemetry as soon as she pronated her right arm. Her baseline sinus rhythm changed to atrial fibrillation with rapid ventricular response that was initiated by a premature atrial contraction. She converted back to normal sinus rhythm immediately on supination of her arm. Electrophysiologic testing and three dimensional mapping has been considered along with ablation of the focus if deemed appropriate.

Discussion: Atrial fibrillation induced by specific movement of the right arm has not been described in the literature. This case can be explained by anomalous cervical input to the right or left atrium that can trigger atrial fibrillation by movement of the arm. Further work up with electrophysiologic study and mapping of the focal origin of atrial fibrillation will help us in identifying the cause and subsequent decision regarding therapeutic interventions.

OSLER'S TRIAD COMPLICATED BY PROSTHETIC AORTIC VALVE

ABSCESS Nizar Noureddine, MD; Yousef Darrat, MD; Paulette Wehner, MD, Department of Cardiovascular Services, Marshall University Joan C. Edwards School of Medicine, Huntington, WV

Introduction: The frequency of occurrence of prosthetic valvular endocarditis (PVE) is approximately 1-4 %. Furthermore, most cases occur early after valve replacement surgery. PVE is often complicated by conduction abnormalities. These conduction disturbances are considered to represent extension of infection from the valve to the annulus and surrounding myocardium. The prosthetic abscess due to PVE constitutes a severe complication of an aortic valve replacement, causing high mortality, despite combined medical and surgical treatment. The incidence of complete heart block complicating PVE is unclear; one study has reported an incidence as high as 22%. Case **Description:** A 59 year old white male with a past medical history significant for mechanical prosthetic aortic valve replacement presented with altered mental status associated with headache and fever. He was started on empiric antibiotics for bacterial meningitis and probable endocarditis although no vegetations were detected on transesophageal echocardiogram (TTE). On the fifth day of his hospital stay he developed high grade atrioventricular block which necessitated temporary transvenous pacemaker insertion which raised the suspicion for complicated PVE. Blood and cerebrospinal fluid cultures failed to grow microorganisms. A computerized tomography (CT) scan of the head revealed bilateral cerebellar infarcts, possibly secondary to septic emboli. Since the prosthetic aortic valve was not well visualized on TTE, a transesophageal echocardiogram was performed that showed an abscess adjacent to the prosthetic aortic valve. The patient was subsequently transferred for surgical intervention of cardiac abscess secondary to prosthetic valve infective endocarditis.

Discussion: The presence of a cardiac abscess is a poor prognostic factor in infective endocarditis. The diagnosis must be made at an early stage when surgical treatment is optimal. Therefore, conduction abnormalities can be used as early markers of severe complication in patients with PVE. The most valuable investigation is transoesophageal echocardiography with a sensitivity of over 80% and a specificity of about 95%.

THE DIAGNOSTIC PREDICAMENT OF SECONDARY ADRENAL INSUFFICIENCY Prasanna Santhanam, Saba Faiz Saleem and Tipu Faiz Saleem. Department of Internal Medicine, MUSOM.

Objective: To propose an approach for the diagnosis of secondary adrenal insufficiency (AI) by the illustration of two clinical situations. Methods: Case 1: A 43 year old lady had undergone transphenoidal resection for a non-functioning pituitary tumor. Twelve weeks later, she had an adequate response to the High dose ACTH Stimulation Test (HST). However, she developed symptoms of fatigue and dizziness on discontinuation of the prior instituted steroid replacement therapy. We performed the Insulin Tolerance Test (ITT) to rule out AI. Case 2: A 65 year old lady was hospitalized for fatigue, urinary tract infection and a laboratory finding of hyponatremia. She had no signs of dehydration or edema. The HST showed adequate baseline and stimulated cortisol levels of 9 and 20 ug/dl respectively. She was initially diagnosed with SIADH secondary to medication use. Despite being faithful with fluid restriction, she had recurrence of symptomatic hyponatremia during the course of hospitalization for transient ischemic attack. The Overnight Metyrapone Test (OMT) was performed on this patient to evaluate for secondary AI. We reviewed the literature to compare the utility of 8AM cortisol, HST, low dose ACTH stimulation test (LST), OMT and ITT for the diagnosis of secondary AI. **Results**: On definitive testing, by the Insulin Tolerance Test (ITT) in case 1 and Overnight Metyrapone test (OMT) in case 2, secondary AI was diagnosed in both the cases. **Conclusion**: Literature review has shown that although LST is superior to 8AM cortisol and HST in predicting the functional status of Hypothalamic Pituitary Adrenal Axis (HPAA) in chronic secondary AI, some situations need further testing with either OMT or ITT based upon clinical suspicion and judgment on a case by case basis.

AN UNUSUAL PRESENTATION OF PHEOCHROMOCYTOMA AS STRESS INDUCED CARDIOMYOPATHY. Padma Venkatraman, Airon Kaibes, Prasanna Santhanam and Tipu Faiz Saleem. Department of Internal Medicine, MUSOM.

Introduction

Stress-induced cardiomyopathy, also Broken Heart Syndrome is a condition characterized by transient apical or left ventricular dysfunction that mimics myocardial infarction. It has been shown in studies that plasma catecholamines are relatively higher in persons with stress induced cardiomyopathy

Case Report. A 78 year old lady with a history of paroxysmal atrial fibrillation and hypertension presented with chest pain and shortness of breath and was found to have an elevated troponin. The heart catheterization was unremarkable and the echocardiogram showed an ejection fraction of 25 % which improved spontaneously to 55 % over the next few months. She was admitted to the hospital again with dyspnea and diagnosed with congestive heart failure. The ejection fraction once again declined to 30 % but spontaneously improved to 50 % over the course of a few days. She was diagnosed with stress-induced cardiomyopathy. The patient subsequently developed episodic palpitations, paroxysmal headaches and sweating. The 24 hour urinary metanephrines was found to be very high. Repeat 24 hour urinary mentanephrines under stable conditions in the endocrine clinic were also high . CT scan showed a 5.4 x 4.1 x 5.7 cm right adrenal mass with central necrotic and cystic changes. The patient underwent excision of the right adrenal mass and the histopathology was conclusive for pheochromocytoma. The patient is now symptom free.

Conclusion Pheochromocytoma is a catecholamine secreting tumor of the adrenal medulla. Pheochromocytoma should be suspected in a patient with Stress induced Cardiomyopathy.

GENDER DIFFERENCE AND THE SEVERITY OF NOCTURNAL OXYGEN DESATURATION IN OBESE PATIENTS. Saif Mashaqi, Maurice Mufson and Imran Khawaja. Marshall University School of Medicine, Huntington, WV

Introduction: Obesity Hypoventilation Syndrome (OHS) is more predominant in obese males with BMI > 30. It is characterized by nocturnal hypoxemia, chronic daytime alveolar hypoventilation defined as PaCO2 > 45 mm Hg and PaO2 < 70 mm Hg. In this study, we looked at the gender difference in these patients on the degree and duration of nocturnal oxygen desaturation.

Methods: A convenience sample of 199 from a total of 281 persons with nocturnal oxygen desaturation (NOD) in our ambulatory practice between July 1, 2007 and December 1, 2009 was examined. Out of these, 110 patients required nocturnal oxygen. Twenty five patients (21 F, 4 M) were found to have NOD without a known cause and were included in the study group. Eighty five (60 F, 25 M) patients had underlying cause for their NOD and were excluded. We evaluated BMI, nadir of oxygen desaturation (percentage), duration of oxygen saturation <90% (minutes), FEV1 (percentage), PaO2 (mm Hg) and PaCO2 (mm Hg). No study patient had COPD, interstitial lung disease, obstructive sleep apnea, congestive heart failure or neuromuscular disorders.

Results: Among 25 patients with NOD in the study group, women outnumbered men 5:1. Nineteen of 21 women and all 4 men were obese (median BMI, F 42 [28-59], M 46 [35-50]). The nadir of oxygen desaturation (median F 80 %, M 86%), duration of oxygen saturation < 90% (median F 93 minutes, M 26 minutes), FEV1 (median F 82 %predicted, M 66% predicted), PaO2 (median F 67mm Hg, M 82mm Hg) and PaCO2 (median F44mm Hg, M 41 mm Hg) were not significantly different between women and men (t test, independent samples).

Conclusion: Although our study did not show a statistical difference in the degree or duration of oxygen desaturation between 2 genders but interestingly we found an idiopathic form of NOD which unlike OHS is five times more prevalent in females. Almost all women had underlying obesity and 50% of these females did not have any day time hypercapnea. To our knowledge, this "idiopathic NOD" has not been described in the literature and appears to be a separate entity from OHS that is five times more prevalent among obese females.

FIGHTING OBESITY: SHOULD MEDICAL INTERVENTION START EARLIER? Audra L Pritt and Patricia Lutz. Department of Pediatrics, Joan C. Edwards School of Medicine, Huntington, WV.

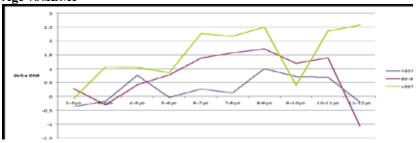
Purpose: To identify the age with the most dramatic change in BMI (body mass index) in obese children compared with normal weight children.

Methods: A retrospective chart review of 12 year old children who had a regular visit at least every other year at a University Pediatric clinic was performed. Children's age, gender, and BMI were obtained. Changes in annual BMI results were compared between obese (>95%tile), overweight (85-95%tile), and normal weight (<85%tile) children.

Results: A total of 100 charts were reviewed of which 23% were obese, 17% were overweight, and 60% were of normal weight. Male to Female ratio was ~1:1. The average BMI change per year in the obese (OB) group was higher compared with overweight (OW), and normal weight group (1.51 vs. 0.73 vs. 0.27, respectively, pvalue= NS). In the obese group, no specific age range was identified to suggest initiation of an age specific clinical intervention (Table below).

<u>Group</u>	No. in group	<u>Age</u>	ΔBMI
Normal	60	8-9	1.0 <u>+</u> 1.95
OW	17	8-9	1.7 <u>+</u> 1.16
OB	23	11-12	2.6 <u>+</u> 4.25
p-value	NS		





Conclusions: The incidence of obesity among our children was higher than national reported data (22% vs. 16%). On annual average, obese children had a greater increase in BMI compared to overweight and normal weight children. No specific age range was identified to implicate clinical intervention.

SEX DIFFERENCES IN EPICARDIAL FAT MICRORNAS IN PATIENTS WITH CORONARY ARTERY DISEASE

Kevin Johnson¹, Chris Adams², Carla Cook¹, Jia Fei¹, Todd Gress², Paulette Wehner², Nepal Chowdhury³, Arthur Mcunu³, Edward Setsor³, Nalini Santanam¹. Department of Pharmacology, Physiology & toxicology, ²Department of Medicine, ³Department of Thoracic Surgery, Joan C Edwards School of Medicine, Huntington, WV

Coronary Artery Disease (CAD) is a growing problem in the United States. CAD has been correlated to the presence of epicardial fat (EF), which provides useful and harmful functions to the body. EF gives the heart extra energy in times of high demand as well as cushions the heart against harsh movements. However, it increases resistance and artery remodeling which can prove to be harmful. This study looks at samples of EF and compares them to subcutaneous fat (SF) in their expression of micro RNAs (miRNA). MiRNAs are 18-25 nucleotides long and regulate gene expression. They influence the expression of a gene by degrading or repressing the target mRNA. MiRNA expression in EF has never been looked at and the opportunity to do so was intriguing. We collected EF and SF samples from male and female (n=20/sex) patients undergoing the coronary artery bypass graft procedure and randomly selected RNA samples to analyze miRNA. The human miRNA microarray consisting of over 88 miRNA relevant to humans was performed on the RNA isolated from EF and SF obtained from patients (n=8/sex). Threshold values were then used to compare miRNA expression in the EF of each patient. The SF samples from the respective patients were used as the control group when determining miRNA expression. Upon completion and initial review of the data, we found several interesting things. Females had no up regulated expression while males had 27 up regulated miRNAs in EF. Females had 13 down regulated miRNAs while males had 16 down regulated. MiR 122, MiR 196-b, MiR 302c, and MiR 210 all showed decreased expression in both males and females and remains a cause for further study. The data we collected and presented only scratches the surface of what we intend to find out about gene expression in EF and possibly how that can be targeted in regards to CAD. Validation studies are in progress. Identification of unique miRNAs in EF in patients will be useful as future therapeutics.

SEX DIFFERENCES IN EPICARDIAL FAT BIOMARKERS IN PATIENTS UNDERGOING CORONARY BYPASS GRAFT SURGERY-WEST VIRGINIAAPPALACHIAN HEART STUDY. Christopher Adams, Carla Cook, Todd Gress, Nepal Chowdhury, Kevin Johnson, Paulette Wehner, and Nalini Santanam. Department of Medicine; Department of Pharmacology, Physiology, & Toxicology, Joan C Edwards School of Medicine, Department of Cardiothoracic Surgery, St. Mary's Hospital & Heart Center, Marshall University, Huntington, WV

Background: Obesity is a growing health crisis, which predisposes one to increased risk to cardiovascular disease. The Appalachian region which includes West Virginia has the highest incidence of obesity. Obesity alters both the mass and function of abdominal fat. Recent studies have recognized the importance of epicardial fat (the fat that surrounds the heart and arteries) in the pathophysiology of coronary artery disease (CAD). The adipokines secreted by the epicardial fat have an immediate paracrine and endocrine effect on the underlying heart and arteries. There is a direct correlation between changes in epicardial fat function with increased risk to CAD. Methods: Our earlier studies in animal models of aging showed age and sex mediated differences in epicardial fat biomarkers. There was a decrease in biomarkers in older and female rats compared to younger and male rats. In order to investigate if these changes in epicardial fat specific biomarkers correlates with sex differences in humans with CAD, we obtained blood, epicardial and subcutaneous fat from men and women (n=20/sex, ages 30-80 years) undergoing coronary artery bypass graft (CABG) surgery at the St. Mary's Heart Center, Huntington, WV (IRB approved study). Results: Our preliminary results indicate sex differences in both circulating levels of adiponectin (total and high molecular weight-HMW) and tumor necrosis factor-α and the ratio of gene expression of adiponectin, peroxisome-proliferator activated receptor γ and interleukin-6 in epicardial fat compared to subcutaneous fat. Correlation analysis of biochemical findings to clinical outcomes (using Society of Thoracic Surgeon's database) showed an inverse correlation between circulating adiponectin levels (both total and HMW) to previous myocardial infarction or congestive heart failure and serum creatinine and a positive correlation with high density lipoprotein. The patients who underwent urgent CABG procedure had lower adiponectin levels compared to an elective procedure. **Conclusion:** Our results so far have identified unique correlations between epicardial fat biomarkers and coronary events. Further analyses are being conducted to validate our results.

MYCOBACTERIUM FORTUITUM SOFT-TISSUE INFECTION AFTER BILATERAL MASTECTOMY. Ryan Kerr, Jose Mario Fontanilla and Thomas C. Rushton. Section of Infectious Diseases, Department of Medicine, Joan C. Edwards School of Medicine, Huntington, WV.

Introduction: We report a case of a soft tissue infection due to a rapid grower, *M. fortuitum* (MF), after a failed total reconstruction after bilateral mastectomy. MF is a soil-borne organism that has been associated with cosmetic and reconstructive surgical procedures. Antimicrobial regimens typically used to treat tuberculosis are ineffective in NTM infections.

Case report: A 47 year old woman was diagnosed with BRCA 1 geneassociated breast cancer. She elected to undergo bilateral mastectomy followed by reconstruction via tissue expanders. Seven days later she developed erythema and pain at the incisions. The tissue expanders were removed and the patient was treated with clindamycin. Aerobic and anaerobic cultures were negative. Because of continued discomfort, fever and drainage, a second debridement was performed. *Pseudomonas aeruginosa* and MF were isolated. She has responded to a triple regimen of a fluorquinolone, doxycycline and linezolid

Discussion and Conclusion: MF should be suspected in infections that are protracted and non-responsive to standard therapy. Macrolides, tetracyclines and fluoroquinolones usually have activity against MF, but resistance has been reported. Guidelines recommend susceptibility testing of all isolates. Finally, long term therapy is generally required to effect a cure.

AN UNUSUAL PRESENTATION OF GERMINOMA WITH NEGATIVE INITIAL NEURO-IMAGING: Samia Kanooz , Abid Yaqub and James Bailes, Jr., Departments of Pediatrics and Internal Medicine. JCESOM, Marshall University Huntington, WV.

Introduction:

Germ cell tumors represent 1-2% of pediatric CNS tumors. MRI is the preferred imaging test of choice but initial false negative results have been reported. We describe here a case where the initial MRI of brain was negative initially but showed progressive abnormalities later in the course of disease.

Case Report:

A 15 year old boy presented to the pediatric endocrinology clinic with stunted growth and polyuria. He had low IGF-1 level and an inappropriately low urine specific gravity. His brain MRI was normal. He was started on Human Growth Hormone therapy for a presumed idiopathic growth hormone deficiency. He was also started on DDAVP for a diagnosis of idiopathic cranial diabetes insipidus. He showed a favorable response with improved growth rate but continued to have poor academic performance at shool. At the age of 18 years, he was started on levothyroxine replacement therapy. He developed motor in-coordination and ataxia. A repeat MRI of brain showed thickening of pituitary stalk and multiple areas of increased signal intensity on T2 images in left basal ganglia, bilateral internal capsule and anterior aspect of corpus collosum. He was started on hydrocortisone therapy for an empiric diagnosis of neurosarcoidosis. He showed marked clinical improvement on steroids; however his follow-up MRI showed progression of the above described lesions. Subsequently, he underwent brain biopsy which confirmed the diagnosis of pure germinoma.

Conclusion:

A high index of suspicion should be exercised before a diagnosis of idiopathic cranial diabetes insipidus is made especially in the presence of other anterior pituitary hormone deficiencies. In a published case series, initial MRI examination was normal in 4 out of 9 cases of biopsy proven intracranial germinomas A case can be made for routine serial MRI examination of brain at regular intervals if the initial MRI of brain does not reveal any abnormality.

EFFECT OF QUERCETIN AND ANTIOXIDENTS ON THE GROWTH OF HUMAN MELANOMA. Sarah Miles, Linda Eastham, Carson Donald, Katie Osley, Elisa Evans, Laura Recchi and Richard Niles. Department of Biochemistry and Microbiology, Joan C. Edwards School of Medicine, Huntington, WV 25704.

Melanoma is the most aggressive form of skin cancer and is often resistant to typical chemotherapeutic agents. Quercetin, a bioactive plant flavonoid, has been shown to inhibit the growth of cancer cells including breast, endometrial, and pancreatic. Our goal was to evaluate the growth inhibitory potential of quercetin (Qu) on human melanoma. We also assessed the sensitivity of melanoma cells to Qu treatment in combination with the antioxidants Ascorbic Acid (AA), and N-acetyl cysteine (NAC).

Time course growth studies were performed using varying concentrations of Qu on radial growth phase (SbCl2, WM3211), vertical growth phase (WM3211, WM3248) and metastatic (WM9,WM239) melanoma cells as well as normal human melanocytes (HEMn-LP). Growth studies were also conducted to determine the effect of combining Qu with the antioxidants AA and NAC on WM1366 and WM9 cell proliferation.

Our results showed that, after a single treatment of Qu, HEMn-LP, and five of the melanoma cell lines were very sensitive to its anti-proliferative effects, with WM1366 (VGP) cells being much less sensitive to Qu. However, the WM1366 and WM9 cells appeared more sensitive following daily treatments with Qu as opposed to a single dose treatment with this phytochemical at the beginning of the experiment. Combining Qu with 1mM AA appeared to enhance the growth inhibitory effects of Qu in these same cell lines. Interestingly, several of the melanoma cell lines are sensitive to 1mM AA treatment alone. NAC alone had no effect on growth in any of the cell lines tested and cotreatment with $10\mu M$ Qu did not augment the effect of Qu.

Our study demonstrates that melanoma cancer cells appear to be sensitive to the anti-proliferative effects of Qu. Furthermore, the growth inhibitory effects of Qu can be increased by daily treatment and co-treatment with the antioxidant AA. This data provides evidence that it is potentially the parent compound rather than a Qu metabolite that is responsible for its anti-proliferative effects. Further research, including the use of animal models, will help elucidate the potential role of Qu as a chemopreventive or chemotherapeutic agent for the treatment of melanoma.

SENSING FORCE OF A MUSCLE THAT ACTIVELY ENGAGES THE SUBSTRATE: TESTING SENSORY RESPONSES OF TARSAL CAMPANIFORM SENSILLA USING A 'BIONIC' PREPARATION. Sasha N. Zill, Sumaiya Chaudhry, Elizabeth Duke, Bridget Keller and David Neff. Department of Anatomy and Pathology, Joan C. Edwards School of Medicine, Huntington, WV.

Many animals adapt posture and locomotion to the properties of the substrates upon which they stand and walk, but the neuronal mechanisms underlying these adaptations are poorly understood. We have studied responses of tarsal campaniform sensilla, receptors that encode forces as cuticular strains in the tarsi (feet) of cockroaches. Previous experiments showed that the receptor discharges to contractions of the retractor unguis muscle, which engages the tarsus during walking on many substrates. We developed a model of force distribution in the tarsal segments as a third-order lever: muscle contractions that pull on the claws produce resisting forces in the last tarsal segment, which serves as a fulcrum. This should result in axial compression along the length of the tarsus and generate sensillum discharge when the claws engage with the substrate. We have performed physiological experiments to test this model. Axial forces applied to the end of the fifth tarsal segment produce discharges in tarsal sensilla that encode the force velocity and magnitude, as predicted by the model. Morphological studies using confocal microscopy suggest that mechanical coupling may occur through a ridge of cuticle that extends from the cuticular cap of the sensillum to the joint condyle.

We are currently using a new preparation in which displacements are applied directly to the retractor apodeme (tendon) using a computer-controlled linear motor. Close joint packing following claw engagement is clearly observed during 'bionic' movements of the tarsus. Sensory recordings show that sensillum firing does not occur during movements of the tarsus but follows engagement of the claws with an object. Thus, all data to date support the idea that the tarsal sensilla do not directly detect the body load (as do other groups of campaniform sensilla in the leg) but are activated by resisted contraction of the muscle that engages the substrate. We plan to further characterize this system to understand how engagement with the substrate is detected and controlled during posture and locomotion. Support: NSF Grant IBN-0235997.

OMEGA 3 FATTY ACIDS TO SLOW PROGRESSION OF INDOLENT B-CELL MALIGNANCIES W. Elaine Hardman*, Theodore R. Witte*, Alexander Salazar*, Gabriela Ballester#. and Oscar Ballester#, *Marshall University School of Medicine, #Edwards Comprehensive Cancer Center, Huntington, West Virginia

Early stage chronic lymphocytic leukemia (esCLL) is an indolent B-cell malignancies which progress to chronic lymphocytic leukemia (CLL)] at varying rates but once malignant, current therapies have limited efficacy. Inhibition of activation of the transcription factor NFkB has been shown to induce apoptosis and inhibit cell proliferation in CLL cells, thus targeting the NFkB pathway has been identified as a strategy for therapy of this malignancy. In preclinical studies, the omega 3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been shown to reduce the activation of NFkB in normal and cancer cells. We hypothesize that consumption of an omega 3 fatty acid supplement will suppress activated NFkB and slow progression to malignancy in patients with indolent B-cell malignancies. We conducted a pilot study to determine the optimal dose, the safety, feasibility and efficacy of omega 3 fatty acids to alter proposed biomarkers that would be expected to correlate with clinical benefit. The 8 participants consumed an omega 3 supplement at 3, 6 or 9 capsules per day, in increasing doses for one month at each dose. We found that: omega 3 was increased in membranes of both red and white blood cells (WBC), that sensitivity of the WBCs to doxorubicin was increased and that NFkB activation was suppressed, all in a dose responsive manner. Blood coagulation (collagen/ADP and, collagen/EPI aggregation) parameters remained within normal range. Our long term goal is to develop effective strategies that prevent or slow progression of indolent B-cell malignancies. Funding was from a pilot grant from the Marshall University Cell Differentiation and Development Center.

DIFFERENTIATION INDUCTION WITH ALL-TRANS RETINOIC ACID (ATRA) PARALLELS REACTIVE OXYGEN SPECIES (ROS) GENERATION IN SK-N-SH NEUROBLASTOMA CELLS

Anne M. Silvis, and Kelley K. Kiningham. Department of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, Huntington, WV.

All-trans retinoic acid is the main signaling retinoid in vivo and one of the most potent inducers of differentiation for human neuroblastoma in vitro. The redox status of a cell is crucial in regulating various cellular processes, with accumulation of ROS leading to oxidative modifications. Therefore, cells mount an adaptive response via upregulation of antioxidant enzymes such as superoxide dismutases, peroxidases, and catalase (CAT). Retinoids are known to alter the levels of ROS and expression of these endogenous antioxidants in various cancer models. In SK-N-SH cells, ATRA increased 4-hydroxynonenal adducts, a marker of lipid peroxidation, within 48 hours. This was paralleled by a significant increase in NMDAR1 (a neuronal differentiation marker) expression; and a significant decrease in glutathione (an endogenous antioxidant) production. After 72 hours, there was a subsequent increase in manganese superoxide dismutase (MnSOD) activity, which is a source of H2O2. H2O2 can be degraded by reacting with either glutathione peroxidase (GPx) or CAT; however, after 96 hours ATRA treatment, data suggest a significant increase in H2O2. Furthermore, preliminary data demonstrated no change in CAT expression and a decrease in GPx activity within 96 hours. Therefore, the lack of CAT or GPx upregulation suggests that H2O2 remains in the cell as a key signaling mediator. As it has been shown in other models, we hypothesize that H2O2 in our model promotes neuronal differentiation. Altogether, these data demonstrate early initiation of oxidative stress by ATRA and a subsequent adaptive response via upregulation of MnSOD, which may promote ROS formation and subsequently enhance neuronal differentiation. In order to enhance the effectiveness of ATRA in the treatment of neuroblastoma, a better understanding of specific signaling pathways involved in its use is needed; thus altering intracellular redox status may prove to be therapeutically beneficial to patients diagnosed with neuroblastoma. (Funding: Centers for Biomedical Research Excellence 1P20RR020180 (KKK) and 5P20RR016477; WV-INBRE 5P20RR016477).

CHRONIC ACETAMINOPHEN ATTENUATES AGE-ASSOCIATED INCREASES IN CARDIAC ROS AND APOPTOSIS IN THE FISCHER BROWN NORWAY RAT

Sunil Kakarla¹, Jacqueline C. Fannin¹, Anjaiah Katta¹, Satyanarayana Paturi², Kevin M. Rice², Ernest M. Walker Jr.³, and Eric R. Blough^{1, 2}

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There is a growing need for pharmacological agents to manage cardiovascular disease in the rapidly growing elderly population. Here we determine if acetaminophen is efficacious in decreasing age-related increases in cardiac reactive oxygen species (ROS) and apoptosis in aging Fischer344XBrown Norway rats. Compared to 6-month control animals, indices of oxidative (superoxide anion [O2•-], 4-hydroxy-2-nonenal [4-HNE], and 8-OHdG8-OHdG) and nitrosative (protein nitrotyrosylation) stress were markedly increased in 33-month old rat hearts. Thirty three month animals that had been treated with acetaminophen (30mg/kg/day p.o. for six months) exhibited diminished age-related increases in cardiac ROS levels and TUNEL positive nuclei and these changes were accompanied by improvements in the Bax/ Bcl2 ratio, diminished evidence of caspase-3 activation and increased phosphorylation of protein kinase B (Akt). Taken together these results suggests that acetaminophen may attenuate the age associated increases in the cardiomyocyte apoptosis, possibly via diminishing age associated elevation in ROS production.

17-AAG TREATMENT INDUCES A DIVERSE RESPONSE IN HUMAN AML CELLS. Jennifer M. Napper and Vincent E. Sollars. Department of Biochemistry and Microbiology, Joan C. Edwards School of Medicine, Huntington, WV.

17-N-Allylamino-17-demethoxygeldanamycin(17-AAG) is a potent heat shock protein 90(Hsp90) inhibitor currently undergoing phase III clinical trials. The goal of this study was to ascertain the specific effects of 17-AAG treatment in human acute myelogenous leukemia (AML). To that end, the human leukemia cell lines HL-60, KG-1a, THP-1 and Kasumi-3 cells were treated with varying doses of 17-AAG followed by analysis of toxicity, apoptosis, proliferation, and cell cycle. After 48 hours of treatment, it was evident that the different cell types exhibited diverse responses to treatment. Cell cycle analysis revealed that the cells accumulate in G2/M phase within 96 hours of treatment, although the effect was not equivalent among the cell lines. Therefore, possible mechanisms for the differing responses to treatment were explored. THP-1 cells, the most susceptible to G2/M arrest, up-regulate p21 with 17-AAG treatment. We also uncovered evidence that Kasumi-3 cells, which undergo apoptosis with 48 of treatment, may express mutant p53. KG-1a cells, the most resistant, regained sensitivity to 17-AAG by combining treatment with verapamil, a P-glycoportein inhibitor. Exploiting these differences may allow for more effective combinatory treatments in patients with AML.

HYPOXIA INDUCIBLE FACTOR-1A REGULATES MICROPHTHAMIA-ASSOCIATED TRANSCRIPTION FACTOR EXPRESSION IN HUMAN MELANOMA Sandeep S. Joshi, Jun Fan, and Richard M. Niles From Department of Biochemistry and Microbiology, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV 25755

Our lab has shown that human melanoma cells express hypoxia inducing factor- 1α (HIF- 1α) under normoxic conditions. Gene array studies revealed that Microphthalmia-associated transcription factor (MITF) was a target gene of HIF-1α. These findings were verified by qRTPCR. Knockdown of HIF-1α significantly reduced the expression of MITF mRNA and protein in melanoma cells. The MITF family consists of isoforms that differ in their transcriptional initiation sites. MITF-A is the largest and most ubiquitously isoform while the MITF-M form is missing exon 1 and is selectively expressed in melanocytes. We verified that MITF-M mRNA was highly expressed in normal human melanocytes relative to all melanoma cell lines. MITF-A and M mRNA were strongly down regulated in radial growth phase melanoma cell lines. However, MITF-A levels were higher in vertical growth phase melanoma and highest in metastatic melanoma. The ratio between MITF-A to -M expression showed a clear shift from MITF-M to -A in melanoma cell lines relative to melanocytes. Insilico investigation of the MITF-A gene promoter revealed two hypoxia response element (HRE) consensus sequences. Transfection of a luciferase reporter plasmid containing MITF-A promoter encompassing these sites into WM9 and WM239 melanoma cells showed ~80 and ~20 fold increase in luciferase activity relative to vector lacking the MITF promoter respectively. Knock down of HIF-1α expression resulted in a >60% decrease in luciferase activity relative to control cells. Moreover mutation in both HRE element in MITF-A promoter reduced its luciferase reporter activity > 30% relative wild type in WM9 melanoma cells. Chip assay revealed there is direct binding of HIF-1α to the MITF-A promoter in WM9 cells. In preliminary investigation MITF Knock down studies in WM9 melanoma cells showed it might be involved in cell survival. Overall our data suggest that MITF is a direct target of HIF-1α and its high expression levels in metastatic melanoma cells may account for the increased amount of MITF-A found in these cells

NUCLEAR-MEDIATED FUNCTION OF CHMP1A IN THE REGULATION OFATM SIGNALING ACTIVITY FOR THE CONTROL OF HUMAN PANCREATIC TUMOR CELL GROWTH Matthew Harlow, Sumanth Manohar, Ryan Mackie, Jing Li, Maiyon Park Department of Biochemistry, Marshall University School of Medicine, Huntington, WV

Chromatin modifying protein 1A (Chmp1A) is a member of the Endosomal Sorting Complex Required for Transport family that functions in the sorting and/or degradation of receptor mediated proteins via the endocytic pathway. Recent reports indicate that Chmp1A has additional functions: Howard's group reported that Chmp1A regulates cell cycle progression and chromatin condensation. We showed that Chmp1A over-expression leads to inhibition of cell and xenograft tumor growth, and that nuclear localization of Chmp1A is required for the mediation of the inhibitory effects of all-trans retinoic acid of human pancreatic tumor cells. Chmp1A appears to regulate tumor growth through the stabilization of P53. P53 is a substrate of an ataxia-telangiectasia mutated (ATM) kinase, and ATM activation is closely related to chromatin modification. We hypothesize that Chmp1A, through its nuclear localization, regulates nuclear ATM signaling activity and pancreatic tumor growth.

We are testing our hypotheses in human pancreatic ductal tumor (PanC-1) cells. Preliminary data indicates that Chmp1A over-expression led to an increase in phospho-ATM at serine 1981 (an indicator of activation) in the nucleus. Immuno-staining identified the co-localization of ectopically induced Chmp1A with phospho-ATM and its target P53 whose intensity was closely reflected that of Chmp1A expression. ATM kinase assay indicated that Chmp1A over-expression increased ATM kinase activity as evidenced by an increase in the level of phospho-P53 compared to control. Also, ATM inhibitortreated PanC-1 cells de-repressed Chmp1 A mediated-growth inhibition and P53 stabilization. To test the significance of the nuclear localization signal (NLS) domain of Chmp1A we generated NLS-deletion and minimal NLS-domain of Chmp1 A that was detected mainly in the cytoplasm and nucleus, respectively. We are currently generating stable clones of PanC-1 cells to conditionally over-express these deletion constructs. Once it is generated, we will test the effect of the NLS domain of Chmp1A on signaling activity of ATM and P53, and pancreatic tumor cell growth.

CHMP1A MEDIATED CHROMATIN MODIFICATION AND CELL CYCLE REGULATION IN HEK 293T AND PANC-1 CELLS Ryan Mackie, Matthew Harlow, Sumanth Manohar, Jing Li, Maiyon Park Department of Biochemistry, Marshall University School of Medicine, Huntington, WV

Chromatin modifying protein 1A/Charged multivesicular body protein (Chmp1A) is a member of the Endosomal Sorting Complex Required for Transport (ESCRT-III) family that functions in the sorting and/or degradation of receptor mediated proteins via the endocytic pathway. Using cell cultures, we recently provided evidence that Chmp1A functions as a novel tumor suppressor in the pancreas (published in Cell Cycle, 2008). Our conclusion is based on the results that first, non-tumorigenic HEK 293T cells form tumors in nude mice when Chmp1A is silenced. Second, Chmp1A protein is either reduced and/or mis-localized in the ductal cells of human pancreatic tumors. Third, over-expression of Chmp1A in human pancreatic ductal tumor cells (PanC-1) resulted in cell growth and tumor xenograft inhibition. We also reported that Chmp1A, especially through its nuclear localization, mediates the growth inhibition observed in all trans retinoic acid (ATRA) treated pancreatic tumor cells (published in Molecular Cancer, 2009). In both ATRA-dependent and -independent cases, Chmp1A regulates tumor growth by the control of P53 signaling activity. Dr. Stanley Hollenberg's group has reported that Chmp1A over-expression induced phosphorylation of Histone3 and chromatin condensation. Although chromatin structure can be changed by various modifications of histone family members and other chromatin interacting proteins, the role of Chmp1A in altering chromatin structure and consequent gene expression has not been fully explored. Nor has any connection been made between Chmp1A-mediated chromatin modifications and signaling activities, including cell cycle signaling. We are in the process of addressing these questions by over-expression of various constructs of Chmp1 A as well as silencing Chmp1A by shRNA in pancreatic tumor cells and HEK 293T cells. We will discuss the detailed modifications of histones mediated by Chmp1A, the significance of nuclear localization of Chmp1A in these processes and subsequent impact on cell cycle progression.

TYROID MALTOMA Reem H. Kheetan, Department of Internal Medicine, Marshall University School of Medicine, Huntington, WV

Mucosa-associated lymphoid tissue (MALT) lymphomas account for less than 1% of all primary thyroid malignancies. They typically arise as neoplastic transformations within areas of autoimmune thyroiditis. Although they tend to have an indolent course, these rare lymphomas often present a diagnostic challenge.

A 64 year old female presented for the evaluation of asymmetrically enlarging goiter of one year duration. Initially she was treated with thyroid hormone suppression therapy for one year for the management of her goiter. Her goiter increased in size despite medical management. Physical exam revealed diffuse enlargement of the right lobe with firm consistency and no tenderness. Mild enlargement of the left lobe was also appreciated. She had normal thyroid function tests and negative thyroid antibodies.. Serial ultrasound examinations of her thyroid showed progressive enlargement of right lobe of thyroid. CT scan revealed an enlarged thyroid gland extending inferiorly into the superior aspect of inferior mediastinum. Because of progressively increasing size of right thyroid lobe and her complaint of increasing pressure sensation in her neck she was referred to an ENT surgeon for consideration of thyroidectomy. She underwent a total thyroidectomy with removal of left peritracheal lymph nodes. Final tissue pathology showed extra nodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALTOMA). She was referred to an oncologist for further management. Further diagnostic studies failed to reveal any evidence of metastatic involvement. An upper GI endoscopy showed a small gastric ulcer and showed evidence of Helicobacter pylori MALT lymphomas are low grade B cell lymphomas that occur primarily in the stomach but also in nongastrointestinal sites, such as the thyroid gland. Thyroid lymphomas are rare malignancies, where MALT lymphoma account for 1% of all thyroid malignancies. They are indolent lymphomas, although in 30 percent of cases dissemination to other mucosal sites, bone marrow, or lymph nodes is found on diagnosis. They might present 20-30 years after the onset of autoimmune thyroiditis and may manifest as the sudden enlargement of pre-existing thyroid mass. Treatment recommendations for MALT lymphoma of the thyroid are still evolving. Successful treatment currently lies in the use of multimodality approach involving surgery, radiotherapy and chemotherapy.

In conclusion, thyroid MALT lymphomas are uncommon thyroid malignancies that typically arise in the presence of long standing lymphocytic thyroiditis. They generally have an indolent course. A high index of suspicion is recommended in patients with compressive goiter who have long standing history of lymphocytic thyroiditis, particularly if the thyroid enlarges suddenly.

PARTIAL EPICONDYLECTOMY WITH DIGITAL PALPATION OF THE ULNAR NERVE: A NEW SURGICAL TECHNIQUE Beatrice Grasu, and Daniel Felbaum, Department of Neuroscience, Marshall University School of Medicine, Huntington, WV

Cubital tunnel syndrome is the second most frequent entrapment neuropathy in the upper extremity. This occurs because the ulnar nerve is constricted by the medial epicondyle upon flexion of the forearm. The standard repair of this malady is by anterior transposition of the ulnar nerve or complete epicondylectomy. We propose a new technique that alleviates this pressure that removes less of the medial epicondyle and maintains the nerve in its natural location. Furthermore, a partial medial epicondylectomy results in shorter operating times and less scar tissue.

The procedure initially resembles a total epicondylectomy with an incision along the medial aspect of the elbow joint. An oscillating drill is used to shave the least amount of bone from the medial epicondyle. Simultaneously, digital palpation is used during forearm flexion after each shave to assess the pressure alleviated on the ulnar nerve. When constriction of the digit is minimized to the surgeon's satisfaction, the medial epicondyle is believed to be shaved down to its necessary width. This completely resolves the ulnar neuropathy. Patients report complete satisfaction with resolution of their pre-operative symptoms at similar success rates of the previously employed techniques.

The purpose of this clinical note is to describe a partial medial epicondylectomy as a successful alternative to anterior transposition of the ulnar nerve or complete medial epicondylectomy. The current management and treatment of cubital tunnel syndrome will also be discussed.

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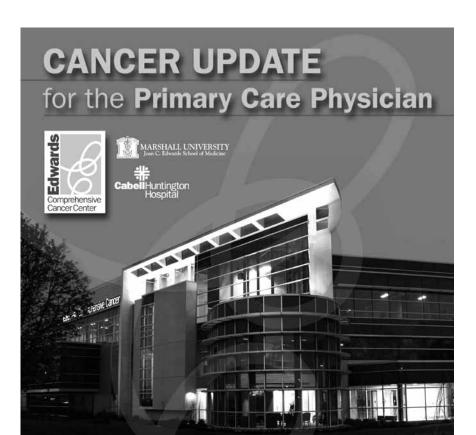












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