



Pediatric Headlines

February 2008

Texas Tech University Health Sciences Center of Amarillo

Special Words from Dr. Benjamin



**Bonna G Benjamin,
MD, FAPSA, FAAP**

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of Pediatrics**

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**Paul K Nolan, MD
Pediatric Pulmonologist**

This is the time of year when we renew old acquaintances, reflect on the past year and look forward to the new one. As a department of pediatrics, we want to share in the renewal and reflections. We have had some changes and additions we would like to share. Dr. Fred McCurdy, our regional chair was promoted to associate dean of faculty development and assistant dean of education. He consented to remain as program director (an enormous plus for our residency training with his extensive experience in education) but could not continue with the duties of the chair also. Dr. Bonna Benjamin was named the interim regional chair of pediatrics. She has been in Amarillo practicing as a pediatric surgeon since 1995 with Dr. Habersang's group until 2004 when that practice merged with Texas Tech to become a large multispecialty pediatric group. The current department of Pediatrics includes general pediatricians, neonatologists, pediatric intensivists, cardiologists, endocrinologists, gastroenterologists, hematologists, oncologists, pulmonologists, infectious disease specialists, nephrologists,

geneticists and surgeons. We are pleased to announce the addition of several new faculty members: One of three new general pediatricians, Dr. Kashif Ali started out our year by joining the full time faculty. Dr. Oluyemisi Fatunde another general pediatrician recently came to us from a practice in California and Dr. Vinod Sethi, also a general pediatrician came from Ohio in March. Emily Howard, PA joined Texas Tech in July to supplement the general pediatric clinic provider staff and Michael Doyle NP joined the special needs clinic with a special interest in diabetes. Cynthia Pride Dowell, NP joined the 1400 Coulter clinic in December. Dr. Golder Wilson, a geneticist, previously a consultant, joined the faculty Jan 1.

We are looking forward to a new year with many opportunities to interact with the extended "family" of pediatrics in new outreach, our annual symposium in April, and collaborative projects to have the best of education and patient care.

Bonna G. Benjamin, M.D., FAPSA, FAAP

Macrophage Activation Syndrome Associated Severe Diffusion Capacity Reduction, Mild Pulmonary Artery Hypertension in Systemic Juvenile Idiopathic Arthritis

By Paul K. Nolan, MD, Curt Daniels, MD, Fredrick Long, MD, Megan K. Dishop, MD, Peter Baker, MD, Margarita Guarin, MD, Elizabeth D. Allen, MD, and Robert Rennenbohm, MD (Texas Tech University HSC, Amarillo, TX; Columbus Children's, Columbus, Ohio; Texas Children's Hospital, Houston, Texas)

INTRODUCTION: Pulmonary Artery Hypertension (PAH) with severe diffusion capacity (DLCO) reduction complicating systemic juvenile idiopathic arthritis (SJIA) is extremely rare, only one case being reported.¹ In children with JRA, Pulmonary Function Tests (PFT) rarely show DLCO impairment and if present is usually only to a mild to moderate.² We describe a case of SJIA complicated by a severely reduced DLCO with mild PAH.

FEBRUARY 2008

Introducing: Pediatric Clinic Medical Director



Marita Sheehan, MD

Dr. Sheehan is a Professor of Clinical Pediatrics, and is also the Assistant Academic Dean for the School of Medicine of Amarillo. She has been part of the Texas Tech Faculty in various roles since 1986. Her wealth of Pediatric knowledge and experience includes a specialization in Adolescent Medicine. It is an extreme honor to introduce our new Clinic Medical Director.

CASE PRESENTATION: A 13 year old female with SJIA and partial Macrophage Activation Syndrome (MAS) developed dyspnea and tachycardia during the 5th month of active disease. During the 9th month, she experienced a life threatening MAS episode. PFT showed hypoxia and severe hemoglobin (hgb) corrected DLCO at 24% without obstruction or restriction. High Resolution Chest CT with angiography and Ventilation Perfusion scan showed no interstitial pulmonary fibrosis or macrovascular thromboembolism. Despite aggressive immunosuppressive therapy with pulsed methylprednisolone, cyclosporine A and methotrexate, the patient's dyspnea and hypoxia worsened. Heart catheterization at month 13 demonstrated mild PAH with mean pulmonary artery pressure (mPAP) of 37 mm Hg without intrapulmonary or significant intracardiac shunting. Bosentan was started in month 14. The patient experienced a second life threatening MAS episode in month 15. Etoposide was instituted to suppress the activated macrophages, which was followed by rapid clinical improvement in the MAS. Open lung biopsy at month 16 showed changes on light microscopy (LM) of pre-plexogenic pulmonary hypertension with intimal thickening and on electron microscopy (EM), multi-lamellated thickening of the alveolar capillary basement membrane (BM) (figure). There was no evidence of pulmonary fibrosis or thrombosis. The patient's Hgb DLCO reached its nadir of 21% by month 16. By month 32, the diffusion had risen to 73% and the mPAP had normalized to 22mm on heart cath. Currently the patient remains on etoposide cycling three weeks on, one week off and is now off bosentan. She maintains normal oxygen saturations off supplemental oxygen while ambulating.

DISCUSSIONS: The severe hypoxia and diffusion capacity limitation described were markedly out of proportion to degree of PAH found. The etiology of the hypoxia is the ultramicroscopic structural changes at the level of the alveolar capillary endothelium. Similar pathologic microvascular endotheliopathy lesions have been described on electron microscopy of the pulmonary alveolar capillary basement membrane in patients with plexogenic primary pulmonary hypertension.^{3,4} The likely pathologic cascade that led to these BM changes was likely excess release of endothelin-1 and cytokines from the activated macrophages, which triggered further endothelin-1 synthesis and release from the vascular endothelium.⁵⁻⁷

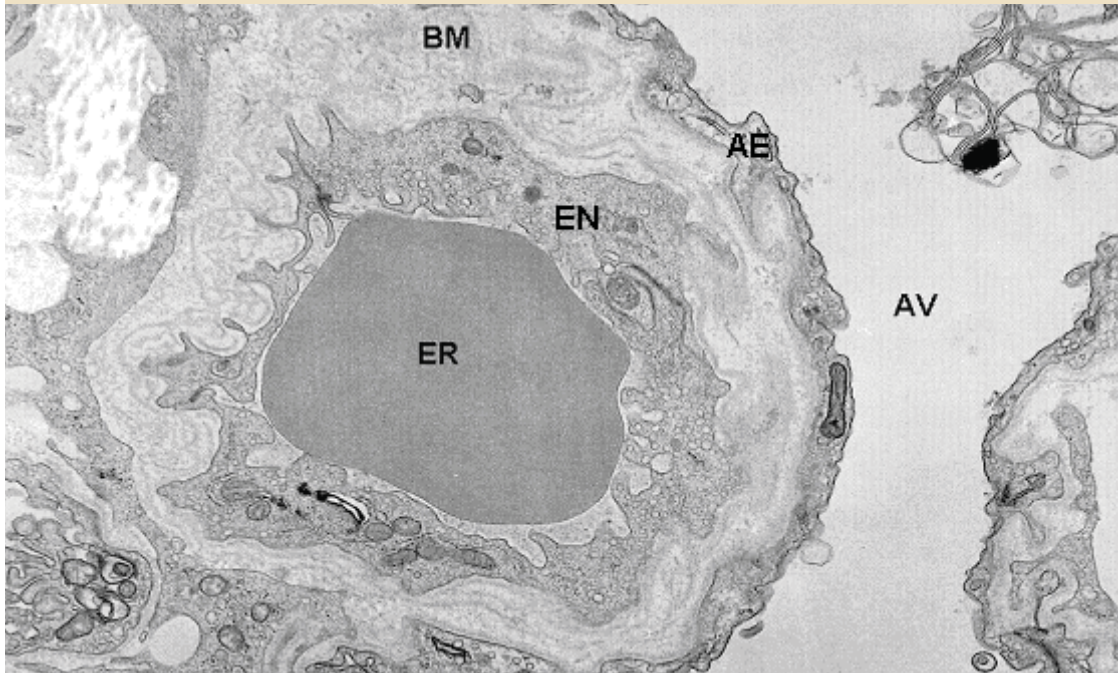
CONCLUSION: Patients with SJIA-related MAS can develop immune-mediated endotheliopathy in the pulmonary microvasculature resulting in severe reduction of oxygen diffusion and secondary PAH. The first clinical evidence of this endotheliopathy may be unexplained tachycardia and subtle dyspnea on exertion. Pulse oximetry and pulmonary function testing with diffusion studies should be considered in patients with active systemic JIA rheumatoid disease who are experiencing MAS. Immune mediated pulmonary microvascular endotheliopathy and pulmonary hypertension should be strongly suspected in the presence of significant diffusion capacity reduction and/or hypoxia. Early lung biopsy with electron microscopy should be pursued if the diagnosis is in question. If the pulmonary hypertension is confirmed on heart catheterization, therapy with the endothelin-1 receptor blocker, bosentan, should be pursued.

When macrophage mediated endotheliopathy is present and unresponsive to conventional therapies, treatment with oral etoposide can be life saving.

The authors are indebted to the young lady whom they have described. The authors also acknowledge Jim Barrish and Dr. John Hicks (Texas Children's Hospital, Houston, TX) for their assistance with the ultrastructural examination in this case.

This case presentation was presented in abstract at Chest 2005 and was awarded "Best Case Presentation in Pulmonary Hypertension".

Figure: Electron micrograph of the lung biopsy showing alveolar capillary endothelium (EN) and multi-lamellated basement membranes (BM) with increased diffusion distance between the alveolar-epithelium (AE), the alveolar air space (AV) interface and the intraluminal erythrocyte (ER). (8000 x magnification).



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Cardiac Outreach



Lana Little, RN, BSN

Lana has worked with Dr. Luckstead in Pediatric Cardiology for 8 years. She was with MIHIA for 2 ½ years at Texas Tech, then left before joining Pediatrics four years later. Lana takes care of the EKG's, Holter and Event Monitors, medication refills for the cardiac patients, and coordinates with Dallas/Ft. Worth for Pediatric cardiology surgeries. She participates in the Women's Bible Study at Amarillo South, loves to cook, and enjoys her family & pets.