2004 Health Sciences SIPs

Research Abstracts

Clinical Abstracts (these are the titles of the papers; the abstracts are descriptions of the clinical experiences)

Enhanced CCL7 and CCR5 Gene Expression in Usual Interstitial Pneumonia

By Esther Choi
Dr. Cory Hogaboam
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Abstract

There has been a struggle to diagnose and manage idiopathic. interstitial pneumonia, where the etiology of the disease is unknown and challenging to investigate. There has been considerable research effort directed toward elucidating the cellular and molecular mechanisms through which fibroblasts are triggered and remain activated during progressive, fibrosing disease of the lung parenchyma. Idiopathic pulmonary fibrosis (IPF) or otherwise known as Usual Interstitial Pneumonia (UIP) is a relentless progressive disease, which usually leads to death within 5 years of diagnosis. Symptoms of UIP diagnosed patients include dyspnea, restrictive lung dysfunction and impaired gas exchange. It is seen through this study that chemokines are increased and may contribute to the remodeling events in Idiopathic Interstitial Pneuomonia (IIP). Differentiating between the different subtypes of IIP is the focus of this study. Therapies for some of the IIP types have been inefficient and unsatisfactory. Concomitant expression of inflammatory CC chemokines and their corresponding receptors in surgical lung biopsies (SLBs) obtained at disease diagnosis was done in order to identify each form of IIP according to their factors that activate pulmonary fibrosis. Gene Array analysis helped examine the upper and lower lobe of SLBs from UIP patients. There was an increase in CCR5 gene expression in the SLBs of the UIP patient group relative to those with non-specific interstitial pneumonia (NSIP). Respiratory bronchiolhatory bronchiol ELISA protein analysis of the SLBs obtained from patients suspected of having a form of IIP showed increased expression of CCL7 and CCL22 gene in UIP patients and increased expression of CCL5 (RANTES) in NSIP-fibrotic patients. This study has provided further support that inflammatory CC chemokine ligands and CC chemokine ligand receptors are highly expressed in SLBs obtained from IIP patients compared to SLBs from non-IIP patients.

Pieces of the Puzzle: Preliminary Evidence that Nuclear Factor-κB and Nerve Growth Factor Play a Role in Thalidomidoinduced Peripheral Neuropathy

Author: Carly N. Higgins

***Supervisor:** Dr. Craig Harris- Reproductive Toxicology, University of Michigan*

Thalidomide is best known for its role in causing severe birth defects such as limb growth retardation and phocomelia in developing embryos. Little research was performed following the thalidomide tragedy of the late 1950s, and its teratogenic mechanisms remained a mystery In the past ten years, however, there has been renewed interest in thalidomide as it has proved to be therapeutic for a variety of disease states. Unfortunately, long-term thalidomide users often develop irreversible peripheral nenropathy. Thalidomide is known to induce oxidative stress and recent research has shown that nuclear factor-kappa B (NF-κB), a redox-sensitive transcription factor involved in limb outgrowth, is modulated by this induced oxidative stress. The effects of these changes on limb bud outgrowth have been demonstrated and we believe that these mechanisms may be connected with the lesser-known mechanism of thalidomide-induced peripheral nenropathy. Primary rat embryonic dorsal root ganglia (DRG) cultures (gestation day 12) were treated with 100 μM thalidomide and then evaluated using immunohistochemishy Observation of NF-κB showed an upregulation of the transcription factor's activation and translocation in the neurons of 5-day-old cultures, but not 14-day-old cultures, after thalidomide treatment. This indicates a connection between thalidomide and NF-κB redox regulation in DRG, and raises many new interesting questions regarding the effects of cell age and cell type on this phenomenon Nerve growth factor's (NGF) response to thalidomide treatment in DRG was also evaluated in this experiment. We provide preliminary evidence that thalidomide induces upregulation and secretion of NGF by astrocytes and subsequent binding to neuronal ceils. It is not certain yet whether or not this event is connected with the observed NF-κB activation, but we provide strong evidence that NGF also plays an important role.

Carl Hinshaw
Dr. James Tyburski M.D.
Professor of Surgery
Wayne State University

"Cytokine effects on secretory phospholipase 4 activitin in *in* vitro rat lung pericytes."

Increased levels of secretory phospholipase Az ($sPLA_2$) have been associated with alterations in microvascular permeability, and with poor prognosis in cases of sepsis. This study evaluates the effects of upregulating cytokines on $sPLA_2$ activity in rat lung pericytes. Rat lung pericytes were harvested and cultured Second passage pericytes were incubated with 10 µg/ml and 50 µg/ml interleukin-la (II-I), interleukin-6 (IL-6), and tumor necrosis factor (TNF) for twenty-four hours. The supernatant was then assayed for $sPLA_2$ activity. Rat lung pericytes exposed to IL-1 showed increased activity to 10 and 50 µg/ml. Administration of IL-6 resulted in no change in $sPLA_2$ activity from control. Pericytes exposed to TNF showed increase $sPLA_2$ activity only at 50 µg/ml. These results suggest that IL-1 and TNF, but not IL-6 play a role in the alteration of microvascular permeability via increases in $sPLA_2$ activity, and may be significant in the pathway leading to sepsis.

Correlation of Intraouerative and Early Postoperative Transvalvular Gradients Following Aortic Valve Replacement

by Lauren Levy
Supervisor: David S. Bach, MD
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ABSTRACT

Intraoperative transesophageal echocardiography (TEE) provides imaging that is useful in planning and guiding many cardiac surgical procedures, particularly in aortic valve replacement (AVR). In order to assess valvular function, surgeons routinely request hemodynamic data derived from TEE (in the form of gradients), following implantation of the prosthetic valve. Although aortic gradients are commonly assessed, there are multiple conflicting factors that may affect their reliability in the operating room.

The present study wus performed to determine the correlation of intraoperative and postoperative gradients following aortic valve replacement (AVR), in order to assess the relevance of measuring gradients intraoperatively. Intraoperative and follow-up echocardiography reports including aortic gradient measurements were obtained for 28 patients that underwent AVR at the University of Michigan Hospital. Scatter graphs with corresponding linear regression equations were constructed and analyzed using the Pearson linear coefficient to determine if a correlation existed between gradients. Separate graphs, constructed by valve type, were also similarly analyzed.

Gradients varied unpredictably between intraoperative and postoperative echocardiograms. Statistical analysis indicated that gradients measured in the operating room after AVR are not predictive of those at follow-up (R^2 was 0. IO for mean gradients and 0.20 for peak gradients). These findings were not isolated to valve type. The results of this study suggest that measuring intraoperative gradients following AVR surgery may not be relevant to the immediate assessment of aortic valvular function.

Mieroleakage Comparison of Adhesive Systems in Class V Composite Restorations

By
Nathaniel P. Mutch

Advisors:

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Abstract:

The development of adhesive systems continue to progress towards a reduction in microleakage at cavity margins. The objective of this study was to compare the microleakage in class V composite restorations using several self-etch bond agents and a standard total-etch control. Class V cavities were prepared on the buccal and lingual surfaces of 20 third molars previously stored in 0.2% sodium azide. Ten preparations for each of the three self-etch bonding systems (AdheSE, SE bond, UniFil) and one total etch control (Excite) were all restored with resin composite (4-Seasons). Restored teeth were finished, placed in distilled water for 24 hours, and thermocycled between water baths of 5 and 55°C with a l-minute dwell time for 1000 cycles. Apices were then sealed with epoxy resin and two coats of varnish applied to within 1mm of the cavity margin Teeth were placed in 0.5% basic fuschin dye for 24 hours, rinsed and embedded in se&curing resin. A slow speed diamond saw was used to cut embedded teeth buccal-lingually to produce multiple sections for each restoration. Under a light microscope (40X) microleakage was ranked (O-4 ordinal scale) with the consensus of two evaluators at the occlusal and cervical marigins. Data were analyzed with Kruskal-Wallis One-Way Analysis of Variance and a Pairwise Sii Test (confidence interval = 0.05). A statistically significant difference was determined between the cervical and occlusal margins that was material-dependent at $p<0.05$. At the occlusal margin the total-etch system (Excite) provided a superior seal compared to 2 (AdheSE and Unifil) of the 3 self-etch systems (SE bond, AdheSE and Unifil). At the cervical (dentin) margin each of the 3 self-etch systems demonstrated less microleakage compared to the total-etch control.

J. Kalli Fortune
Abstract for Clinical SIP

The clinical portion of my SIP was at the Tuba City Indian Medical Center and the Tuba City/Moenkopi Family Wellness Center in Tuba City, Arizona. I lived on the Navajo reservation the majority of the summer and created an internship under the supervision of Dr. Diana Hu. Three to four days of the week, my time was spent at the Wellness Center. I helped create and run the Summer Youth Enrichment Program, part of the Wellness Center's Prevention of Diabetes program. We designed the mornings to educate the children on the importance of exercise, normally through actually teaching the activity. The afternoons were designed to educate the children on nutrition, including how to make healthy snacks and to know basic nutrition information. The goal was to educate children while they are still young enough to change the habits learned from their parents, and hopefully help in the battle against the epidemic of obesity and diabetes that is plaguing the reservation. The other portion of my internship was spent at the medical center, assisting doctors in a variety of fields. While some time was spent merely shadowing, I was able to assist doctors with patients in Emergency, Labor & Delivery (specifically, midwifery), Pediatrics and Family Medicine. I also made house calls with Field Health nurses elsewhere on the reservation.

On-site supervisor: Diana Hu, MD
Location: Tuba City Indian Medical Center
Tuba City/Moenkopi Family Wellness Center
Tuba City, AZ

Erica Lake
Dr. Sanjay Dalal
Nephrology Center of Kalamazoo
Kalamazoo, Michigan

Internship at Nephrology Center of Kalamazoo

When I first began thinking about the topic that 1 would write my SIP on, I was unsure as to what direction I should even take. I asked my aunt for help in fmding someone to allow me to follow the around, and she introduced me to Dr. Sanjay Dalal, a nephrologist. After my first visit, I knew that I had chosen a difficult field, and that is what enticed me to write my SIP on Lupus Nephritis.

For the most part, I followed Dr. Dalal around to see his patients and try and pick up on the different symptoms, look at the different labs and determine what could be the problem. When I first got to the practice, Dr. Dalal just had me follow him with any questions that I had about what I had seen in the rooms with the patients. I had an enormous list of questions because I had never speculated how many different organ systems could be involved witb the kidney, and how many systems depended on the life of the kidney, mainly, the circulatory and endocrine systems.

Once 1 became comfortable with the basic labs and questions, Dr. Dalal let me look at the labs in front of the patients, and try to assess the problems with my current knowledge. At first, this was somewhat difficult, however, after some time, it became more easy to look for just the right number depending on the problem that the patient was having.

Through this internship, I became very familiar with looking for symptoms of patients not just through what they were visiting for, but also watching them. What is not said is often the best determinant of what could be ailing the patient. I was made knowledgeable of how to read many different types of blood labs. I am now more confident in the correct way, in my mind, of how to treat a patient in terms of level of intimacy and friendship, while maintaining professionalism.

As far as my SIP was concerned, some of the patients that we saw had Lupus, an autoimmune disease that was very difficult because of it's mimicking symptoms lack of cure. Dr. Dalal said that it was a very complicated disease. After seeing about the third patient with this disease, and noting that all the symptoms were in fact different, I decided to write my SIP on Lupus Nephritis, which is lupus, plus a malfunctioning kidney.

The Chiropractic Approach On Down Syndrome, An Abstract

Phillip D. Kotzan

On-Site Supervisor:
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White Lake Chiropractic P.C
White Lake, MI

Down syndrome is due to autosomal trisomy resulting in 47 somatic chromosomes rather than the usual 46. The chromosomal defect is associated with chromosome 21. Though the disorder is not neurological, many neurological deficits are common, along with congenital heart defects, visual and auditory problems, atlanto-axial instability, and a weakened immune system. Since these problems are genetically determined and permanently present, the health care world has shown minimal progress towards helping the conditions of people with this disorder. The chiropractic realm of health care has recently advanced its concern for people with Down syndrome by investigating the degree to which each patient is assisted both neurologically and structurally through chiropractic care. A plethora of case studies have been released as to the benefits seen within hundreds of patients with Down syndrome. Until the health care world is presented with a greater understanding of the intricate interrelationships of the nervous system, its chemical neurotransmitter substances and all other physical, mental or emotional forces that may affect improvement within individuals with Down syndrome, little published research, besides case studies will be seen in the next few years. The future of thousands of people with Down syndrome could improve upon the crossing of disciplinary lines and allowing alternative medical practices to join the efforts of those traditional health care practitioners to fully understand and care for Down syndrome. Therefore, the following work attempts to piece together the understanding of Down syndrome and chiropractics, and how the latter can be applied to provide some of the best documented relief to the symptoms of Down syndrome.

Clinical SIP in the Emergency Department

Stéphanie Maurissen
Dr. Danny Greig
MidMichigan Medical Center: Emergency Department

My clinical Senior Individualized Project consisted of following and assisting Dr. Danny Greig throughout his rotations. I assisted in suturing, in explaining conditions and medications to patients, in copying and doing other secretarial duties, etc. Throughout the 12-week project, I witnessed extraordinary procedures, such as intubation of patients and inflation of a collapsed lung. I enjoyed the array of conditions we saw (from chest pain to broken bones to infections).

We saw at least 21 patients during the IO-hour shifts physicians complete three to five times a week. These shifts ranged in time slots; each physician would spend two-three days on one shift, then have two-three days off, and then move to another shift clockwise on the rotation (to aid the body's circadian rhythm). The shifts were from 6:00-16:00, 9:00-20:00, 15:00-1 :00, and 20:00-6:00.

There are a few general principles that have stuck out as summarizing my experience. The first is the team/family network found during any shift. The physician is of course in charge of patient care but works together with other physicians and the nurses. When unsure of something, the team would get together and analyze a patient's history or diagnostic results. When a nurse had a question, the physician took the time to explain the plan and analyze the thoughts the nurses might bring up. When times became stressful, nurses would order x-rays and do anything to help the physicians out. It felt completely like a large extended family.

Another aspect is that the patient is the customer and has all rights as such. When he/she refused a certain test or wanted to leave, the consequences were laid out to him/her but the treatment would be stopped if refusal was persistent. If the patient left against the advice of the physician, he/she had to sign a form "Against Medical Advice" saving the physician from any bad situation that might arise in the future.

Another important point is the amount of compassion I have seen given to patients by the employees of the department. Each time a patient enters the E.R., they are treated with utmost respect. Even if they are mentally ill, their needs are taken care of and nurses talk to them as though they were normal, alert and responding. Patients are treated as people not as numbers.

The dedication of the nurses and physicians is the last point I would like to talk about. I have really been impressed with the dedication of everyone in regards to the patients and their care. Physicians stay "overtime" to follow their patients throughout their stay in the department. They feel responsible for the well-being and the diagnosis of the patients they started to see. This is something that is not seen in a lot of workplaces; usually, when a shift is over, an employee leaves and doesn't finish up loose ends. Another part of this same idea is how much the physicians love what they are doing. They look forward to each new case and hope they will be able to help. When they don't know what is causing a patient's complaint, they look it up in reference books or talk to one another about it. This is dedication!

Review paper: Congestive Heart Failure: Physiopathology, Etiology, and Therapeutics

Clinical SIP Summer Internship Abstract

Anne M. McCue
On-Site Supervisor: D/Sgt. Rob Rayer
Firearms/Toolmarks Division
Michigan State Police, Northville Forensic Laboratory

It is oftentimes not realized, but because the requirements for graduate study are almost identical to those required for most medical schools, forensic science is an excellent choice for anyone considering an alternative to medical school. My summer in 2003 consisted of a full-time, volunteer internship position at the Michigan State Police Crime Lab in Northville, MI. Specifically, I worked in the firearms and toolmarks division, although on some days I was able to move around into the other departments (such as latent prints, DNA, and trace evidence). It was a really fascinating experience, and I learned not only a lot about the science of forensic investigation, but also about the structure and workings of the Michigan State Police as a unit. In general, I spent most of my time assisting with evidence processing, organizing, and examining in the firearms lab. Although I was understandably not allowed to perform many of the aspects of evidence examining by myself, my responsibilities grew as time wore on. In the lab, I learned how to do preliminary examinations and labeling **of** firearms **and toolmarks** evidence, and also how to do some comparing of test shots and evidence on a comparison microscope. Some of the jobs I did also consisted of office work: I helped design some evidence examining worksheets constructed a PowerPoint presentation for a lecture being given on the firearms and toolmarks department. I also performed research for the division on evidence sterilization techniques, labeled crime scene photographs, and assisted in crime-scene re-enactments. On some of the more relaxed days, I was given the opportunity to learn about the bomb squad, which at the time was part of the division, and learned how to shoot a gun. I learned a great deal as well about the legal process involved in forensic investigation and was able to go to court and witness the testimony of forensic scientists on two occasions. Finally, I was able to organize a contact database of all the police agencies the crime lab works with.

Paper Title: The Forensic **Investigation of Gunshot Wounds with** a **Special Emphasis on Cranial Defects**

Jaime Pulling
Dr. Eduardo Crotte
Kalamazoo Radiology
Dr. Timothy Swartz
Rheumatology P.C.

MY CLINICAL, EXPERIENCE

For my clinical experience, I had the opportunity to work with two doctors in completely different aspects of the health field for five weeks each. For the first five weeks I was working with Dr. Eduardo Crotte, radiologist, of Kalamazoo Radiology and partner of Bronson Hospital. And for the second five weeks, I worked with Dr. Timothy Swartz, rheumatologists, at Rheumatology P.C. Both experiences were very eye opening and exciting, but when it came time to pick a topic for my SIP review paper, I chose gout, a rheumatic disease.

While working with Dr. Crotte, I was exposed to several types of radiology, but specialized in mammography. In my first weeks, I was given the break down of procedures for specific radiographic techniques, taught the diirence in color scheming between x-ray film, MRI images, and ultrasound, and listen to many, many dictations of films in preparation for the coming weeks. For the final three weeks of my internship, I was often in a reading room with a stack of films ranging from MRI's to x-ray films. It was my job to view through these films individually, separate and identity anatomy, and determine whether or not there was anything abnormal. After completing the piles of film, Dr. Crotte and I would review them together and I would explain to him what I observed. This was a great problem solving experience because radiologists are given the patient's symptoms, then expected to find on film why those symptoms are occurring. I also enjoyed this internship because of both the hospital and clinic settings. The only downfall to this field of medicine is the lack of patient contact.

As opposed to radiology, rheumatology allowed me to receive an abundance of hands on clinical experience with patients. Daily, I would see patients with Dr. Swartz that had a variety of diseases such as gout, rheumatoid arthritis, fibromyalgia, etc. I learned the physical and clinical differences between each of these diseases, and was eventually able to make my own assessments (not in front of the patient though, this was done at a time between myself and Dr. Swartz only). During my internship, I was also able to assist Dr. Swartz in testing and procedures, such as joint mobility testing, steroid injections, and blood lab reviews. This hand on experience was an excellent learning tool, and also worked my problem solving abilities. I was lucky to work with two very excellent doctors that taught me an important lesson of doctor patient relationships, and that a sense of humor is sometimes the best medicine.

During my experience at the rheumatology clinic, I was a little disappointed because I was only able to see two patients with active gout flares, but I was able to see a few more without symptoms and ask about their experiences with the disease. This hands on experience made me more enthusiastic to begin the research for my SIP review paper on gout.

Gout: An Overview of the Etiologies, Stages, Diagnosis, Treatments, and Future Outlooks.

Contemporary Management of Brain Metastases
John Sharpe

Abstract

An extensive ten-week internship under experienced neurosurgeon, Anthony L. Asher, M.D., F.A.C.S., was carried out at Carolina Neurosurgery and Spine Associates (CNSA), the nation's largest community-based neurosurgical group. Members of CNSA are involved in leadership positions in a variety of national brain tumor organizations and modern clinical research in the field of neurosurgery Several of the group's most recent clinical studies are related to the control of brain metastases. Dr. Asher is the director of neurooncology at Carolinas Medical Center, where most of the group's research is conducted. While working under Dr. Asher, responsibilities included independent research of material for contemporary book chapters, participation in patient care conferences, communication with other neurosurgical offices across North America, and acting as editorial assistant for Self-Assessment in Neurological Surgery (SANS) 2004. Presented by the Congress of Neurosurgeons, SANS 2004 is a nationwide online self-assessment tool, which now offers Continuing Medical Education (CME) credit for neurosurgeons. Herein are reported experiences and data obtained during this internship, including, but not limited to, observation of novel clinical research tools, clinical examinations, and neurosurgical treatments for various central nervous system disorders, in addition to a deeper understanding of neuroanatomy, patient examination, surgical technique, and health care in general. More aspects of this internship are further documented in the journal. The final products of this experience were the journal that follows and the preceding composition regarding management of brain metastases.