THE UNIVERSITY OF MANITOBA

DEPARTMENT OF INTERNAL MEDICINE
POSTGRADUATE EDUCATION PROGRAM

RESIDENT RESEARCH DAY
MAY 27, 2008

SCIENTIFIC PROGRAM
THEATRE B, BMSB
DEPARTMENT OF INTERNAL MEDICINE
RESIDENT RESEARCH DAY PROGRAM
THURSDAY, MAY 27, 2008
THEATRE B, BMSB

0905  Welcoming remarks / 2006 Published Prize Announcement
Dr. D. Houston
Chair, Dept. of Internal Medicine Resident Research Day

ORAL PRESENTATIONS

Time will be adhered to with 10 minutes for presentation and 5 minutes for questions.

0915  (Clinical Investigation)
Characteristics and Outcomes of ESRD in the ICU
Bradford Strijack  Supervisor: C. Rigatto

0930  (Case Report)
A May-Thurner Head Turner
Chris Wiebe  Supervisor: D. Houston

0945  (Case Report)
Adult Onset Still's Disease with Hemophagocytic Syndrome
Marcus Blouw  Supervisor: D. Robinson

1000  (Case Report)
Macrovascular Involvement in Scleroderma: Case Report
Marc Fournier  Supervisor: D. Robinson

1015-1030  Break

1030  (Clinical Investigation)
CD8+ T-Cell and Antibody Responses to Annual Influenza Vaccine Components
Yoav Keynan  Supervisor: K. Fowke
1045  (Case Report)
Reversible Cerebral Vasoconstriction Syndrome: A Sheep in Wolf’s Clothing
Peter Hughes  Supervisor: B. Schmidt

1100  (Clinical Investigation)
A Population Based Study of Breastfeeding in Inflammatory Bowel Disease: Initiation, Duration and Effect on Disease in the Post Partum Period
Dana Moffatt  Supervisors: A. Ilnyckyj
C. Bernstein

1115  (Case Report)
Unexpected Clotting in a Cardiopulmonary Bypass Circuit
Michael Semus  Supervisor: D. Houston

1130-1200  Break

1200-1300  Keynote Address

Some Random Thoughts on Clinical Research

Dr. R. Meyer
Edith Eisenhauer Chair in Clinical Cancer Research Director,
National Cancer Institute of Canada Clinical Trials Group
Professor, Departments of Oncology and Medicine
Queen’s University

1315  (Clinical Investigation)
Survival After Bone Marrow Transplant in Rural and Urban Manitobans
Kristjan Paulson  Supervisor: M. Seftel

1330  (Case Report)
Functional Pheochromocytoma in a Woman with Eisenmenger’s Syndrome
Michael Karolak  Supervisor: S. Zieroth

1345  (Clinical Investigation)
The Utility of Tissue Doppler Imaging for the Noninvasive Determination of Left Ventricular Filling Pressures in Patients with Septic Shock
Andrew Czarnecki  Supervisor: D. Jassal
1400  (Case Report) Meningococcal Serotype Y Myopericarditis
Joel Nkosi  Supervisor: D. Jassal

1415  (Clinical Investigation) Adequacy of Bone Marrow Aspirate and Trephine Biopsy in 2007
Emily Rimmer  Supervisor: D. Houston

1430  (Case Report) An Acute Crohn’s Flare Inducing a Takotsubo’s Cardiomyopathy: Was There EKG Evidence?
Owen Mooney  Supervisor: S. Zieroth

1445-1515  Break

1515  (Clinical Investigation) End-of-Life Communication with Hospitalized Terminally Ill Patients
Tim Hiebert  Supervisor: K. Wiebe

1530  (Clinical Investigation) Trastuzumab Mediated Cardiotoxicity in the Setting of Adjuvant Chemotherapy for Breast Cancer: A Real World Population Based Study
Deepa Wadhwa  Supervisor: D. Jassal

1545  (Clinical Investigation) Intensive Care Unit Admissions Among Patients Infected with the Human Immunodeficiency Virus - A Manitoba Perspective
Michael Chapman  Supervisor: K. Kasper

1600  (Case Report) Akinetic Mutism with Waxy Flexibility and Increased Spontaneous Blinking
Atheer Al-Kaabi  Supervisor: A. Yankovsky

1615  (Case Report) An Unusual Case of Splenomegaly and Pancytopenia
Trevor Hutchison  Supervisor: C. Moltzan

1630  (Case Report) Plasmapheresis: A Potentially Puzzling Proposition
David Dawe  Supervisor: C. Moltzan
Characterization of *Pseudomonas Aeruginosa* Isolates Obtained from Patients in Canadian Hospitals: Results of the CANWARD Study 2007

Andrew Walkty

Supervisor: G. Zhanel

Closing Remarks

- Dr. D. Houston
- Dr. D. Roberts
Characteristics and Outcomes of ESRD in the ICU
Strijack B, Roberts D, Rigatto C

Abstract:

Context: It is well established that patients developing acute renal failure (ARF) requiring dialysis in the intensive care unit (ICU) have a very high mortality, approaching 50%. It is often assumed that end-stage renal disease (ESRD) patients admitted to ICU have similarly adverse outcomes. However, very sparse data exist describing the outcome of end-stage renal disease (ESRD) patients admitted to the ICU. We hypothesized that ESRD patients admitted to ICU experience a mortality rate much lower than ICU patients with acute renal failure requiring dialysis.

Objective: To describe the clinical characteristics and outcomes of ESRD patients admitted to an ICU.

Design and Methods: Population-based historical cohort study using a prospectively maintained ICU database capturing all patients admitted to ICU in Winnipeg, Canada.

Results: Between 2000 and 2006, 34,976 patients were admitted to the ICUs; 1174 of these were known ESRD, 1242 developed ARF requiring dialysis, and remaining cohort of 32,560 constituted the non-dialysis group (controls). This last group was further subdivided into quartiles (n=8142 each) based on admission serum creatinine: Q1, mean creatinine 50; Q2, mean creatinine 77, Q3 mean creatinine 99, Q4, mean creatinine 209. The median age at admission was 56.8 in ARF group, 53.3 in the ESRD group, and in the control group (Q1 57, Q2 62, Q3 67, Q4 70). The most common admitting diagnoses in ARF group was septic shock, ESRD septic shock, in Q1, Q2, Q3 MI and Q4 septic shock. In hospital, mortality (Graph 5) was 44.6% in the ARF cohort, 23.9% in the ESRD cohort, Q1 7.9%, Q2 5.8%, Q3 9.4%, and in Q4 22.9%. Mean length of stay in days was 10.9 in ARF group, 4.8 in the ESRD group, and in the control group (Q1 4.7, Q2 3.5, Q3 3.8, Q4 4.7). The mean TISS score per day calculated over the first three days of admission was 38.6 in the ARF cohort, 27.9 in the ESRD cohort, Q1 27.8, Q2 23.9, Q3 28.3, Q4 31.6.

Conclusions: ESRD patients admitted to the ICU have outcomes similar to patients without severe renal failure, and much lower than ICU patients developing ARF requiring dialysis. Crude measures of resource utilization (TISS, length of stay) were also similar between ESRD and patients without severe kidney failure. The perception that ESRD patients have poor ICU outcomes does not appear justified.
A May-Thurner Head Turner

Chris Wiebe MD, Don Houston MD, PhD, FRCPC

May-Thurner syndrome (MTS) is a relatively rare but underappreciated cause of lower extremity deep vein thrombosis (DVT). We discuss a case of a 24-year-old female who presented to the emergency department with a two-week history of back pain and left leg pain and a one-day history of dyspnea. Her pain had worsened gradually over the week prior to admission to the point she was unable to ambulate. She was found to have a DVT by ultrasound and a pulmonary embolism by CT chest. A cause of the patient's significant back pain was not revealed by history, physical, or computer tomography (CT) of the spine. Therefore, the possibility of MTS was considered and later confirmed by CT venogram. After 5 days of conservative management with intravenous heparin she had not improved. Intravenous tissue plasminogen activator was administered on the fifth through seventh days of her admission to achieve thrombolysis with good results. Intravascular stent placement was performed on day seven without complications.
ADULT ONSET STILL'S DISEASE WITH HEMOPHAGOCYTIC SYNDROME

Abstract
Dr. Marcus Blouw, R2 Internal Medicine, University of Manitoba (Winnipeg, Manitoba)
Dr. David Robinson, Associate Professor, Internal Medicine and Rheumatology, University of Manitoba
(Winnipeg, Manitoba)

Introduction: Adult Onset Still's Disease (AOSD) is a rare inflammatory disorder of uncertain etiology and pathogenesis. It is characterized by daily fevers, arthritis, rash and clinical and biochemical evidence of systemic inflammation. Disease severity ranges from mild, self-limited constitutional symptoms to chronic disabling disease or fatal multi-organ dysfunction. AOSD can present similarly to infectious, malignant, allergic and autoimmune conditions, making for much difficulty in diagnosing this entity.

Case: A previously healthy 35-year-old male patient presents to hospital with symptoms of fever, malaise, arthralgia, myalgia, rash and odynophagia for seven days. He also reports an unintentional 30 lb weight loss, frequent sweating and chills and increased fatigability over the preceding two months. He has not recently traveled, nor been in contact with anyone who has been ill or in hospital. He is a non-smoker and does not use illicit drugs. He does not have a family history of malignancy or of rheumatologic diseases.

Physical examination reveals fever (39.2°C) and tachycardia (101 bpm). There is a diffuse salmon-colored maculo-papular rash on the trunk and arms. There is splenomegaly. The remainder of the physical exam is unremarkable. Empiric treatment with broad-spectrum antibiotics is initiated.

Complete blood count reveals white blood cell count of 1,200/ml with 93% neutrophils, thrombocytopenia (platelets = 79,000/ml) and hemoglobin of 130mg/L. Liver enzymes are elevated with a predominant hepatocellular pattern of injury. Markers of systemic inflammation are elevated including C-Reactive Protein (CRP: 135) and ferritin (13,564). Erythrocyte sedimentation rate is normal (4mm/hr). Bone marrow biopsy and aspiration reveals hemophagocytosis with increased activation of macrophages. Investigation for a source of infection or malignancy is exhausted.

Diagnosis of Adult Onset Still's Disease with hemophagocytic syndrome is made. The patient is treated with intravenous corticosteroids with abrupt improvement of his symptoms. The antibiotic agents are discontinued.

Discussion: We present a typical case of AOSD complicated by hemophagocytic syndrome. The clinical similarity to a wide variety of infectious and malignant conditions often necessitates an exhaustive series of investigations, and can lead to delays and/or difficulty in diagnosis. Hemophagocytic syndrome, a rare entity itself, is only an infrequent component of AOSD, which can make the diagnosis even more challenging.

Over the previous decade, a minimum of eleven confirmed cases of AOSD have been diagnosed and followed in the Rheumatology Clinic at our institution. These cases have significant variability of clinical signs, symptoms and outcomes. A brief description of this cohort will be presented along with a summary of the most widely accepted criteria for the diagnosis of AOSD. Consideration of the possibility of AOSD may result in earlier diagnosis in patients with undiagnosed fever or systemic inflammation.
Macrovacular Involvement in Scleroderma: Case Report
M R Fournier, B.Comm, M.D. and D Robinson, M.D., FRCPC
Health Sciences Centre, Winnipeg, Manitoba

Scleroderma is a chronic multisystem disorder of connective tissue. It is characterized by fibrosis of skin and internal organs, most frequently kidneys, lungs, gastrointestinal tract, and lungs. A widespread obliterative vasculopathy of small arteries and arterioles is the pathological hallmark.

A 46-year-old female presented to the Emergency Department with complaints of transient left monocular blindness and left arm numbness. She described three similar episodes of left eye blindness lasting no longer than five minutes over the past year. Clinical examination was consistent with diffuse scleroderma with advanced skin changes over the extremities and trunk, marked joint destruction and decreased oral aperture. The patient had a known diagnosis of significant pulmonary fibrosis and had received both cyclophosphamide and azathioprine. Bilateral carotid bruits and normal appearing fundi were found on examination. Catheter angiography of the great vessels, carotids, and vertebral arteries was pursued. Notable findings included 50% eccentric stenosis of the origin of the left common carotid and 100% occlusion of the left subclavian with revascularization of the left axillary artery by retrograde flow via the vertebral artery. A diffusion weighted MRI with flair was normal with no focal lesions identified. The patient was admitted to hospital for further observation and placed on clopidogrel.

Large vessel macroocclusive disease has been rarely reported in patients with scleroderma. Underreporting almost certainly exists, as ischemic changes in extremities are apt to be blamed on the more prevalent small vessel occlusion typical of scleroderma. Mechanisms of large vessel disease are unknown. This patient was a lifelong non-smoker with no known risk factors for atherosclerosis apart from her connective tissue disease. A proportion of scleroderma patients with vascular insufficiency may benefit from evaluation for large vessel involvement.
CD8+ T-cell and antibody responses to annual influenza vaccine components

Presenter: Yoav Keynan MD.
Supervisor: Dr. Keith Fowke PhD.

Objective:
Antibodies against influenza hemagglutinin are correlated with protection while influenza-specific CD8+ T-cells assist in the elimination of virus and subsequent host recovery. In the absence of these cells viral clearance is delayed.
The recommended 2006--07 trivalent influenza vaccine virus strains: A/New Caledonia/20/1999 (H1N1)-like(NC), A/Wisconsin/67/2005 (H3N2)-like(WISC), and B/Malaysia/2506/2004-like(MAL) antigens. Of these three strains one, the A/New Caledonia/20/1999 has been circulating in the past 6-7 years and included in vaccine preparations (thus referred to as “old” strain).
We compared the antibody and CD8 responses to new and “old” vaccine components among healthy adults at baseline and following annual influenza vaccination as well as responses among influenza immunization naïve population.

Methods:
Healthy subjects were recruited in Winnipeg (University of Manitoba) after institution ethics board approval. Prior to flu vaccination, PBMC were isolated and plasma was frozen for hemagglutination inhibition assay (HIA). The PBMC’s were stimulated with whole influenza viruses: H1N1-A/New Caledonia/20/99; H3N2-A/Wyoming/2/2003 and B/Malaysia/2506/2004. The procedure was repeated 7 and 30 days after immunization. The data was acquired using BD LSRII flow cytometer and analyzed on FACSDiva software. Gating on CD8+ lymphocytes, the IFNy and IL-2 response as well as the memory subset of the responding cells was determined.

Results:
HIA was performed on all samples for each of the three vaccine components. Mean baseline titers were 52 (CI 95.0-130.7), 18.86 (CI 95-6.45-31.26) and 4.857 (CI 95.3.005-6.709) for New Caledonia/20/1999 (H1N1), A/Wisconsin/67/2005 (H3N2) and B/Malaysia/2506/2004 respectively. There was a non-significant increase in HIA titer for NC and statistically significant increase in IgG antibody titers for WISC and MAL.
IL-2 and IFNy production by effector CD8+CD45RA-CCR7- T-cells increased after in-vitro stimulation with influenza NWisc and MAL but not when stimulated with influenza A/New Caledonia.

Conclusions:
Higher pre-immunization titers against the “old” strain were detected, however the titer failed to increase after vaccination, while HIA titers against “new” strains showed significant increase after vaccination. IL-2 and IFNy production by CD8+ T-cells increased thirty days following influenza vaccination, in response to “new” strains but not when stimulated with influenza A/New Caledonia/20/99- “old” strain. The implications are that re-vaccination with same strain may prohibit development of CD8 response and might decrease the potential protection against heterologous influenza virus, thought to be mediated to a large extent by these cells.
REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME: A SHEEP IN WOLF’S CLOTHING

Peter S. Hughes, Brian J. Schmidt and Ruth Ann Marrie
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Reversible cerebral vasoconstriction syndrome (RCVS) is a relatively recently recognized condition that typically presents with recurrent, thunderclap headaches. Although there is often no identifiable trigger, several precipitating factors have been identified including pregnancy, childbirth, exercise, and vasoactive drugs such as nasal decongestants, selective serotonin reuptake inhibitors (SSRIs) and cannabis. Although subarachnoid hemorrhage, ischemic infarction and seizures occur in some patients, in rare instances leading to disability or death, the outcome is usually benign.

Distinguishing between RCVS and primary central nervous system (CNS) vasculitis is diagnostically challenging. A characteristic radiographic finding in both diseases is ‘beading’ of the cerebral vasculature on digital subtraction angiography, representing adjacent areas of vasodilatation and vasoconstriction. A key feature of RCVS, however, is the disappearance of these lesions within one to three months on repeat angiography. Accurate recognition of RCVS is critical in order to avoid the risks and potential morbidity associated with long-term immunosuppressive treatment of vasculitis.

We present two cases of RCVS. The first is that of a 48-year-old woman who presented to the emergency department complaining of severe, pounding headaches that began abruptly and lasted for approximately 30 minutes. Her neurological examination was normal. A computed tomography (CT) scan of her brain revealed a small amount of subarachnoid blood over the frontal convexity, and an angiogram revealed numerous arteries with regions of focal narrowing. Blood results, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and autoimmune markers, were within normal limits. The patient was given a tapering dose of prednisone. Six weeks later, a second cerebral angiogram was normal. After eight months the patient remained headache-free, and the steroid was stopped. She has had no recurrences over the past 11 years.

The second patient was a 56-year-old woman who reported a 10-day history of thunderclap headaches lasting between 30 minutes and three hours. Two of the headaches were postcoital. Her neurological examination was unremarkable. Imaging revealed a small subarachnoid hemorrhage overlying her right parietal lobe, as well as two small intraparenchymal hemorrhages. An angiogram demonstrated multiple areas of ‘beading’ involving the small arteries of the brain. The CRP was 18.5, but systemic autoimmune markers were negative. The patient was diagnosed with RCVS and treated with a five-day course of methylprednisone. Also, verapamil was started. Her headaches resolved by the time of discharge, and a follow-up angiogram performed one month later confirmed the diagnosis.

These cases illustrate that the presentation of RCVS can overlap with that of subarachnoid hemorrhage secondary to cerebral aneurysm rupture, and can have angiographic features suggesting CNS vasculitis. Serial angiography is important in order to make the diagnosis. Failure to treat RCVS promptly may increase the risk of permanent, potentially devastating consequences. Misdiagnosing RCVS as CNS vasculitis may expose the patient to inappropriate immunosuppressive therapy.
A population based study of breastfeeding in inflammatory bowel disease: initiation, duration and effect on disease in the post partum period.
Dana C. Moffatt MD. Alexandra Ilnyckyj MD, FRCPC, Charles N. Bernstein MD, FRCPC

INTRODUCTION: Previous studies report that women with inflammatory bowel disease (IBD) have lower rates of initiation of breastfeeding (BF). It has also been suggested that initiation of BF is associated with an increased rate of disease relapse of autoimmune disorders including IBD. This study aimed to quantify the rates of initiation and duration of BF in women with IBD, the discontinuation rate of medications to facilitate BF and to assess the impact of BF on disease relapse.

METHODS: The population-based University of Manitoba IBD Research Registry, was used to identify the target group. Women who were of childbearing age (16-40) from 1985-2006 were contacted by mail and formed the sample. They completed a self-administered questionnaire regarding pregnancy, lactation history and disease state during the postpartum 12 months. Data for initiation and duration of BF were compared to regional data for all women compiled by Manitoba Health, the single health insurance provider for the population.

RESULTS: Two hundred and four women met study criteria. 132/204 (64.7%) responded to the survey: 88/132 (66.7%) had Crohn’s disease (CD), 39/132 (29.5%) had ulcerative colitis (UC), 4/132 (3%) had indeterminate colitis (IC). Amongst these 132 women there were 156 live births. 130/156 (83.3%) of infants born to women with IBD were breastfed at birth, (82% of babies born to CD mothers, compared to 84% born to UC mothers with UC, p=0.8) Median duration of BF for both groups of women was 22 week while on average female population of Manitoba initiated BF 81.5% of the time and 50% of patients persisted with breastfeeding for 20 weeks (p=0.78). In CD 26% of those who initiated BF vs 29% of those that did not initiate BF, reported a disease flare in the post partum period, a difference that was non-significant (p =0.24). In UC, 29% of those who initiated BF vs 44% of those who did not initiate BF developed disease flare in the post partum period a difference that was non-significant (p=0.44). These differences in disease flare were still insignificant when adjusted for the fact that 10% of mothers who breastfed, discontinued their IBD medications in the post partum period.

CONCLUSIONS: Women with IBD are just as motivated as the general population to initiate and continue breastfeeding in the post partum period. Although previously thought to be a risk factor for disease flare, breastfeeding was not associated with an increased risk in our population. Also, rates of disease flare appeared to be equal despite a significant percentage of women discontinuing their medications in the post partum period in order to breastfeed.
A 63-year-old male was taken to surgery for elective repair of severe aortic stenosis and tricuspid insufficiency and concomitant single vessel cardiac bypass grafting. His past medical history was significant for longstanding type 2 diabetes mellitus, ischemic heart disease and he had no history of heparin exposure in the preceding year. There was no personal or family history of bleeding or clotting disorders, solid tumors, hematological malignancy, or heparin allergy. After opening the sternum, 35,000 units of heparin was administered and standard aorto-bicaval cannulation was performed. The activated clotting time (ACT) was noted to be greater than 999 seconds prior to initiating bypass. Shortly after the bypass circuit was initiated, clot was recognized in the venous arm of the circuit and the oxygenator. The circuit was immediately shut down. The ACT was confirmed to be >999 and a heparin assay revealed serum levels greater than 1 unit/mL. The operation was aborted due to concern of an undiagnosed clotting disorder. Postoperatively the patient had no clinical evidence of embolic disease.

Investigations were undertaken to try to understand the cause of clotting in the bypass circuit. Testing for heparin-induced thrombocytopenia was negative. A qualitative d-dimer was negative, excluding disseminated intravascular coagulopathy. Additional laboratory testing was done to rule out an identifiable hypercoagulable disorder. The patient has normal antithrombin III levels by both antigen and functional assays, and does not have the factor V Leiden mutation. A serum protein electrophoresis did not demonstrate a monoclonal paraprotein. We also considered the possibility of temperature-dependent effects that may have been activated upon entering the bypass circuit. A screen for cold agglutinin was negative. However, the evening after surgery, platelet aggregates were noted on a blood smear prepared from the patient's blood that had been collected in heparin and cooled; no aggregates were seen in a sample collected in EDTA. At this point, we hypothesized there might be a calcium or heparin dependent, cold-dependent antibody causing platelet agglutination, as described by Hall et al. [Am J Hem. 69:45].

To test this hypothesis we brought the patient back to the clinic for further blood work.

METHODS: Blood was collected in four different anticoagulant solutions: heparin (25U/ml), EDTA (3.45mg/ml), danaparoid (31U/ml) and heparin+EDTA. A blood film was made immediately from each sample on slides warmed to 37C. The blood samples were then incubated for 10 minutes at 22, 30 and 37 degrees. At this time platelet agglutination was assessed in two ways: the apparent platelet count was measured by an automated hematology analyzer (Sysmex), and a second blood smear was prepared and examined for aggregates. Blood of two controls was processed in the same manner. RESULTS: In samples incubated in EDTA, no platelet aggregation was noted. Marked aggregation was found in the heparin-anticoagulated samples after 10 minutes of incubation. This effect was negated by addition of EDTA to the heparin solution. In the controls, the platelet aggregation with heparin was more pronounced with increasing temperature, with an average apparent platelet count of 11.9% at 37C when compared to the EDTA control, and little effect at 22C. This in vitro platelet-activating effect of heparin has been previously described [J Clin Invest. 65:64]. Danaproid showed a weaker propensity to promote platelet aggregation. In the patient, the platelet aggregation effect with heparin at 22C was more pronounced than in the controls.

The mechanism by which clotting occurred in our case is not fully elucidated. The patient may have platelet aggregation induced by hypothermia, as described by Hall and colleagues. Their observations confirmed platelet aggregation in whole blood cooled to 24 degrees Celsius. Furthermore, they identified a subgroup of subjects (14% of healthy volunteers) in which heparin exposure amplified this phenomenon. But if this phenomenon is capable of causing clotting in the bypass circuit and if it is as prevalent as Hall et al. report, bypass circuit failure should be a prohibitively common problem. Moreover, even in our patient, the aggregating effect of heparin was more pronounced at 37C rather than at colder temperatures. Although the effect of heparin is clearly calcium-dependent, it does not seem entirely specific since danaparoid (another large glycosaminoglycan molecule) appeared to elicit a similar though weaker effect. Possible mechanisms for the patient's events would include a transient antibody mediated effect, which has spontaneously resolved, or a physico-chemical interaction between the platelets and the tubing used in the cardio-pulmonary bypass circuit.
SURVIVAL AFTER BONE MARROW TRANSPLANT IN RURAL AND URBAN MANITOBANS

PRIMARY INVESTIGATOR: DR. KRISTJAN PAULSON
RESEARCH SUPERVISOR: DR. MATTHEW SEFTEL

Objective: Manitobans in different parts of the province have vastly different access to health care. People from Winnipeg have easy access to specialists and subspecialists, while people from Northern Manitoba can live hundreds of kilometres from health care resources. Stem cell transplantation is an intense treatment that is only offered in Winnipeg. We hypothesized that rural Manitobans would have worse outcomes after stem cell transplant than urban Manitobans.

Methods: We used data from the Manitoba Blood and Marrow Transplant Program database. Information on all Manitobans who have undergone a hematopoietic stem cell transplant at Health Sciences Centre was analyzed. We looked at every patient's address based on postal code at time of diagnosis, age at diagnosis, type of transplant, disease (including stage), date of transplant, and if each patient is alive or has deceased. We used a Kaplan-Meier plot to compare survival of rural Manitobans and urban Manitobans. In addition, we compared survival based on distance from Health Sciences Centre.

In addition, we obtained data from the Manitoba Cancer Registry on Hodgkin's Lymphoma. Hodgkin's disease was chosen to analyze in more detail because the diagnosis is more uniform than other forms of lymphoma, and bone marrow transplant should be a standard therapy for patients with aggressive disease who relapse after initial treatment. We looked at the proportion of rural and urban Manitobans who received a transplant compared to the number of rural and urban Manitobans who were diagnosed with Hodgkin's lymphoma.

Results: In total, 468 Manitobans received a hematopoetic stem cell transplant between 1990 and 2006. 179 patients were from rural Manitoba (all locations aside from Winnipeg), and 285 patients were from Winnipeg. We compared rural Manitobans to urban Manitobans based on gender, graft type (allogeneic versus autologous), age at time of transplant (less than 40, 40 to 60, and greater than 60), year of transplant (1990-1995, 1996-2000, and after 2001), and high and low risk disease (low risked being defined as acute leukemia in first remission, lymphoma in first remission, chronic myeloid leukemia and non-malignant diseases, with all other cases defined as high risk). There were no significant differences in baseline data between rural and urban Manitobans. Rural Manitobans were slightly more likely to have received an allogeneic transplant (47% versus 39%), and were slightly more likely to have high risk disease (23% versus 16%), but these differences were not statistically significant.

Survival data was compared at 5 years. Rural Manitobans were less likely than urban Manitobans to be alive in five years (45% versus 37%, p = 0.06). In addition, patients were stratified based on their distance from Health Sciences Centre (less than 20 km, 20 km – 200 km, and over 200 km). Patients who lived less than 20 km from HSC were more likely to be alive after five years, and those furthest were least likely to be alive in 5 years. Using log rank comparison statistics, this was statistically significant (p=0.026).

Between 1990 and 2006, 432 Manitobans were diagnosed with Hodgkin's Lymphoma. 182 (42%) of these patients were from rural Manitoba (again, defined as all locations outside Winnipeg), and 250 (58%) were from Winnipeg. Based on data from the 2006 census, 54% of all Manitobans live in Winnipeg. However, 69% of patients undergoing transplant for Hodgkin's Lymphoma were from Winnipeg.

Conclusions: Based on the results of our research, rural Manitobans do worse after hematopoetic stem cell transplant than urban Manitobans. The exact reasons for this are unclear. There could be delays in diagnosis or treatment, meaning that rural Manitobans have more advanced disease. There could also be inadequate follow up, meaning rural Manitobans may have more complications from transplant. In addition, rural Manitobans are less likely to undergo hematopoetic stem cell transplantation. This could be because they are less likely to be offered transplant, or are less willing to undergo transplant.
FUNCTIONAL PHEOCHROMOCYTOMA IN A WOMAN WITH EISENMENGER'S SYNDROME

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A 58 year old female with a history of Eisenmenger's syndrome and third degree atrioventricular block with a permanent pacemaker implanted presented to her physician with complaints of headaches, hot flashes and vomiting. She was subsequently diagnosed with a functional pheochromocytoma based on elevated normetanephrine and vanilmandelic acid levels as well as a CT confirmed right adrenal mass. A significant amount of controversy ensued regarding optimal preoperative management for possible resection of the neoplasm. Her baseline functional status was NYHA Class 3 and she had adapted very well to her severe cyanotic heart disease as evidenced by her ability to carry out full time work during the spring. She could walk up one flight of stairs and 2 street blocks. Physical examination was notable for mild volume overload, signs of severe pulmonary hypertension and peripheral cyanosis. Previous bloodwork showed a hemoglobin of 204 g/L and a platelet count of 125 000. Her polycythemia was controlled by intermittent phlebotomies. Serial echocardiograms showed severely elevated right ventricular systolic pressures of 100 mm Hg, a 2.5 cm muscular VSD, preserved biventricular function but no shunting of blood between ventricles. She was only controlled on Labetalol 200 mg twice daily and occasional doses of 20 mg of Furosemide. Overall, she seemed only moderately affected by her neoplasm and was not very eager to proceed with surgical treatment. Multiple consultations were obtained from General Surgery, Endocrinology, Transplant Cardiology, Anesthesia, Hematology and the case was referred to Toronto General Hospital Department of Cardiology. This case report highlights important considerations in the perioperative approach to a patient with congenital cyanotic heart disease as well as reviews the complex pathophysiology of Eisenmenger's syndrome.
THE UTILITY OF TISSUE DOPPLER IMAGING FOR THE NONINVASIVE DETERMINATION OF LEFT VENTRICULAR FILLING PRESSURES IN PATIENTS WITH SEPTIC SHOCK

Czarnecki A1, Mousavi N2, Kumar A1, Jassal DS2
Departments of Internal Medicine1 and Cardiac Sciences2
University of Manitoba
Winnipeg, Manitoba

Objective: To determine whether echocardiographic Doppler assessment is accurate in estimating pulmonary arterial wedge pressure in patients with septic shock.

Methods: A retrospective chart review was performed of 253 patients admitted with a diagnosis of septic shock from 2006 to 2007 inclusive. Of the total patient population, 36 patients fulfilled the inclusion criteria, having undergone both trans-thoracic echocardiography and pulmonary artery catheterization within 24 hours. Spectral Doppler indices including peak early (E) and late (A) transmitral velocities, E/A ratio, and E-wave deceleration time were measured. Tissue Doppler indices including S', E' and A' velocities were determined. Pulmonary artery wedge pressure values measured invasively were compared to the dimensionless index of E/E' in each patient.

Results: The mean age was 65±15 years with 24 males (66%). The mean left ventricular ejection fraction was 55±10%. On echo assessment, 25% of patients had evidence of mild left ventricular diastolic dysfunction while 14% of patients had moderate diastolic dysfunction. Pulmonary artery wedge pressures ranged from 8 to 30 mm Hg with a mean of 17±6 mmHg. The mean E/E' was 12±8. Linear regression analysis between pulmonary artery wedge pressure and E/E' demonstrated a strong correlation (r=0.8, p<0.05).

Conclusion: Tissue Doppler indices using trans-thoracic echocardiography is a feasible and strong predictor of pulmonary artery wedge pressure in patients with septic shock. Whether Tissue Doppler imaging can be used to guide hemodynamic management while avoiding the complications associated with pulmonary artery catheterization requires further study.
MENINGOCOCCAL SEROTYPE Y MYOPERICARDITIS

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Introduction: Involvement of the pericardium is a well-recognised but rare complication of meningococcal disease. Isolated meningococcal pericarditis is defined as purulent pericarditis without clinical evidence of meningococcaemia or meningitis. Although uncommon, it carries the risk of complication with tamponade or constriction. This is the first case report of meningococcal serotype Y myopericarditis in the English literature to our knowledge.

Case presentation: An 18 year old male was referred to our institution for evaluation of acute pleuritic chest discomfort. He was normothermic, tachycardic, tachypneic, and normotensive. Jugular venous pressure was elevated without muffled heart sounds or a pericardial rub. His mentation was clear with a supple neck. Skin was normal. Electrocardiography was in keeping with stage I pericarditis with a normal chest radiograph. Echocardiography showed a small generalized effusion with a severe global LV systolic dysfunction with an EF of 25-30% without features of tamponade physiology. He was admitted for treatment of myopericarditis presumably viral.

On day 2, he deteriorated with further elevation of jugular venous pressure, some drop in blood pressure, pulsus paradoxus and muffled heart sounds. Repeat echocardiography confirmed tamponade. Percutaneous pericardiocentesis was performed for about 500 mls of exudative fluid. When cultured, it grew Neisseria meningitis serotype Y. Blood cultures were negative.

Following pericardiocentesis and initiation of parenteral antibiotics, the patient improved markedly. After a few days, the pericardial catheter was removed and he was discharged for outpatient intravenous antibiotics. On follow up several weeks later at the cardiology clinic he was doing well and the ejection fraction had improved to 50-60%.

Discussion: Isolated meningococcal pericarditis represents one of three previously described patterns of cardiac involvement in meningococcal disease. It is extremely rare with less than 30 cases reported in the English literature to date. Neisseria meningitis serotypes C, B, W135 have been previously described to cause pericarditis, tamponade and constriction. This is the first case of meningococcal serotype Y myopericarditis. The presentation is often non-specific with acute chest pain, fever and elevation of markers of inflammation making distinction from the benign and more common viral or idiopathic pericarditis difficult. Tamponade is a common complication which is easily treated when recognized promptly. Repeat echocardiography should be performed early in patients with presumed viral or idiopathic pericarditis not rapidly improving on symptomatic treatment. Fluid analysis may help suggest an indication for antibiotics. It has been suggested that the less common complication of constriction, which is usually an indication for invasive pericardectomy, can be prevented by early initiation of antibiotics. The role of antibiotics in undifferentiated pericarditis remains undetermined.
ADEQUACY OF BONE MARROW ASPIRATE AND TREPHINE BIOPSY IN 2007.
Dr. Emily Rimmer1, Dr. Donald Houston1,2, Dr. Kristine Roland3. 1Department of Internal Medicine, 2Section of Hematology/Oncology, 3Department of Pathology. University of Manitoba. Winnipeg, Manitoba.

OBJECTIVES: To review the bone marrow aspirates and trephine biopsies performed at the Health Sciences Centre in Winnipeg, Manitoba in 2007 and evaluate them in terms of published criteria for adequacy.

METHODS: 1012 bone marrow aspirates and biopsies were identified from January 1 - December 31, 2007. Bone marrow biopsies performed on children (age <18 years) and specimens referred from other centers were excluded. A total of 779 bone marrow aspirates and biopsies were evaluated. The length of interpretable marrow and total length of each biopsy were measured. The indication for biopsy, ward, and operator for each biopsy were recorded. The bone marrow biopsies were compared to published criteria for adequacy: 1.6 cm prior to processing, 0.8 cm of interpretable marrow, and 1.1 cm of interpretable marrow when the clinical question is of infiltration by malignancy.

RESULTS: Using the less stringent 0.8 cm length of interpretable bone marrow adequacy criterion, the overall adequacy is 67% (474 / 709). Residents are least likely to obtain adequate marrow samples. When the more stringent 1.1 cm of interpretable marrow adequacy criterion is used, the overall adequacy is 40% (283 / 709). Among operators, residents and registered clinical assistants are least likely to obtain an adequate bone marrow biopsy of 1.1 cm.

<table>
<thead>
<tr>
<th></th>
<th>Hematologist</th>
<th>Registered clinical assistant (RCA)</th>
<th>Resident</th>
<th>Oncologist</th>
<th>Medical student</th>
</tr>
</thead>
<tbody>
<tr>
<td># Performed</td>
<td>272</td>
<td>269</td>
<td>141</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Adequacy 0.8 cm</td>
<td>81% (220/272)</td>
<td>62% (168/269)</td>
<td>50% (71/141)</td>
<td>55% (5/9)</td>
<td>54% (7/13)</td>
</tr>
<tr>
<td>Adequacy 1.1 cm</td>
<td>57% (155/272)</td>
<td>26% (71/269)</td>
<td>34% (48/141)</td>
<td>44% (4/9)</td>
<td>38% (5/13)</td>
</tr>
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CONCLUSIONS: A large number of bone marrow biopsies performed during the study period are inadequate. A multidimensional intervention – of which this presentation is a component – including education and procedural changes will be implemented in order to improve the quality of bone marrow biopsies performed.
AN ACUTE CROHN’S FLARE INDUCING A TAKOTSUBO’S CARDIOMYOPATHY: WAS THERE EKG EVIDENCE?
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Supervisor: Dr. Shelley Zieroth
University of Manitoba

Takotsubo’s cardiomyopathy is a well documented but incompletely understood phenomenon in which transient apical or mid-ventricular ballooning mimics a myocardial infarction, in the absence of coronary artery disease.

A 64-year-old woman with a history of ulcerative colitis was transferred from a peripheral hospital in cardiogenic shock. The patient had presented to the emergency room with complaints of profuse bloody diarrhea. Computed axial tomography showed a diffuse pancolitis and the decision to transfer the patient to a tertiary care centre was made. Electrocardiogram’s (EKG) upon arrival to intensive care unit (ICU) revealed diffuse ST-elevation in both the inferior and lateral leads. Cardiac resuscitation was employed with vasopressors and inotropes. Coronary angiography and thrombolytic therapy was delayed secondary to acute renal impairment attributed to the patient’s very tenuous blood pressures on arrival. Echocardiography revealed a depressed ejection fraction (35-40%), hyperkinetic proximal left ventrical with ballooning of the apical area, consistent with Takotsubo’s cardiomyopathy. The patient clinical course was complicated by severe thrombocytopenia thought to be attributable to sepsis-induced disseminated intravascular coagulation. Aggressive supportive therapy was continued and the patient recovered. Repeat EKG’s showed complete resolution of ST-changes with relatively complete normalization of the tracing. Repeat echocardiography also revealed normalization of both the ejection fraction and wall motion abnormalities. The patient went on to require hemodialysis for her acute renal failure and the diagnosis of ulcerative colitis was changed to Crohn’s disease upon development of enteric fistulas causing E. coli sepsis.

This case illustrates the interesting phenomenon of a stress-induced cardiomyopathy (Takotsubo’s). Typical EKG findings have been described and can aid in differentiating a stress-induced cardiomyopathy from an acute myocardial infarction. These typical changes are important to recognize because of the treatments of both conditions are vastly different. Although the prognosis is good, further treatment considerations, i.e. anti-coagulation for possible apical thrombus, must also be addressed.
END-OF-LIFE COMMUNICATION WITH HOSPITALIZED TERMINALLY ILL PATIENTS

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Kim Wiebe, Assistant Professor, Department of Internal Medicine, University of Manitoba, Winnipeg, MB

Objectives: Communication is a key element of high quality end-of-life care. Poor communication by healthcare providers with seriously ill, hospitalised patients regarding prognosis, patient wishes, goals of therapy, and other end-of-life issues compromises patient care. This study describes end-of-life communication with terminally ill, hospitalised patients. It is hypothesised that many terminally ill patients admitted to tertiary care internal medicine wards have severe, chronic non-oncologic disease and that discussions between healthcare providers, the patient, and patient’s families about disease prognosis and end-of-life issues often are not addressed, or only occur very late in the disease process.

Methods: Inpatients on the internal medicine wards at the Health Sciences Centre, Winnipeg, Manitoba who died or were discharged with a designation of palliative care between July 1, 2006 and December 31, 2006 were included. Patients were identified using the Winnipeg Regional Health Authority (WRHA) internal medicine database. Demographic data, functional status, comorbid diseases, admitting diagnoses were obtained from the WRHA database. Information regarding disposition, comorbidities, advanced care plan (ACP) status, and discussions regarding end-of-life issues was obtained via a retrospective chart review. Data was analysed with SAS version 9.2.

Results: There were 182 discharges that met the study criteria. Retrospective review was completed on 158 available medical charts (87%). One hundred twenty five patients died (69%) and 57 (31%) were discharged from the ward. A chronic disease was identified in 147 patients (93%) and 109 (69%) were admitted with a complication or deterioration of their chronic disease. Active malignancy was present in 80 patients (44%). ACP status prior to admission was either non-existent or unknown in 104 patients (66%). Discussions of ACP status at the time of admission were documented in 73 charts (46%). Subsequently, at least one more end-of-life discussion occurred in 75% of cases. Only 6 patients (4%) died with an ACP level of 4 or unknown. Amongst patients who died, the final ACP conference occurred within 2 days of death in 59 patients (47%). Documentation regarding end-of-life discussions was poor, there was low patient involvement (38%), and few discussions documented the presence of both an attending physician and trainee (8%). Compared to patients with malignancy, the non-oncologic group had worse functional status, higher rates of resuscitation (22% vs 1.5%, p<0.001) and ICU admission (25% vs 2.9%, p<0.001), were more likely to die in hospital (86% vs 46%, p<0.0001), and were less likely to receive palliative care services (11% vs 72%, p<0.0001).

Conclusions: The majority of study patients were designated DNAR prior to death or discharge. A significant proportion of terminally ill inpatients suffered from chronic non-malignant disease and appeared to receive a different, and possibly inferior, level of end-of-life care. Discussions concerning end-of-life issues in terminally ill inpatients were often poorly documented, frequently did not include the patient and may have not appropriately included trainees. Further research is needed to elicit the reasons for these findings as well as guide improvements in the delivery of high quality in-hospital end-of-life care.
Background: Trastuzumab provides considerable therapeutic benefits in the adjuvant setting of breast cancer, resulting in a 50% decrease in the risk of relapse and 33% decrease in the risk of death. Although widely adopted, trastuzumab is known to increase the cardiotoxic effects of anthracyclines. The incidence and management of trastuzumab-mediated cardiotoxicity in real-world practice, outside of clinical trials, has not been well described.

Objective and methods: The aim of the study was to evaluate the incidence of cardiac dysfunction, characterize its natural history, and identify the degree of reversibility using cardiac MRI, in a real-world population of HER-2 positive breast cancer patients receiving trastuzumab in the adjuvant setting.

Results: Out of 152 patients (mean age 52±10 years), 36 (24%) developed trastuzumab mediated cardiomyopathy, the majority asymptomatic. Factors that predicted the development of Trastuzumab mediated cardiac dysfunction were a preexisting history of hypertension, smoking history, family history of coronary artery disease and the use of diuretics. Within 3 months of treatment with trastuzumab, there was a difference in LVEF between the normal cohort and those patients who developed LV systolic dysfunction (61±5 % vs. 51±8%, p<0.01). During the 6 month follow-up, 34/36 patients demonstrated subepicardial linear delayed enhancement of the lateral wall of the left ventricle on cardiac MRI, confirming trastuzumab induced myocarditis. At 6 months, although 20 patients experienced some recovery of LVEF, 10 had no change in LVEF and 6 developed further decline in LVEF.

Conclusion: Approximately 1 in 4 women will develop LV systolic dysfunction after treatment with adjuvant trastuzumab in the real world, necessitating careful patient selection and close serial monitoring using noninvasive cardiac imaging.
INTENSIVE CARE UNIT ADMISSIONS AMONG PATIENTS INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS – A MANITOBA PERSPECTIVE

Michael Chapman MD; Ken Kasper MD. Department of Internal Medicine, The University of Manitoba, Winnipeg, Manitoba, Canada.

Objectives: To describe the patient demographics, stage of Human Immunodeficiency Virus (HIV) infection, admission diagnoses, antiretroviral use and survival in patients infected with HIV admitted to the Intensive Care Unit (ICU) in the province of Manitoba.

Methods: A retrospective chart review of all HIV infected patients admitted to one of five university-affiliated intensive care units from July 1988 to March 2008. Data collected included patient demographics, co-morbid illness, stage of HIV infection at admission, diagnosis, antiretroviral use, APACHE II scores, admission CD4 counts, hemoglobin values and serum albumin values, as well as survival to ICU discharge.

Results: A total of 109 HIV positive patients on 126 separate admissions were analyzed. 72% of admissions were male patients and the mean age was 41 (range 20-76). ICU mortality was 29%. Among patients admitted, 40% were co-infected with the Hepatitis C virus and 37% and 34% of patients chronically used drugs and alcohol respectively. An additional 14% of patients had diabetes, 10% had ischemic heart disease and 8% were known to have hepatic cirrhosis. 25% of patients were newly diagnosed HIV positive during their stay in the ICU. Of these patients, 84% were classified in clinical category A according to the CDC HIV classification system. Of the known HIV infected patients, 32% were in clinical category A, 18% were classified in clinical category B and an additional 24% were in clinical category C. 19% of patients were last known, prior to their admission, to have a CD4 count greater than 500 cells/mm³, 25% had counts between 200 and 499 cells/mm³ and 54% had a CD4 count of less than 200 cells/mm³. 70% of patients were not actively taking antiretroviral medication prior to their admission, compared to 30% who were on active antiretroviral therapy. 9% of patients were started on antiretrovirals as part of their in-hospital management. The respiratory system was the principal organ system involved in 49% of admissions. Cardiac causes led to 13% of admissions and neurologic disease led to 10% of admissions. Drug overdose led to 7% of admissions. A sepsis syndrome complicated 30% of admissions. 32 patients were diagnosed with *Pneumocystis jirovecii* pneumonia (PCP). 32 patients were diagnosed with bacterial pneumonia. Acute Respiratory Distress Syndrome (ARDS) complicated the admission of 11 patients. 3 patients were diagnosed with CNS lymphoma in the ICU and bacterial and cryptococcal meningitis was each diagnosed in 1 patient. 11 patients had hepatic failure and 10 patients had renal failure. An acute coronary syndrome led to 11 admissions and bacterial endocarditis led to 4 admissions. The mean hemoglobin values on admission was 101g/L (range 42-176) and the mean serum albumin value was 22g/L (range 7-38). The mean APACHE II score for ICU admissions was 19 (range 4-51).

Conclusions: A significant portion of patients is being diagnosed with an HIV infection in the ICU in Manitoba. Hepatitis C and chronic drug and alcohol use are significant co-morbid illnesses in this local population. Respiratory disease was the principal organ system involved in nearly half of the admissions to the ICU and PCP and bacterial pneumonias were equally represented. Further analysis of independent predictors of mortality in this local patient population is warranted as well as changes in patient characteristics over time.
Akinetic mutism is a motionless state of hypersomnolence. Notwithstanding the ability to visually track, the patient is mute, or whispers barely audible monosyllables. Typically, there are no voluntary or restless movements. Anterior cerebral artery (ACA) infarction is a known cause of akinetic mutism. We report a case of ACA infarction with akinetic mutism and two clinical signs not previously reported.

A 66-year old lady was found by family members sitting in a chair unresponsive. On examination, she blinked rhythmically and almost continuously up to 120 blinks per minute. A video clip will demonstrate the blinking. She was completely mute. There were no spontaneous movements noted and she did not follow commands. When either arms or legs were moved, they maintained their new position for a prolonged period, indicating waxy flexibility. Electroencephalography (EEG) was normal. Diffusion-weighted magnetic resonance imaging (MRI) showed an acute left ACA infarct involving the medial frontal gyrus.

Akinetic mutism with waxy flexibility is difficult to differentiate from catatonia. The lack of a psychiatric history and any other features of catatonia, such as peculiar motor mannerisms or repetitive limb motions, made this diagnosis unlikely. The continuous rhythmic blinking is reminiscent of absence seizures, but this was ruled out with a normal EEG. It is essential that this unique presentation of ACA infarction be recognized so that treatment can be appropriate and timely.
Extra-pulmonary sarcoidosis is uncommon and although the spleen is a recognized site of involvement, the presence of splenomegaly with pancytopenia is an unusual presentation of sarcoidosis.

A 62-year-old woman presented to her doctor with fatigue and upper extremity joint pain. Initial laboratory investigations revealed a leukopenia, thrombocytopenia, and positive antinuclear antibody (ANA). She was referred to a rheumatologist for further investigations and was found to have a positive anti-double-stranded (anti-ds) DNA antibody and a low C4. The diagnosis of systemic lupus erythematosus (SLE) with some components of Sjogren’s syndrome was made and because she was relatively asymptomatic, no treatment was initiated. A year later, she again presented to her doctor with fatigue and myalgias, and was found to be pancytopenic with splenomegaly noted on abdominal ultrasound. She was seen by a different rheumatologist who repeated an autoimmune work-up and this time her ANA and anti-ds DNA antibody were both negative. The diagnosis of SLE was questioned and a referral to haematology was made for evaluation of a possible malignancy. On presentation to the haematology clinic she gave a history of fatigue for 1 year, worse in the last 3 months. She also reported night sweats for 3 months and left upper quadrant abdominal pain. On examination there was no cervical, axillary, or inguinal lymphadenopathy. The abdomen was soft and mildly tender to palpation in the left upper quadrant. There was a visible fullness in the left upper quadrant and the spleen was palpated 10 cm below the costal margin. Laboratory evaluation confirmed the pancytopenia. A bone marrow biopsy was done. A computed tomography (CT) scan of the chest, abdomen, and pelvis was done and showed massive splenomegaly, abdominal lymphadenopathy, and multiple bilateral pulmonary nodules. The diagnosis of lymphoma or myelofibrosis was entertained; however, the bone marrow biopsy was normal. She was referred to respirology for further evaluation of the pulmonary nodules. A bronchoscopy and transbronchial biopsies were performed. The results of the biopsies indicated sarcoidosis. It was presumed that this was also the cause of her pancytopenia and splenomegaly. She refused treatment with Prednisone. Six months after the diagnosis of sarcoidosis she continued to have significant tenderness and pressure secondary to the splenomegaly. This lead to a splenectomy being performed and the pathology confirmed sarcoidosis.

This case illustrates the atypical nature in which sarcoidosis can present, and the need to keep sarcoidosis in the differential diagnosis of splenomegaly and pancytopenia. Although it is a rare presentation, in the absence of findings consistent with lymphoma, appropriate investigations for sarcoidosis should be done.
Case Report Abstract

Plasmapheresis: A Potentially Puzzling Proposition
David Dawe, PGY-1 and Dr. Catherine Moltzan

We present the case of an 83-year-old woman who initially presented with hematuria and an elevated creatinine in 2003. She had been experiencing recurrent episodes of palpable purpura on her lower legs for the previous three years that always resolved with prednisone. She further had a known history of splenic marginal zone lymphoma with associated splenomegaly on CT scan. Her creatinine was 124 and her urinalysis showed >100 RBCs and red cell casts. Her subsequent workup revealed substantially decreased complement levels, negative ANCAs, ANA, and M-protein, but an elevated cryoglobulin level. She was treated with prednisone, cyclophosphamide, and three courses of plasmapheresis resulting in dissipation of the rash and improvement in her creatinine to 85. Four years later she returned to hospital with palpable purpura, elevated creatinine, anemia, bilateral leg pain and leg weakness. She was initially treated with solucortef and cyclophosphamide for presumed recurrence of cryoglobulin-induced vasculitis. Her cryocrit was 51%, confirming the etiology, and she therefore received two plasmapheresis treatments. Her rash began to resolve and her kidney function improved. We transferred her back to Dauphin to continue her convalescence. During both of these admissions, she did not improve until plasmapheresis was initiated. Plasmapheresis would then seem to be the treatment of choice in patients with cryoglobulinemia-induced vasculitis. However, accepted wisdom and anecdotal reports are sometimes disproved when rigorously tested. We will review the evidence for the use of plasmapheresis in patients with cryoglobulinemia.
Characterization of *Pseudomonas aeruginosa* Isolates Obtained from Patients in Canadian Hospitals: Results of the CANWARD study 2007.
Andrew Walkty, MD\(^1\), Melanie DeCorby, M.Sc\(^2\), James Karlowsky, PhD\(^{1,2}\), Daryl Hoban, PhD\(^{1,2}\), George Zhanel, PhD\(^{1,2}\)
Departments of Medicine and Clinical Microbiology, Health Sciences Centre\(^1\); Department of Medical Microbiology, Faculty of Medicine, University of Manitoba\(^2\), Winnipeg, Manitoba, Canada

**Introduction:** *Pseudomonas aeruginosa* is an important nosocomial pathogen. The purpose of this study was to determine the frequency with which *P. aeruginosa* isolates are obtained from different areas of Canadian hospitals (medical wards, surgical wards, emergency rooms (ERs), intensive care units (ICUs)) and to evaluate their antimicrobial susceptibility profiles.

**Methods:** From January to December 2007, inclusive, 12 sentinel hospitals across Canada submitted clinical isolates from patients attending ERs, medical and surgical wards, and ICUs. Each centre was asked to submit clinical isolates (consecutive, one per patient/infection site) from blood (360), respiratory (200), urine (100), and wound/IV (50) infections. Susceptibility testing was performed using CLSI broth microdilution methods.

**Results:** To date, 5851 bacterial isolates have been collected as part of the CANWARD study. *P. aeruginosa* was the third most common bacteria isolated from surgical and medical wards, the fourth most common isolated from ICUs, and the fifth most common isolated from ERs. Antimicrobial susceptibility data was available for 328 *P. aeruginosa* isolates. The breakdown of these isolates by specimen source was: respiratory (60%), blood (14%), urine (11.8%), and wound (14.3%). The rank order of antimicrobial susceptibility was as follows (% susceptible): amikacin (92.1%) = piperacillin/tazobactam (92.1%) > meropenem (85.7%) > cefepime (65.2%) > ciprofloxacin (64.6%) > gentamicin (60.7%) > levofloxacin (57.3%). Resistance to meropenem, levofloxacin, and cefepime was more frequently observed among isolates obtained from patients in an ICU (p values of 0.0019, 0.0079, and 0.0815 respectively). Twenty-seven isolates (8.2%) were multi-drug resistant (MDR resistant to at least 3 different antimicrobial classes). Amikacin and piperacillin/tazobactam were the most active antimicrobials versus the MDR isolates, while the fluoroquinolones were the least active. MDR isolates were more likely to be obtained from patients in an ICU (p value 0.0161) and less likely to come from a bloodstream source (p value 0.0301).

**Conclusions:** *P. aeruginosa* is common among clinical specimens from patients in Canadian hospitals. Amikacin and piperacillin/tazobactam were the most active antimicrobials evaluated, irrespective of hospital area. Isolates resistant to individual antimicrobials (meropenem, levofloxacin, cefepime) and MDR isolates were more commonly obtained from ICU patients.