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OF OHIO

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IN THE COURT OF CLAIMS OF OHIO

YONG HUI SHEFFIELD, ET AL.,	:	
Plaintiffs	:	Case No. 2013-00013
v.	:	Judge Dale A. Crawford
THE OHIO STATE UNIVERSITY MEDICAL CENTER,	:	
Defendant	:	

DEFENDANT'S EXPERT DISCLOSURE

In accordance with the Court's scheduling order, defendant hereby identifies the following witnesses as experts:

1. Peter J. Papadakos, M.D., critical care medicine, report attached.
2. John Askins, R.N., B.S.N., report attached.
3. David W. Woodruff, M.S.N., R.N.-B.C., report attached.
4. Jenny Beerman, R.N., M.N., report attached.
5. Miguel-Angel Perales, M.D., hematology, report attached.
6. Bruce Farber, M.D, infectious disease, report attached.

ON COMPUTER

Respectfully submitted,

MIKE DEWINE
Ohio Attorney General

KARL W. SCHEDLER (0024224)
DANIEL R. FORSYTHE (0081391)
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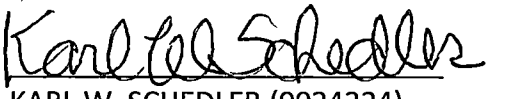
(614) 466-7447
COUNSEL FOR DEFENDANT

CERTIFICATE OF SERVICE

I hereby certify that a copy of Expert Witness Disclosure was sent by regular U.S. Mail, and by electronic mail, on this 21st day of July, 2014 to:

Michael J. Rourke
Robert P. Miller
495 S. High St., Suite 450
Columbus, Ohio 43215
Counsel for Plaintiff



KARL W. SCHEDLER (0024224)
Assistant Attorney General

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ATTORNEY GENERAL'S OFFICE
COURT OF CLAIMS DEFENSE

June 30, 2014

Daniel R. Forsythe, J.D.
Senior Assistant Attorney General
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June 28, 2014

Re: Yong Him Sheffield et al, v The Ohio State University Medical Center, Court of Claims Case No. 2013-00013

At the request of your office, I have reviewed the medical records and images of Mr. Daniel Sheffield during his hospitalization at Ohio State University Medical Center. I also reviewed the Deposition of Paul Gallett, R.N.

In brief:

Daniel Sheffield was a 69 y/o male with a history of follicular lymphoma s/p allogeneic stem cell transplant, admitted with neutropenic fever, acute respiratory failure, hypotension, and sepsis on 6/13/2012 to Wexner Medical Center of Ohio State. During that admission, he was treated for Norcardia pneumonia, atrial fibrillation, and CMV viremia.

His past medical history is remarkable for prostate cancer, hypotension, depression, and the above lymphoma.

On 7/5/2012, a left internal jugular center venous catheter was removed by Mr. Paul Galett, R.N. in the supine position and pressure was applied for 15 minutes and a dressing placed. Approximately 40 minutes later, Mr. Sheffield went into a coma while having a meal. CT imaging showed air in the brain and read as either from Norcardia or air embolism by several consultants. Treatment was done with hyperbaric oxygen along with supportive therapy. No recovery occurred and the family withdrew care, and the patient expired at 9/25/2012.

Assessment:

Based on my review of the available data, I do not believe Mr. Sheffield suffered from an air embolism, due to the line being extracted by Mr. Gillett. Mr. Gillett extracted the line in the supine position and placed direct pressure for 15 minutes. No hematoma was noted on the neck, which supports that pressure was applied. A dressing was placed. The event occurred approximately 40 minutes after the line was removed outside the window of time an embolism is expected due to clot formation, return of fascial planes and muscular approximation.

No evidence of air in the lungs was ever noted, a classic finding of air embolist. Also, no intercardiac shunts were ever documented either by murmur or echocardiogram.

In summary, I believe Mr. Sheffield's death was not a consequence of the line being removed. All standards of care were met.

Sincerely,

Peter J. Papadakos, M.D., F.C.C.P., F.C.C.M., F.A.A.R.C.
Professor of Anesthesiology, Surgery, Neurosurgery, and Neurology
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Assistant Attorney General
Court of Claims Defense Section
150 East Gay Street, 18th Floor
Columbus, Ohio 43215

July 10, 2014

Re: Yong Hui Sheffield, ET AL. –v- The Ohio State University Medial Center
Case No 2013-00013

Dear Mr. Forsythe,

As requested I have reviewed the records sent to me of Mr. Sheffield. He was admitted to Wexner Medical Center of Ohio State University on 6/13/2012. Mr. Sheffield presented to the ER with complaint of elevated temperature, 103 degrees, became hypotensive with sepsis and hypoxic with respiratory failure. He was found to be neutropenic. In addition he suffered from CMV viremia, Norcardia pneumonia, renal insufficiency and atrial fibrillation.

Past medical history includes Non-Hodgkin's lymphoma, pneumonia, acute renal failure, anemia, DVT in lower extremity, carcinoma of prostate, depressive disorder, and epileptic seizure.

Mr. Sheffield had a central venous catheter placed in order to provide medication, fluids and care. On 7/5/2012 this catheter was removed. Mr. Sheffield experienced what is described as a seizure some 40 to 50 minutes after the removal of this catheter. Imaging studies, laboratory studies and hyperbaric treatment were done. Mr. Sheffield expired on 9/24/2012 from sepsis.

Allergies include chlorhexidine, penicillins, vancomycin and sulfa drugs.

As requested I have focused my review on the standards of care involving the left internal jugular catheter removal. This catheter was removed on 7/5/2012. Mr. Sheffield was instructed on the procedure for the removal of the catheter, placed flat and requested to hum. Pressure was held on the removal site for approximately 15 minutes and gauze dressing was applied to the site. He remained in bed for at least 30 minutes per the time line of the records. He tolerated the removal of the catheter well and was talking with his family and eating with the assistance of his wife following the removal.

The procedure followed was within the standards of care for removal of a central line. Mr. Sheffield understood the procedure due to prior education by his nurse. He was placed in a flat position as tolerated by him and according to standards. There is a question about a pillow being under his head during the catheter removal. The position of the catheter site would not have been altered significantly and still leave access for removal of the catheter, if in fact there were a pillow there. He was requested to hum which required him to exhale, which results in a valsalva response. Studies have shown this to be effective in reducing the possibility of an air embolism. This procedure is accepted and has been shown to be as effective as a valsalva maneuver. Pressure was held on the site for approximately 15 minutes with gauze. This is acceptable as well and practiced in facilities. A gauze dressing was applied with tape, which is also an acceptable practice.

It is my opinion that nurse Gullett followed acceptable standards of practice in the removal of a central line. Nurse Gullett's actions were that of a prudent nurse and his care was within acceptable standards. This opinion is stated with a reasonable degree of nursing certainty and is based on review of the records sent to me as well as my education, training and experience over the past 36 years as a registered nurse.

Sincerely,

John Askins RN

John Askins RN

RECORDS REVIEWED

1. Medical Records Wexner Medical Center of Ohio State University, 6/13/2012 to 8/16/2012.
2. Discharge Summary by Dareth N. Gilmore,CNP and and Sumithira Vasu M.D., MBBS.
3. Expert Report, DanGzesh M.D.m 9/15/2013 and 6/12/2013.
4. Expert Report, Carolynn Cassutt RN, CRNI, CLNC, VA-BC, 6/15/2013.
5. Deposition, Paul Gullett RN,Volume 2, 6/10/2014

David W. Woodruff, MSN, RN-BC, CNS, CNE
571 Ledge Road
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(330) 888-9446

July 15, 2014

Mr. Daniel Forsythe
Court of Claims Defense Section
150 East Gay Street, Floor 18
Columbus, OH 43215

Re: Sheffield, et al. vs. The Ohio State University Medical Center

Dear Mr. Forsythe,

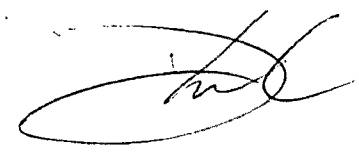
The following is a report of my opinions in regard to the appropriateness of the nursing care that Daniel Sheffield received by the staff from Ohio State University Medical Center on July 5, 2012. The items that I reviewed in order to reach my opinions were: the medical records of the Ohio State University Medical Center from June 13, 2012 to September 25, 2012, the plaintiff's complaint, and deposition transcript of Paul Gullet, RN, and the OSUMC Patient Standards of Practice.

As a result of my review, I found that the nursing care that Daniel Sheffield received met the standard of care required of a reasonable and prudent nurse. The nurses caring for Mr. Sheffield assessed him, planned appropriate interventions for him, implemented those interventions, and evaluated the effectiveness of the interventions.

Mr. Sheffield was admitted to The Ohio State University Medical Center on June 13, 2012 with sepsis. On July 5, 2012, Paul Gullet, RN removed a central venous catheter from Mr. Sheffield's internal jugular vein using accepted and standard nursing practice. Thereafter, Mr. Sheffield developed respiratory distress, and later, altered mental status. There is no evidence from my review that the removal of the catheter resulted in Mr. Sheffield's subsequent symptoms or caused injury to Mr. Sheffield. The central catheter was removed following the accepted standard of care.

Therefore, it is my opinion, to a reasonable degree of nursing certainty, that the nurses at The Ohio State University Medical Center followed the appropriate standard of care in their treatment of Mr. Sheffield. I reserve the right to amend my opinions if additional information becomes available.

Respectfully,



David W. Woodruff, MSN, RN-BC, CNS, CNE

July 21, 2014

Daniel Forsythe
Karl W. Schedler
Court of Claims Defense Section
Office of the Ohio Attorney General
150 East Gay Street, Suite 1800
Columbus, OH 43215

RE: Daniel Sheffield

Dear Mr. Forsythe and Mr. Schedler:

Per your request, I have reviewed excerpts of the medical records from The Ohio State University Medical Center regarding Mr. Sheffield's final hospitalization, which included the Admission, History and Physical and Transfer Notes, the Progress and Discharge Notes, Orders, and Nursing Flow Sheets. Also reviewed were the Plaintiff's Amended Complaint with Affidavits of Merit, Plaintiff's Identification of Expert Witnesses and Expert Reports (Dan Gzesh, M.D. and Carolynn Cassutt, R.N.), Deposition of Paul Gullett, R.N., with exhibits, taken June 10, 2014, and the following policies: OSUMC Patient Care Standards of Practice: Intravascular Access Devices and Mosby's: Central Venous Catheter; Removal.

My opinions are based on my education that includes a master's degree in nursing, teaching at several colleges of nursing, 43 years of full and part time staff nursing in medical-surgical and critical care settings, teaching and caring for patients in the geriatric and nursing home settings, and lectures and publication on documentation, chain of command, and critical care issues. I devote approximately 90 percent of my professional time to the active clinical practice of nursing, being at the bedside of patients and the students that I teach. My curriculum vitae is attached at the end of my report.

Since 1971, my nursing duties and responsibilities have included and continue to include, in addition to the clinical and academic training of professional nursing students, weekly clinical nursing care of patients like and similar to Daniel Sheffield. As a practicing nurse since 1971, I have special knowledge, training and experience in medical and surgical nursing, with a clinical nursing emphasis in the nursing care of adult patients, involving direct nursing diagnosis, assessment, care and treatment to patients experiencing lymphoma, stem cell transplantation, sepsis, and the use and removal of central venous catheters.

Daniel Sheffield was a 69 year old male who had a history of Non-Hodgkin's lymphoma and was status post Allogenic Stem Cell Transplant. Mr. Sheffield presented to the Ohio State University Medical Center on **June 13, 2012** with a diagnosis of septic shock. He was admitted to the Medical Intensive Care Unit (MICU) and started on IV antibiotics.

Following Mr. Sheffiel's admission to the MICU, he required intubation, vasopressors, and hemodialysis. His condition slowly improved and he was weaned from the vasopressors and was extubated. Mr. Sheffield was transferred to the BMT (Bone Marrow Transplant) Unit. Mr. Sheffield

was receiving physical therapy and occupational therapy with plans for discharge to an acute rehabilitation center.

On **July 5, 2012,** an order was written to discontinue a left IJ (internal jugular) temporary central venous access device (CVAD) catheter. Mr. Sheffield's nurse, Paul Gullett, R.N., prepared to removed the CVAD that evening at approximately 1800. Nurse Gullet documented that the CVC was removed per sterile procedure while Mr. Sheffield's bed was placed in the flat position. The sutures were removed, and Nurse Gullet instructed Mr. Sheffield to hum a song while he removed the catheter. Nurse Gullet stayed with Mr. Sheffield as he applied pressure to the exit site for 15 minutes.

At approximately 1840, Nurse Gullett was called to Mr. Sheffield's room by his family who stated that Mr. Sheffield was short of breath. Upon Nurse Gullett's arrival to the room, Mr. Sheffield was sitting up in a chair complaining of shortness of breath. His room air oxygen saturation was 89%. Nurse Gullett stopped his antibiotic infusion. Mr. Sheffield was on oxygen and IV fluids. He called for help, and when no one came, he ran to get his charge nurse. When Nurse Gullett returned to the room, Mr. Sheffield was unresponsive and he was quickly moved from the chair to the bed.

Mr. Sheffield was breathing on his own and was placed on oxygen at 4 liters. The physician arrived at the bedside. Mr. Sheffield continued to be unresponsive and was taken for an emergent CT scan of the brain at 1900. The CT scan revealed evidence of a stroke. Upon Mr. Sheffield's return to the floor, the neurology service was consulted and evaluated him at 1915. Mr. Sheffield remained unresponsive and was intubated. Further CT scans of the brain were completed and revealed a cerebral air emboli. The neurology service noted that it was unclear how the air emboli were introduced.
Over the next couple of weeks, Mr. Sheffield remained unresponsive. Follow-up brain scans continued to show acute areas of infarcts. On **September 24, 2012**, Mr. Sheffield's condition deteriorated. He expired that afternoon at 1600 due to severe sepsis and immobility from a stroke.

Opinions of Nursing Care

I am familiar with the national standard of nursing care and know it to be that level of reasonable care, skill and diligence that nurses would ordinarily have and exercise in the same or similar cases.

In my opinion, the nursing care Mr. Sheffield received while at Ohio State University Medical Center met the standard of care. It is my opinion Nurse Gullett safely positioned Mr. Sheffield in a flat position when he removed the CVAD catheter. Though a Trendelenburg position is common, many patients are unable to tolerate this position for periods of times. Having a patient supine allows the heart, positioned in the anterior portion of a man's body, to be slightly above the catheter site, which is in the internal jugular vein in the neck. Mr. Gullett does not recall if he removed Mr. Sheffield's pillow. However, if a pillow was in place, it would elevate the head and not the lower portion of the neck, where the internal jugular vein is located.

There are several techniques that are safe when removing a CVAD catheter. It is my opinion Mr. Gullett met the standard of nursing care by removing the CVAD catheter by having Mr. Sheffield exhale during the procedure. Nurse Gullett, per his deposition, recalls that he asked Mr. Sheffield to

hum during the removal. I have been a nurse for 43 years, and have witnessed physicians and nurses removing CVAD catheters safely by having patients hum. Understanding the mechanism of humming provides insight into exhaling, which is the goal during CVAD catheter removal. During humming, the glottis opens and closes intermittently, to increase intra-thoracic pressure and force expiration. A patient is required to exhale during humming. The mechanism of humming resembles those of a Valsalva maneuver. What is ultimately achieved during humming is a patient must take a deep breath to sustain humming, and prevent inhalation, which is the goal of safe CVAD catheter removal.

It is my opinion Nurse Gullett safely sealed the site of the CVAD catheter by applying pressure with sterile gauze at the sight for 15 minutes. Petroleum-based ointment is no longer used in many institutions and no longer stocked on many supply carts. It is my opinion that firmly applying direct pressure over the insertion site with sterile gauze meets the standard of nursing care. In the past several years, holding pressure with a sterile gauze until homeostasis is achieved, and then placing tegaderm or tight tape over the sight, is accepted procedure and what a reasonable and prudent nurse would do. Nurse Gullett testified that at no time was the wound open to air.

There is dispute in the records and deposition of Nurse Gullett as to how long Mr. Sheffield remained in his bed before he was in a chair to eat his dinner. Nurse Gullett testified that he stayed with Mr. Sheffield for 15 - 30 minutes for the CVAD catheter removal and then left the room to retrieve an antibiotic. Nurse Gullett estimated in his deposition that locating the antibiotic and signing out for it would have taken about 5-10 minutes, in addition to the time he spent removing the CVAD. When Nurse Gullett returned to the room, he noted that Mrs. Sheffield was assisting her husband to eat. Mr. Sheffield was in a chair. Nurse Gullett testified that Mr. Sheffield was doing "okay" at that time. Nurse Gullett, according to his testimony, spent another 5-10 minutes in Mr. Sheffield's room, setting up the tubing for the antibiotic to be hung through his PICC. It remains unclear how long Mr. Sheffield remained in bed after the removal of his CVAD, but more likely than not, it was greater than 30 minutes. Allowing Mr. Sheffield out of bed outside of 30 minutes of the CVAD removal, meets the standard of nursing care.

It is clear, from the above paragraph and the deposition of Nurse Gullett, that greater than 30 minutes elapsed before Mr. Sheffield experienced some difficulty breathing. When Mrs. Sheffield requested Nurse Gullett to check on her husband, Nurse Gullett appropriately assessed him by checking his oxygen saturation and found it to be 89% on room air. He did a quick neurological assessment and found Mr. Sheffield to be oriented. Mr. Sheffield knew his name and where he was. Nurses Gullett immediately stopped the antibiotic and started normal saline through his IV. He auscultated his lungs and noted that Mr. Sheffield had some rhonchi on the left side. He called out for help, then left quickly to locate help. Mr. Sheffield was breathing and oriented to person and place when he left the room with his family. Nurse Gullett quickly got help. When Nurse Gullett and two nurses returned to the room, Mr. Sheffield had quickly changed. They found him unresponsive. They got Mr. Sheffield back to bed and laid him flat. As Mr. Gullett testified, he did not suspect an air embolism, based on the time that had lapsed. In his nursing judgment, Nurse Gullett knew he needed help, and obtained it from his charge nurse. When they found Mr. Sheffield unresponsive, they placed Mr. Sheffield flat in bed and called for additional assistance. They also obtained the floor's crash cart. Dr. Bittenbender, an on call

physician, also came into the room to assist with Mr. Sheffield.

Mr. Sheffield's change of condition was unusual following the removal of his CVAD catheter. Nurse Gullett reacted with care and quickly obtained help for Mr. Sheffield when his condition acutely changed. It is my opinion that the nursing care given to Mr. Sheffield met the standard of nursing care.

Thank you for asking me to review information on Mr. Sheffield's nursing care. Should knew information, such as additional depositions, statements, or other discoveries become available to me, I reserve the right to amend or change my opinions.

Respectfully submitted,

Jenny Beerman, RN, M.M.
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Case No 2013-00013

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Court of Claims Defense Section
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July 18, 2014

Re: *Yong Hui Sheffield et. al. v. The Ohio State University Medical Center*
Court of Claims Case No. 2013-00013

Dear Mr. DeWine and Mr. Forsythe,

At your request I have reviewed the medical records of Mr. Sheffield (Appendix 1) and provided an expert opinion regarding his life expectancy.

Expertise

I am a medical oncologist licensed in the State of New York. I serve as Deputy Chief of the Adult Bone Marrow Transplant Service at Memorial Sloan Kettering Cancer Center in New York, where I have been on faculty for over 13 years and also direct the Adult Stem Cell Transplant Fellowship. I am a Special Contributing Faculty Member at the Gerstner Sloan Kettering Graduate School at MSK and an Associate Professor of Medicine at Weill Cornell Medical College. I am a member of a number of scientific associations and serve on the Alliance for Clinical Trials in Oncology (former CALGB) Transplant Committee, the American Society for Blood and Marrow Transplantation (ASBMT) Educational Committee and Committee on Practice Guidelines, and the National Marrow Donor Program (NMDP) System Capacity Initiative Working Group and Curriculum Sub-Group. I also serve as Co-Chair of the Center for International Blood and Marrow Transplant Research (CIBMTR) Graft Sources and Manipulation Working Committee and chair the Digital Education Working Group of the American Society of Hematology (ASH). My clinical practice focuses on allogeneic and autologous stem cell transplantation for hematological malignancies. I have served as a reviewer for several study sections and journals, have been invited to give presentations at national and international meetings and have authored over 70 peer-reviewed manuscripts, editorials, reviews and book chapters.

Review of the medical case

Mr. Sheffield was a 69 year-old man with follicular non-Hodgkin Lymphoma (NHL), originally diagnosed in 2006, who underwent a reduced intensity allogeneic hematopoietic stem cell transplant (HCT) from a 10/10 matched unrelated male donor in October 2011. He was diagnosed with follicular NHL, Stage IVA, grade 2 in 2006. Between 2006 and 2011, he required six courses of chemotherapy, including two courses of fludarabine/rituximab (2007 and 2008), rituximab/cyclophosphamide/vincristine/prednisone

(RCVP) with rituximab maintenance (2009), cyclophosphamide/adriamycin/vincristine/prednisone (CHOP, 2010), experimental therapy with CAL101 (2010) and bendamustine/rituximab (2011). His treatment course was complicated by two episodes of pneumonia, including pneumonia due to respiratory syncytial virus (2010), acute renal failure due to vancomycin, and persistent neutropenia (low white blood cell count) in 2011 that required a delay and reduction in the dose of his chemotherapy as well as immune suppression with cyclosporine.

His prior medical history was notable for prostate cancer diagnosed in 2006 and treated with brachytherapy (implanted seeds), depression, glaucoma, and tonsillectomy. His pre-transplant evaluation was notable for cardiac function just below normal (left ventricular ejection fraction of 54%), slightly decreased pulmonary function (adjusted diffusion capacity – DLCO – of 79%), and imaging studies that showed that he was in complete remission after his most recent therapy. His Karnofsky performance status (KPS) was 90 and calculated hematopoietic cell transplantation-comorbidity index (HCT-CI, see Appendix 2 for bibliography) was 6 based on prior malignancy, abnormal pulmonary function, and depression.

He was admitted for transplant from 10/31/11 to 11/30/11. He underwent a standard reduced intensity allogeneic HCT after conditioning with busulfan/fludarabine/antithymocyte globulin and received tacrolimus/methotrexate for prevention of graft-versus-host disease (GVHD). He had a complicated transplant course with neutropenic fever, mucositis (mouth and throat sores) that required holding the last planned dose of methotrexate, high blood pressure attributed to tacrolimus, and reactivation of cytomegalovirus (CMV) in the blood. In addition, on 11/17/2011, he was noted to have mental status changes with expressive aphasia and evidence of seizure activity on an electroencephalogram (EEG). He was treated with ativan and dilantin (anti-seizure drug), and tacrolimus was discontinued as it was assumed to be the offending agent and is known to cause neurological complications in a minority of patients. Tacrolimus was replaced by mycophenolate mofetil (MMF), another drug commonly used to prevent GVHD. On 11/21/11, he was noted to have a skin rash and diarrhea consistent with a clinical diagnosis of acute GVHD and was started on intravenous steroids (methylprednisolone). A colonoscopy performed on 11/28 supported the diagnosis of acute GVHD.

Shortly after discharge, he developed increasing levels of CMV in the blood and was started on valgancyclovir (a drug to treat CMV). About two weeks after his discharge, he was readmitted with worsening skin rash, which now covered 45% of his skin, consistent with stage 2 skin acute GVHD and was again treated with high dose intravenous steroids. Another immunosuppressive drug, sirolimus, was added for GVHD treatment.

He then remained out-patient from 12/20/11 until 6/12/12. His course during that time was notable for presence of BK virus in the urine, which is associated with urinary symptoms and can also lead to hemorrhagic cystitis and in some cases nephropathy, a seizure on 2/7/12, and recurrent CMV in the blood, which required a second round of treatment with valgancyclovir (March 2012). Throughout this time, he continued to be treated for skin GVHD with involvement of up to 70% of the skin surface and was maintained on 3 immunosuppressive agents, MMF, sirolimus and prednisone.

He was readmitted on 6/13/12 in the setting of neutropenic fever and septic shock. He was transferred to the ICU, where he required intubation, mechanical ventilation and the use of drugs to support his blood pressure. He had acute renal failure and required continuous veno-venous hemofiltration (CVVH), a type of dialysis often used in ICU patients who are not stable enough for dialysis. In addition, his blood tests also revealed liver damage likely related to the septic shock and he experienced an episode of

atrial fibrillation with rapid ventricular rate. He was treated with broad spectrum antibiotics as well as foscarnet for his CMV. The diagnostic work-up was notable for the presence of CMV in the blood and possible CMV pneumonitis, and pneumonia due to nocardia, an infection typically seen in patients whose immune system is compromised, such as patients with HIV/AIDs, cancer or after transplant. He also had evidence of inflammation of the colon on a CT scan. With aggressive supportive care, he improved clinically and, on 6/19/2012, he was able to be extubated and discontinued CVVH. While he remained very debilitated from the septic shock episode and his underlying condition, he was making progress with physical therapy and the plan was to transfer him to a rehabilitation facility, when the critical events of 7/5/12 occurred. After a prolonged course, the patient expired on 9/24/12.

Expert Opinion

Despite significant advances over the past decades, with better patient selection, novel conditioning regimens and improved supportive care, allogeneic HCT remains a high risk procedure with significant morbidity and mortality reserved for patients with advanced disease, for whom no other curative option is available. Mr. Sheffield was diagnosed with advanced lymphoma (stage IV) and had received several courses of chemotherapy, including investigational therapy, and his disease was proving increasingly resistant. In addition, he also had significant complications during his treatment prior to transplant.

There are several tools that can be used to predict the expected survival in a patient who undergoes a stem cell transplant for lymphoma, and the likelihood of survival varies during the treatment course based on response to therapy and development of complications.

At the time of his diagnosis in 2006, based on his age greater than 60 and stage IV disease, he was considered intermediate risk and his estimated 10-year overall survival was only 50%, using a prognostic tool called the Follicular Lymphoma International Prognostic Index (FLIPI) (1). If he had additional risk factors at that time, such as 4 or more sites of lymph nodes involved, a high LDH or a low hemoglobin, he would then have had been classified as high risk with an estimated 10-year overall survival of only 35%.

At the time of transplant, survival can be predicted by results of studies reporting outcomes for specific diseases as well as the use of the hematopoietic cell transplantation-comorbidity index (HCT-CI), which predicts the risk of complications and likelihood of survival due to the patient's underlying conditions and known risk factors. An analysis of the Center for International Blood and Marrow Transplant Research (CIBMTR) included long-term outcomes of 283 patients with lymphoma who received an unrelated donor allogeneic HCT. In the 62 patients with follicular lymphoma, overall survival was 40% at 5 years after transplant (2). Single-center series have reported better results but are subject to biases including patient selection that is not typically found in registry data where all transplants are included. The CIBMTR study also reported treatment-related mortality (TRM) of 44% at 1 year, and 52% at 5 years for the whole cohort. TRM was also significantly increased in patients over 40. Treatment-related or non-relapse mortality is predicted in part by patients' underlying medical conditions, which is captured in the HCT-CI and predicts outcomes after transplant (3). The patient had a HCT-CI score of 6 and KPS (performance status) of 90, and therefore falls into risk group III (out of four potential risk groups). The HCT-CI predicts a 2-year non-relapse mortality of 30% and 2-year survival of 41% for patients in this group.

As noted above, the patient had a complicated transplant course that included GVHD. GVHD is one of the main complications of an allogeneic HCT and is associated with significant morbidity and accounts

for 10 to 20% of all deaths after an allogeneic HCT (4). The severity of acute GVHD predicts treatment-related mortality and survival (5). Based on skin involvement of 70% in the patient's case, he would be classified as grade 3 GVHD, which is associated with a survival at 2 years of less than 50%.

Finally, patients undergoing allogeneic HCT who require ICU level care have extremely poor outcomes. In a large retrospective multicenter study of 209 patients who were admitted to an ICU after HCT, 1-year survival for all patients was only 21% and dropped further to 10.6% in patients requiring mechanical ventilation (6). In this study, the authors identified several factors associated with poor prognosis: patients requiring mechanical ventilation patients in the setting of late complications of HCT, especially in the presence of other organ failures such as shock or liver dysfunction. The use of corticosteroids, typically given for GVHD was also a poor prognostic factor. All of these poor risk factors were present in the case of Mr. Sheffield.

In summary, Mr. Sheffield was an older man with advanced lymphoma, who required several lines of treatment and had significant medical issues prior to transplant. Based on these factors, his risk of dying as a result of complications was estimated at 30% at 2 years from the time of transplant. However, this risk increased significantly due to several complications during his early transplant course, including neurological toxicity attributed to tacrolimus, CMV reactivation, and GVHD. Most patients with GVHD do not die of GVHD itself but of complications of GVHD or the drugs used to treat GVHD. In many patients, infectious complications often lead to a patient's death. This is certainly the case for Mr. Sheffield, where his final admission was precipitated by neutropenic fever and septic shock in the setting of CMV infection and nocardia pneumonia, not an uncommon scenario in GVHD. Finally, given the resultant multiorgan failure, with acute renal failure and liver compromise, as well as requirement for mechanical ventilation, his long-term prognosis would have been extermely guarded. Based on the clinical course and literature reviewed, Mr. Sheffield's probability of one year survival prior to events of 7/5/11 would therefore have been estimated to be very low, in the order of 10%-20%.

My opinions are stated with a reasonable degree of medical certainty and are based on the materials I have reviewed to date and may change based on review of new or additional material or data.

Miguel-Angel Perales MD

Appendix 1 – Materials reviewed

- Pre-Transplant Records [OSUMC 00422-00437, OSUMC 001235-001239, OSUMC 002061-002063]
- Transplant Admission (10/31/11 – 11/30/11) [OSUMC 002818-003104, 002335-002350, OSUMC 002335-002466]
- Post-Transplant Admission (12/12/11 – 12/20/11) [OSUMC 003585-003594]
- Post-Transplant Office Records [OSUMC 002192-002200, OSUMC 002131-002141, OSUMC 004811-4830]
- Final Admission (6/13/12 – 6/20/12, 6/20/12 – 9/25/12)
    - Admission Note, H&P, and Transfer Note [OSUMC 004836-004852, OSUMC 004950-004954]
    - Discharge Note [OSUMC 005700-005703]
    - Consults [OSUMC 005704-005712]
    - Progress Notes [OSUMC 005759-005867]

Appendix 2 – Bibliography

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HOFSTRA NORTH SHORE-LIJ
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July 20, 2014

Mr. Karl Schedler
Ohio Attorney General
150 East Gay Street Floor 18
Columbus, Ohio 43215

RE: Yong Hui Sheffield v. Ohio State University Medical Center
Claim No 2013-00013

Dear Mr. Schedler:

At your request I had the pleasure of reviewing the relevant documents regarding this case. These have included medical records from the hospitalization of Daniel Sheffield included admission notes transfer notes history and physical discharge note consults radiology and cardiology reports nursing flow sheets orders and progress notes. In addition I was given the multiple imaging studies including echocardiography chest x-ray MRI CT scans and vascular duplex studies.

The patient in this case was a 69-year-old male with a history of non-Hodgkin's lymphoma status post left allergenic stem cell transplant in 11/11. The procedure was complicated by graft-versus-host disease and he has been on chronic immunosuppressive therapy since then including prednisone. His post transplant course was also complicated by CMV viremia requiring valcyte therapy. The patient had a past history of seizures, cancer the prostate, hypertension, acute renal failure, and DVT.

The patient was admitted to Ohio State University Medical Center on June 13, 2012 with neutropenic fever. His ANC at that time was less than 100. He was placed on empiric antibiotics including Zyvoxx, ciprofloxacin, and aztreonam because of penicillin and vancomycin allergies. At the time of admission he became severely hypotensive and was treated with fluid resuscitation requiring over 3 L. He had a central line to manage his lipids. The patient had a BAL done shortly after admission and ultimately grew Nocardia. The major focus of this case revolves around the period of time shortly after his CVP line was removed on 75 2012. The CVP line was removed because he had had a PICC line placed and it was low longer needed. He became hypoxic following this procedure and subsequent studies revealed evidence of air in the venous sulci and intravascular. Follow-up studies revealed a right frontal infarct right

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temporal infarct right basal ganglia infarct as well as left-sided infarcts. An echocardiogram was done which failed to reveal pulmonary hypertension or a patent ductus.

The major allegation in this case is that there was a deviation during the removal of the central venous line that resulted in an air embolus. In my opinion to a reasonable degree of medical certainty the following can be stated in

- This patient had no evidence of a patent ductus or VSD that would allow for a paradoxical embolus to develop. There was also no evidence of significant pulmonary hypertension that would have allowed a right-to-left shunt. Therefore, there is no reasonable physiologic explanation for how an air embolus from a CVP line would cause multiple bilateral strokes.
- This patient was severely immunosuppressed. He had previously received an allogeneic bone marrow transplant and was on chronic prednisone therapy. In addition the patient came in with neutropenia, which also placed him at dramatically increased risk of getting multiple opportunistic and bacterial infections. He was being treated for a pulmonary Nocardia infection which would require at least 6 months of therapy. Nocardia is an opportunistic bacterial infection that infects immunosuppressed host. Although Nocardia usually enters through the lung and causes pulmonary disease, the 2 other sites of metastatic spread that are commonly reported include the brain and subcutaneous tissues. The patient had significant bilateral cerebral disease not limited to one focal area. Due to his penicillin allergy, he was being treated with a variety of antibiotics that did not normally cross the blood-brain barrier.
- Nocardia can be an explanation for the air in the brain, and this certainly seems more reasonable that to postulate that removal of a cvp line was responsible for the latter in the absence of pulmonary hypertension and a right to left cardiac shunt.

I reserve the right to add to the report as additional information becomes available. I hold all my opinions to a reasonable degree of medical certainty.

Sincerely,

Bruce Farber M.D.