



Patient Safety Review Committee 2011 Annual Report

Office of the Chief Coroner
Province of Ontario
June 2012

Table of Contents

Message from the Chair	i
Committee Membership	iii
History	1
Purpose	1
Structure and Size	2
Limitations	2
Summary of Cases Reviewed in 2011	4
2011-01	4
2011-02	8
2011-03	16
2011-04	23
2011-05	27
2011-06	32
2011-07	36
2011-08	40
2011-09	44
2011-10	47
2011-11	51
2011-12	55
Special Review: Pneumonitis Deaths Following Chemotherapy	59
Special Review: Deaths Following Laparoscopic Bariatric Surgery	63

Message from the Chair

“Primum Non Nocere”

This oft-quoted phrase translates to, “First, do no harm.” Its origins are uncertain, although the Hippocratic Oath includes the promise to “abstain from doing harm.”

As healthcare providers, our motivations are to improve health, relieve suffering and cure disease. The possibility that our very actions might inadvertently cause harm to those whom we are striving to help is difficult to accept. But the unfortunate fact is that medical error results in the loss of thousands of lives every year in Canada. Many of these deaths are preventable.

Do medical errors occur because doctors and nurses are careless, or incompetent, or bad people? Generally, no. Most often, errors occur because of underlying system flaws that make it easy to make a mistake, and more difficult to avoid making an error. Two medications that look or sound alike, placed side by side in a medication cabinet; connectors that allow a ventilator to be inadvertently connected to an outlet delivering regular air instead of oxygen; these are just two examples of medical errors waiting to happen because of system flaws.

In Ontario, all coroners are medical doctors. There is tremendous value to a death investigation system where the investigations – and in particular, medically-related deaths - are conducted by physicians with extensive clinical expertise and a first-hand understanding of the health care system and its weaknesses.

The goal of the Patient Safety Review Committee of the Office of the Chief Coroner is to review cases where a medical error or other system issue is thought to have caused or contributed to a death. This multi-disciplinary Committee examines the root causes of these tragic outcomes and generates recommendations aimed at preventing similar deaths in future. These recommendations are disseminated from the Chief Coroner through local, provincial and national organizations in order that the lessons learned from one death may be used to prevent many.

This 2011 Annual Report of the Patient Safety Review Committee includes summaries of the twelve cases reviewed by the Committee this year, and the 45 recommendations that arose from these cases. In addition, the PSRC reviewed the results of two special reviews: one related to a series of cases of pneumonitis following administration of a chemotherapy agent, and the second related to a series of unexpected post operative bariatric surgery deaths.

We are fortunate to have had four new members join the Committee in 2011: Dr. Jonathan Dreyer brings his extensive experience in emergency medicine and pre-hospital care; Dr. Anne Matlow is a world-recognized expert in patient safety with a background in infectious disease; Ms. Julie Greenall is a clinical pharmacist and the Interim Operations Leader for the Institute for Safe Medication Practices (ISMP) Canada; and Dr. Kris Cunningham is a forensic pathologist and the Medical Director of the Provincial Forensic Pathology Unit in Toronto. These four join an already formidable group of clinicians and researchers on the

Committee. I would also like to recognize and thank Dr. Edward Etchells, who left the Patient Safety Review Committee this year after many years of dedicated service.

One of the realities of our system is that many, but not all, deaths related to fatal adverse events during medical care are reported to a coroner. In the coming months, the Office of the Chief Coroner will work with hospitals and health care providers with the aim of ensuring that all deaths in Ontario arising from a sentinel event are investigated by a coroner. All such cases represent opportunities for systemic improvements, and by enhancing their reporting, these opportunities can be acted upon.

This year, I was invited to join the Centre for Patient Safety at the University of Toronto as a core member. As Chair of the Patient Safety Review Committee and a representative of the Office of the Chief Coroner, this affiliation will further strengthen and formalize our academic mandate, and will foster further collaboration in the coming years aimed at improving the safety of health care in Ontario.

On behalf of the Committee, thank you for your interest in patient safety, and in the work of the Patient Safety Review Committee.



Dr. Dan Cass

Committee Chair and

Deputy Chief Coroner - Investigations

Committee Membership

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University of Toronto

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President and CEO
Institute for Safe Medication Practices
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History

In Ontario, the traditional means of disseminating information critical to patient safety that comes to light via coroners' investigations has been through the coroners' inquest process. Due to the complexity of such investigations however, an inquest (if held) may not take place for several years after the death in question. Further, it may be challenging for an inquest jury comprised of members of the lay public to fully grasp the complex medical details in such cases in order to make practical recommendations aimed at preventing a similar death in future.

To help expedite the review of coroners' cases with actual or perceived systemic patient safety implications, and where possible to make recommendations to prevent future similar deaths through more immediate actions, the Office of the Chief Coroner established the Patient Safety Review Committee in 2005.

Purpose

The purpose of the Patient Safety Review Committee (PSRC) is to assist the Office of the Chief Coroner in the investigation and review of healthcare-related deaths where system-based errors or issues appear to be a major factor. The PSRC develops recommendations aimed at the prevention of similar deaths in future, which are sent to the relevant agencies and organizations by the Chief Coroner for Ontario. The patient and public safety mandate of the Office of the Chief Coroner is derived from the *Coroners Act*:

Chief Coroner and duties

4. (1) The Lieutenant Governor in Council may appoint a coroner to be Chief Coroner for Ontario who shall,
 - (d) bring the findings and recommendations of coroners' investigations and coroners' juries to the attention of appropriate persons, agencies and ministries of government;

Disclosure to the public

18. (3) The Chief Coroner shall bring the findings and recommendations of a coroner's investigation, which may include personal information as defined in the *Freedom of Information and Protection of Privacy Act*, to the attention of the public, or any segment of the public, if the Chief Coroner reasonably believes that it is necessary in the interests of public safety to do so. 2009, c. 15, s. 10.

In this context, the use of the word "error" does not imply blame or responsibility on the part of any individual or organization. For the purposes of this committee, "error" is defined as a system design characteristic that either permits unintended adverse events to occur (latent error) or does not detect deviations from the intended path of care (active error). System design would

include not only the design of care processes, but also the management of access to care (such as delays in receiving care). The presence of such errors does not mean that an individual or organization should be assigned blame or responsibility for an unintended outcome. The mandate of the PSRC, like that of the Office of the Chief Coroner, is one of fact-finding, not fault-finding.

The aims and objectives of the Patient Safety Review Committee are:

1. To provide expert opinion about the cause and manner of death in health care-related cases where systems-based errors appear to be a major factor.
2. To assist coroners to improve the investigation of deaths within, or arising from, the health care system in which systems-based errors appear to have occurred.
3. To stimulate educational activities for professionals through identification of systemic problems, referral to appropriate agencies for action, collaboration with professional regulatory bodies and the dissemination of an annual report. Emphasis will be placed on speedy dissemination of information.
4. To provide expert evidence at inquests on request.
5. To conduct or promote research, where appropriate.
6. To undertake random or directed reviews when requested by the Chairperson.
7. To help identify the presence or absence of systemic issues, problems, gaps, or shortcomings of each case to facilitate appropriate recommendations for prevention.

Structure and Size

The Committee membership consists of respected practitioners from various disciplines related to health care. The membership is balanced to reflect wide and practicable geographical representation and representation from all levels of institutions, including teaching centres, to the extent possible. Other individuals with specialized knowledge or expertise are invited to participate in Committee reviews when required and at the discretion of the Chairperson.

In 2011, the Patient Safety Review Committee was comprised of thirteen members, including the Chairperson and Executive Lead. The Committee membership, and its balance, is reviewed regularly by the Chairperson and by the Chief Coroner, as requested.

Limitations

The Patient Safety Review Committee reviews coroners' cases that are referred by a Regional Supervising Coroner. These cases, and the issues arising from them, may be brought to the attention of the Regional Supervising Coroner through the investigating coroner, family of the deceased, or other organizations, agencies or individuals.

The Patient Safety Review Committee is advisory to the coroners' system and may make recommendations to the Chief Coroner through the Chairperson.

The consensus report of the Committee on a given case is limited by the data provided. Efforts are made to obtain all relevant data relating to the death.

The Committee's opinion is subject to the limits imposed on coroners' investigations and inquests by the *Coroners Act*.

Members of the Committee do not give opinions outside the coroners' system about cases the Committee has reviewed. In particular, members of the Committee will not act as experts at civil trials for cases that have been reviewed by the Committee.

Members do not participate in discussions or prepare reports of clinical cases where they might have a conflict of interest, whether personal or professional.

Medical records, draft and consensus reports and the minutes of the meetings are confidential documents. Redacted versions of case reports (i.e., with personal and organizational identifiers removed) are considered public documents and are available upon request from the Executive Lead. Meetings of the Committee are not open to the public.

Summary of Cases Reviewed in 2011

In 2011, the Patient Safety Review Committee reviewed twelve cases which resulted in 45 recommendations. Recommendations were distributed to agencies and organizations which were felt to be able to impact or affect implementation. These organizations were asked to respond within one year of the time the recommendations were received and indicate what action they had taken on these recommendations.

Case Reviews

Case 2011-01

Date of Death: May 20, 2010

Age: 90 years

OCC File number: 2010-6125

History:

The decedent was a 90-year-old female who presented to the Emergency Department (ED) of Hospital A (a large academic health sciences centre) on May 15, 2010, nine days after falling on the sidewalk when her foot became caught in a hole. After the fall, she experienced persistent chest pain (unlike angina), which led to further immobility and a reduction in her oral intake.

Her past medical history included: chronic obstructive pulmonary disease (COPD) with an approximately one pack-per-week smoking history; congestive heart failure; type II diabetes controlled by diet, prior myocardial infarction, chronic renal insufficiency and a previous carotid endarterectomy.

She was admitted to the Internal Medicine service on May 15, 2010, for pain management and further investigations. During her admission, pulmonary embolus was ruled out and she was diagnosed with chest wall pain due to the fall. On May 17, she was transferred to the Geriatrics service (which is physically located on the same unit as General Internal Medicine). On May 19, she was also diagnosed with pneumonia.

Early on May 20, her condition deteriorated and she was transferred to the “Step Up” unit (also within the same General Medicine floor). She was noted to have shortness of breath, oxygen desaturation and acute renal failure, believed to be related to volume depletion. (Her creatinine level had risen from 146 micromoles/L to 408 micromoles/L).

At 0935 hours, she was found to be unresponsive with a low respiratory rate and an oxygen saturation of 90% on an FiO₂ of 35%. At that time, a review of the orders and the medication administration record revealed that on May 17, when she was transferred to Geriatrics, her pain management had been changed; morphine was discontinued and hydromorphone (Dilaudid) was ordered. However, the morphine discontinuation order was not transcribed, and she continued to receive both narcotics. She was given naloxone 0.2 mg IV at 0955 hours and became awake and responsive, confirming the clinical suspicion of narcotic toxicity.

At 1030 hours, nursing notes indicate the patient to be “stable” with “no change in condition.” At 1100 hours, the nurse notes the decedent to have a decreased level of consciousness, respiratory rate and heart rate. At 1102 hours, she was found to be

unresponsive and in respiratory arrest. At that time, she had no heart sounds and her pupils were noted as being dilated. The physician was called at 1102 hours. As there was a Do Not Resuscitate (DNR) order, further resuscitation was not initiated and she was pronounced dead at 1105 hours.

Pain Management:

A summary of the narcotic orders, as well as the narcotic medications administered, is shown below:

Date	Narcotic Orders	Narcotic Administered
May 15	Morphine SR 15 mg po BID Morphine 5 mg po q 2-3 h prn	Morphine SR 15 mg x 1
May 16		Morphine SR 15 mg x 2 (1000 and 2200)
May 17	D/C Morphine SR Start Dilaudid (hydromorphone) 2mg po q6h (standing dose) and; Dilaudid 2mg po q4h prn	*Morphine SR 15 mg x 2 Dilaudid 2 mg x 2 (1800 and 2400)
May 18		*Morphine SR 15 mg x 2 Dilaudid 2 mg x 4 (0600, 1200, 1800, 2400)
May 19	D/C prn Morphine Hydromorph Contin (controlled-release hydromorphone) 3mg po TID	*Morphine SR 15 mg x 2 Dilaudid 2 mg x 2 (0600 and 1200) Hydromorph Contin 3 mg @ 2200
May 20	Narcotics held	? Hydromorph Contin 3 mg @ 0800 (not documented)

* - Morphine SR doses administered after discontinuation order

Post Mortem:

The post mortem examination revealed evidence of chronic heart and kidney disease, as well as evidence of pneumonia. Toxicology testing revealed the following:

Morphine 780 ng/ml (fatal reference > 200 ng/ml)
Hydromorphone 56ng/ml (fatal reference > 77 ng/ml)

The toxicology report indicates that, "Toxicity is dependent on tolerance. When combined would produce more pronounced CNS [central nervous system] depression."



Death was attributed to narcotic intoxication, with significant pneumonia, heart and kidney disease.

Cause and Manner of Death:

Cause of Death:

1a) Narcotic (morphine and hydromorphone) toxicity

Contributing factors:

2) Congestive heart failure; renal failure; pneumonia

Manner of Death: Accident

Discussion:

A number of issues in this case were identified by the Patient Safety Review Committee. These included both general issues (such as the role of care plans in the management of the frail elderly patient; medication reconciliation and medication management practices), and issues specific to this case.

In terms of specific issues, two in particular were identified which were felt to merit further attention. Naloxone was administered by bolus dose when signs of narcotic toxicity were identified. The decedent responded well to this treatment, and her clinical status improved dramatically. However, the half-life of naloxone (approximately 20-30 minutes) is much less than the half-lives of the narcotic drugs (morphine and hydromorphone) causing the decedent's respiratory and central nervous system depression. As such, when the effect of the naloxone wore off, the decedent became re-sedated, leading to her respiratory arrest and death. When naloxone is administered for reversal of the effects of narcotic toxicity, it is important for clinicians to appreciate the need for a naloxone infusion following bolus dose administration until such time as the effect of the narcotic medication(s) has worn off.

Once re-sedation occurred, the decedent began to again deteriorate in terms of her level of consciousness and her respiratory status. Because this was not recognized in time to prevent further progression of her symptoms, this resulted in a respiratory arrest followed by a cardiac arrest. As the decedent had a "DNR" order, further resuscitation was not attempted. The Committee felt that the DNR order may have affected the way in which the care team managed the decedent, and in particular, the decision-making around whether or not to proceed with further reversal of the narcotic medications. As the Committee has encountered previous cases in which the issue of DNR status in the setting of iatrogenic and reversible narcotic toxicity has been identified, the Committee felt that this issue merited further review by an expert in bioethics.

PSRC Recommendations:

To Hospital A:



1. The hospital should initiate a quality improvement process to ensure appropriate review and checks of transcription of physician orders.
2. The hospital should review the processes, documentation, and clinical practice related to narcotic ordering, dispensing and administration in this case.

To Hospital A, the Ontario Nurses Association (ONA), and the Registered Nurses Association of Ontario (RNAO):

3. Institutions should implement interdisciplinary care plans for the frail elderly aimed at prevention of known complications associated with hospital admission.

To Hospital A; RNAO; the Ontario Hospital Association (OHA); Accreditation Canada

4. Institutions should implement medication reconciliation when transfers to another service or unit take place.

To OHA; RNAO; Canadian Society of Hospital Pharmacists; College of Physicians and Surgeons of Ontario (CPSO):

5. Institutions should ensure that processes are in place such that, when a bolus dose(s) of naloxone is administered, there is consideration given to the initiation of a naloxone maintenance infusion when appropriate, depending on the half-life of the narcotic involved. Nurses, pharmacists and physicians should be reminded of the need for naloxone infusions in such situations.

The Chair of the Patient Safety Review Committee will prepare this case study for submission to the *CPSO Dialogue*.

(Chair's note – this case was published in the June, 2011 edition (Volume 7, issue 2) of CPSO Dialogue.)

In addition to the above, the Patient Safety Review Committee will seek the input of the Joint Centre for Bioethics at the University of Toronto regarding issues arising (in this case, and a previous case reviewed by the Committee) related to the management of potentially reversible conditions (whether arising from errors or not) in patients with DNR orders in place.

(Chair's note – This case, and another case with similar end-of-life issues, were reviewed by a bioethicist. The results of these reviews were presented to the PSRC, and will be the subject of a future peer-reviewed publication with an aim of educating care providers about the complex issues surrounding the management of reversible medical errors in the patient with a Do Not Resuscitate order in place.)

Case 2011-02

Date of Death: February 4, 2010

Age: 54 years

OCC File number: 2010-1319

History:

The decedent was a 54-year-old woman who died on February 4, 2010, of bleeding complications resulting from the attempted removal of a vena cava filter for the treatment of venous thromboembolic disease.

In February 2009, the decedent presented to the Emergency Department (ED) at Hospital A (a large, academic health sciences centre) with an ischemic left arm. She also gave a history of a transient ischemic attack (TIA) one week prior for which she presented to a different ED. Initial investigations revealed no obvious cardiac thrombus or vegetations, and no obvious right to left shunt. She had evidence of a dilated right ventricle and tricuspid regurgitation, which raised the possibility of previous pulmonary emboli.

These two events, occurring in short succession, raised the possibility of an embolic focus and/or a hypercoagulable disorder. The ischemic arm was felt to be due to an arterial embolus, and an embolectomy was performed under local anaesthesia. During attempts to achieve anticoagulation following the procedure, she was noted to be “relatively Coumadin [warfarin] resistant” and a Hematology consultation was obtained. Initial workup for hypercoagulable disorders was negative.

Further investigations demonstrated the presence of a patent foramen ovale, with evidence of a deep venous thrombosis to support the diagnosis of paradoxical embolus to the left arm.

The decedent subsequently experienced an embolic stroke while in hospital which underwent conversion to a hemorrhagic stroke secondary to anticoagulation. Computerized tomography (CT) of the chest confirmed the presence of multiple pulmonary emboli. An inferior vena cava (IVC) filter was placed, and the decedent’s oral contraceptive was stopped. She was maintained on sildenafil for significant pulmonary hypertension. She subsequently underwent percutaneous closure of the patent foramen ovale. Warfarin and ASA were prescribed.

The decedent was followed as an outpatient in a Pulmonary Hypertension clinic and Thrombosis clinic. Further investigations revealed evidence of chronic pulmonary thromboembolism without significant pulmonary hypertension. The plan was to wean the decedent off of the sildenafil over a two-month period starting in November 2009.

In December 2009, the decedent was seen in the Thrombosis Unit. The clinic note from this visit summarizes the case to date noting the improvement in the pulmonary hypertension on medication (which was being decreased), and the recent CT and angiography that showed

pulmonary artery webs secondary to previous emboli. The consultant planned to complete the hypercoagulable testing. The consultant's note states, "I think it is reasonable for her to have her IVC filter removed if everything else is stable." Follow up was planned for January 2010 with repeat ultrasounds to ensure there was no clot on the IVC filter.

In January 2010, the decedent was seen again in the Thrombosis Unit. Her hypercoagulable testing to date was negative (although it is noted that she still required protein C and protein S level testing when off warfarin). An ultrasound that day showed no clot in her deep venous system and IVC filter, and that the IVC was patent with no clots. The consultant suggested to the patient that the filter be removed, quoting a 10% chance of not being able to remove the filter. Due to her high risk state for thrombosis, the consultant planned a warfarin reversal program prior to the IVC filter removal accompanied by bridging with low molecular weight heparin. The plan was for long term anticoagulation therapy due to significant problems with clots and pulmonary hypertension. Warfarin was stopped on January 25, 2010.

On February 1, 2010, the decedent was admitted to Hospital A for IVC filter removal by Vascular Interventional Radiology. Her pre-op hemoglobin (from December 8, 2009) was 113. The procedure began at 1050 hours. The decedent was given sedation (50 micrograms fentanyl x 4 doses and 1 mg midazolam x 4 doses between 1050 and 1255 hours).

At 1300 hours, the decedent developed bradycardia (heart rate 32) with low blood pressure. Atropine 0.6 mg was given along with IV fluids running "wide open." It was identified that the IVC had been torn and an occlusion balloon was placed in the IVC at 1305 hours. Additional intravenous access lines were inserted in the right internal jugular (IJ) vein and left hand. Further occlusion balloons were inserted. The decedent's blood pressure and pulse stabilized. She was cross-matched for multiple units of packed red blood cells (pRBCs).

Over the next approximately two hours, several attempts were made to deflate the occlusion balloons, with each attempt resulting in a drop in blood pressure and the need to re-inflate the balloons. During this period, the decedent began to complain of nausea and severe abdominal pain, and was given 50 micrograms of fentanyl and 25 mg of diphenhydramine. The occlusion balloons were successfully deflated the final time at 1516 hours. Approximately 5 litres of normal saline and one unit of packed red blood cells (pRBCs) (started at 1530 hours) were administered during, and immediately following, the procedure.

The decedent was transferred from the Interventional Radiology suite to the Cardiovascular Intensive Care Unit (CVICU) at 1615 hours. She had a right IJ sheath in place. There was an order for her to receive three units pRBCs, as well as orders for bloodwork.

A chart note from Vascular Radiology on February 1, 2010 read, in part: "Despite numerous techniques we were unable to retrieve IVC filter. IVC perforation with subsequent venous pseudoaneurysm that remains patent even as pt. has stabilized. If pt. remains stable and you [follow up with] CT to assess patency of pseudoaneurysm, please do a C-phase (unenhanced) initially."

A Procedure Report by Vascular Radiology (dictated on February 4, 2010) indicated:

- Attempted IVC Filter Removal (Celect).
- Inferior Vena Cavagram showing no clot in the filter, some filter tilt with legs projecting beyond the confines of the IVC. This was felt to be in small venous sleeves (i.e. still within the vena cava).
- A description of the various techniques and snares used to try to remove the filter.
- The patient then developed pain, and the procedure was abandoned.
- Cavagram demonstrated contrast extravasation indicative of iatrogenic IVC injury. At this point, the patient went hypotensive.
- An Atlas 18 mm diameter x 40 mm long balloon was inflated under low pressure to tamponade the IVC inferior to the filter. The second RIJ had been removed. To have more access, a right femoral vein 8 Fr sheath was placed.
- A 16 mm diameter x 40 mm Atlas balloon was placed and used for injection of contrast. This showed persistent extravasation. A portion of the balloon and guidewire distally was extraluminal as well.
- The balloon from the RIJ was deflated and repositioned more superiorly where it was all intracaval. The inferior 16 mm balloon was inflated. Initial inflation for 10 minutes, followed by 10 minute observation - the patient then became hypotensive with abdominal pain.
- Contrast injection showed continued extravasation in what appeared to be a venous pseudoaneurysm. The 16 mm balloon was reinflated for 30 minutes. After deflation, there was still extraluminal contrast in what was thought to be a venous pseudoaneurysm. The patient remained stable.
- The balloons and wire were removed. The right femoral access was removed. The right internal jugular sheath was sutured in place.

The procedure report goes on to state: “The conclusion is that the filter was not removed and that some of the legs are reoriented. There has been iatrogenic injury to the IVC. The patient was unstable for some time, but improved prior to leaving the department. The vascular surgery team is aware and has assumed management responsibilities for this patient.”

It is important to reiterate that this Procedure Report was not dictated until February 4 (the day following the decedent’s discharge; and the day of her death) and was not available to those providing care to the decedent during her admission.

A consultation note by Vascular Surgery from February 1, 2010 read, in part:

Caval Injury - For removal of IVC filter today in VIR (Vascular Interventional Radiology). Difficult procedure; completion angiogram showed extravasation IVC below renals. Patient became hypotensive; balloon inflated in Vena Cava – stabilized. Balloons x 10 min → unstable; Balloon x 30 min → stable. Angio final showed some extravasation vs pseudoaneurysm.

[On examination]: 90/60 P95 98% [room air] Tender RLQ RUQ no peritonitis no visible hematoma

[Assessment / Plan]: 1 needs aggressive resuscitation, pRBCs and fluid
2 if has continued runs of instability will need OR intervention
3 Thromb [Thrombosis service] to see.

On February 2, the decedent received oral and intravenous narcotic medications for pain. She was re-started on warfarin, as well as an infusion of IV heparin. Bloodwork, including CBC, was ordered. Her hemoglobin was noted to be 124, and she was noted to be complaining of abdominal pain. Her vital signs were documented at 1115 hours as being pulse 90 and blood pressure 140/80.

On February 3, the IV heparin was stopped and low molecular weight heparin (LMWH) was started. Oral narcotics were continued. Her hemoglobin and INR results were:

Date	Time	Hb	INR
08 Dec 2009		113	
01 Feb 2010	1323 hours	92	1.24
01 Feb 2010	1452 hours	71	
01 Feb 2010	1925 hours	125	1.29
01 Feb 2010	2320 hours	128	
02 Feb 2010	0334 hours	124	1.14
02 Feb 2010	1700 hours	110	
03 Feb 2010	0630 hours	106	1.1

On February 3, the Vascular Surgeon indicated that the hemoglobin was stable and that the patient may be discharged.

A nursing note from 1240 hours February 3 stated, “pt. taken for a walk, feels nauseous and weak, returned to bed, Dr. A [Vascular] notified, no new orders, patient is still for discharge home.” A further nursing note at 1400 hours on February 3 stated, “discharged home, denies having pain.”

Discharge instructions, as documented in the Vascular Surgery Discharge Note, were:

- Fragmin [LMWH] x5 days while Coumadin is given and INR to be checked on Saturday.

- Follow-up appointment with vascular surgeon on 26 Feb 2010.
- Call the Vascular surgeon if any concerns.

According to the Coroner's Investigation Statement (CIS), family members of the decedent stated that they felt that she had not done well after the procedure, and that prior to discharge on February 3, she had been complaining of feeling very weak and unwell.

The day after discharge (February 4, 2010), while at home, she went into the bathroom for a shower at about noon and her husband discovered her collapsed a few minutes later. Cardiopulmonary resuscitation (CPR) was started and 911 was called. Emergency personnel noted the bruising at various IV sites and on the abdomen, vomitus in the airway, and fixed and dilated pupils. They attempted resuscitation and transported her to the ED at Hospital B where a pulse was detected and further resuscitation attempted. According to the CIS, "Unfortunately as Ms. X's blood pressure came up, she started to bleed from the injury to the vena cava again and she was pronounced dead in the Emergency Department" at Hospital B.

Post Mortem:

- 500 ml serosanguinous fluid on right pleural cavity;
- 500 ml serosanguinous fluid in peritoneal cavity;
- Massive retroperitoneal hematoma extending down retroperitoneum to pelvic cavity, approximately 1.5 - 1.8 litres of clotted blood;
- Inferior vena cava in place partially distorted inferior vena caval umbrella (filter) associated with laceration of mid segment of inferior vena cava and massive retroperitoneal hemorrhage. Post traumatic recent intravenous thrombosis of distal segment of inferior vena cava and extending into both right and left iliac veins;
- Intestines extensive dissecting hemorrhages noted at mesenteric root to small bowel.

Cause and Manner of Death:

Cause of Death:

- 1a) Massive acute retroperitoneal hemorrhage; due to
- 1b) Iatrogenic laceration of inferior vena cava; due to
- 1c) Attempted for removal of inferior vena cava filter; for the treatment of
- 1d) History of multiple pulmonary emboli.

Manner of Death: Natural

Discussion:

An Interventional Radiologist with experience with the insertion, management and removal of IVC filters was contracted to review the case and to provide their opinion and recommendations. The comments from the expert reviewer are summarized below:

Indication for filter placement in February 2009: Complication of anticoagulation (hemorrhagic conversion of embolic stroke) during treatment of pulmonary embolus. This is a recognized accepted indication.

Follow up of thrombosis / pulmonary hypertension throughout 2009: Multiple clinic visits document her improvement on medication for pulmonary hypertension. She remained on anticoagulant therapy (warfarin) although INR from Dec 2009 was sub-therapeutic. Eventually the thrombosis specialist suggested that the IVC filter be removed.

Removal of IVC filter: The successful retrieval of any IVC filter is promoted by good centering of the filter on placement within the lumen of the IVC so that the apex is available for grasping at the time of removal. Unfortunately filters do not remain stationary. The IVC is a dynamic tube with changes in diameter, pressure and flow, all of which contribute to movement of the filter device.

All of the available devices have been noted to penetrate the wall of the IVC. This has been defined by some authors as seeing the leg or arm of the filter extend beyond the confines of the IVC by 3 mm or more. There has been some debate in the literature whether all extension beyond the wall represents true penetration or whether it is IVC wall tenting or perhaps entry into a small vein. This has been seen with filters dating back to the initial models, and has been thought to be rarely symptomatic (0.3%). It can cause significant problems like chronic pain syndrome, or pseudoaneurysm of the aorta or renal artery etc. It has not been noted to be a contraindication to removal of a retrievable filter.

Studies involving series CT imaging have demonstrated that tilting of IVC filters and penetration of the wall of the IVC occurs within the first 3 – 4 months after insertion.

There is only one study with Level 1 evidence (i.e. prospective randomized data), Decousis et al, NEJM 1999, that has resulted in the perception that all filters should be removed. This paper studied patients with types of filters which are no longer in use. The conclusions of this study - that filters were protective against pulmonary embolus in the initial 3-4 months, but lead to increased incidence of deep venous thrombosis in the long term - have provided the impetus for removal of all of these devices.

This has lead to some innovative and daring techniques for removal (including the loop snare technique utilized in this patient). Reports of these methods suggest that the technique was applied in patients when the usual methods of snare or recovery cone were not successful. The procedure times recorded for these aggressive techniques were between 5 and 60 minutes. The procedure time for this patient was 2 hours and 35 minutes until the vasovagal episode followed by angiogram confirming the torn IVC.

One of the ongoing concerns of the national and international bodies about IVC filters is now patient follow up. In Canada, the devices are placed by Interventional Radiology when the patient is an inpatient. The report of placement will indicate that removal is possible via Interventional Radiology, but there is then a disconnect that occurs in arranging that procedure. The decision that it is time to remove the filter is not the Interventional Radiologists to make. That properly lies with the Hematology / Respiriology team as was

seen in this case. Whether that decision could be made sooner in this patient is doubtful. As above, there is no guarantee that the device will lie in good position for removal even after a few months. There are however, large numbers of patients who do not come for removal. Even with a regular reminder to the physician and patient, the attempted retrieval rate is only 30% in some series.

It is not clear from the record that there was effective communication between the services involved in the decedent's care as to the seriousness of the complication. The typed Radiology Procedure Report is clear, but would only be available after February 5 having been dictated on February 4, 2010. It indicates that there is clearly a laceration of the IVC large enough that an 18 mm balloon was partly outside the wall of the IVC. The emergency treatment using balloon tamponade is depending on thrombosis of either the IVC itself or of the retroperitoneal clot to tamponade this hole. A covered stent was not placed and no mention of consideration of this device was made. The seriousness of the leak seen on angiography does not seem to be reflected in the chart notes following up the patient over the next few days.

Although the hand written preliminary Interventional Radiology report suggests that CT be done, there is no order for this examination and it was never performed. Since the patient originated in the Imaging Department, it would have been expedient to move directly to CT once the patient had stabilized and blood was hung. This may have provided direct visual evidence to determine / confirm that surgical repair was necessary if the size of the retroperitoneal hemorrhage was known. The Interventional Radiologist should feel that he/she can order and arrange this CT emergently.

With the hemodilution of 5.3 litres of normal saline, the service seems to have been happy with a Hgb of 128 after 4 units of pRBCs. The declining hemoglobin during the two day admission with a discharge Hgb of 106 seems to have been ignored. This should have suggested ongoing blood loss since all IVs had been on TKVO ["to keep vein open"], so dilution would not play a role. I do not see any hematocrit results to help in that regard.

The patient is then restarted within 24 hours on the anticoagulation with IV Heparin, warfarin, ASA and switched to Fragmin on discharge. There is some suggestion that the patient was not well at the time of discharge and as noted had dropped her Hgb, had some abdominal pain, was still receiving oxycodone for pain.

Finally, it is unclear how much the physicians at Hospital B knew about the patient's most recent history to aid them in their resuscitation when the patient arrived.

Recommendations from Expert Reviewer:

1. Encourage the Interventional Radiologist involved to publish this case. The series of advanced techniques for removal of filters published to date indicate no mortality.
2. Improve communication between services when complications arise.

3. Interventional Radiologists should arrange further investigations on patients who are under their care for procedures if they feel it is required.
4. Interventional Radiologists should remain in the care loop of this type of patient. They are the ones who saw the problem occur.
5. Trending charts of Hgb are presumably available online at Hospital A. This should have been reviewed prior to discharge.
6. A physician, perhaps an Interventional Radiologist, should maintain a record and contact patients and their physicians following placement of IVC filters to inquire if it is time for removal. Earlier retrieval is still easier than late. This may result in a lower failed retrieval rate.
7. A new prospective study of the current filters would be ideal, but the devices are changed frequently.
8. No mention of bridging low molecular weight heparin on Interventional Radiology documents, only notes that warfarin was held. This needs to be asked since there are not routine tests for the effects of LMWH on anticoagulation and clinical services often send patients for procedures feeling that being anticoagulated with these drugs is acceptable since the PTT and INR are normal.

PSRC Recommendations:

To the Diagnostic Imaging Section of the Ontario Medical Association (OMA):

1. When complications occur during an interventional radiology procedure:
 - The Interventional Radiologist (IR) should initiate / obtain appropriate investigations and consultations;
 - Direct communication should take place between the IR and any service assuming the responsibility of care for the patient to ensure that the accepting service is fully aware of the circumstances and severity of the complication.
2. Whenever a device such as an IVC filter is inserted, the IR (in collaboration with the referring physician and/or the patient's primary care provider) should take responsibility for following up these patients to ensure that removal occurs as appropriate.

To Hospital A:

3. The hospital should review the processes and the clinical care provided in the case; particularly the decision-making around investigation, further stabilization and decision to discharge.
4. The Hospital should report this case to Health Canada, if it has not already done so.

5. The Hospital should encourage the clinicians involved in the care of the decedent to seek publication of the details of this complication in the peer-reviewed literature. If the authors felt it to be appropriate, part of such a publication could include a recommendation for further research in this area.

Case 2011-03

Date of Death: April 25, 2010

Age: 19 years

OCC File number: 2010-5628

History:

The decedent was a 19-year-old woman with a history of hemoglobin SS disease on hydroxyurea therapy (although there is some question as to her compliance with this medication). During her childhood, she was followed at Hospital A (a tertiary / quaternary care pediatric hospital) for her Sickle Cell disease.

Her past history, as summarized in a note from Hospital A, included:

- avascular necrosis right hip (developed jaw pain and stopped bisphosphonate August 2008);
- moderate airflow obstruction identified by pulmonary function tests (underlying diagnosis of sickle cell with anemia not corrected);
- normal sleep study 2005;
- no evidence of cardiac compromise.

Around the time of her 18th birthday, the decedent was referred by Hospital A to Hospital B (a large, adult academic health science centre located near Hospital A) for further follow up and management. It is not clear from the medical records whether the decedent was ever assessed or treated at Hospital B.

On the morning of April 22, 2010, the decedent was transferred by ambulance from home to Hospital C (a large community hospital near her home) with pain that she described as more severe than her typical sickle crisis pain. Her pain was described as “all over”, especially in the left knee and right elbow.

Most of that day was spent in the Emergency Department (ED). She was assessed by the ED physician who attempted to stabilize her pain. She was noted to be afebrile with mild tachycardia and borderline low blood pressure. A standardized pre-printed order sheet was completed for the “Emergency room management of adult patients with a sickle crisis.”

Her long-standing sickle cell history complicated the establishment of vascular access. This precluded easily obtaining blood work, which is recognized as an essential component of sickle crisis management. Analgesics (morphine and hydromorphone) were provided

subcutaneously until a peripheral intravenous of the central circulation (PICC) line was established at 1615 hours. Non-narcotic analgesics (ibuprofen) were also used.

She was seen by a Hematologist in the early part of the afternoon and admitted to hospital. She was moved from the ED to a medical floor. Efforts to control her pain, as well as intravenous fluid resuscitation, were continued. In the early evening, her vital signs suggested that her status was improving as her heart rate and blood pressure seemed to be more appropriate for her age.

Laboratory information showed that she was moderately anemic, although not different from what was her historical norm. She appeared to have a white blood cell stress response to the sickle crisis, and had objective signs of sickle crisis with morphologic changes as well as biochemical indicators of sickle activity. Throughout the day, it appeared from the clinical notes that some of the interactions between the patient/family and various caregivers may not have been smoothly harmonious.

The dosage and timing of analgesic medications administered on April 22 were as follows:

- hydromorphone 2 mg SC at 1055 hours
- morphine 4 mg SC at 1150 hours
- ibuprofen PO 400 mg at 1255 hours
- morphine 4 mg SC at 1300 hours
- morphine 4 mg SC at 1430 hours
- hydromorphone 0.5 mg at 1536 hours SC
- hydromorphone 1 mg IV at 1755 hours
- hydromorphone 1 mg IV at 1915 hours
- hydromorphone 1 mg IV at 2030 hours
- ibuprofen PO 400 mg at 2145 hours
- hydromorphone 1 mg IV at 2300 hours

Totals:

Hydromorphone: 2.5 mg SC + 4 mg IV = 6.5 mg total

Morphine: 12 mg SC

On April 23, the clinical notes suggested some improvement and the patient began to mobilize. There was variable pain control. The laboratory findings supported a component of stabilization. There was no sign of acidosis as her bicarbonate level was in the upper range of normal. She appeared to be adequately hydrated as she continued to void well.

The dosage and timing of analgesic medication administered on April 23 were as follows:

- hydromorphone 1 mg IV at 0005 hours
- hydromorphone 1 mg IV at 0145 hours
- hydromorphone 1 mg IV at 0335 hours
- hydromorphone 1 mg IV at 0520 hours
- hydromorphone 1 mg IV at 0745 hours
- hydromorphone 1 mg IV at 0950 hours

- hydromorphone 1 mg IV at 1125 hours
- hydromorphone 3 mg IV at 1200 hours
- hydromorphone 1.5 mg IV at 1430 hours
- hydromorphone 3 mg IV at 1600 hours
- hydromorphone 3 mg IV at 2000 hours
- hydromorphone 1.5 mg IV at 2210 hours
- hydromorphone 3 mg IV at 2359 hours

Total:

Hydromorphone: 22 mg IV

On April 24, there was a deterioration in the decedent's status with the development of a fever (maximum recorded temperature = 38.7°C), and an increased heart rate (as high as 156/minute at one point). The origin of the fever was not obvious and urinalysis was negative. A broad spectrum antibiotic was started by mouth.

The decedent slept most of the day. Shallow breathing was questioned by the physician although the decedent did not complain of any pleuritic pain or cough. Although not consistently reported, the respiration rate was only slightly increased at 20 in the early evening. With minimal oxygen supplementation however, she maintained excellent oxygen saturation throughout the day.

Laboratory tests from earlier in the day showed that the hemoglobin continued to decrease. An improvement in her leukocytosis seen the previous day was now reversed with an increase in WBC. There were no signs of acidosis as the bicarbonate remained normal. It would seem that she continued to be well hydrated as she was voiding well.

Vital signs done at 2230 hours showed a temperature of 38.2 C, heart rate of 156/min, blood pressure of 109/66 mm Hg, respirations of 20/min. Her pain was described as "10/10." She was noted to be drowsy for much of the evening and an anti-nauseant was not given because of this.

At 2359 hours she refused her routine hydromorphone dose.

The dosage and timing of analgesic medication administered on April 24 were as follows:

- hydromorphone 1.5 mg at 0252 hours
- hydromorphone 3 mg IV at 0400 hours
- hydromorphone [?dose - MAR record not clear] at 0605 hours
- hydromorphone 3 mg at 0800 hours
- Tylenol 3 tablets at 1045 hours
- hydromorphone 4 mg at 1200 hours
- hydromorphone 4 mg at 1600 hours
- hydromorphone 4 mg at 2000 hours
- Tylenol 3 tablets at 2030 hours
- [hydromorphone refused at 2359 hours]

Totals:

Hydromorphone: 19.5 mg IV (plus 0605h dose - ?3mg) ~ 22.5 mg IV

Codeine: 120 mg PO

Shortly after midnight on April 25, she was given water. At this time, she was noted to be very drowsy. At 0100 hours, she was given a dose of diphenhydramine at her bedside. At 0203 hours, she was able to get out of bed with assistance and use the commode. She indicated that her nausea was improved, and that she wanted to sleep. She was given her hydromorphone dose (4 mg IV) at 0200 hours. At 0425 hours, she was noted to be “sleeping comfortably.” At no time over the course of the hours prior to her death was she noted to have respiratory distress or desaturation.

She was found vital signs absent at approximately 0600 hours and resuscitative efforts were unsuccessful.

Post Mortem:

A post mortem examination was performed. The preliminary examination did not reveal a cause of death. Subsequent testing revealed evidence of a right ventricular infarction due to sickle cell crisis to which the cause of death was initially attributed.

Subsequently, toxicology testing was performed. Testing of the hospital admission blood sample was negative. Testing of the femoral blood sample obtained at post mortem revealed a hydromorphone level of greater than 200 ng/mL (with a value of greater than > 77 ng/mL being potentially fatal, particularly in an opiate-naïve individual.).

The pathologist gave the cause of death as Acute Hydromorphone Toxicity.

Discussion:

The Regional Supervising Coroner (RSC) responsible for the case reviewed the clinical notes in detail. The RSC identified a number of areas of potential concern, including perceived gaps in terms of the dispensing of narcotics to sickle cell patients, monitoring for signs of narcotic toxicity, and monitoring the effectiveness of pain management using objective measures. As a result of these concerns, the RSC referred the case for review by the Patient Safety Review Committee.

An expert review of this case by a community-based Hematologist, whose practice includes sickle cell patients, was obtained. The Hematologist was asked to comment on the care provided and to identify any potential recommendations aimed at preventing deaths in similar circumstances in future.

NB: It should be noted that the expert’s review was conducted based on the medical records as provided from Hospital C, as well as the initial post mortem and toxicology reports. The expert was not provided with the additional information



obtained later through further investigation – namely: full quantitative toxicology testing on all samples; independent review of clinical, pathological and toxicological findings; and direct information from the investigating coroner with respect to the clinical condition of the decedent in the hours immediately preceding her death (see “Further Investigation” below).

Expert review:

An excerpt of the expert’s comments is included below:

My global sense of this case is that the initial management (April 22) was very appropriate. Every effort was made to establish symptom control (using a standard pre-printed order sheet in the ED) and to reduce the sickle crisis process.

The second day (April 23) appears to show variable symptom management and some objective signs of improvement.

On the third day (April 24), some significant changes take place in the health status that may not have been fully appreciated by all of the people involved in her care.

There are some components of the record that suggest some aspects of this person's health were not obvious to her current caregivers.

- *She had been at Hospital C a year earlier and yet no mention is made whether or not her hemoglobin was significantly different from that visit. The summary note from Hospital A does provide some sense of her typical hemoglobin range.*
- *As noted in the Coroner’s Investigation Statement (CIS), there were no blood cultures drawn and a chest x-ray wasn’t done. While perhaps not so obvious on admission, these might have been useful with the development of respiratory changes and a fever*
- *It is concerning that a heart rate of 156 (April 24) was not addressed by contacting the on-call physician*

Questions have been raised about pain management / narcotic use in this case. In general, I don't get the sense that at any time the dosages were inappropriately high. I think it would have been reasonable to increase the frequency of vital sign monitoring with the use of narcotics in a case like this. Pain scales were noted by the nurses and I think had the vital sign frequency been more often this would have been noted. While noted in the emergency room record, the use of non-narcotic medications (which is often helpful) were not used routinely here after admission.

I note that there was no standard "Medicine Admission Orders." Such orders might have helped the care team to think about more frequent monitoring. The availability of a Pain Management Consultation Service (sometimes including a Clinical Nurse Specialist in pain management) can be very helpful in the management of sickle cell patients.

A question is raised about the changes in hemoglobin. A hemoglobin of 78 g/L in most young people would not mandate transfusion and would be a function of the physiologic status. I don't think the transfusion was necessarily indicated here.

The question here as well is about sickle cell anemia / crisis and sudden death. From reviewing the literature, it would appear that pulmonary and cardiac etiologies probably account for the majority of the sudden deaths in sickle cell crisis patients. I note that the autopsy findings showed congestion and edema in the lungs, but curiously no sickle cells; while there were such findings in the heart and brain. I'm not sure if one can interpret postmortem sickle findings as necessarily clinically relevant and an explanation for mortality. However, the literature seems to be somewhat devoid of reports of toxic drug overdose as a notable cause of sudden death.

My impression of this unfortunate case is that this young woman had a sudden death due to a sickle crisis-related cardiac event which may have been provoked either by infection or more remotely thromboembolism although the latter was not obvious on postmortem examination. While more attention might be paid to narcotic administration and assessment I do not think this young woman died of a hydromorphone overdose.

Further Investigation:

The Patient Safety Review Committee had difficulty reconciling the discrepancy between the conclusions of the expert reviewer and the results of the toxicology testing. A plan was developed for further investigation of this case. This included:

- Testing of all hospital blood samples, as well as re-testing of post-mortem samples by the Centre for Forensic Sciences in order to ensure that the toxicology results were accurate;
- Root cause analysis to be conducted by the hospital (assisted by the Institute for Safe Medication Practice and a clinical pharmacologist) in order to better understand the circumstances of the narcotic administration and to identify any potential sources of medication error or other factors which may have resulted in hydromorphone toxicity in this case;
- Review of all clinical, pathologic and toxicologic information by a second forensic pathologist.

A synopsis of the results of these efforts is shown below.

Toxicology

- Hospital blood samples revealed no evidence of narcotic toxicity ante-mortem
- Hydromorphone levels were below the limit of detection (<3.13 ng/mL) on the samples drawn April 22nd ~1700h and April 23rd ~0600h.
 - Hydromorphone level <13 ng/mL on sample drawn April 24th ~0600h.
- Post-mortem samples revealed clearly toxic hydromorphone levels
 - Femoral blood – 310 ng/mL
 - Heart blood – 140 ng/mL
 - Ratio in heart to femoral blood = 0,46; within the accepted range for post-mortem redistribution of hydromorphone

Hospital Review

- Explored possibilities including dosing error, interacting / potentiating agents, and dose accumulation in the decedent from factors not taken into account when titrating dose
- Medications dispensed via automated medication dispensing machine
 - Records do not support larger dose being taken in error
 - No evidence to support administration of medication intended for another patient
 - Some evidence of vials of hydromorphone, containing larger doses than required for the dose to be administered, being removed from dispensing machine – not clear whether this was temporally or causally related to the death
- No evidence of administration of another potentiating substance (such as hydrocodone); not supported by toxicology testing.

Review of Pathological Findings

A review of the macroscopic and microscopic findings, as well as the toxicology testing results, was conducted by a second forensic pathologist. This revealed post mortem findings of sickle cell anemia, pulmonary edema with frothy fluid in airways, patchy acute infarction of the right ventricle, and mild to moderate pulmonary fat microembolism (the latter felt to be due to bone infarction). The cardiac findings and fat emboli were felt to be sub-lethal complications of sickle cell disease. The second pathologist concluded that, “the best interpretation of the clinicopathologic and toxicologic findings is: Hydromorphone Intoxication during therapy for Sickle Cell Crisis.”

Cause and Manner of Death:

Cause of death:

1a) Hydromorphone Intoxication during therapy for Sickle Cell Crisis

Manner of Death:

Accident

PSRC Recommendations:

To Hospital C, the Ontario Hospital Association, and the Ontario Medical Association Section on Hemaology:

1. Institutions should initiate the use of standard admission order sheets for sickle cell patients. Such standard order sheets could include: investigations; medication dosage and administration; monitoring of patients receiving narcotics; triggers to contact MD, etc.
2. Clinicians caring for sickle cell patients should consider the use of Pain Service / Clinical Nurse Specialists to assist in management of sickle patients

Case 2011-04

Date of Death: October 31, 2010

Age: 61 years

OCC File number: 2010-13909

History:

The decedent was a 61-year-old male who was brought to hospital by ambulance on October 25, 2010 after spending approximately 24 hours in a bus shelter. He was noted to be tremulous, confused, and febrile. His past medical history included: renal transplantation, coronary artery disease, alcohol abuse, intravenous (IV) drug use, depression, hypertension and Hepatitis C.

Upon admission, the lab results were: blood cultures positive for *Staphylococcus aureus*, creatinine 141 $\mu\text{mol/L}$ (normal range 44-106) and potassium 4.1 mmol/L (3.5-5.0).

Following evaluation by the Internal Medicine service, the decedent was admitted to hospital with the following diagnoses:

1. Ethanol withdrawal;
2. Confusion;
3. Impaired liver function;
4. Elevated white blood cell (WBC) count; and
5. Possible acute on chronic renal failure.

Summary of Events in Hospital:

A thorough admission history was documented on October 25, 2010 and extensive, detailed daily notes were found in the medical chart. A daily plan was clearly articulated by the medicine team on October 25, 26, 27 and 29, 2010.

The decedent was maintained on normal saline infusion throughout his admission. Initially, the rate was 125 mL/hr with no added KCl (potassium chloride). This was reduced to 75cc/hr with no added KCl on October 25 and 26. The KCl appears to have been added on October 27-28 when lab tests showed that the decedent's serum K⁺ was dropping, with a low of 3.5 noted on October 27.

A "Do Not Resuscitate" (DNR) order was written on October 27, 2010.

Complete blood count (CBC), electrolytes and renal function tests were ordered daily until October 29, at which time a standing order was written to measure "CBC, lytes, creatinine, urea, liver enzymes M/W/F [every Monday, Wednesday and Friday]."

An addendum note from one of the medical teams on October 29 indicated a creatinine of 150 and urea of 28.3. These results were listed in the note under lab results (i.e. in handwriting), but not specifically addressed in the notes, assessment or plan.

On Friday, October 29, 2010 at 2045 hours, the physician's orders indicated that CBC and creatinine were ordered for Saturday morning.

On Saturday October 30, 2010 at 1200 hours, a telephoned physician's order was made to continue IV normal saline. Also on that day, a physician note (with no time documented) indicated a creatinine level of 182 and blood urea nitrogen (BUN) level of 32.2. There were no electrolyte levels from the lab and no electrolyte values were listed in the physician's note. The plan was documented as: "plastics consult (hands), continue IV fluids, reassess in a.m."

On October 30, 2010 at 2102 hours, the nursing notes indicated that the decedent was not voiding and that a bladder scan showed 600 mL retention. The doctor on call was notified and ordered an in-and-out catheter. This was done and only 300 mL of concentrated urine was drained. The decedent stated that he was "still feeling full." A bladder scan showed 600 mL so the in-and-out catheter was done again, still with no output.

At 2130 hours, the physician's orders were to insert a Foley catheter to straight drainage. Nurse's notes at this time indicated that the Foley catheter was inserted as per the doctor's instructions and still there was no drainage. The nurses continued to monitor the decedent.

At 2145 hours, nursing notes indicated that there was still no output and that the decedent was complaining of abdominal pain. The doctor was notified by telephone. There were no new orders and the instructions were to continue monitoring and to have a plastic surgeon in to see the decedent regarding his hand.

There was a change of Duty Nurse at approximately 2330 hours on October 30, 2010. At 0100 hours on October 31, the nurse's notes indicated that the catheter was in situ and was draining (although no amount was specified).

At 0300 hours on October 31, 2010, the nursing notes indicated that there were no signs of restlessness or discomfort.

By 0500 hours on October 31, 2010, the nursing notes indicated that there was scant urine noted on the Foley catheter. The doctor was paged and at 0530 hours, a bolus order was obtained. At 0530 hours, the physician's orders were to "give 500cc bolus with 20 KCL x 1 to run for 2 hours, then resume NS with 20KCl @ 75cc/hr."

Again on October 31 (at no specified time), the Significant Events Form detailed the events as follows:

- 0845 hours – the decedent was restless with a BP of 85/45 and pulse of 56. O₂ saturation could not be read. O₂ by nasal prongs was applied.
- 0845 hours – the Yellow team was paged and biochemistry phoned reporting that K⁺ = 6.9. The doctor was paged again.

- 0900 hours – the decedent was non responsive and they were unable to get a BP.
- 0910 – the Rapid Response Team was paged and arrived.
- 0915 hours - Yellow team paged again.

The patient was pronounced dead at 0925 hours on October 31, 2010.

A later note on October 31 from the on-call resident (time not indicated) was listed in the record's Progress Notes section. The note was written after the patient's death, and stated that the decedent had been complaining of abdominal pain in the night, but was found sleeping comfortably when seen. Comment is made about no blood having been drawn the day before, but that all potassium levels prior had been low normal. The note also stated that the resident was called to assess the patient's dehydration (i.e. dry membranes, chapped lips). The note also described a 500mL bolus of normal saline ordered + 20 mmol KCL to run over two hours, after checking last K+ value of 4.8. The patient was described as stable in the morning. The note also stated that bloodwork results showing K+ were not available until after the patient's death (the level that morning, in fact, was later found to be elevated at K+=6.9). In the note, the resident physician lists cause of death due to multiple contributing factors.

On October 31, 2010, at 1000 hours, an entry in the Progress Notes section, following the note by the doctor, described being called to the arrest, recounts the history of the patient's demise from the RN (i.e. patient alert at 0800 hours, decreasing level of consciousness at 0845 hours, agonal respirations, dropping BP, etc.). The note goes on to say that the team was paged at 0915 hours, though no mention of reported pages at 0845 hours and 0900 hours that went unanswered.

In their notes written subsequent to the decedent's death, both the on-call resident and Yellow team resident remark "unable to check lytes on Oct 30" – however in reviewing orders, no electrolytes had been ordered for October 30.

A table summarizing electrolyte levels throughout the decedent's stay is produced below:

Date	Time	Hg (130-190)	Cr (3.0-7.0)	Urea (44-106)	K (3.5-5.5)
25 Oct 2010	0905	150	141	25.1	4.1
26 Oct 2010	0625	99	124	24.6	4.1
27 Oct 2010	0600	105	109	20.6	3.5
28 Oct 2010	0600	111			
28 Oct 2010	0800		122	23.3	3.7
29 Oct 2010	1200	123	150	28.3	4.8
30 Oct 2010 (Sat)	0700	128	182	32.2	*none*
31 Oct 2010 (Sun)	0720	121	235	38.3	6.9



Discussion:

The decedent was known to have some degree of renal failure, noted on admission, and was known to have a climbing creatinine level in the days leading to his demise. It was clear that urine production was dwindling on October 30 and 31. Serum electrolytes were not ordered to be routinely tested on October 30 and therefore not available for review when the patient was first assessed by the on-call resident at 1200 hours on October 30. While the rising creatinine was seen in the resident note written at 1200 hours on October 30, it was not identified as a problem. No electrolytes were subsequently ordered during October 30 or early in the morning of October 31.

When the “in and out” catheterization was ordered, little urine was found and subsequent urine output was described as scant to nil. Concern about the lack of urine output was noted by the nurse on duty, and the indicated response from the on-call physician to this was to “monitor.”

Nursing notes from October 31, 2010 at 0100 hours note that a Foley catheter was “in situ and draining” – but no amounts of output were described until 0500 hours when the word “scant” was used. It seems clear from the record that the patient, already known to have some degree of renal failure on admission, was suffering from further failure of his renal system.

The notes written after the decedent’s death by both resident physicians pointed out the lack of serum potassium levels in the last 48 hours of the decedent’s life though neither addressed the rising creatinine or well-documented and identified condition of renal failure. The subsequent IV bolus with added potassium increased the presumed already-rising serum potassium, likely triggering events leading to the death of the patient. The decedent suffered from some degree of renal failure and the addition of potassium to the intravenous fluids ordered early in the morning of October 31 (which were also used for the fluid bolus) likely contributed to the cardiac arrest that occurred later that morning.

In reviewing the notes and orders sections of the decedent’s chart, there appeared to be either a lack of awareness on the part of the care team of the impaired renal status of the patient (as was indicated by the history of renal failure, the minimal urine output, or the rising trend in serum creatinine), or possibly of the potential harm of infusing potassium in a patient with known renal failure. It is unclear if this was due to deficiencies in knowledge on the part of one or more members of the team, or whether this related to other factors that were not identified.

It is not clear from the notes to what degree the junior resident involved in this case was supervised. Workload, fatigue, other events competing for attention, or other such issues may be relevant which cannot be identified through review of the chart. Lack of responsiveness of the on-call team to urgent pages in the hour leading up to the patient’s death (as was documented in the nursing notes) was a concern, although there is no context in which to interpret this (i.e. were the pagers working, were there other emergencies, etc.).

In addition, a “Do Not Resuscitate” or DNR order had been entered on the decedent’s chart in the days preceding his death. Changes in care following the decision to enact DNR orders on patients have been documented in the medical literature. It is possible that the change of status to DNR may have inadvertently changed the level of care provided to the decedent.

It seems clear that a lack of appreciation of either the worsening renal status of the decedent, or an unawareness of the potential harm in infusing potassium in patients with impaired renal failure, are the most likely immediate factors contributing to the death of this individual.

It is not possible to see beyond these factors to identify what hospital or system issues may have had a role in the demise of this patient. Staff involved in this type of care is reminded of the physiology surrounding renal failure and of the potential harmful role of supplemental potassium in these patients.

PSRC Recommendation:

To Hospital A:

1. A Quality of Care Review should be conducted into this death, if this has not already occurred. This review should focus on issues including, but not limited to: policies and procedures related to the administration of fluid boluses; monitoring of electrolytes and renal function, particularly in patients receiving parenteral electrolyte replacement; and degree of autonomy versus supervision of junior trainees.

Case 2011-05

Date of Death: June 18, 2009.

Age: 42 years

OCC File number: 2009-3884

History:

The decedent was a 42-year-old woman who underwent a right radical mastectomy for breast cancer in 1997. She subsequently was found to have a lytic lesion in her T9 (ninth thoracic) vertebra in 2001. She was treated with radiation and chemotherapy in 2007. From 2008 onwards, the decedent experienced recurrent difficulties with swallowing, and underwent repeated bouginage for the treatment of esophageal stricture.

On June 16, 2009, the decedent was admitted to hospital through the Emergency Department (ED) for rehydration due to esophageal stricture. Past history of radiation and chemotherapy was noted. The decedent was noted to have metastases to bone and possibly brain. Resuscitation status was “DNR” (Do Not Resuscitate).

The decedent was ordered morphine for management of pain. On June 16, 2009 she received two doses of morphine - 8 mg and 2 mg; metoclopramide and dimenhydrinate were also ordered and given. On June 17, three doses of morphine given: 2 mg, 4 mg and 2 mg.

On June 18, 2009 the current morphine order was written as: “Morphine 2-3 mg IV q4h prn; hold if respiratory rate less than 10.” At 0120h, 2mg of morphine was given intravenously. At 1300 hours, 3 mg of intravenous hydromorphone was inadvertently administered instead of the ordered morphine.

At 1420 hours, the medication administration error was detected. The patient was noted to be sleeping and vital signs stable. An urgent message was sent to the medical resident via the internal hospital web-based paging program. This program does not require an immediate response, and no response was documented.

At 1435 hours, the patient was noted not to be breathing by her sister who was with her. Nurses reassessed the patient and called the physician “STAT.” Due to the patient’s DNR status, no resuscitation measures were implemented. Death was formally pronounced at 1500 hours.

Because of the temporal relationship between the medication error and the decedent’s death, the coroner was notified. The coroner’s investigation included an examination of the medication room located on the unit. An excerpt from the Coroner’s Investigation Statement documents the findings:

“The hydromorphone stock is [Dilaudid (Sandoz)] and there are 10 vials of 2 mg/ml in brown glass with a green metal top. Morphine sulfate is manufactured also by Sandoz in a white package with green stoppers and brown glass containers of 2 mg/ml each. These narcotics were all kept together in a locked narcotic drawer on this ward at the nursing station.”

Following the coroner’s investigation, the case was referred for review by the PSRC. The Institute for Safe Medication Practices (ISMP) Canada was asked to assist in this case review. The report included photographs of similar products to those found on the nursing unit:

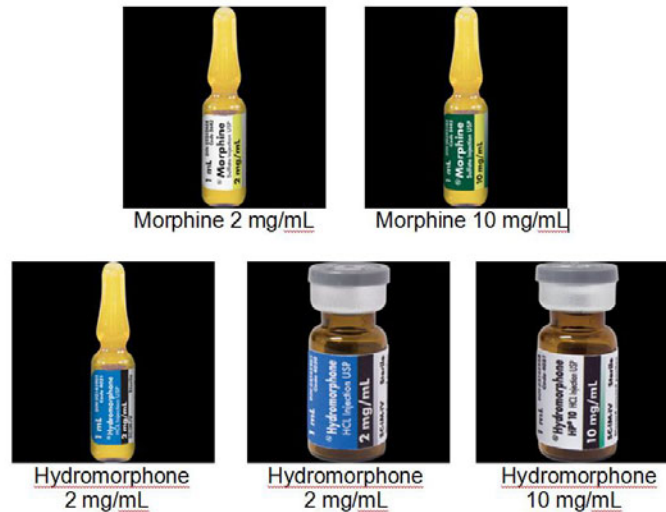


Left: Hydromorphone 10 mg/mL (2009) Right: Hydromorphone 2 mg/mL (2009)

Morphine and Hydromorphone (Sandoz Canada) current physical appearance is shown below (The style of the caps on hydromorphone vials have changed since 2009.)

Available from: <http://www.sandoz.ca/site/en/products/catalogue/index.shtml>;

<http://www.sandoz.ca/site/en/products/catalogue/index.shtml>.



Post Mortem:

Diagnoses:

1. Metastatic carcinoma consistent with primary breast origin, widespread;
2. Post mortem toxicology:
 - Hydromorphone 17 ng/mL “within a range expected following therapeutic administration.” Therefore it was felt by the forensic pathologist that “the administration of hydromorphone prior to death is unlikely to have materially contributed to the death.”
 - Morphine – not detected

Cause of death: Metastatic breast carcinoma

Discussion:

Substitution errors in which hydromorphone is administered instead of morphine are not uncommon. In an aggregate analysis of reported incidents involving hydromorphone published by ISMP Canada in 2006, such errors represented 75% of reported harmful “incorrect drug” incidents involving hydromorphone.¹ Incidents in which vials of higher concentration hydromorphone (e.g. 10 mg/mL) were readily available and inadvertently used instead of morphine were noted to be of particular concern. Look-alike/sound-alike

¹ Shared Learning – Reported Incidents Involving Hydromorphone. ISMP Canada Safety Bulletin 2006; 6(9). Available from: <http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2006-09Hydromorphone.pdf>.

medication names are a recognized contributing factor to this type of error, combined with a lack of understanding on the part of practitioners about the potency of hydromorphone (5-8 times as potent as morphine). Product packaging and labeling can also contribute to confusion. In this case, it is not clear from the coroner's narrative description whether the product labeling contributed in any way to the substitution error.

The pathologist concluded that since the hydromorphone level fell "within a range expected following therapeutic administration," the medication error was unlikely to have contributed to the death. However, it should be noted that toxicity of opioids is dependent on the tolerance of the individual and as hydromorphone is approximately 5-8 times as potent as morphine, a 3 mg dose of hydromorphone would be equivalent to 15-24 mg of morphine, which could have had a significant clinical impact. The decedent was in a compromised physical state due to her illness and weighed less than 50 kg, which would be expected to increase her susceptibility to the effects of this potent medication. For these reasons, the Committee felt that "Accidental Narcotic Overdose" should be listed as a contributing factor in the death.

It was noted that prior to the PSRC review, Hospital A had conducted a quality of care review and had implemented a number of changes aimed at preventing a similar incident in future.

PSRC Recommendations:

The following recommendations have been adapted from a 2006 ISMP Canada Safety Bulletin that focused on medication incidents involving hydromorphone²:

To the Ontario Hospital Association, the College of Nurses and the College of Pharmacists:

1. Educate and inform clinicians about the differences between hydromorphone and morphine.
2. Remove parenteral hydromorphone from patient care areas whenever possible, in particular high concentration hydromorphone. If hydromorphone cannot be removed, segregate it from other opioids.
3. Require redundancies such as independent double checks before administration of parenteral opioids, and especially morphine (due to the repeated confusion with hydromorphone).

² Shared Learning – Reported Incidents Involving Hydromorphone. ISMP Canada Safety Bulletin 2006; 6(9). Available from: <http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2006-09Hydromorphone.pdf>.

4. Consider the development and use of medical directives to empower nurses to administer naloxone when indicated in situations of narcotic toxicity, especially in the setting of accidental overdose.
5. Implement guidelines and practices for assessment, monitoring and documentation of opioid therapy (e.g., vital signs, pain and sedation scales).

To Health Canada:

6. Reduce look-alike potential (e.g., add auxiliary labels that include the brand name equivalent, i.e., [hydromorphone – for Dilaudid]).
7. Encourage the use of Tallman letter on Hydromorphone product labeling (HYDROmorphine) to distinguish the name of morphine. This Tallman letter format should be used in the pharmacy in-house labeling as well as the computer look up for the product.

To Hospital A:

8. For urgent situations, immediate direct communication should occur with the most responsible physician / on-call resident, rather than relying on the hospital's web-based communication system alone.

To the Chief Coroner:

9. It would be valuable to provide investigating coroners with specific guidelines when investigating deaths that are known, or suspected to have resulted from, a medication error. Such guidelines might include:
 - In the event of medication substitution errors, if at all possible, obtain photographs of the medications involved.
 - In the event of a medication error, it is helpful to have some understanding of how the error was discovered. (For example, did the nurse who discovered the error notice that empty or used vials of the administered medication were lying around? Was the discrepancy noticed when doing the shift count (narcotics)?)

To the Chair, Patient Safety Review Committee:

10. Draft a report summarizing similar cases reviewed previously by PSRC, with a view to developing broader system recommendations, such as
 - the development of an equivalency-based system for narcotic administration
 - the development / dissemination of analgesic equivalency charts and other tools readily available at the point of medication preparation to reduce the likelihood of accidental over-administration of narcotic analgesics.

In this report, specific attention should be paid to the issue of narcotic administration in Long-Term Care Homes.

Incidental finding:

In this incident, a decision was made not to administer naloxone because there was a “Do Not Resuscitate” (DNR) order in effect. DNR orders are intended to apply to situations where the cause of death is related to the patient’s underlying condition, rather than to preventable adverse events. This is being addressed as a separate issue by the PSRC in conjunction with a similar case.

(Chair’s note – This case, and another case with similar end-of-life issues, were reviewed by a bioethicist. The results of these reviews were presented to the PSRC, and will be the subject of a future peer-reviewed publication with an aim of educating care providers about the complex issues surrounding the management of reversible medical errors in the patient with a Do Not Resuscitate order in place.)

Case 2011-06

Date of Death: December 25, 2010

Age: 65 years

OCC File number: 2010-16634

History:

The deceased was a 65-year-old woman with acute myelogenous leukemia (AML) who was being treated with induction chemotherapy as an inpatient at Hospital A (a large, tertiary care teaching centre). Her past medical history was significant for right-sided (T2N2) breast cancer treated in 2001 with surgery, adjuvant chemotherapy (6 cycles of FEC-100), adjuvant radiotherapy and anti-estrogen therapy. She also had a remote cholecystectomy.

The patient was diagnosed with AML on November 1, 2010 when she was seen at Hospital A after a 3-week history of suffering from symptoms of fever, lethargy, shortness of breath on exertion and signs of pancytopenia. A bone marrow biopsy confirmed AML with the presence of 40-50% blasts. Cytogenetics performed at that time revealed a chromosomal abnormality (t(3;21)) which may have resulted from previous anthracycline-based chemotherapy used to treat her breast cancer nine years prior. This cytogenetic profile was associated with a poor prognosis. An electrocardiogram (ECG) performed at that time was normal. A nuclear cardiology (MUGA) scan also performed at that time demonstrated normal cardiac function with an left ventricular ejection fraction (LVEF) of 60%.

She was admitted to Hospital A for induction chemotherapy. Risks and benefits were discussed with her and her husband, and she decided to proceed with chemotherapy. This consisted of cytarabine and daunorubicin at 60mg/m² (3+7 protocol) and started on November 7, 2010.

The patient was an inpatient at Hospital A during the entire induction period, as she was closely monitored on a daily basis. Side effects of febrile neutropenia persisted during the initial 30 days; multiple anti-bacterials and antivirals were used along with blood product transfusions. There were also episodes of electrolyte imbalances that were appropriately

corrected on a daily basis. This included hypokalemia, hypomagnesemia, hypophosphatemia and hypocalcemia. The patient appeared hemodynamically stable throughout this initial induction period.

After 30 days, a repeat bone marrow biopsy was performed on December 8, 2010. This demonstrated 30% residual blasts. Consideration of second induction chemotherapy (salvage chemotherapy) with Imatinib and Amsacrine was presented to the patient and she consented to continue with chemotherapy. A repeat MUGA scan performed on December 13, 2010 identified a drop in LVEF of 10% (from 60% to 50%). An ECG also performed on December 13, 2010 was normal except for mild tachycardia. Daily ECGs (December 13, 14, 15) were performed and tachycardia was consistent and stable. The ECG performed on December 16, 2010 revealed a prolonged QT interval along with a heart rate of 100 beats per minute. Normal electrolyte profile was present on that day.

On December 16, 2010, the patient began complaining of a new frontal headache that was treated with Tylenol, codeine and hydromorphone. Imatinib was started on that day to begin the second induction (salvage) chemotherapy. On December 17, 2010, the frontal headache persisted with new onset of postural dizziness. Electrolyte panel performed in the morning was relatively normal (specifically, the potassium level was normal). The CBC persisted to be abnormal, reflecting pancytopenia of AML. An ECG performed that morning continued to demonstrate a prolonged QT interval. At 2130 hours on December 17, 2010 amsacrine (AMSA) chemotherapy infusion was started. The patient was found to be non-responsive at 2232 hours with vital signs absent and a code blue was performed. The patient was resuscitated and transferred to Hospital B ICU where it was determined there was severe irreversible anoxic brain injury with chronic on acute subdural bleeds. There was no neurologic recovery, supportive care was withdrawn and the patient died on December 25, 2010.

[Note from Chair, PSRC – The timing of the chemotherapy infusion was incorrectly stated in the original version of the PSRC report to be 2200 hours. The correct time, as noted above, is 2130 hours on December 17, 2010. In addition, the timing that the patient was found unresponsive has been amended to 2232 hours, instead of 2230 hours as was originally reported.]

Post Mortem:

A post mortem examination was performed on December 26, 2010.

The conclusions of the coroner's investigation were:

Cause of death: 1(a) Anoxic encephalopathy following cardiorespiratory arrest during chemotherapy for leukemia.

Manner of Death: Natural

Discussion:

The investigating coroner reviewed the documentation and ordered an autopsy. The documentation demonstrated that the patient sustained a cardiorespiratory arrest during the infusion of chemotherapy for AML. There was evidence of a prolonged QT on the ECG the

day of the collapse along with electrolyte abnormalities immediately after the resuscitation. These included hypokalemia, hypocalcemia and hypomagnesemia, possibly contributing to the cardiac rhythm disturbance causing cardiorespiratory arrest.

At autopsy, there was no pathologic evidence of residual or persistent leukemia in the bone marrow. There was evidence of bleeding diathesis with multiple gastrointestinal mucosal hemorrhages, multiple small white matter hemorrhages, and a chronic subdural hemorrhage. The brain also demonstrated diffuse anoxic change secondary to the cardiorespiratory arrest.

The final conclusion from the coroner's report is that the underlying cause of the cardiorespiratory arrest was not clear based on the postmortem findings. However, the cardiorespiratory arrest could have been caused by a cardiac arrhythmia/rhythm disturbance related to the effects of chemotherapeutic drugs or other medications or an obscure cause (e.g. genetic channelopathy).

Following referral of this case to the Patient Safety Review Committee, an independent oncologist was asked to review the case and identify any issues or recommendations arising from this review. The expert identified two specific considerations in this case:

1. AML has been associated with prior anthracycline-based chemotherapy as evident in this case for the previous breast cancer treatment. Anthracyclines are known to be cardiotoxic, usually causing a dilated cardiomyopathy, and proper monitoring of cardiotoxicity in assessing the LVEF either by MUGA or 2D-echocardiography. It is assumed that the patient received a total epirubicin dose of 600 mg/m^2 for her previous breast cancer treatment (maximum cumulative cardiotoxic dose is considered to be 900 mg/m^2) in 2001. [Of note, there was no documentation in the chart as to the type of chemotherapy this patient received for her prior breast cancer.] Induction chemotherapy consists of more anthracycline therapy (daunorubicin) and therefore careful cardiac monitoring needs to be re-assessed. Any excessive drop in LVEF of $>10\%$ should be concerning when considering more chemotherapy that can be potentially cardiotoxic. A cardiology consult should be considered if salvage chemotherapy with potential cardiotoxic agents is being considered. The use of amsacrine was considered as an alternate for salvage chemotherapy in this case because of the safer cardiotoxic profile. However, a 10% drop in LVEF was noted and a prolonged QT was also noted immediately prior to the amsacrine treatment.
2. AMSA chemotherapy (amsacrine) is considered an alternative antineoplastic agent for the induction treatment of elderly patients with AML who have underlying cardiac disease. It is an alternative to anthracycline-based induction chemotherapy with daunorubicin. However, it has been associated with cardiac arrhythmias, specifically in patients who had prior anthracycline therapy. Fortunately, these are considered rare (1%), but can be higher with patient factors of hypokalemia, previous anthracycline exposure, and QT prolongation on ECG. In fact, cardiotoxicity is considered acute with AMSA infusion and cardiac arrests can occur as AMSA is infused or within four hours after completion. The mechanism is

unclear. However, hypokalemia and QT prolongation are the two factors that are significant contributors to a potential fatal cardiorespiratory arrest. Therefore it is recommended that **potassium levels be monitored immediately before and during AMSA infusion and cardiac rhythm be monitored during and after AMSA administration** (BCCA product monograph, JCO 1996).

The product monograph (from Erfa Canada Inc., prepared August 16, 2005) contained the following warning³:

Patients with hypokalemia are at increased risk of ventricular fibrillation. The risk of developing arrhythmias can be minimized by ensuring a normal serum potassium level immediately prior to and during AMSA PD administration. Careful monitoring of cardiac rhythm is recommended for detection of cardioactivity. Fluid or electrolyte imbalance should be corrected prior to AMSA PD administration.

The following excerpt is taken from the British Columbia Cancer Agency Cancer (BCCA) Drug Manual (revised September 1, 2008) product monograph for amsacrine ⁴:

The exact mechanism by which amsacrine causes arrhythmias is unknown, though QT interval prolongation does occur. Hypokalemia, which also causes QT prolongation, may contribute to the risk of developing arrhythmias. This risk may be minimized by ensuring a normal serum potassium level immediately prior to and during amsacrine administration. As arrhythmias typically occur during or immediately following infusion, monitor cardiac rhythm during and after drug administration. Fluid imbalance should also be corrected prior to amsacrine administration. Patients with arrhythmias may receive amsacrine with careful monitoring and correction of electrolyte abnormalities.

In this case, AMSA was administered in a non-monitored setting. The chemotherapy was administered at 2200 hours and the patient was left alone in her room. The potassium level was drawn in the morning and was normal, however a prolonged QT was persistently evident within 48 hours of AMSA administration. The patient was found unresponsive with absent vital signs immediately following the AMSA infusion. It is unclear whether the arrest occurred during or after the infusion. The potassium level was significantly low at 2.8 during the cardiopulmonary resuscitation. A potassium level immediately prior to the AMSA infusion was not available.

PSRC Recommendations:

To Hospital A, all Ontario Cancer Centres and OMA Sections on (i) Hematology and Medical Oncology and (ii) Cardiology:

1. The hospital (and oncologists / cancer centres) should review their internal processes and practices related to the infusion of amsacrine, specifically when there are patient risk factors present that may be contributory to an acute cardiotoxic event, such as a cardiopulmonary arrest. As per the product monograph, AMSA

infusion should be administered with careful monitoring of potassium levels and cardiac monitoring. These guidelines should be adhered to.

2. Previous chemotherapies that are cardiotoxic should be carefully documented in the clinical record.

References:

1. Journal of Clinical Oncology, 4:918-28. 1996
2. Leukemia Research, 32:3:491-494, 2008
3. AMSA product monograph – ERFA Canada Inc. August 16, 2005. Accessed May 7, 2011, via Health Canada Drug Product Database - <http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>
4. BCCA Amsacrine product monograph, Sep 2008. Accessed May 7, 2011 via BCCA website: http://www.bccancer.bc.ca/NR/rdonlyres/DC04BEFB-BF13-4A48-91A8-976A9650C6B8/30156/Amsacrinemonograph_1Sept08.pdf.

(Chair's note – A Regional Coroner's Review was conducted with Hospital A following the release of the PSRC recommendations. At the time of this annual report, Hospital A has suspended the use of amsacrine and is using alternate chemotherapy agents. The Hospital has indicated that, should the use of amsacrine be considered in future, it would only be reintroduced in the setting of a strategy that includes appropriate cardiac monitoring.)

Case 2011-07

Date of Death: December 2, 2009.

Age: 28 years

OCC File number: 2009-15613

History:

This case involved a 28-year-old male with developmental delay, autism and hearing impairment secondary to a chromosomal abnormality. The deceased displayed limited verbal communication and was living with his parents. He had a remote history of asthma in childhood, but had no problems with this for many years. There was no history of cardiac or pulmonary abnormalities.

The deceased presented for anterior cervical discectomy and fusion (ACDF) on an outpatient basis for treatment of progressive cervical myelopathy secondary to developmental cervical stenosis and C₄₋₅ disc protrusion. A cervical segmentation abnormality was noted leading to some difficulty identifying the level of vertebral involvement, but was considered unlikely to affect treatment. At the time of surgery, he was classified as a non-traumatic incomplete tetraplegic based on the American Spinal Injury

Association Impairment Scale (ASIA-C). Preoperative medications included sertraline and risperidone. Allergies to penicillin and peanuts were reported.

On November 25, 2009, the deceased underwent uncomplicated ACDF through a right-sided approach at a large urban academic hospital (Hospital A) with tertiary neurosurgical care facilities. Surgery and anesthesia lasted approximately two hours and fifteen minutes. A fibreoptic intubation was performed (apparently electively), following the induction of general anesthesia. A history of difficult intubation was noted in relation to previous anesthetics in childhood, but note is made on both the anesthetic record and pre-admission anesthesia consultation that an adequate glottic view had been reported following recent intubation for MR imaging. The procedure was completed without incident. The bone graft and titanium plate were placed without difficulty. Minimal blood loss was reported. The surgeon was satisfied with hemostasis at the conclusion of surgery. The deceased received a total of 125 mcg of fentanyl and 30 mg of ketorolac intraoperatively. He also received 1 mg of granisetron (long acting antiemetic) at the conclusion of surgery. Local anesthetic solution was infiltrated into the incision by the surgeon at the time of wound closure.

The deceased arrived in the Post-Anesthetic Care Unit (PACU) at approximately 1015 hours. Vital signs were stable throughout his postoperative stay. He was discharged from the PACU to the day surgery unit at 1315 hours. Pain scores and nausea assessments were reported to be zero. There is no record that further analgesics were administered postoperatively. His stay was uneventful. The surgical dressings were reported to be intact with “scant oozing.” No significant change in neck circumference was reported (41.5 cm preop, 42 cm at 1315 hours and 1445 hours). He was reviewed by the anesthesiologist prior to discharge (time not recorded) and noted to be suitable for discharge and that his parents were satisfied that he had returned to his baseline condition. He was discharged at 1600 hours (almost six hours following surgery) with a discharge score of 9/10 (scoring 1 out of 2 on activity level as he continued to require assistance consistent with preoperative status).

The deceased went home accompanied by his parents following discharge. He ate dinner at 1730 hours. He received oxycodone (5 mg) and possibly plain acetaminophen (notes unclear) at approximately 2100 hours and went to bed between 2130 – 2200 hours. His mother slept in the same room. The deceased was noted to be restless at approximately 0130 hours and was directed back to bed by his mother and possibly received ibuprofen (chart unclear).

Between 0330 – 0400 hours, he was noted to have loud, labored breathing and was checked by his mother. He was noted to be lying supine with his eyes open and ashen-grey in colour. Shortly thereafter, he ceased breathing. Cardiopulmonary resuscitation (CPR) was started by his parents and 911 was called. Emergency medical services (EMS) arrived promptly and reported pulseless electrical activity (PEA) with narrow complex bradycardic rhythm. CPR was continued until a pulse was restored approximately two minutes later. Several attempts at intubation were unsuccessful at the scene although manual ventilation was described as adequate.

The deceased was transported to Hospital B at 0535 hours where he was intubated successfully by the emergency physician. Blood pressure at admission was 143/77 and the

Glasgow Coma Score was reported at 3. He had a witnessed seizure following intubation. Femoral lines were placed and sedation was commenced with fentanyl, midazolam and rocuronium. Neck circumference was reported to be 17.5 inches (45 cm) at 0655 hours. A chest X-ray was reported to show extensive pulmonary consolidation consistent with aspiration. He was transferred to Hospital A at 1015 hours.

At Hospital A, systemic cooling was instituted for the cerebral ischemic insult. Reference to a neck hematoma was made repeatedly in the clinical notes although evidence of a neck hematoma was not reported in CT studies of the chest or head available in the material provided.

Neurologically, the deceased's prognosis remained dismal. Despite multiple anticonvulsant mediations, attempts to withdraw sedation under electroencephalograph monitoring were confounded by the development of status epilepticus. In light of his poor prognosis, life support was withdrawn following discussions with his parents. He was pronounced deceased at 2152 hours on December 2, 2009.

Post Mortem:

Autopsy findings included evidence of hemorrhage within the right side of the neck with a hematoma that encased the thyroid and trachea and extended into the retropharyngeal space. On section, the trachea was reported to be widely patent. Extensive foreign material was also noted throughout the lungs consistent with severe aspiration pneumonia. This was considered an acute event with no evidence of old or recurrent aspiration. Admission blood samples were not available for toxicology studies. Cause of death was reported as complications of cervical spine surgery.

Discussion:

In reviewing the circumstances surrounding this death, the PSRC made the following observations:

1. Perioperative care appears to have been appropriate. The deceased was discharged almost six hours after surgery in good condition under the care of his parents. There did not appear to be any factors in the immediate postoperative period that would have predicted subsequent events.
2. Care following discharge appeared to have been appropriate and attentive. This included the deceased's mother sleeping in his room to observe his condition during the first postoperative night.
3. The case material does not offer sufficient information to definitively determine the factors that contributed to the deceased's respiratory and cardiac arrest during the night following surgery. An extensive neck hematoma was noted. Although, at the time of autopsy, the hematoma did not appear to compromise tracheal patency, it encapsulated the trachea and extended into the retropharyngeal space. It is certainly most plausible that distortion of the airway or glottis led to an episode of obstruction

and would be consistent with the report of labored breathing noted prior to his cardiac arrest. Aspiration of gastric contents also occurred, although this is more likely to represent an event arising secondary to CPR, failed intubation and a prolonged period of unconsciousness with an unsecured airway.

4. The surgeon and hospital have done an extensive review of the events surrounding this patient's unfortunate death as well as a review of the institutional experience with ACDF as an outpatient procedure. The review concluded that there have been no other patients, among the series of 76 cases, who died as a consequence of complications. The surgeon concluded that the deceased's developmental delay and limited communication skills may have contributed to difficulty recognizing complications, particularly early signs of airway compromise, if they arose in the postoperative period. As a consequence, changes have been made in the selection criteria for outpatient ACDF and in the post-discharge information provided to patients and their families.
5. Reports of the risk of complications following ACDF are quite variable including the incidence of neck hematoma which is a well-recognized, potentially fatal, complication. In a recent retrospective review of more than 1000 *inpatient* ACDF procedures, an incidence of 5.6% was reported.¹ Forty-two percent of these patients underwent surgical re-exploration. There were no deaths attributed to hematoma. None of the patients were noted to have a pre-existing bleeding diathesis or coagulation disorder, or other factors reported to correlate with increased risk. As a consequence, identifying evolving neck hematoma may be challenging even in the inpatient setting where neck measurements are routinely performed and complaints of excessive discomfort may be addressed more promptly.
6. Experience with outpatient ACDF is limited.² A few relatively small series have been reported with few serious complications. Given limited literature experience with outpatient ACDF, an academic neurosurgical practice would seem to be an appropriate environment to develop experience and evaluate the benefits and risks associated with this treatment option.

PSRC Recommendations:

To the College of Physicians and Surgeons of Ontario; Ontario Medical Association Section on Neurosurgery; Ontario Hospital Association and Hospital A:

1. Patients with developmental delays and communication impairment should not undergo a cervical discectomy and fusion (ACDF) on an out-patient basis.

Committee comments: The PSRC agreed that it is possible that the presence of developmental delay and communication impairment increased the deceased's vulnerability to an adverse event arising in the postoperative period and supported the surgeon's recommendation that patients with these conditions should not undergo this procedure on an outpatient basis, notwithstanding potential benefits

associated with recovery in a familiar environment, at least until sufficient experience is available to fully understand the attendant risks of serious complications.

2. It is recommended that the surgeon and perioperative care team review their selection criteria for candidates suitable for cervical discectomy and fusion to ensure that patients with other conditions or circumstances that may contribute to increased vulnerability should disqualify patients from this care pathway until the risk associated with the complications that arise on an outpatient basis is more fully defined.

Committee comments: The PSRC was concerned that a focus on developmental delay /communication should not detract from an appreciation of the fact that serious complications following ACDF are well recognized, although relatively rare. The care team should also consider other factors, including but not limited to: medical disability; cognitive impairment; lack of availability of a responsible attendant following discharge to support patient for first post operative night; or circumstances that would compromise a timely return to hospital should complications arise.

3. It is recommended that the perioperative care team ensure that supporting instructions and information provided to patients undergoing this procedure on an outpatient basis include an appreciation of the types of adverse events that may be encountered and an understanding of how they would be recognized and addressed.

Committee comments: Serious complications following ACDF, such as neck hematoma, can arise subtly, at least initially, and inpatient care routines typically include assessments such as neck circumference measurements and experience evaluating postoperative neck discomfort, that may alert the care team to adverse events.

References:

1. Fountas KN, et al. Anterior cervical discectomy and fusion associated complications. *Spine* 2007;32:2310-2317.
2. Villavicencio AT, et al. The safety of instrumented outpatient anterior cervical discectomy and fusion. *Spine J* 2007;7:148-153.

Case 2011-08

Date of Death: February 4, 2011
Age: 91 years
OCC File number: 2011-1362

History:

The decedent was a resident of a long-term care home. She was admitted to an acute care hospital (Hospital A) from January 20 – 31, 2011 for treatment of pneumonia and influenza.



She was identified as high risk for aspiration while in hospital. She returned to the long-term care home on January 31, 2011.

On February 1, 2011, she was returned by ambulance to Hospital A from her long-term care home with symptoms of aspiration pneumonia. She was described by her caregiver/ family as alert and participating in conversation the evening prior; however, the following morning she was much less alert, and was noted to be short of breath with gurgling respirations. She was assessed by a physician in the Emergency Department (ED) of Hospital A and at 1616 hours, orders were written for levofloxacin 500 mg IV and metronidazole 500 mg IV. The metronidazole was given at that time.

A note written at 1804 hours indicated, “P[atien]t appears more alert.” At 2004 hours, the records reflect, “Admitted with aspiration pneumonia. Orders received. Pharmacist called re p[atien]t’s allergy to cipro[floxacin]. Dr. XX aware, reports to continue with [antibiotics].” (Reportedly, the decedent had received ciprofloxacin on the prior admission with no adverse effects.) The decedent remained in the Emergency Department pending the availability of an inpatient bed. Notes later that evening indicate that the decedent was breathing without distress, but continued to have a congested cough.

A note written the following day (February 2) indicated, “RN notified MD that patient unable to swallow po [oral] meds – MD aware. When p[atien]t alert and able to swallow safely, will trial po meds.” At 1548 hours, the nursing assessment reflected a worsening of the decedent’s respiratory status: “↑ RR [respiratory rate] noted 48. Wheezing noted – upper lobes congested. O₂ sat 69% on 3L NP [nasal prongs]. MD paged – aware of sat level – to place new orders. ↑use of accessory muscle use noted.” Subsequent notes documented an improvement in oxygen saturation on 35% oxygen. There were episodes of desaturation noted which improved with repositioning. The decedent was noted to open her eyes to voice. The order for ciprofloxacin was changed to moxifloxacin 400 mg intravenously every 24 hours. The first dose of moxifloxacin, scheduled for February 2 at 2000 hours, was not given. The Medication Administration Record (MAR) stated, “Medication IV not available. None in night cabinet. Tablets only.” The first dose of moxifloxacin was not given until February 3 at 2109 hours (more than 24 hours after the first scheduled dose).

On the morning of February 3, the decedent was still in the Emergency Department awaiting an inpatient bed. At 0710 hours, a nursing note stated, “P[atien]t won’t rouse to painful stimuli. P[atien]t non-verbal. Airway patent.” At 0822 hours, the notes stated, “Shallow labored breathing. P[atien]t unable to be roused by voice or painful stimuli. P[atien]t on 15L NRB [non-rebreather oxygen mask], saturating 97%. P[atien]t shallow breathing, ↓A/E [decreased air entry] lower lobe.” At 1130 hours, the decedent was transferred to the medical ward.

A note from the attending physician written subsequently (not timed) states, “Patient’s condition deteriorating, increasing shortness of breath, appears distressed, in pain. Active stage of dying. Spoke with family (daughter, son, grandchildren). Comfort care. SC → IV morphine standing.” An order was written at 1530 hours on February 3 for morphine 4 mg subcutaneously every four hours (as a standing order) and morphine 2 mg subcutaneously every hour prn [as needed] for pain.

Two doses of morphine 2 mg were given (at 1614 and 2029 hours) with documentation of good effect. Of note, the standing doses of morphine 4 mg (scheduled for 1800 and 2200 hours) were not given, and notes reflect that this was because of the prn doses that had been administered. An assessment note at 2330 hours stated, “Nurse took vitals: BP low, O₂ sats were low, did head to toe assessment, totally lethargic.”

At 0146 hours on February 4, the medication record documented the administration of morphine 4 mg subcutaneously (routine dose scheduled for 0200 hours). At 0400 hours, the decedent was found vital signs absent. No resuscitation was attempted as per her advance directive.

Through the narcotic medication count process, it was identified that the decedent had received hydromorphone 4 mg instead of the prescribed morphine 4 mg. At 0930 hours, a note written by the attending physician stated, “Made aware of medication error overnight. Morphine 4 mg was to be given. Hydromorphone given instead. Called patient’s son and disclosed medical error. Discussed steps to be taken to investigate the error.”

The Office of the Chief Coroner was advised of the death. This was reported on the basis of being a threshold (i.e. 10th death from the long-term care home), and not on the basis of the medication error. The coroner was informed of the medication error in the course of his investigation. It was subsequently determined that while an automated medication dispensing system with barcode checking of medication administration had recently been introduced on the unit, this system was not used when the dose in question was given.

Post Mortem:

No autopsy and no toxicological testing were conducted per the wishes of the family.

Discussion:

The hospital conducted a review of the incident and identified several opportunities for improvement. Some of the resulting recommendations were focused on care standards and processes specific to this particular case. In addition, systemic recommendations were made, including:

- Review the appearance of the medications involved, as well as their location in the narcotic cupboard;
- Encourage staff to bring [mobile medication dispensing cart] into the medication room when obtaining medications to avoid reliance on memory.

PSRC Recommendations:

In addition to the recommendations made by the hospital, the Patient Safety Review Committee made the following recommendations:

To the Ontario Hospital Association (OHA); College of Nurses of Ontario (CNO); Ontario branch of Canadian Society of Hospital Pharmacists; Ontario College of Pharmacists:

1. Review opioids available in patient care units and ensure that medications stocked are available in the least number of doses, concentrations, and forms that will meet essential patient needs between replenishment (not exceeding 72 hours).³
2. If a medication is not available in the formulation prescribed at the time the dose is scheduled to be given, attempts should be made to obtain the medication (or a suitable alternative, as determined by the prescriber) as soon as possible. Clinicians should not wait until the time of the next scheduled dose to administer the medication, particularly in the case of long-acting medications with infrequent dosing.

To the Ontario Hospital Association and College of Nurses of Ontario:

3. Regular reviews should be undertaken with staff to ensure awareness of, and compliance with, established standards of practice, including but not limited to:
 - Assessment of patients receiving opioids for pain management, including palliative / comfort measure orders, should always include a critical evaluation of vital signs, including quality of respirations, before and after administration, to ensure that opioid administration is appropriate given the patient's current status, and that the patient has responded as expected.^{4,5}
 - Review nursing workload and numbers of patients assigned per nurse, coverage of breaks, and strategies to ensure continuity of care over the course of a shift.
 - Educate nursing staff about how system-based strategies (such as automated medication dispensing systems and independent double checks) support them to achieve safe medication administration.
[Committee comments: There are sometimes misconceptions that following the 5 "rights" (i.e. right patient, right drug, right dose, right route, right time) alone is sufficient to prevent errors. In fact, this is the intended outcome, not the process to achieve the goal.⁶]
 - Identify medications for which a manual independent double check is mandatory, such as opioids and other high-alert medications⁷, if an automated dispensing system is not being used.

³ Medication Safety Self-Assessment for Hospitals, Canadian Version II, 2006, Item 85.

⁴ Shared Learning — Reported Incidents Involving Hydromorphone. ISMP Canada Safety Bulletin 2006; 6 (9).

⁵ CNO Practice Standard: Medication (revised 2008) p. 4: "Nurses use their knowledge, skill and judgment in the assessment of the client, the medication and the practice supports prior to administering medication.", Cited 20Jun2011; available from: http://www.cno.org/Global/docs/prac/41007_Medication.pdf

⁶ The five rights: A destination without a map. ISMP Medication Safety Alert! 2007;12(2).

⁷ High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. ISMP's List of High-Alert Medications. Available at: www.ismp.org/Tools/highalertmedications.pdf.

Case 2011-09

Date of Death: August 18, 2010
Age: 82 years
OCC File number: 2010-10425

History:

The deceased was receiving treatment for advanced breast cancer. Approximately one week prior to her death, she was referred to a home palliative care service as she was no longer able to travel to hospital for assessment and care. The day prior to her death, she was assessed at home by the palliative care physician who wrote a prescription that included:

*M-Eslon 10 mg;
S: i po q12h
M: 60 (sixty)*

*Morphine solution 5 mg/mL
S: 1/2 -1 mL q2h prn pain
M: 100 mls*

One dose of M-Eslon (sustained-release morphine) was administered at 1030 hours on the day of the patient's death. Over the course of the day, she became unresponsive and died that evening. When the palliative care physician came to pronounce the patient's death, it was discovered that M-Eslon 100 mg capsules had been dispensed by the pharmacy instead of the prescribed 10 mg capsules.

Post Mortem findings:

Post-mortem toxicology (femoral blood):
Morphine 160 ng/mL
Codeine < 0.050 mg/L

Pathologist's note:

"Toxicological analysis of post mortem blood showed a concentration of morphine that was lower than the concentration seen in fatalities due to acute morphine toxicity. Codeine was present at therapeutic concentrations. Individuals on long-term codeine become cross-tolerant to morphine, which implies that her concentration of morphine was effectively less than measured. The levels of codeine and morphine are consistent with end-of-life care."

Discussion:

This case was reviewed by ISMP Canada and the results of that review presented for discussion by the PSRC. It was felt that the dispensing error likely resulted from misinterpretation of the handwritten prescription, which at first glance appears to be for M-Eslon 100 mg. (See Figure 1.)



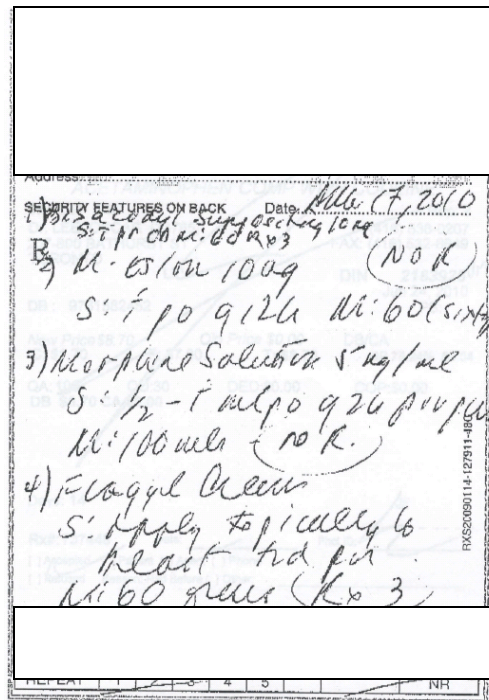


Figure 1: Prescription

Concerns were identified regarding the dispensing of M-Eslon 100 mg for this patient:

- A scheduled dose of 100 mg q12h not in line with an “as needed” dose of 2.5-5 mg
- The patient’s prior narcotic consumption was minimal. Per the pharmacy records:
 - 30 Tylenol # 3 tablets dispensed 24 June 2010;
 - 100 Tylenol # 2 tablets dispensed 20 Aug 2009.

The forensic pathologist noted that “the levels of codeine and morphine are consistent with end-of-life care”; however, the toxicology report noted that “morphine toxicity is highly variable and depends on the tolerance of the individual to the drug.” Given that, per the palliative physician’s assessment on 17 Aug 2011, the patient was taking only occasional (1-2 tablets/day) of Tylenol #2 and #3; 100 mg of morphine represents approximately 11 times the equivalent dose of two Tylenol # 3 tablets daily (60 mg codeine)⁸.

While the levels of codeine and morphine may be consistent with those seen in palliative patients, it is important to note that this patient had very limited tolerance to opioids, which may be more important than the actual blood levels. It is therefore likely that, considering the patient’s clinical condition at the time of the unintended overdose, while the morphine may not have directly caused the patient’s death, it seems likely that it would have had a substantial clinical effect.

⁸ Opioids: Approximate analgesic equivalences. Opioids general monograph. Canadian Pharmacists Association. Compendium of Pharmaceuticals and Specialties. 2011, p.1760.

PSRC Recommendations:

To the College of Physicians and Surgeons of Ontario:

1. Remind prescribers of best practices in handwriting prescriptions, including:
 - Avoiding the use of cursive script when expressing measurement units;
 - Ensuring sufficient space between the numerals and the measurement units to optimize readability;
 - Including the alphabetic as well as the numeric units on prescriptions (e.g., 10 (ten) mg), especially on high-alert medications.
2. Work to expedite computerized prescribing systems to eliminate legibility problems with handwritten prescriptions.

To the Ontario College of Pharmacists:

3. For all new narcotic prescriptions, review the patient's history to ensure dosing is appropriate given prior narcotic use.
4. Confirm the appropriateness of the medication and dose for the patient, per the expected standards of pharmacy practice.⁹
5. Identify high dose narcotics as medications requiring additional review prior to dispensing.
6. Identify high alert medications for which an independent double check should be conducted when a second qualified staff member is available in the pharmacy.

⁹ National Association of Pharmacy Regulatory Agencies (NAPRA) Model Standards of Practice. Cited 1Sept2011; available from:
[http://www.ocpinfo.com/Client/ocp/OCPhome.nsf/object/Model_Standards/\\$file/Model_Standards.pdf](http://www.ocpinfo.com/Client/ocp/OCPhome.nsf/object/Model_Standards/$file/Model_Standards.pdf)

Pharmacists, when providing patient care as part of the care provided when dispensing medications or medication therapies:

9. review each prescription for a medication that a patient is taking for the first time to ensure that this medication is the most appropriate for the specific patient, including collecting and interpreting relevant patient information to ensure that:

- there are no significant drug interactions or contra-indications, and
- the medication is the most appropriate in view of patient characteristics, other conditions and medications, and
- the dose and instructions for use of the medication are correct

10. rectify prescriptions for medications that patients are taking for the first time that pose risks to a patient by:

- making changes to the prescription in accordance with authorities granted to pharmacists by laws / regulations / policies / guidelines, and/or
- contacting a prescriber to recommend changes in the prescription, and/or
- refusing to dispense the medication

Case 2011-10

Date of Death: February 3, 2011
Age: 80 years
OCC File number: 2011-1320

History:

The decedent was an 80-year-old male with a past history significant for hypertension and hypercholesterolemia. He was a cigarette smoker. His medications included ramipril – 10mg daily, atorvastatin – 20mg daily. He had no surgical history.

On February 2, 2011, the decedent was witnessed by his family to have a 30-40 second period during which he had a blank stare and was not responding. When he began speaking again, he stated that he had 6/10 pain in his lower abdomen with no radiation. He felt comfortable lying down, but felt very weak and dizzy when he sat up. When he did sit up, he became diaphoretic.

The family of the decedent called 911 following the episode of unresponsiveness. He was transferred by ambulance and reached the Emergency Department of Hospital A (a community teaching hospital located in a major urban centre) at 1437 hours. His vital signs at triage were noted to be exactly the same as the vitals obtained by the paramedics at the decedent's home; heart rate 85, respiratory rate 20 and blood pressure 130/73. The triage nurse noted that the patient had abdominal pain and was weak and that his abdomen was hard. The patient was assigned a Canadian Triage Acuity Score (CTAS) 3 out of a possible 5. This classification reflected an acuity of "urgent." CTAS guidelines recommend that a person assigned a CTAS score of 3 be assessed by a physician within 30 minutes of presentation, and that if this is not possible, that they be reassessed by a nurse every 30 minutes¹.

The decedent was apparently assessed in the Emergency Department by a physician at 1730 hours, approximately three hours after arrival. The vitals in the physician's note were precisely the same as the vitals noted by the ambulance personnel and in the triage note. The abdomen was noted to be soft with no pulsations felt. A computerized tomography (CT) scan was ordered to rule out diverticulitis, an intravenous was started and a stool sample was obtained for culture and sensitivity and C. difficile. The decedent was also to be placed in a monitored area and orthostatic vitals were to be done.

At 1800 hours, the decedent's blood pressure was 123/87 with a heart rate of 116 when lying down. On standing, the blood pressure dropped to 72/63 with a heart rate of 130. The decedent was transferred to the monitored area and his systolic blood pressure was noted to be 81.

A CT of the abdomen and pelvis with contrast was performed at 1837 hours. A large infrarenal abdominal aortic aneurysm measuring 7.4 cm AP x 8.1 cm transverse was noted. At the mid portion of the aneurysm, there was rupture with frank extravasation of contrast

noted. There was a large associated retroperitoneal hematoma measuring approximately 7.8 cm AP x 13 cm transverse. The hematoma was compressing and displacing the right kidney.

Blood transfusions were ordered and arrangements for transfer to a vascular surgery centre commenced.

CritiCall Ontario was utilized to organize transfer. A total of 65 telephone calls were made between CritiCall and vascular surgery centres, first locally, then to surrounding regions. In general, there were significant difficulties locating on call physicians. In one case, there was blatant lack of cooperation, with a physician stating that he had “never accepted a CritiCall transfer in eight years.” Availability of intensive care unit (ICU) beds was also a critical factor. Information regarding the availability of a vascular surgeon and the availability of ICU beds was not coordinated. Facilities were not available in the urban centre or surrounding regions, and ultimately a surgeon and ICU bed were obtained at Hospital B (a community hospital located approximately 135 km away from Hospital A). The decedent was accepted for transfer at 2104 hours.

Prior to transfer, the decedent was successfully intubated. He was transferred via air ambulance to Hospital B. He arrived at 0030 hours on February 3, 2011 and was taken directly to the operating room. By this time, he had received 20 units of packed red blood cells. Neither platelets nor coagulation factors had been transfused and the decedent was oozing from all puncture sites. The abdomen was very distended and tense, pulses were not palpable, and pupils were fixed. The surgeon at Hospital B determined that surgery was not indicated as there was no possibility of success.

The decedent was transferred to the ICU for compassionate care and died shortly thereafter.

Post Mortem:

A post mortem examination was not performed.

Cause of Death:

1a) Ruptured abdominal aortic aneurysm

Contributing factors:

Hyperlipidemia; Hypertension

Manner of Death:

Natural

Discussion:

This is a case of an 80-year-old man who presented to a hospital in a large urban centre and did not receive timely access to care for a life-threatening vascular emergency.

It would appear that the Emergency Department triage process (and the initial physician assessment) relied upon vital sign measurements made previously by paramedics rather than

a reassessment of vital signs. The severity of the decedent's illness was not initially appreciated by the triage nurse or the emergency physician, which resulted in a significant delay in diagnosis.

Once the diagnosis was made and it was determined that he could not be treated in the hospital in which he was located, CitiCall Ontario was contacted and immediately began trying to arrange a transfer – initially within the urban centre, and then within the surrounding regions. Transfer was ultimately arranged to a community hospital located a significant distance away.

CitiCall Ontario made 65 telephone calls while trying to organize the transfer. The response to calls from CitiCall Ontario are well documented and include responses of frank unprofessionalism (one hospital), confusion as to which vascular surgeon was on call (two hospitals), lack of coordination between critical services such as vascular surgery and ICU (most hospitals), and an overall lack of willingness to accept responsibility in a life-threatening situation.

Given the prolonged time required for transfer, the patient management at Hospital A was not felt to have been optimal. Although intubated, there was no management of coagulation given the massive transfusion of 20 units of packed red blood cells.

Despite the ultimate willingness by Hospital B to accept the decedent in transfer, by this point, the decedent's condition had deteriorated to a point where surgical intervention was not possible and compassionate end of life care was provided.

PSRC Recommendations:

To Hospital A:

1. The hospital should review this case, with particular attention to:
 - a. The need for vital signs to be re-acquired at appropriate points in the triage and treatment process, and not merely transcribed from previous care providers' notes;
 - b. The identification of patients with vascular compromise and appropriate triage and urgency of physician assessment of such patients;
 - c. Best practices in the management of patients requiring massive transfusion (including the principles of balanced transfusion, etc.)

Committee's comments: Triage processes at Hospital A were felt to merit review. Vitals recorded at triage should be newly acquired and not transcribed from the ambulance report. It would appear that had signs and symptoms of vascular instability (postural hypotension and presyncope) been appreciated earlier, the patient would likely have been assessed as CTAS 2 which may have led to a timelier physician assessment. In addition, emergency physicians and others involved in resuscitation need to understand and apply best practices in order to avoid the development of transfusion-related coagulopathy where possible.

To the Ministry of Health and Long-Term Care and Local Health Integration Networks (LHINs):

2. A “No Refusal” policy should be introduced at a regional level such that unstable patients with life or limb-threatening conditions who require urgent access to tertiary case resources will be accommodated within a region in a timely way.

Committee’s comments: The Committee has previously reviewed similar cases in which delays in identifying a centre willing to accept a patient with a life or limb-threatening problem contributed directly to the death. The Committee is aware that a pilot project of a “Life or Limb - No Refusal Policy” is currently underway within one LHIN. The Committee strongly supported the prompt expansion of this model to all LHINs in the province in order to avoid situations such as are described in this case.

3. Hospitals that participate as receiving centres for Criticall patients must ensure that processes exist to facilitate timely access to the on-call physician for each service. If such calls are not responded to in a timely way, a back-up method (ideally involving the chief of the service) needs to be readily available. It is also critical that appropriate coordination occurs within the institutions such that on call physicians are aware of, and can access, ICU resources where available.
4. Financial incentives / disincentives should be aligned with the acceptance / refusal rates of Criticall referrals

Committee’s comments: The Committee was struck by the difficulty experienced by CritiCall staff and by the obstacles encountered in identifying an accepting centre. These included the inability of some centres to identify or contact the on-call vascular surgeon, and a lack of communication between the on-call surgeon and the ICU in making decisions on accepting the patient. In addition, it was felt that centres that accept a disproportionately greater share of CritiCall transfers should be financially rewarded for this, and that the converse should be true for centres that accept less than their share of transfers.

To Criticall:

5. The Medical Director of Criticall should take appropriate steps (including involvement of the College of Physicians and Surgeons of Ontario) when issues of professionalism (disrespectful conduct; persistent issues with lack of availability when on call; etc.) are identified.

Committee’s comments: There was major compromise in the process because the physician on-call system had broken down, including at major teaching hospitals. The inability to identify or contact the on-call surgeon suggests that there may be professional practice issues, particularly given the fact that physicians are financially compensated for periods on call. In addition, the attitude expressed by some of the on call physicians contacted by CritiCall was felt to be unprofessional and unacceptable. The Medical Director of CritiCall should raise these issues with the College of Physicians and Surgeons of Ontario when appropriate.

References:

1. Bullard MJ, Unger B, Spence J, Grafstein E and the CTAS National Working Group. Revisions to the Canadian Emergency Department Triage and Acuity Scale (CTAS) adult guidelines. *Can J Emerg Med* 2008;10(2):136-42.

Case 2011-11

Date of Death: March 22, 2011
Age: 52 years
OCC File number: 2011-3469

History:

The decedent was a 52-year-old male who presented to Hospital A (a community hospital located within a large, urban centre) by ambulance on Friday, March 19, 2011. He had a history of left-sided chest pain commencing the preceding day following crack cocaine use. He was triaged promptly at 1431 hours, assigned a Canadian Triage Acuity Score (CTAS) of 2 (emergent), and admitted to the Emergency Department (ED) with a diagnosis of myocardial infarction. Initial treatment consisted of supplemental oxygen, intravenous fluid and sublingual nitroglycerin. ASA was withheld temporarily due to a history of peptic ulcer disease and possible recent gastrointestinal bleeding. His initial blood pressure was reported as 92/70 mmHg and his heart rate was 84 beats per minute. The initial troponin I level (collection reported at 1454 hours) was 15.7 µg/L (ref <0.10).

The decedent's past medical history was complicated by gastritis and peptic ulcer disease which had historically caused him considerable discomfort. He apparently underwent investigation for chest pain in 2007 that included a myocardial perfusion study that was negative at that time. He also had a history of hypertension, cigarette smoking (40 pack/yr), substance abuse (marijuana and crack cocaine), hyperlipidemia and was reportedly noncompliant with medications.

The Acute Coronary Syndrome protocol was commenced following assessment in the Emergency Department, consisting of ASA, clopidogrel, nitroglycerin, metoprolol, intravenous heparin and atorvastatin. He was assessed by consultants in Internal Medicine and Cardiology. He was also reviewed by an Intensive Care Unit (ICU) physician. Notes and documentation related to his care were felt to be clear and thorough. A referral to Hospital B (a tertiary care teaching centre located in the same city as Hospital A) for cardiac catheterization was apparently completed on March 19 through the Cardiac Care Network (CCN).

The decedent remained in the Emergency Department for over two days awaiting transfer to Hospital B, the anticipated destination for coronary angiography and possible intervention. Several notes confirm that he had been triaged for angiography and his disposition was managed expectantly. He was known to have experienced an extensive

posterior/inferior/lateral myocardial infarction, the troponin I level peaked on March 20 at 73.9 µg/L and an echocardiographic study completed on March 21 reported extensively abnormal left ventricular wall motion with the ejection fraction estimated at 30-35%.

Following some apparent confusion in relation to arrangements for cardiac catheterization, the decedent became increasingly hemodynamically unstable during the early morning hours on Monday, March 22, 2011. This followed episodic hypotension and intermittent chest pain arising over the two days that followed his admission. A central line was established and inotropic/vasopressor support was initiated. In response to persistent chest pain and progressive dyspnea, a trial of bi-level positive airway pressure (BiPAP) was initiated. Despite this, the decedent continued to deteriorate and sustained a cardiac arrest shortly after 0400 hours. He was intubated and resuscitation was continued for approximately 45 minutes, but a viable rhythm could not be reestablished and he was pronounced deceased at 0455 hours.

The case was referred to the coroner as a consequence of the delay experienced accessing cardiac angiography and possible intervention.

Records indicated that a referral request for angiography was completed by a physician at Hospital A and dated Friday, March 19, 2011. The referral date, completed by the CCN coordinator, was recorded as March 21; the fax transmittal stamp on the CCN referral form contained in the records obtained from Hospital B recorded fax transmission to the CCN Coordinator at 0754 hours on March 20, 2011.

A note by the CCN coordinator on March 21, 2011 noted that the referral was received, but no cardiac ICU bed was available at Hospital B. The situation was apparently discussed with the Cardiac ICU attending physician at Hospital B and confirmation was noted that Hospital A was seeking a referral for cardiac catheterization only at that point (presumably with return to Hospital A following the procedure and not anticipating admission to Hospital B). A subsequent note at 1500 hours indicated episodes of hypotension and extensive MI and the expectation that the decedent would require transfer to a Cardiac ICU bed at Hospital B. In the absence of an available bed, Hospital A was advised to contact CitiCall to arrange transfer to another centre.

Nursing notes from Hospital A on March 20, 2011 at 1550 hours indicated a referral for cardiac catheterization had been sent to Hospital B. On March 21, 2011 at 1025 hours, a note indicated that a call was received regarding an outpatient catheterization appointment (i.e. with return to Hospital A following the procedure). Information regarding the patient's 'unstable' condition was apparently provided to the CCN Coordinator at Hospital B, and Hospital A was apparently informed that a Cardiac ICU bed would be needed but was not available, and advised to pursue 'alternative arrangements.' (It was not clear from the notes to whom at Hospital A this information was communicated.) An ICU Progress Note dated March 21 (not timed) indicated that Hospital A was 'awaiting triage for angiography.' No further notations were found in the material reviewed that referred to further plans for obtaining access for coronary angiography at another centre.

Post Mortem:

A post mortem examination was not performed.

Cause of Death:

1a) Acute Coronary Syndrome

Contributing factors:

Hypertension, dyslipidemia, smoking, cocaine use

Manner of Death:

Natural

Discussion:

The decedent remained in the Emergency Department of Hospital A for over two days awaiting transfer to Hospital B, the anticipated destination for coronary angiography and possible percutaneous coronary intervention (PCI). Notes confirm that he had been triaged for angiography and his disposition was managed expectantly. He was known to have experienced an extensive non-ST elevation myocardial infarction (NSTEMI) and was continuing to experience intermittent episodes of chest pain and hypotension.

Based on his presentation, the decedent would have been risk stratified as a high-risk NSTEMI patient. Medical management of this condition at Hospital A appears to have been appropriate. The role for coronary angiography in unstable angina /NSTEMI is more controversial than for patients experiencing a STEMI. Given the clinical circumstances and high risk nature of his condition, timely access to coronary angiography may not have altered the unfortunate sequence of events that led to his death.

Nevertheless, considerable confusion seemed to surround the circumstances of his transfer:

- i. Timing and sequence of events surrounding the referral transmission are unclear. Referral documents indicated that the referral form was completed at Hospital A on Friday March 19 and faxed to Hospital B the following morning. The referral was reported to have been received by the CCN Coordinator on March 21 and discussions between Hospital B and Hospital A regarding the disposition of this patient occurred initially on Sunday March 21. The basis for this substantial discrepancy is unclear.
- ii. The decedent appears to have spent the two days following admission in the Emergency Department (ED) at Hospital A. In the face of unstable angina/NSTEMI and the apparent expectation, at least initially, that coronary angiography would be performed at Hospital B as an outpatient (i.e. treat and return) procedure, it is not clear why admission to a high acuity environment (e.g. ICU / CCU) at Hospital A was not arranged, as a cardiologist and intensivist appear to have been involved in his care in the ED.

- iii. Available documentation does not define the decedent's triage status as determined by CCN. It appeared however, that he was deemed appropriate for urgent angiography and that the primary obstacle to access to this procedure, once triage was completed, was the newly-appreciated need for a Cardiac ICU bed that was not available at Hospital B. At that point, over forty hours had elapsed since his presentation and his condition had deteriorated. It is unclear what steps were taken by Hospital B or CCN to assist staff at Hospital A to secure access to these services or what steps were taken by staff at Hospital A to seek an alternate accepting hospital with cardiac catheterization facilities.
- iv. It is not clear whether the availability of these services was influenced by the fact that his presentation occurred on a weekend.

PSRC Recommendations:

To the Cardiac Care Network (CCN):

1. If a referred patient is risk-stratified as high risk, and requires urgent access to resources that are not available to provide the necessary care:
 - a. Communication should occur directly between either the CCN coordinator or the on-call CCU physician at the tertiary site and the most responsible physician caring for the patient at the referring site
 - b. The CCN coordinator should facilitate the referral to other tertiary centres, either through the CCN or through CitiCall Ontario

Committee's comments: There appeared to be some confusion and miscommunication between the two hospitals and the Cardiac Care Network regarding the status of the decedent's referral for interventional cardiology, and the need for Hospital A to pursue alternate arrangements. It was felt that more direct communication involving the most responsible physician would be of assistance. Further, it was felt that better communication and coordination between the CCN coordinator, the sending facility and CitiCall Ontario was needed.

To the Ministry of Health and Long-Term Care and the Local Health Integration Networks:

2. A "No Refusal" policy be introduced at a regional level such that unstable patients with life or limb-threatening conditions who require urgent access to tertiary care resources (including interventional cardiology), will be accommodated within a region in a timely way.

Committee's comments: The Committee has previously reviewed similar cases in which delays in identifying a centre willing to accept a patient with a life or limb-threatening problem contributed directly to the death. The Committee is aware that a pilot project of a "Life or Limb - No Refusal Policy" is currently underway within one LHIN. The Committee strongly

supported the prompt expansion of this model to all LHINs in the province in order to avoid situations such as are described in this case.

Case 2011-12

Date of Death: July 3, 2011
Age: 80 years
OCC File number: 2011-7920

History:

The decedent was an 80-year-old male who was found to have an incidental, solitary pulmonary nodule in his right lung following routine radiographic imaging of his chest in April 2011 to assess a previously implanted endovascular stent within his thoracic aorta. This nodule was reported to be pleural based within the right upper lobe and approximately 1.4 cm in greatest dimension.

An ultrasound-guided fine needle aspirate of this nodule in the anterior segment of the right upper lobe was obtained on April 26, 2011 and reported as 'Positive for Malignant Cells / Non-Small Cell Carcinoma.' A whole body Positron Emission Tomography – Computed Tomography (PET-CT) scan was performed which demonstrated that the nodule was 15 mm x 13 mm and metabolically active. No evidence of metabolically active foci was identified within the intrathoracic lymph nodes or elsewhere to suggest metastatic disease. [Of note, in the body of this PET-CT report, the nodule is recorded as being in the right middle lobe; however, in the summary of the same report, the nodule is reported as being in the right upper lobe. All other clinical notes indicate that the nodule was present in the anterior segment of the right upper lobe.]

The decedent was subsequently assessed by an internal medicine specialist to evaluate his pre-operative status. His past medical history included apparent familial corneal dystrophy with multiple surgeries for this condition, chronic obstructive pulmonary disease in the setting of a > 50 pack/year smoking history, hypertension, hypercholesterolemia, diabetes mellitus (type II), angina pectoris, peripheral vascular disease, mild pulmonary fibrosis of unknown etiology, surgical management of a descending thoracic aneurysm with endovascular stents, right and left carotid artery bypass, arthritis of the neck and back and benign prostatic hypertrophy. Following the endovascular aneurysm stenting with selective 'debranching' of the aorta in 2010, the decedent sustained a presumed infarction of tissues supplied by the anterior spinal artery resulting in motor and sensory deficits necessitating the use of a walker for mobilization. Although the decedent was noted to have an elevated risk of cardiovascular complications given his significant atherosclerotic vascular disease, he was felt to have been medically optimized for surgery that was booked for June 17, 2011 at Hospital A, a large, university-affiliated tertiary care hospital. The planned procedure was for bronchoscopy followed by video-assisted thorascopic resection of the pleural based pulmonary nodule.

The operative notes from the surgery on June 17, 2011 indicated that bronchoscopy did not reveal evidence of any endobronchial lesions and that pleuroscopy of the visceral and parietal pleura as well as the diaphragm did not show evidence of malignant disease. The lungs did show evidence of anthracosis, emphysematous changes and signs suggestive of some degree of pulmonary fibrosis. The surgeon performed a wedge resection of the right upper lobe in the vicinity of the nodule. Palpation of the resected specimen failed to reveal a nodule. Intra-operative review of the preoperative Computed Tomography scan with a radiologist confirmed that the nodule was radiographically located in the anterior segment of the right upper lobe and not in the adjacent right middle lobe. An intra-operative consultation with another surgeon and pathologist failed to identify a nodule in two wedge resection specimens or in the remaining right upper lobe of lung.

A decision was made to resect the remaining right upper lobe through a converted thoracotomy. It was felt that given the decedent's pulmonary function test results and preoperative status, he could tolerate the more extensive resection. A mediastinal lymph node dissection for staging purposes was also performed. The remaining operation was reported to have been unremarkable. Following the operation, extensive dissection of the lobectomy specimen by both the surgeon and the pathologist failed to identify the pulmonary nodule.

The decedent was initially clinically stable following the operation. However, within the ensuing first postoperative day (POD#1), he began to require increasing amounts of oxygen for respiratory insufficiency and sustained new onset atrial fibrillation. The decedent was extubated on POD#1. Blood gases on POD#2 revealed an acidosis (7.25/55/62/24) and a moderately elevated leukocyte count (WBC 16.6). The decedent was afebrile. Chest radiography demonstrated evidence of atelectasis as well as small effusions. In subsequent days, the acidosis appeared to become largely corrected; however chest X-rays in the ensuing days revealed evidence of airspace disease that was associated with an elevated leukocyte count (ranging from ~15-25 over the course of his admission post-operatively). The decedent was started on piperacillin / tazobactam on POD#2 and was provided three days of methylprednisolone starting on POD#3. His oxygenation continued to slowly deteriorate over multiple days requiring bi-level positive airway pressure support (BiPAP) starting on POD#4. In addition, vasopressor support was added and vancomycin was added on POD #8 to assist with the persistent leukocytosis and worsening radiographic evidence of airspace disease in his lungs (left more than right). Blood cultures eventually grew an *Enterobacter* species and the decedent was started on ciprofloxacin on POD#12.

On POD#10 the decedent had what was interpreted to be an upper gastrointestinal bleed (melena stools) that was associated with a moderate drop in hemoglobin (to a range of 80-95). Oesophagogastroduodenoscopy (OGD) revealed the presence of a duodenal ulceration that was clipped. A second OGD the subsequent day following more melena stools, revealed superficial ulceration and 'oozing' of the adjacent mucosa of the duodenum that subsequently stopped bleeding.

In the few days prior to his death, the decedent's respiratory status was deteriorating with increasing vasopressor support requirements and development of sepsis. A family meeting was held and it was decided that aggressive, life sustaining medical therapy would be

discontinued and comfort measures initiated. The decedent died soon afterward on post-operative day 16.

The initial surgical pathology report did not identify a malignant tumour in the resected specimens. The initial cytology of the pulmonary nodule and surgical specimen was subsequently reviewed by a surgical pathologist with specialization in pulmonary pathology at a tertiary care facility. He supported the initial diagnoses of a non-small cell carcinoma in the fine needle aspirate specimen (poorly differentiated) and did not identify evidence of malignancy in sections of the formal resection specimens of the right upper lobe. Molecular genetic testing for confirmation of identity to confirm that pathological specimens had not been mixed up, confirmed that the fine needle aspirate specimen belonged to the deceased and that no misattribution of samples had occurred.

A revised surgical pathology report from the hospital where the surgery took place was produced following embedding of all of the remaining tissue from the lobectomy specimen (104 blocks). A 0.8 cm poorly differentiated squamous carcinoma was ultimately identified.

Post Mortem:

No post mortem examination was conducted.

Discussion:

Although initially thought to be pathologically negative, subsequent assessment of the entire right upper lobectomy specimen *did* identify a poorly differentiated non-small cell carcinoma. This finding diagnostically correlated with the fine needle aspirate specimen obtained pre-operatively. Identity of specimens was confirmed with molecular genetic testing. The tumour proved extremely difficult to identify; indeed, it eluded intraoperative identification by two surgeons and a pathologist with the assistance of a radiologist.

The decedent was elderly and had multiple significant co-morbidities. As a result of failing to identify a tumour nodule at the time of surgery (despite concurrent intra-operative pathology and radiology consultations), a more extensive resection was conducted in order to attempt to definitively treat the patient. The clinical pre-operative status of the decedent was felt to be sufficient to tolerate the modified surgical procedure.

On review by the PSRC, there were no recommendations identified with respect to the process used to attempt to identify the nodule intraoperatively. Committee members raised concerns with respect to some of the management decisions in this case; namely, the decision to proceed with an open thoracotomy versus aborting the procedure and re-localizing the nodule via imaging prior to trying again with endoscopic approach, and the decision to extubate the decedent early in the post operative period despite signs of respiratory distress. It was felt that it would be appropriate to recommend that Hospital A conduct a quality of care review of this case.

Recommendation:

To Hospital A:

1. A Quality of Care Review of this case should be conducted, with particular attention to the decision-making around proceeding with open resection, and early extubation.

Special Review – Pneumonitis Following Chemotherapy

Background:

Two deaths of patients with breast cancer who had been undergoing adjuvant chemotherapy with docetaxel (Taxotere) were identified in one cancer centre (Hospital A) in Ontario. The two individuals died within a short period of time, in the Intensive Care Unit (ICU), of what initially appeared to be pneumonia. However, the clinical findings (later confirmed on post mortem examination) were more consistent with pneumonitis, suspected to be due to the chemotherapy they had received.

The expected rate of pulmonary complications from docetaxel is around 2%. This had been the baseline rate of pulmonary complications (with no attributable deaths) observed in patients being treated with docetaxel in Hospital A between 2006 and 2010.

However, in the summer and fall of 2010, there was noted to be a significant increase in symptomatic pneumonitis among patients to whom this drug was administered at Hospital A. During this time period, a total of thirteen patients receiving docetaxel developed varying levels of dyspnea. They ranged in age from their mid-30s to their mid-60s, and had various co-morbid illnesses; however, the respiratory illness they developed was consistent and similar, and no patients of Hospital A who had not received this drug developed a similar acute respiratory distress syndrome. The rate of respiratory complications observed in patients receiving docetaxel at Hospital A between October and December, 2010, was 32%.

Several of the patients affected ultimately were unable to continue employment, and at least one remained long-term oxygen dependent. As noted, two of the thirteen affected patients died. Neither of the patients who died had any significant health problems except their (treated) breast cancer, and neither was expected to die when they did.

Investigation:

A review of the fatalities and illness thought to be due to docetaxel pneumonitis ensued. It was determined that none of the patients who became ill, including the two who died, had received radiation at the time of their illness. None had any prior underlying respiratory illness. All subsequently had bronchoscopy and all were grossly normal. Despite chemotherapy, none of them were neutropenic. Two or three of the patients who became symptomatic had received growth factor as part of an accelerated docetaxel regimen. Some were not subjectively unwell, and only after direct questioning regarding exercise tolerance did the extent of their impairment become evident.

Post mortems on the two patients who died concluded that the injury evident in the lungs was consistent with pneumonitis. It was also determined that the significant respiratory difficulties experienced by the other patients who did not die were very likely a consequence of docetaxel.

An expert review was undertaken by the Office of the Chief Coroner. After internal discussion, it was decided that this review would be overseen by the Patient Safety Review Committee (PSRC).

In addition, Hospital A initiated a number of actions aimed at investigating the illnesses and deaths. These actions included the following:

- A full internal review was commissioned of processes within Hospital A related to the use of docetaxel, including the doses used.
- Health Canada was informed of their observations.
- Samples of the drug were provided to the drug manufacturer for analysis.
- Samples of the drug were sent to the local university for analysis by mass spectrometry.
- Samples of the infusion set used were provided to the manufacturer of the infusion set for their review.

Pending the outcome of this review, Hospital A voluntarily suspended the use of docetaxel.

The PSRC commissioned a review by an independent expert (a haematologist / oncologist and clinical investigator from a cancer centre in a different city), which included an assessment of the process of oncology medication ordering, the nursing documentation, medication mixing and administration processes, tracking of side effects, and follow-up. There were no areas of concern identified with any of the identified areas of review; nor was a cause for the unexpected cluster of pneumonitis identified.

It was noted that a comparable drug, paclitaxel (Taxol), is administered through a filter while docetaxel is not. Evidently, at some time in the past this practice changed; however neither the manufacturer nor the Cancer Care Ontario processes recommend use of a filter for docetaxel. During the PSRC review of this issue, a letter was sent from the Chair of the PSRC to Health Canada asking whether they felt that the use of a filter should be recommended during the administration of docetaxel, pending the outcome of this investigation. Health Canada also indicated that their information did not support a recommendation for the use of a filter for this drug.

It was noted early on that all the patients who became ill (and both who died) had received their chemotherapy at Hospital A. Although 25% of patients associated with the cancer centre who were receiving docetaxel infusions did so in peripheral hospitals under the remote supervision of the cancer centre at Hospital A, none of the patients receiving docetaxel in a peripheral hospital developed pneumonitis. No explanation for this observation was identified.

The hospital undertook a quality of care review, incorporating all of the information they had gathered, and there were no consistent factors identified connecting either of the two patients who died or the others who became ill. More than one medication lot was implicated in the patients developing pneumonitis. A variety of nurses, physicians, and pharmacists had been involved in the care of these patients, with no common provider identified.

A subsequent review of all practices associated with mixing and administration of the drug was conducted by the pharmaceutical company that manufactures docetaxel. Only two minor deviations from their protocols were identified: rather than rolling the vial for mixing, it was recommended that it be inverted; and it was recommended that the premixed drug be held for no more than eight hours, and not more than four hours once it is placed into the intravenous bag. (Hospital A had been following the BC Cancer Agency guidelines regarding preparation and stability of docetaxel which allowed for a longer holding period.) Neither of these actions was linked to the resulting illnesses or deaths.

A few of the docetaxel samples examined at Hospital A were found to contain a cloudy white precipitant. The manufacturer recommends that such doses not be administered when this is identified. This observation was not reported in any of the doses which had been infused into patients who developed pneumonitis. Samples of the lot numbers affected (including those which were not clear in solution) were sent to the manufacturer, who deemed that the drug contained in these samples was within normal limits.

In January 2011, another hospital which followed the same guidelines regarding mixing, storage, and administration as those used by Hospital A noted an increase in Type IV hypersensitivity reactions to docetaxel, and also noticed a number of vials with a cloudy precipitant. The vials with the precipitant were quarantined and sent back to the vendor, who reported “there was no manufacturing issue.”

Health Canada reviewed the case reports they had received from across Canada of adverse reactions to docetaxel between January 1, 2009 and February 28, 2011. A total of 39 individual cases of respiratory events were detected, including three deaths. Overall from 1995 to 2011, there were 191 individual cases reported and 16 deaths. It is noted that this represents a five-fold increase from about four “respiratory” cases per year to 20. What is not reported is the denominator; that is to say, how many people received the drug. The change in baseline deaths would not be deemed statistically significant.

On completion of their investigation, Health Canada did not share the detailed conclusions of their investigation into the drug with the PSRC, but reinforced the advice to discard any medication which did not appear clear or which had any precipitation evident. They also reported that the quality of the lot reviewed by the manufacturer “met the specifications required for approval and distribution.” No further information was provided to the PSRC regarding the Health Canada review.

There were some irregularities noted in the mass spectrometry which the university undertook on behalf of the hospital. When comparing the lots in question with non-affected lots, there were some anomalous “spikes” identified. The university was not able to provide an explanation for this observation, or to comment on what, if any, clinical implications might be inferred. The pharmaceutical company indicated that they had no validated methods for testing docetaxel with mass spectrometry, and declined to draw any conclusion from these results.

Finally, there were no findings related to the infusion sets that could be concluded to have had any impact on the stability, solubility or clinical efficacy of the drug.

Conclusions:

There was no cause identified for the observed increase at Hospital A in the incidence of pneumonitis and the two deaths observed in patients receiving docetaxel. The hospital's internal review did not detect any variance from usual practice. The external reviewer likewise did not detect a root cause for the observed phenomenon. The Patient Safety Review Committee of the Office of the Chief Coroner also did not arrive at a conclusion regarding the underlying cause.

Hospital A has instituted a number of changes since these events, and in preparation for re-introduction of docetaxel in their formulary. These include:

- Docetaxel is no longer used for adjuvant chemotherapy, and has been replaced by paclitaxel; docetaxel is still used in some other metastatic cancers.
- Pharmacy records the drug lot number each time the drug is administered to a patient.
- Individual lot numbers are therefore linked to every patient.
- The timing of administration and elapsed time from preparation are noted.
- Refrigeration is now calibrated, monitored, and documented.
- Enhanced vigilance in the completion of safety reports for any unusual observations has been instituted.
- All visits to the emergency department and all admissions to the intensive care unit by oncology patients are reported to oncology service.
- Annual education for staff regarding handling and preparation of chemotherapy agents has been expanded.
- Pending development of Ontario-specific guidelines, the British Columbia Cancer Association (BCCA) guidelines for chemotherapy preparation have been adopted.

Recommendations:

Beyond the actions noted above (including communicating at various points with Health Canada during the review process), no specific recommendations were made by PSRC with respect to this investigation.

Special Review – Deaths Following Laparoscopic Bariatric Surgery

Introduction:

In 2009 and 2010, the Office of the Chief Coroner investigated a series of unexpected post-operative deaths of laparoscopic bariatric surgery patients at one institution. The resulting collaboration between the Office of the Chief Coroner (OCC) and the institution led to a number of system improvements, following which no further post-operative deaths have been identified. The details of this investigation were presented to the PSRC in order to identify any measures that might be applicable to other bariatric centres in Ontario.

Background:

Bariatric surgery refers to the surgical alteration of the gastrointestinal tract in persons with severe obesity (body mass index (BMI) greater than 40, or greater than 35 with co-morbidities) in order to facilitate weight loss and improvement of co-morbid conditions where other attempts at weight loss have failed. Typically, the associated co-morbid conditions include type II diabetes, hyperlipidemia, sleep apnea and hypertension.

Bariatric surgery typically results in significant weight reduction – usually around 60 percent of excess weight within the first year. This results in a dramatic reduction in co-morbidities; for instance, diabetes completely resolves in over three-quarters of those undergoing bariatric surgery. Mortality risk is reduced by 40 percent in the seven years following surgery.

While a variety of bariatric surgery procedures have been described, most procedures are currently performed using a laparoscope. The most common involves the creation of a smaller stomach which is attached to the distal small bowel (Roux-en-Y gastric bypass). Mortality in the first 30 days is typically quoted between 0.5% and 2%, and increases with higher BMI and greater numbers of co-morbidities. The most common serious operative complications include separation of the attached bowel (anastomotic site leak) resulting in infection (3 to 5% incidence), and intra-abdominal bleeding (0.5 – 1% incidence).

Cluster of Post-Operative Deaths

In November 2009, the OCC became aware of a cluster of three post-operative deaths that occurred in laparoscopic bariatric surgery patients from one Ontario centre. The three deaths occurred between September and November, 2009. A collaborative review of prior cases by the OCC and the hospital identified three previous post-operative deaths that occurred in bariatric surgery patients from that centre between March 2008 and April 2009.

The OCC met with the clinical and administrative staff of the hospital to review the findings in these six cases. The cases involved four different surgeons, and two different procedures. The causes of death were anastomotic site leak (3), hemorrhage (2) and multi-factorial (abdominal wall and peri-pancreatic bleeding plus self-administration of excessive narcotic

medications) in one case. The hospital was unable to identify any common factors in these six cases. When averaged out over three hundred bariatric surgery cases performed at the centre over this 18 month period, the rate of complications and post-operative mortality were felt to be within the rates accepted in the literature. During this time, the hospital initiated a number of process improvements for bariatric patients, including more frequent vital signs assessment and blood testing in the post operative period, and new protocols to ensure that any post-operative bariatric patients who returned to the Emergency Department after discharge were assessed by the General Surgery service.

Shortly after this initial investigation, two further post-operative deaths occurred; one each in January and February, 2010. The OCC conducted a Regional Coroner's Review with the hospital, and it was agreed that the hospital would arrange for an external review of the bariatric surgery program to be conducted by the Provincial Medical Director for Bariatric Surgery. The hospital voluntarily suspended the bariatric surgery program temporarily, pending the external review, and notified the Ministry of Health and Long-Term Care and the Local Health Integration Network. It was also agreed that the hospital would continue to pursue accreditation of their bariatric surgery program through the American College of Surgeons.

The external review was conducted over two days at the hospital, and included a review of all aspects of pre-operative, operative and post-operative care within the bariatric program. The major findings from the review were:

- The incidence of surgical complications was found to be within accepted rates. There were no issues identified with surgical skill or technique.
- There were opportunities identified to improve the selection and medical optimization of patients prior to surgery and to enhance post-operative care.
- Strategies identified included the introduction of Clinical Nurse Specialist and formal Medical Director roles; augmenting the nurse-patient ratio on the surgical ward post-operatively; and having a lower threshold for returning the patient to the operating room for diagnostic laparoscopy when a post operative complication was suspected.

All of the recommendations arising from the external review were implemented. In the first year following the review, 450 bariatric surgery cases were performed at the hospital; the 30 day mortality rate was zero. (One late death occurred in a patient between 30 and 90 days following surgery.) Complication rates were at or below the expected rates reported in the literature, and a number of complications were identified and rectified early through the more liberal use of diagnostic laparoscopy.

Since that time, the hospital has earned the distinction of becoming the first non-US bariatric surgery program to be accredited as a "Center of Excellence" by the American College of Surgery. In addition, the program's referral and intake process has been recognized as a "Leading Practice" by Accreditation Canada. More than 1200 bariatric surgery cases have been performed at the hospital since the review, without a single death in the first 30 days following surgery.

The Patient Safety Review Committee felt that there was value in ensuring that the lessons learned through this process be disseminated to other bariatric centres. To this end, the PSRC made the following recommendations:

To MOHLTC Bariatric Services Program and the Ontario Bariatric Network:

1. The hospital's experience should be shared with other Ontario bariatric centres.
2. The provincial medical director for the bariatric surgery program should work with all Ontario bariatric centres to identify and support the implementation of appropriate components of the hospital's initiative at other sites

To Accreditation Canada:

3. Accreditation Canada should consider disseminating the details of this identified "Best Practice" to hospitals offering bariatric surgery programs.

To the Hospital:

4. The hospital should consider peer-review publication of the initiatives implemented and the outcomes achieved.

Questions or comments pertaining to this report may be directed to:

Patient Safety Review Committee
Office of the Chief Coroner
26 Grenville Street,
Toronto, ON
M7A 2G9

Attn: Executive Lead – Committee Management