

Analysis of causes that led to baby Stryker Eoghan Burke's sudden death

Mohammed Ali Al-Bayati, PHD, DABT, DABVT

Toxicologist & Pathologist

Toxi-Health International

150 Bloom Drive, Dixon, CA 95620

Phone: +1 707 678 4484 Fax: +1 707 678 8505

Email: maalbayati@toxi-health.com

Abstract

Stryker is a 55-day-old white male infant who was found dead in his bed on September 6, 2005. Based on the finding of methanol (20 mg/dL) and formic acid (23.2 mg/dL) in a blood sample taken from his heart at the time of autopsy, his parents were accused of poisoning him with methanol. My investigation reveals that the baby died as a result of severe hyponatremia. He had a critically low serum sodium level of 114 mmol/L (normal range: 135-145 mmol/L). Moreover, the gross and microscopic examinations of the brain showed evidence of edema and hypoxia and these lesions are reported in people suffering from hyponatremia.

My investigation also reveals that there is no evidence that the baby suffered from methanol poisoning. He did not show any symptom of methanol poisoning prior to his death. His brain, spinal cord, eyes and optic nerves, heart, lungs, liver, kidneys, pancreas, and other tissues were examined grossly and microscopically and no lesion was observed that indicated intoxication with methanol.

It is likely that the methanol and formic acid detected in Stryker's blood resulted from the contamination of the blood with formalin used to fix tissues. This fixative contains 1 to 1.5% methanol and 3 to 4% formaldehyde. The oxidation of formaldehyde to formic acid is facilitated by formaldehyde dehydrogenase present in the red blood cells.

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Keywords: Acidosis; Alcohol dehydrogenase; brain edema; formic acid; formaldehyde dehydrogenase; growth retardation; head circumference; hyperbilirubinemia; hyperkalemia; hyponatremia; hypoxemia; hypoxemia; hypoxemia; methanol poisoning; pneumothorax; pulmonary edema; sepsis; stillbirth.

1. Summary of the case and findings

Stryker is a 55-day-old white male infant from Ontario, Canada. He was born at 37 weeks of gestation on July 13, 2005 and developed serious health problems at six hours following birth. These include respiratory distress syndrome (RDS), lethargy, pneumothorax, hypoxemia, sepsis, acidosis, hyperkalemia, and hyperbilirubinemia.

Moreover, his echocardiograph exam showed a small atrial and ventricular septal defect with a small patent ductus arteriosus. His mother previously had two stillbirths, one of which was due to Potters syndrome. Stryker was treated with antibiotics and other medications and released from the hospital on July 22, 2005.

Stryker's mother fed Stryker and changed his clothes at approximately 2300 on September 5. The mother and the baby slept and the mother woke up at approximately 0300 on September 6 to feed her baby. She found him cold, white, and not breathing.

The father and the paramedics performed CPR but without success. The paramedics transported the baby to the hospital where they gave him 0.9% sodium chloride solution IV. The baby was pronounced dead in the hospital.

Dr. Chitra Rao performed an autopsy on Stryker's body (Case # ML 05-415) at 1312 on September 6, 2005. Prior to autopsy, Stryker's body was examined by X-rays and showed no evidence of recent or old bony fractures or any other bony abnormalities.

At autopsy, a blood sample was taken and revealed critically low serum sodium level of 114 mmol/L (normal range: 135-145 mmol/L) and normal levels of urea and creatinine in serum. Moreover, blood, skin, tissues, and stool samples were taken for

cytogenic, bacterial culture, and other clinical studies. They showed that the baby did not have bacterial or viral infections.

Rao examined Stryker's body and tissues grossly. She also examined the H & E stained sections of the brain, spinal cord, and other major organs microscopically. In addition, she evaluated certain tissues using electron microscope. Her examination revealed no evidence of injuries caused by trauma and infections.

Her gross and microscopic examinations of the brain showed evidence of edema and hypoxia. She also reported the possibility of mild edema in the lung. In addition, she observed areas of extramedullary hematopoiesis within the liver, the epicardial adipose tissue, and the choroids and sclerae of the right eye. The gross and microscopic examinations of other organs revealed no abnormalities.

Rao sent a blood sample taken from the baby's heart, along with stomach content, to the Centre of Forensic Sciences (CFS) in Toronto for chemical analysis. The CSF reported on January 30, 2006 that Stryker's blood contained formic acid and methanol at the concentration levels of 232 mg/L and 200 mg/L, respectively. Stryker's parents were accused of poisoning their baby with methanol and their other two children were removed from their house and placed with relatives.

Stryker's parents requested that I review the medical data in Stryker's case and the family medical history and provide an opinion concerning the likely cause(s) of their baby's death. I am a pathologist and toxicologist with over twenty years experience in these fields. I have also evaluated many cases of babies and older children who died suddenly due to variety of causes and my investigations have led to explaining the causes of death in these children. I have also served as an expert witness in these cases.

I reviewed the medical evidences and the published medical literature pertinent to Stryker's case. I used differential diagnosis to identify the likely causes that led to Stryker's death. I spent about 200 hours in evaluating the medical evidence and writing a detailed report in this case. The clinical data and studies described in this report reveal the following:

1) Stryker's death was caused by severe hyponatremia. His serum analysis performed on September 6, 2005 revealed a critically low serum sodium level of 114 mmol/L (normal range: 135-145 mmol/L). In addition, the gross and microscopic examinations of the brain showed evidence of edema and hypoxia. Individuals who suffer from severe hyponatremia develop brain edema, hypoxia, neurological problems, and respiratory arrest. For example, Soupart and Decaux stated that an abrupt fall in serum sodium may cause seizure, respiratory arrest, and coma. Hyponatremia produces brain edema and increased intracranial pressure that leads to subsequent neuropathological sequelae or death [Section 6].

2) Stryker suffered from health problems that led to the development of severe hyponatremia. Rao reported the presence of areas of extramedullary hematopoiesis within the liver, the epicardial adipose tissue, and the choroids and sclerae of the right eye. It has been reported that finding areas of extramedullary hematopoiesis within the liver and other tissues of a child or an adult indicates that the individual is suffering from chronic hypoxemia and/or anemia. Moreover, Rao reported that the baby's nail beds of both hands appeared somewhat cyanotic.

Furthermore, Stryker's head circumference growth rate during his 55 days of life was 1.47 cm/month, which is significantly lower than the average rate (2.5 to 3.0 cm/month) for healthy infants similar to his age. These observations indicate that the baby suffered from hypoxemia and possible development problems (Sections 5 and 6).

3) It is possible that there are common factors between Stryker's causes of illness and death and the family history with serious health problems. Stryker's mother had two stillbirths, one of which was due to Potters syndrome. The cause of the second stillbirth was not determined. The mother also had a baby boy born at about one year after Stryker's death who developed health problems at 6 hours following birth which were similar to those observed in Stryker's case (Section 7).

4) There is no evidence that Stryker suffered from methanol and/or formic acid intoxication. I base my medical opinion on the followings clinical observations and medical studies:

a) Stryker did not show symptoms of methanol poisoning during the 48 hours prior to his death. These include neurological signs, vomiting, diarrhea, and other health problems. In humans, the ingestion of toxic levels of methanol usually cause damage to the nervous system, eyes, kidneys, pancreas, and other organs (Section 9.1).

b) Stryker's brain and spinal cord were examined grossly and microscopically by Rao and she did not observe any lesion that would indicate the baby was exposed to methanol and formic acid. She also examined a section of the brain

using an electron microscope and did not observe any lesion that indicated the baby was exposed to methanol and/or formic acid.

Furthermore, Dr. John Provias, neuropathologist examined sections of Stryker's meninges, brain, and spinal cord microscopically and he did not observe changes that are usually associated with methanol toxicity in humans. In particular, his examination revealed no specific changes of methanol toxicity such as patterned or regional neuronal necrosis, areas of tissue necrosis, infarction or hemorrhage. Pathological changes observed in the brain of people who suffered from methanol intoxication are described in Section 9.2 of this report.

c) Dr. Rao examined Stryker's eyes grossly and microscopically and did not observe any lesion that would indicate methanol and formic acid toxicity. Formic acid inhibits mitochondrial cytochrome oxidase activity leading to ocular toxicity. Retinal damage and bilateral optic nerve necrosis and atrophy have been observed in humans intoxicated with methanol. Ocular lesions associated with methanol intoxications are described in Section 9.3 of this report.

d) Dr. Rao examined Stryker's heart, lungs, liver, kidneys, pancreas, and adrenal glands grossly and microscopically and did not observe any lesion that would indicate the baby was intoxicated with methanol and/or formic acid. Moreover, she evaluated tissue samples of liver, skeletal muscle, and heart using an electron microscope and did not find any specific ultrastructural abnormalities. Lesions observed in pancreas and kidneys of individuals intoxicated with methanol are described in Section 9.4 of this report.

e) Clinical studies showed that methanol at the level detected in Stryker's blood (20 mg/dL) did not cause severe toxicity within four hours following ingestion. Methanol has a relatively low toxicity and metabolism is responsible for the transformation of methanol to its toxic metabolites. For example, Kostic and Dart analyzed published cases of methanol poisoning and found 22 cases presented for care within 6 hours of ingestion. A clear acidosis developed only with a methanol level ≥ 126 mg/dL. This level of methanol is more than six times the level of methanol (20 mg/dL) detected in Stryker's blood sample (Section 9).

f) I believe that detecting methanol and formic acid in a single blood sample in the absence of medical data that show methanol intoxication is insufficient to make a case for methanol intoxication. In Stryker's case, the gastric contents and tissue samples were not analyzed for the presence of methanol and formic acid as has been typical protocol in many medical and legal investigations.

For example, Tanaka *et al.* determined the levels of formic acid in the blood, stomach contents, urine, and organs of two men who were fatally intoxicated with methanol. The average formic acid concentrations were 0.28 mg/mL in the blood, 1.37 mg/mL in urine, 0.64 mg/g in the brain, 0.53 mg/g in the liver, and 0.66 mg/g in the kidneys. The average total amount of formic acid in the gastric contents for these men was 65.6 mg.

5) I believe that the methanol and formic acid detected in Stryker's blood resulted from the contamination of the blood with formalin used in the laboratory to fix tissues. Formalin fixative contains 1 to 1.5% methanol and 3 to 4% formaldehyde. The oxidation of formaldehyde to formic acid is facilitated by formaldehyde dehydrogenase present in the red blood cells. For example, human blood oxidized formaldehyde (0.7 mg to 4 mL blood) to formic acid in vitro within four hours (Section 10).

2. Stryker's health problems developed following birth and treatments given

Stryker was born on July 13, 2005 at 37 weeks of gestation via vaginal delivery. His umbilical cord was wrapped around his neck. Stryker's apgar score was 9 both at 1 and 5 minutes. His weight and head circumference were 2830 g and 35 cm, respectively. He was treated with erythromycin ointment (0.5%) in both eyes within two hours following birth. He was also injected with 1 mg of vitamin K (IM).

Stryker appeared healthy; however, at about 6 hours following birth, he developed respiratory distress syndrome (RDS), lethargy, pneumothorax [1]. His respiratory rate was elevated (80-90/minute). He also developed hypoxemia, sepsis, acidosis, hyperkalemia, and hyperbilirubinemia. He was given IV fluid and treated with antibiotics, morphine, and Tylenol as shown in Table 1. In addition, he was given phototherapy as treatment for his jaundice.

Table 1. Some of the treatments given to Stryker at the hospital

Date	Treatments
7/14/05	Morphine 0.3 mg IV Gentamicin, 7.0 mg IV q 12 hrs Ampicillin 280 mg IV q 12 hrs IV Fluids and amino acids
7/15/05	Morphine 0.2 mg IV Gentamicin, 7.0 mg IV q 12 hrs IV Fluids and amino acids
7/16/05	Gentamicin, 7.0 mg IV q 12 hrs IV Fluids and amino acids
7/17/05	Morphine 0.25 mg IV Acetaminophen 40 mg IV Fluids and amino acids
7/18/05	Acetaminophen 40 mg
7/20/05	Acetaminophen 40 mg

Stryker was released from the hospital on July 22, 2005. His weight on July 21 was 2703 g, which was 127 g less than his weight at birth. Below are the results of the clinical tests performed in the hospital and their significance.

2.1 Respiratory distress syndrome, pneumothorax, and acidosis

Stryker developed respiratory distress syndrome at approximately six hours following birth. He was noted to have an increased respiratory rate. The baby was transferred to the neonatal

unit and a chest X-ray was taken on July 14. It revealed a large left-sided pneumothorax necessitating the insertion of a chest tube. This X-ray also showed minimal subsegmental atelectasis and air space disease at both lung bases.

The chest tube was clamped on July 19 and removed from the chest on July 20, 2005. A follow-up chest X-ray showed no re-accumulation of air. The drainage site was healing well at the time of discharge on July 22, 2005.

Stryker's blood analysis performed on July 14 and 15 revealed low pH and PO₂ levels. He suffered from acidosis and hypoxemia (Table 2). His serum analysis revealed that he suffered from hyperkalemia for at least six days (Table 3).

Table 2. Stryker's blood gases measured in July, 2005

Measurements	Values on			Reference range
	July 14	July 14	July 15	
Blood pH capillary	0840	2025	0920	7.35-7.45
PCO ₂ (mm Hg)	7.25	7.28	7.25	38-50
PO ₂ (mm Hg)	48	49	55	75-105
Actual bicarb. (mmol/L)	52L	37L ¹	36L	22-26
Base excess (mmol/L)	20	22	23	-2 to -3
	-7L	-5L	-5L	

¹ Bubble in sample, L: Values lower than normal.

Table 3. Stryker's serum analyses results

Date	Time	Sodium (mmol/L)	Potassium (mmol/L)	Glucose (mmol/L)
7/14/05	0840			6.1
7/14/05	1140	131L	6.6H	5.2
7/14/05	2000	132L		6.3
7/15/05	0920	138	6.1H	
7/15/05	2000	132L		
7/16/05	1515	137		4.8
7/18/05	0845	142	5.2H	4.7
7/19/05	0820	141	5.4H	4.7
7/20/05	0915	138	5.9H	
Reference range		135-145	3.5-5.0	<11.1

2.2 Heart problem

Stryker had an echocardiograph exam on July 14, 2005 that showed a small atrial septal defect (ASD) measuring 5 mm with bi-directional flow and a small mild ventricular septal defect (VSD). Also revealed was a small patent ductus arteriosus (PDA) flowing left to right. A chest X-ray showed Stryker's heart was within the normal limits.

2.3 Bacterial infection

Stryker's blood analysis performed on July 14, 2005 revealed elevated white blood cell and neutrophil counts (Table 4), indicating he had bacterial infection. He was treated with

antibiotics as listed in Table 1 and his white blood cell and neutrophil counts returned to normal on July 17 (Table 4).

Table 4. Stryker's white blood cell counts measured in July, 2005

Measurements	Values x 1000/ μ L			Reference range
	July 14 at 0418	July 14 at 2000	July 17 at 2025	
White blood cell	24.6	23.6	13.2	5.0-21.0
Neutrophil	18.2	18.2	6.5	1.5-10.0
Bands	0.7	0.5		
Lymphocytes	4.2	3.8	5.1	2.0-17.0
Monocyte	0.7	0.7	0.8	0.5-1.9
Eosinophil	0.5	0.2	0.8	0.2-0.8

2.4 Jaundice

Stryker's blood analysis performed on July 14-20, 2005 revealed that he developed Jaundice on July 15. His total bilirubin level reduced to a normal range on July 20. However, his conjugated bilirubin level remained elevated (Table 5). Blood analysis revealed that Stryker did not suffer from anemia between July 14 and 17, and his platelet count was normal (Table 6).

Table 5. Stryker's serum bilirubin levels

Date	Time	Bilirubin Conjugated (μ mol/L)	Bilirubin Total (μ mol/L)
7/14/05	0840	-	117
7/14/05	2000	4	129
7/15/05	0920	4	149
7/15/05	2000	5	190H
7/17/05	0825	6H	274H
7/17/05	2025	7H	283H
7/18/05	0845	9H	311H
7/19/05	0820	9H	258H
7/20/05	0915	10H	214H
7/20/05	0750	9H	148
Reference range		0-5	<170

Table 6. Stryker's hematology measurements in July of 2005

Measurements	Values on			Reference range
	July 14 at 0418	July 14 at 2000	July 17 at 2025	
Red blood cell x $10^6/\mu$ L	4.81	5.12	5.07	4.0-6.6
Hemoglobin (g/L)	171	181	181	145-225
Hematocrit %	50.8	54.4	53.3	45-67
MCV (fL)	106	106	105	95-121
MCH (pg)	35.6	35.3	35.8	28-40
MCHC (g/L)	337	332	341	280-360
RDW	15.6	15.7	14.9	11.5-15.0
Platelet x $10^3/\mu$ L	288	185	277	150-400

3. Stryker's health condition between July 21 and September 5, 2005

3.1 Stryker's health condition and growth rate between July 23 and August 3

Stryker was released from the hospital on July 22 and was fed formula milk.

A physician examined him on July 25, 2005 because there was a concern about his breathing. His pediatrician also examined him on August 3, 2005 [2]. His weight and head circumference were 3233 g (7 pounds and 2 ounces) and 36 cm, respectively. He had gained 529 g since his release from the hospital on July 22 (40.6 g/day). His head circumference had increased 1 cm since birth.

3.2 Stryker's health condition between August 4 and September 4

Stryker was not seen by a physician between August 4 and September 4, 2005. His parents did not notice any alarming condition that required a visit to the doctor. However, Stryker's mother related the following reported observations:

1) The baby had a very strong urine odor. She smelled it in his diapers and sleepers and when he urinated. The baby also had a sweaty body odor. The baby did not smell fresh within hours of taking a bath. The mother also noticed on a few occasions that the baby's head and back were fairly damp when he awoke from a nap. The baby was not overdressed.

2) The baby vomited on a few occasions.

3.3 Stryker's health condition on September 5 and 6

Stryker seemed fine on September 5. His mother gave him a bath in the morning and took him to the neighborhood park. They sat under a gazebo style picnic area for the majority of the day. Stryker was seen and held by the family friends and no one noticed anything unusual concerning the baby's health.

However, Stryker's mother reported that the baby slept a lot, thinking this was due to the fresh air. Furthermore, the mother stated that the baby did not drink the usual amount from his bottle that day. He took approximately one ounce less than normal per feeding. She usually fed him each three or four hours or on demand.

The parents brought Stryker home at night. The mother fed him and changed his clothes for the last time at approximately 2300 on September 5. She did not notice any unusual sign such as Stryker appearing fussy or ill. The mother and baby slept and the mother awoke at approximately 0300 on September 6. The mother was alarmed that the baby had not awakened for his feeding. She looked at him and touched his cheek. He was cold, white, and not breathing.

The mother picked up the baby and ran downstairs screaming for the father. She said that there was something wrong with the baby. The father took the baby from his mother and started CPR. The mother called the ambulance. The paramedics also

performed CPR but without success. The paramedics placed an intra osseous IV line over the right tibia and connected a bag of 0.9% sodium chloride solution. The baby was taken to the hospital and pronounced dead. The mother noticed some formula near the baby's head and ear in hospital. Scene investigation revealed no evidence of any disturbance in the house.

4. Serum analysis and bacteriology and virology studies performed on September 6, 2005 and their significance

The paramedics brought Stryker to the hospital in the morning of September 6 where he was pronounced dead. At autopsy, a blood sample was taken for serum analysis and bacterial culture. Furthermore, skin and tissue samples and stool sample were also taken for cytogenetic and other clinical studies. Serum analysis revealed that Stryker suffered from a severe and fatal case of hyponatremia. Other studies showed that the baby did not have bacterial or viral infections [3].

4.1 Stryker's serum had very low sodium level

Serum analysis performed on September 6 revealed very low serum sodium level of 114 mmol/L (normal range: 135-145 mmol/L). Stryker's average serum level of sodium for the eight samples of blood analyzed in July of 2005 was 136 mmol/L. These data indicate that Stryker was suffering from a severe and fatal case of hyponatremia.

The paramedics gave the baby 0.9% sodium chloride solution and the baby's hyponatremia was not caused by a treatment given in the hospital.

Severe hyponatremia (serum sodium levels less than 120 mmol/L) is usually associated with significantly high morbidity and mortality rates in humans [4]. For example, Howanitz and Howanitz evaluated the records of 166 individuals who had a critically low serum sodium level of 120 mEq/L (120 mmol/L) and found that the mortality rate of hyponatremia was 19% [5].

Stryker's serum urea and creatinine levels were within the normal range, indicating he did not suffer from kidney or liver problems. A normal serum creatinine level also indicates that the baby did not suffer from muscle wasting illness and malnutrition.

4.2 Bacteriology and virology studies did not reveal infections

Culture of Stryker's peripheral blood sample taken at the autopsy revealed growth of mixed organisms consisting of *Klebsiella pneumoniae* and coagulase negative *Staphylococcus* species, indicating post mortem contamination. In addition, a sample of the skin was taken for cytogenetic studies and the results indicated that the specimen received failed to grow in culture. Tissue samples were also taken for viral culture and showed no significant findings.

Electron microscopic examination of the stool specimen showed no evidence of virus and viral antigen was negative for rotavirus and adenovirus. The culture of the stool sample similarly revealed no growth of adenovirus or enterovirus. Culture of the stool sample from small and large bowel was negative for

Salmonella, *Shigella*, *Yersinia enterocolitica*, *Campylobacter* and *E. coli* 0157.

5. Autopsy findings in Stryker's case and their significance

Dr. Chitra Rao performed an autopsy on Stryker's body (Case # ML 05-415) on September 6, 2005 at 1312 at the Hamilton Health Sciences-General campus in Ontario, Canada. Prior to autopsy, Stryker's body was examined by X-rays and showed no evidence of recent or old bony fractures or any other bony abnormalities [3].

Dr. Rao examined Stryker's body and tissues grossly. Also examined the H & E stained sections of the brain, spinal cord, and other major organs microscopically. In addition, certain tissues were evaluated using electron microscope [3]. I reviewed these findings described below (Section 5.1-13) and my review reveals the following significant observations that provide medical explanations for Stryker's sudden death.

1) The gross and microscopic examinations of the brain showed evidence of edema and hypoxia. No other lesions were found in the brain; thus, the baby did not suffer from trauma, infectious diseases, or poisoning with methanol and formic acid. Stryker's serum sodium level was 114 mmol/L (normal range: 135-145 mmol/L), indicating he suffered from severe hyponatremia. Severe hyponatremia is defined as serum sodium levels less than 120 mmol/L [4].

Individuals suffering from severe hyponatremia develop brain edema, hypoxia, neurological problems, and respiratory arrest. For example, Soupart and Decaux stated that an abrupt fall in serum sodium might cause seizure, respiratory arrest, and coma. Hyponatremia produces brain edema and increased intracranial pressure that leads to subsequent neuropathological sequelae or death [6]. Farrar *et al.* conducted retrospective chart review of infants who presented to an urban pediatric emergency department with seizures. They found that hyponatremia was the cause of seizures in 70% of 47 infants younger than 6 months who lacked other findings suggesting a cause [7].

Dr. Rao's examined the H & E stained sections of Stryker's liver, heart, and the right eye microscopically and observed areas of extramedullary hematopoiesis within the liver, the epicardial adipose tissue, and the choroids and sclerae of the right eye [3]. It has been reported that finding areas of extramedullary hematopoiesis within the liver and other tissues of a child or an adult indicates that the individual is suffering from chronic hypoxemia and/or anemia [8-13]. In addition, Dr. Rao reported that the baby's nail beds of both hands appeared somewhat cyanotic. These observations indicate that the baby suffered from chronic hypoxemia.

3) Stryker's head circumference on September 6 and July 13, 2005 was 35 and 37.5 cm, respectively. Stryker's age on September 6 was 55 days. It seems that the growth rate of Stryker's head circumference (1.47 cm/month) is less than that for healthy infants with the same age (2.5-3.0 cm/month). For example, Brandt evaluated head circumference growth rate in cm/month from the prenatal period until the age of 18 months. Measurements were made in 60 appropriate for gestational age

(AGA) preterm infants of very low fetal age and 68 full term infants.

The study found a period of rapid head circumference growth—a growth spurt—that extends from the 31st postmenstrual week until the 6th month after term, after which time the velocity curves flatten in subsequent months. If the age is not corrected for prematurity, the peak of the velocity curve becomes flat and spreads with a mean growth velocity of 3.0 cm, 3.5 cm, and 2.5 cm, in the first, second and third months, respectively [14].

5.1 External examination of the body and measurements taken

Dr. Rao stated that Stryker was well nourished and his weight and other body measurements were within the normal range for his age (Table 7). Examination of the body did not reveal injuries caused by trauma. Examination of bones and skeletal muscles revealed no abnormality. She observed clear fluid oozing freely through both nostrils of the baby and the nail beds of both the baby's hands appeared somewhat cyanotic.

Table 7. Stryker's weight and other measurements taken on September 6

Measurements	Values
Body weight	4600 g
Length from crown to heel	61.0 cm
Crown to rump	43.0 cm
Rump to heel	18.0 cm
Head circumference	37.5 cm
Chest circumference	37.5 cm
Abdominal circumference	38.0 cm
A single arm length	24.0 cm
Foot length	9.5 cm

5.2 Examination of the head and neck

There was no bruising of the scalp and its undersurface. The skull was intact and the sinuses were patent. The tongue was intact. The dissection of the neck revealed no evidence of hemorrhage or bruising of the musculature. The microscopic examination of the H & E stained sections of the right and left middle ears revealed no evidence of significant inflammation.

5.3 Examination of the brain and meninges

5.3.1 Meninges

Gross examination of the fresh dura and fixed dura showed no evidence of sub or epidural hemorrhage or subarachnoid hemorrhage. Microscopic examination of the H & E stained section of the dura revealed no evidence of sub, epi, or intradural hemorrhage, trauma, tissue necrosis, or any other evidence of any pre-existing disease process.

5.3.2 Gross examination of brain

The brain weighed 525 g. External examination of the brain revealed symmetrical cerebral hemispheres showing generalized cortical congestion. The brain on the whole appeared

somewhat soft and showed scattered areas of flattening of the convolutions. There was no evidence of any surface contusion.

The brain was put in formalin fixative on September 6 and the examination of the fixed brain was done on November 10, 2005. It revealed symmetrical cerebral hemispheres with no evidence of surface contusion or hemorrhage. The brain appeared somewhat soft and showed areas of flattening of the convolutions indicative of mild edema. There was no gyral abnormality noted.

Examination of the undersurface of the brain similarly showed no contusions or evidence of herniation. Basal blood vessels revealed no vascular anomaly. In the process of sectioning the cerebrum, the brain matter fell apart with the cut surface appearing glistening. Neither obvious paranchymal hemorrhage nor other gross lesions were noted. Examination of representative sections of the midbrain, pons, medulla, and the cerebellum showed no evidence of trauma or any other lesion.

5.3.3 Microscopic examination of the brain

Dr. Rao examined the H & E stained sections of the brain microscopically and observed generalized parenchymal congestion. Some of the sections appeared highly fragmented due to postmortem autolysis. She observed areas of neuronal spongiosis with a few eosinophilic neurons. There was no evidence of trauma or infection observed.

5.4 Examination of the eyes

Both eyes were removed and showed no evidence of bruising of the periorbital tissue or perineural sheath hemorrhage. Both eyes were put in formalin fixative on September 6, 2005 and the fixed eyes were examined grossly on October 24, 2005. There was no evidence of perineural sheath hemorrhage and on bisecting the eyes, no gross evidence of hemorrhage was observed.

Microscopic examination of the H & E stained sections of both eyes revealed no evidence of retinal hemorrhage. However, a section of the right eye revealed areas of extramedullary hematopoiesis within the choroids and sclerae. Sections taken from both optic nerves including the extra ocular muscles revealed no evidence of perineural sheath hemorrhage and no hemorrhage within the extra ocular muscles.

5.5 Examination of the spinal cord

A posterior approach was taken to expose the spinal cord. Removing the skin revealed no evidence of bruising of the musculature. The vertebrae were dissected and the examination of the spinal cord in situ showed no evidence of hemorrhage or softening. The spinal cord was removed and put in formalin fixative. Examination of the fixed cord with surrounding dura showed no evidence of dural sheath hemorrhage. On serial sectioning, the spinal cord revealed no evidence of trauma or any other abnormality.

Microscopic examination of the H & E stained sections taken from the various regions of the spinal cord showed no evidence of trauma or infection. There was no evidence of epi, sub or intradural hemorrhage.

5.6. Examination of the respiratory system

5.6.1 Upper respiratory system

The airways appeared normal grossly. Larynx, trachea, and bronchi contained a scant amount of mucoid material. Occasional lymph nodes were noted within the tracheobronchial junction.

The examination of the H & E stained sections of the trachea revealed partial lining by a respiratory-type epithelium. The submucosa showed no evidence of significant inflammation. The examination of the H & E stained sections of the main bronchi revealed sloughing of the lining epithelium due to post-mortem autolysis. The submucosa showed congestion but appeared free of significant inflammation. The adjacent lymph nodes showed mild sinus hyperplasia with congestion.

5.6.2 Lungs

The left lung's weight was 48 g before infusion with the formalin fixative and the weight of the lung with fixative was 68.8 g. The right lung weighed 55.5 grams. The cut surfaces of both lungs appeared congested and with questionable mild edema.

The examination of the H & E stained sections of both lungs revealed generalized parenchymal congestion with areas of mild intra-alveolar hemorrhage. There was irregular and variable alveolar expansion with occasional areas showing alveolar collapse. Some of the bronchi included peribronchial lymph nodes showing congestion and slight reactive changes.

Bacterial colonies were present within some of the bronchi and bronchiolar lumen as well as within the alveolar lumen. Some areas showed the presence of aspirated milk with the bacterial colonies. No secondary inflammatory reaction was seen and the changes represented agonal aspiration. None of the sections examined revealed any evidence of bronchiolitis, bronchitis, or pneumonia.

5.7 Examination of the heart

The heart, pericardial sac, and major blood vessels appeared normal grossly. The microscopic examination of the H & E stained sections taken from the right and left ventricles revealed generalized parenchymal congestion, but no evidence of myocardial hypertrophy, myocardial necrosis, or myocarditis. Occasional foci of extramedullary hematopoiesis were noted within the epicardial adipose tissue showing a perivascular arrangement.

5.8 Examination of the thymus, spleen, and bone marrow

5.8.1 Thymus

The thymus weight was 34.12 grams and it appeared normal. The microscopic examination of the H & E stained sections of the thymus revealed normal cortico-medullary differentiation. A few macrophages were noted within the deep cortex. Many Hassall's corpuscles were identified with occasional Hassall's corpuscles appearing dilated and contained detritus.

5.8.2 Spleen

The spleen weighed 15.4 grams and appeared normal grossly. Examination of the H & E stained sections of the spleen microscopically revealed parenchymal congestion.

5.8.3 Bone marrow

The microscopic examination of the H & E stained sections of bone marrow revealed normal cellular representing all three-cell lines.

5.9 Examination of the peritoneal cavity and gastrointestinal tract

The medical examiner reported the following observations:

- (1) There was no fluid accumulation in the peritoneal cavity.
- (2) Pharynx and esophagus appeared normal.
- (3) Stomach contained 30 mL of curdled milk and the mucosa showed no lesion.
- (4) Intestines showed generalized distension due to autolysis and no other mucosal lesion was noted.
- (5) Pancreas weighed 8.4 grams and showed no gross lesion. Examination of the H & E stained sections of the pancreas microscopically revealed parenchymal congestion. There was mild mononuclear cellular infiltration of the periductal region. The islets appeared unremarkable.

5.10 Examination of the liver and gall bladder

The liver weighed 187 grams and appeared normal grossly. Examination of the H & E stained sections of the liver microscopically revealed parenchymal congestion with areas showing minimal fatty change in the form of microvesicles. Occasional foci of extramedullary hematopoiesis were noted. The gall bladder appeared normal.

5.11 Examination of the genito-urinary system

The gross examination of kidneys, urinary bladder, prostate gland, and testes appeared normal. The weights of left and right kidneys were 19 and 20 g, respectively. Microscopic examination of the H & E stained sections of the kidney revealed generalized parenchymal congestion. Small collections of mononuclear cells were noted within the cortical interstitium in one section. Apart from this, there was no evidence of tubular necrosis or inflammation. Immunohistochemical stain done for myoglobin was negative.

5.12 Examination of the thyroid and adrenal glands

The thyroid was in normal position and revealed no gross lesion.

The right and left adrenal glands weighed 2.2 and 2.0 g, respectively. On sectioning, there was no hemorrhage or necrosis noted. Microscopic examination of the H & E stained sections of the adrenals showed medullary congestion.

5.13 Examination of tissues using electron microscope

Tissue samples taken for electron microscopic studies revealed no specific ultrastructural abnormalities in the sections of liver, skeletal muscle, brain, and heart.

6. The clinical significance and likely causes of Stryker's hyponatremia

Stryker's serum analysis performed on September 6, 2005 revealed a critically low serum sodium level of 114 mmol/L (normal range: 135-145 mmol/L). Stryker's average serum level of sodium for the eight samples of blood analyzed in July of 2005 was 136 mmol/L (Table 3). These data indicate that Stryker was suffering from a severe and a fatal case of hyponatremia. Severe hyponatremia is defined as serum sodium levels less than 120 mmol/L and is usually associated with high morbidity and mortality rates in humans [4, 15].

Hyponatremia can be due to sodium loss or fluid excess [15]. The onset of acute hyponatremia is relatively rapid. For example, seven healthy marathon runners collapsed after competing in a marathon. They were hospitalized with pulmonary edema. The mean (\pm SD) plasma sodium level was 121 ± 3 mmol/L, and oxygen saturation was less than 70%. Chest radiographs showed pulmonary edema with a normal heart. Electrocardiograms and echocardiograms were normal. Scanning of the brain showed cerebral edema [16].

Furthermore, severe hyponatremia developed after elective surgery in 15 previously healthy women who subsequently either died or had permanent brain damage. Their average preoperative serum sodium level was 138 mmol/L. These women recovered from anesthesia. However, they developed grand mal seizures, followed by respiratory arrest at about 49 hours following surgery. Their average plasma sodium level was 108 mmol/L. At that time, the urinary sodium level and the osmolality averaged 68 mmol per liter and 501 mOsm per kilogram, suggesting inappropriate secretion of antidiuretic hormone [17].

The clinical evidence indicates that Stryker developed acute hyponatremia and it was likely caused by water retention. The data presented in Table 8 show that his weight gain rate between August 3 and September 6 (40.6/day) was more than twice of that for the period between July 13 and August 3 (19.1 g/day). However, his head circumference growth rates for those two periods are almost equal.

It is possible that Stryker's body retained water within the 24 hours prior to his death that led to lowering his serum sodium to the critical level of 114 mmol/L. Excessive water retention is usually caused by the over release of antidiuretic hormone from the pituitary gland in response to certain illnesses and pain [17].

Stryker suffered from hypoxemia. The medical examiner (ME) reported the presence of areas of extramedullary hematopoiesis within the liver, the epicardial adipose tissue, and the choroids and sclerae of the right eye [Section 5]. It has been reported that finding areas of extramedullary hematopoiesis within the liver and other tissues of a child or an adult indicates that the individual is suffering from chronic hypoxemia and/or anemia [8-13]. In addition, the ME reported that the baby's nail beds of both hands appeared somewhat cyanotic. These observations indicate that the baby suffered from hypoxemia.

Furthermore, Stryker's head circumference growth rate during his 55 days of life was 1.47 cm/month, which is significantly lower than the average rate (2.5-3.0 cm/month) for healthy infants similar to his age. Brandt evaluated head circumference growth rate in cm/month from the prenatal period until the age of 18 months. Measurements were made in 60 cases appropriate for gestational age (AGA) preterm infants of very low fetal age and 68 full term infants. They found that the average growth rates for the first and second month to be 3.0 and 3.4 cm, respectively [14].

Individuals suffering from severe hyponatremia develop brain edema, hypoxia, neurological problems, and respiratory arrest. Soupart and Decaux reported that an abrupt fall in serum sodium may cause seizure, respiratory arrest, and coma. Hyponatremia produces brain edema and increased intracranial pressure that leads to subsequent neuropathological sequelae or death [6].

Arieff and Ayus evaluated four healthy women who underwent elective endometrial ablation for dysfunctional bleeding and developed hyponatremic encephalopathy. The mean (\pm SD) preoperative serum sodium level was 138 ± 1 mmol/L and it was 107 ± 13 mmol/L at the time of diagnosis of hyponatremia. Two of these women developed either hypothermia or hypoxemia. The diagnosis was established before respiratory arrest occurred in three women. The fourth woman suffered respiratory arrest before therapy could be initiated [18].

In addition, Farrar *et al.* conducted a retrospective chart review of infants who presented to an urban pediatric emergency department with seizures. They found that hyponatremia was the cause of seizures in 70% of 47 infants aged younger than 6 months who lacked other findings suggesting a cause [7].

The medical examiner stated that the cut surfaces of Stryker's both lungs appeared congested and with questionable mild edema. No evidence of inflammation was observed in Stryker's lungs. Individuals suffering from severe hyponatremia also developed pulmonary edema.

For example, Ayus and Arieff conducted a retrospective cohort study of 40 adults with postoperative hyponatremic encephalopathy and hypoxia, of whom 30 had noncardiogenic pulmonary edema and 10 had hypercapnic respiratory failure. Among the 30 individuals with pulmonary edema, the serum sodium (\pm SD) was 114 ± 7 mmol/L, arterial pH was 7.24 ± 0.16 , PCO_2 was 45 ± 15 mm Hg, and PO_2 was 42 ± 16 mm Hg [19].

In addition, Kashyap *et al.* reported a case of a young previously healthy female cross country runner who collapsed on completion of a cross country run. The cause of the collapse was non-cardiogenic pulmonary oedema as a manifestation of hyponatraemic encephalopathy [20].

Stryker suffered from severe hyponatremia as indicated by his critically low serum sodium level of 114 mmol/L. However, the medical examiner has overlooked considering hyponatremia in her evaluation of Stryker's case. Hyponatremia should be considered in any investigation dealing with illness or death of a child or an adult even when serum sodium level is moderately low. Hyponatraemia is one of the most common electrolyte abnormalities leading to significant morbidity and mortality [15].

For example, Singhi *et al.* correlated serum sodium concentration at the time of hospitalization with the length of hospital stay and mortality in a prospective study of 727 sick children aged up to 12 years, who sought emergency care. They found that the mortality rate in 510 children with normal serum sodium concentration (≥ 131 mmol/L) was 5.3%. In contrast, it was 17% in 47 children with serum sodium < 125 mmol/L and 9.3% in 170 children with serum sodium between 126–130 mmol/L [21].

Table 8. Stryker's weight gain rate and head circumference growth rate

Measurement	7/13- 8/3/05	8/3- 9/6/05	7/13- 9/6/05
Weight gain (g)	402	1368	1770
Weight gain rate (g/day)	19.1	40.2	32.2
Head circum Growth (cm)	1	1.7	2.7
Head circum. Growth rate cm/month)	1.43	1.50	1.47

7. Problems that Stryker's mother experienced with other pregnancies and possible common factors in Stryker's case.

Stryker's family also lost two babies prior to Stryker's birth due to developmental and other health problems. Stryker's mother had two stillbirths, one of which was due to Potters syndrome. The cause of the second stillbirth was not determined. Stryker's mother also had a baby boy that was born approximately one year following Stryker's death. This baby developed health problems 6 hours following birth that were similar to those observed in Stryker's case.

I believe that the family's history with health problems should be taken into consideration in the evaluation of Stryker's case. Stryker developed severe hyponatremia due to a metabolic problem. It is also possible that he suffered from a developmental problem. His head circumference growth rate (1.47 cm/month) was below the average rate (2.5–3.0 cm/month) for his age as described in Section 6 of this report.

7.1 The first stillborn baby with Potter's facies and abnormalities reported

This baby boy with Potter's facies was born at 38 weeks of gestation via vaginal delivery and died 12 minutes later. He was born on September 21, 2002. An autopsy was performed and the baby had the following abnormalities: (1) marked growth restriction; (2) severe left renal hypoplasia and dysplasia. The kidney's weight was 0.8 g and the expected weight was 13.55 g. (3) Left renal agenesis. (4) Severe pulmonary hypoplasia. The lung's weight was 21.5 g and the expected weight was 62 ± 16.6 g.

7.2 The health condition of the second stillbirth

The second stillbirth was a girl that died *in utero* at 32 weeks gestation. The mother was induced and the infant was delivered vaginally on June 11, 2003. At autopsy, there was evidence of mild maceration consistent with intrauterine demise. The infant had a chronological age of 32 weeks gestation and the growth parameters were consistent with 32–33 weeks gestation.

No developmental abnormalities were identified on external and internal examination. However, there was evidence of fetal distress in the form of a starry-sky appearance in the thymus and meconium aspiration within the lungs. Microscopic examination of tissues did not demonstrate any evidence of infection and all of the cultures taken at autopsy were negative.

It is possible that there is a common feature between this case and Stryker's case. Meconium was observed in the lungs of this infant and aspirated milk with the bacterial colonies was observed in Stryker's lungs. Stryker suffered from severe hyponatremia and hyponatremia causes seizure. I believe that Stryker aspirated because of seizure. It is also possible that this female infant aspirated meconium because she had a seizure induced by a metabolic problem.

7.3 Health problems of Stryker's brother born in August, 2006

Stryker's mother had a baby boy in August of 2006 which was approximately one year following Stryker's death in September of 2005. This baby was delivered prematurely at 35 weeks gestation via cesarean section due to low amniotic fluid and some growth restriction.

This baby developed complications similar to those observed in Stryker's case and at the exact same time frame. At 6 hours following birth, he developed respiratory distress syndrome (RDS), bacterial infections, hyperbilirubinemia, heart murmur, and interstitial disease. In addition, the baby had numerous complications that included myoclonic jerks for the first 3 months of life after every feed, herniated umbilicus, and a reflux problem. His urine also had strong odor similar to baby Stryker.

8. Blood test performed on January 30, 2006 and the allegation of methanol poisoning

At autopsy on September 6, 2005, the medical examiner (ME) took a blood sample from Stryker's heart. She also took stomach content. The ME sent the blood sample (2E93401) and the stomach content (2E93402) to the Centre of Forensic Sciences (CFS) in Toronto to check for the presence of drugs and other chemicals in these samples. The CFS received these samples on September 9 and put them in the storage [22].

The CFS analyzed the blood for the presence of the chemicals listed in Table 9 but the stomach content was not analyzed. The CSF reported that Stryker's blood contained formic acid and methanol at the concentration levels of 232 mg/L and 200 mg/L, respectively [22]. No other chemicals were detected in the blood (Table 9).

Table 9. The result of Stryker's blood analysis

Chemicals	Results
Formic acid	232 mg/L
Methanol	200 mg/L
Acetaminophen	Not detected
Barbiturates	Not detected
Cannabinoid metabolites	Not detected
Cocaine metabolite	Not detected
Codeine	Not detected
Dextromethorphan	Not detected
Diphenhydramine	Not detected
Hydrocodone	Not detected
Hydromorphone	Not detected
Levorphanol	Not detected
Morphine	Not detected
Pseudoephedrine	Not detected
Salicylate	Not detected

The CSF released this report on January 30, 2006, which is about five months following the autopsy.

The CFS's report alleged that baby Stryker was poisoned with methanol based on the finding of methanol and formic acid in Stryker's blood sample. It seems that CSF did not analyze the stomach content for the presence of methanol and formic acid. Moreover, samples from major organs were not taken in this case to check for the presence of methanol and formic acid as has been the protocol in many medical and legal investigations.

For example, Ferrari *et al.* investigated fifteen cases of fatal massive methanol intoxication. Body distribution of methanol and formic acid, as the main metabolite, was analyzed in blood and in different organs (brain, kidney, lung and liver). Formic acid concentrations were found to be between 30 and 1100 mg/L in the samples under study. A good correlation was found between the blood and the brain [23].

In addition, Tanaka *et al.* determined the levels of formic acid in the blood, stomach contents, urine, and organs of two men who were fatally intoxicated with methanol. Formic acid was measured by headspace gas chromatography [24]. The postmortem concentrations of formic acid in the samples taken from these two men and the total formic acid in the stomach contents are listed in Table 10. The average formic acid concentrations were 0.28 mg/mL in the blood, 1.37 mg/mL in urine, 0.64 mg/g in the brain, 0.53 mg/g in the liver, and 0.66 mg/g in the kidneys. The average total amount of formic acid in the gastric contents for these men was 65.6 mg.

Furthermore, Wu Chen *et al.* measured the methanol levels in the blood, tissues, and gastric contents of a man that died as a result of methanol intoxication. Methanol determinations were performed on a Hewlett-Packard 5840A gas chromatograph with flame ionization detection using a glass column packed with 0.2% Carbowax 1500 on Carbowax.

The man was found unconscious and brought to a hospital. On admission to the emergency room, he was comatose in metabolic acidosis with high anion and osmolal gaps. His serum methanol was 583 mg/dL and his serum ethanol and ethylene glycol were negative. He was treated with ethanol, bicarbonate, and hemodialysis. He died 40 hours after admission.

The postmortem methanol concentrations in his body fluids were as follows: bile 175 mg/dL, vitreous humor 173 mg/dL, and blood 142 mg/dL. Urine sample was not available for analysis. Postmortem methanol concentrations in his tissues are given in decreasing order: brain 159 mg/100 g, kidney 130 mg/100 g, lung 127 mg/100 g, spleen 125 mg/100 g, skeletal muscle 112 mg/100 g, pancreas 109 mg/100 g, liver 107 mg/100 g, and heart 93 mg/100 g. The total amount of methanol in his gastric contents was 73 mg [25].

Table 10. Distribution of formic acid in biological samples taken from two individuals poisoned with methanol

Sample type ¹	Individual #1	Individual #2
Blood	0.32 mg/mL	0.23 mg/mL
Urine	2.27 mg/mL	0.47 mg/mL
Brain	0.11 mg/g	1.17 mg/g
Liver	0.54 mg/g	0.51 mg/g
Kidneys	0.13 mg/g	1.19 mg/g
Stomach contents (Total)	108 g	23.2 g

¹Tanaka *et al.* [24].

9. Medical observations and studies that invalidate the allegation of methanol poisoning presented in the case of baby Stryker

It has been alleged that Stryker's death was caused by methanol poisoning based on the finding of methanol (20 mg/dL) and formic acid (23.2 mg/dL) in the blood sample taken from Stryker's heart at autopsy. My review of the medical evidence in this case clearly shows that Stryker did not show evidence of methanol and/or formic acid intoxication. I base my medical opinion on the following clinical observations and medical studies:

1) Stryker did not show any symptom of acute methanol poisoning during the 48 hours prior to his death. These include neurological signs, vomiting, diarrhea, and other health problems. In humans, the ingestion of toxic levels of methanol usually cause damage to the nervous system, eyes, kidneys, pancreas, and other organs. Symptoms of methanol toxicity in humans are described in Section 9.1.

2) Stryker's brain and spinal cord were examined grossly and microscopically by the medical examiner (ME) who did not observe any lesion that would indicate the baby was exposed to methanol and formic acid. The ME also examined a section of the brain using an electron microscope and no lesion was observed that would indicate the baby was exposed to methanol and/or formic acid.

Furthermore, Dr. John Provias, neuropathologist examined sections of Stryker's meninges, brain, and spinal cord microscopically and he did not observe changes that are usually associated with methanol toxicity in humans. In particular, his examination revealed no specific changes of methanol toxicity such as patterned or regional neuronal necrosis, areas of tissue necrosis, infarction or hemorrhage [26]. Pathological changes

observed in the brain of individuals who suffered from methanol intoxication are described in Section 9.2.

3) The ME examined Stryker's eyes grossly and microscopically and no lesion was observed that would indicate methanol and formic acid toxicity. Formic acid inhibits mitochondrial cytochrome oxidase activity leading to ocular toxicity. Retinal damage and bilateral optic nerve necrosis and atrophy have been observed in people intoxicated with methanol [27-30]. Ocular lesions associated with methanol intoxications are described in Section 9.3.

4) The ME examined Stryker's heart, lungs, liver, kidneys, pancreas, and adrenal glands grossly and microscopically and no lesion was observed that would indicate the baby was intoxicated with methanol and/or formic acid. Moreover, she evaluated tissue samples of liver, skeletal muscle, and heart using an electron microscope and no specific ultrastructural abnormalities were found. Lesions observed in pancreas and kidneys of people intoxicated with methanol are described in Section 9.4.

9.1 Stryker did not show symptoms of intoxication with methanol

Initially, methanol poisoning in individuals induces nausea, vomiting, abdominal pain, and mild central nervous system depression. Then, uncompensated metabolic acidosis develops within approximately 12 to 24 hours, depending upon the methanol dose ingested. It is usually associated with visual function impairment, ranging from blurred vision and altered visual fields to complete blindness [31].

For example, Osterloh *et al.* evaluated four individuals after ingestion of a methanolic copying fluid. All individuals were initially intoxicated. Twelve to twenty-four hours later, signs and symptoms included nausea, abdominal pain, hypokalemia, acidosis. Pathologic ocular findings were observed in two individuals [32].

In addition, Pamies *et al.* reported a case of a 46-year-old male who presented to the emergency room seven hours after ingesting a toxic level of methanol. He complained of abdominal and back pain. He was tachypneic, tachycardic, hypertensive and hypothermic. Laboratory results were significant for a severe metabolic acidosis, a serum osmolality of 465 and serum methanol level of 493 mg/dL [33].

Furthermore, Kalkan *et al.* reviewed the records of 113 children and adults who suffered from methanol intoxication. Clinical signs in all cases were central nervous system symptoms (45.1%), metabolic acidosis (23.0%), visual symptoms (21.2%) and gastrointestinal symptoms (10.6%) [34].

Stryker did not show any symptoms of methanol poisoning during the 48 hours prior to his death. On September 5, his mother gave him a bath in the morning and she took him to the neighborhood park. They sat under a gazebo style picnic area for the majority of the day. Stryker was seen and held by the family friends and no one noticed anything unusual concerning the baby's health. In addition, his mother fed him and changed

his clothes at approximately 2300 on September 5. She did not notice any unusual sign such as appearing fussy or ill.

Stryker's mother found Stryker cold, white, and not breathing in his bed at approximately 0300 on September 6, which is four hours after she fed him. Clinical studies showed that methanol at the level detected in Stryker's blood (20 mg/dL) did not cause severe toxicity within four hours following ingestion. Methanol has a relatively low toxicity and metabolism is responsible for the transformation of methanol to its toxic metabolites.

Methanol is oxidized in the liver by alcohol dehydrogenase to formaldehyde and the oxidation of formaldehyde to formic acid is facilitated by formaldehyde dehydrogenase. Acidosis is caused by the accumulation of formic acid. There is a direct correlation between the formic acid concentration and increased morbidity and mortality. Formic acid has been shown to inhibit cytochrome oxidase in the mitochondria [31, 35, 36].

Kostic and Dart analyzed published cases of methanol poisoning and found 22 cases that presented for care within 6 hours of ingestion. A clear acidosis developed only with a methanol level ≥ 126 mg/dL [37]. This level of methanol is more than six times the level of methanol (20 mg/dL) detected in Stryker's blood sample.

Furthermore, Hantson *et al.* evaluated a 26-year-old woman who ingested 250 to 500 mL methanol during the 38th week of pregnancy. Her initial serum concentrations of methanol and formic acid were 230 mg/dL and 33.6 mg/dL, respectively. She had a mild metabolic acidosis. Gynecologic examination and fetal monitoring failed to detect fetal distress. The woman was treated with ethanol infusion, bicarbonate administration and three courses of hemodialysis. Delivery occurred six days after the methanol exposure, when methanol was no longer detected in maternal blood. No further complications were noted in the mother and her newborn [38].

The methanol concentration in the serum of this woman is more than 11 times the concentration of the methanol detected in Stryker's blood (20 mg/dL). In addition, the formic concentration in the serum of the woman described above was 1.4 times higher than the concentration of formic acid reported in the blood in Stryker's case.

9.2 Stryker's CNS showed no damage specific for methanol and formic acid

Stryker's brain, spinal cord, and meninges were examined grossly and microscopically by the medical examiner (ME) and no lesion was observed that would indicate the baby was exposed to methanol and formic acid (Section 5). The ME also examined a section of the brain using an electron microscope and observed no lesion that would indicate the baby was exposed to methanol and/or formic acid.

Furthermore, Dr. John Provias, neuropathologist was consulted to evaluate Stryker's brain and spinal cord after the Centre of Forensic Sciences (CFS) reported that methanol and formic acid were found in Stryker's blood sample. Dr. Provias examined sections of Stryker's meninges, brain, and spinal cord

microscopically and did not observe changes that are usually associated with methanol toxicity in humans.

In particular, his examination revealed no specific changes of methanol toxicity such as patterned or regional neuronal necrosis, areas of tissue necrosis, infarction or hemorrhage. He stated, “Despite extensive sampling, including multiple sections of basal ganglia, specific changes of methanol toxicity, such as patterned or regional neuronal necrosis, areas of tissue necrosis or infarction or hemorrhage, are not seen.” [3, 26]

Severe pathological changes have been observed in people who suffered from methanol intoxication. For example, Roberge *et al.* evaluated a fatal case of subacute methanol toxicity and found diffuse brain involvement, including bilateral putaminal necrosis and cerebral edema with ventricular compression [39].

The detection of pathological changes in the brain of people who suffered from methanol intoxications are not limited to autopsy cases. Such changes have also been detected by computed tomographic scans (CT) and magnetic resonance imaging (MRI) in people who showed symptoms of methanol intoxication. For example, McLean *et al.* evaluated two individuals who suffered from severe methanol poisoning. Computed tomographic scans in both individuals demonstrated bilateral symmetrical infarction of the frontocentral white matter and putamen [40].

Moreover, Patankar *et al.* performed head CT scans on four individuals who presented with a history of methanol poisoning. They observed prominent hypodense lesions in the lentiform nuclei and peripheral white matter and hemorrhage [41]. Also, Gaul *et al.* evaluated the brain of an individual who suffered from severe methanol intoxication using MR and CT scans. They observed bilateral hemorrhagic necrosis of the putamen and caudate nuclei, extensive subcortical necrosis, and symmetric bilateral necrosis of the pontine tegmentum and optic nerves [42].

Furthermore, Anderson *et al.* reported a case of a 47-year-old man with significant methanol intoxication who had enhancing lesions in the caudate nuclei, putamina, hypothalamus, and subcortical white matter by MRI [43]. In addition, Takao *et al.* reported the serial magnetic resonance imaging (MRI) findings in a case of a 50-year-old man who had accidentally ingested methanol. This man was almost blind and became comatose. The MRI showed bilateral putaminal lesions with restricted diffusion. The MRI, which was performed on the third day after admission, showed new lesions in the subcortical white matter [44].

9.3 Formic acid causes ocular toxicity and Stryker’s eyes were normal

The medical examiner evaluated Stryker’s eyes grossly and microscopically and did not see evidence of ocular and optic nerve damage (Section 5). Formic acid inhibits mitochondrial cytochrome oxidase activity leading to ocular toxicity. Retinal damage and bilateral optic nerve necrosis and atrophy have been observed in individuals who suffered from methanol intoxication [27-30].

For example, Brent *et al.* evaluated 11 consecutive individuals who presented with methanol poisoning at a hospital. Seven of them initially had visual abnormalities [45]. Moreover, Sharpe *et al.* conducted histopathologic evaluation of the brain and optic nerve of four individuals who died as a result of intoxication with methanol. They observed myelin damage behind the lamina cribrosa in each nerve. Demyelination also occurred in cerebral hemispheric white matter in one individual [46].

Furthermore, Naeser evaluated the eyes and optic nerves microscopically in a 37-year-old man who died as a result of methanol poisoning. He observed bilateral central necrosis of the optic nerves from behind the lamina cribrosa to the orbital apex [29]. Also, Fujihara *et al.* evaluated the retina of a 37-year-old man who suffered from methanol intoxication. The retinal profiles were evaluated by optical coherence tomography (OCT) and fluorescein angiography during the course of treatment. OCT demonstrated peripapillary nerve fiber swelling and accumulation of intraretinal fluid in the acute phase. In the chronic phase, the retinal thickness was diffusely decreased [27].

9.4 Stryker’s kidneys and other organs showed no evidence of methanol toxicity

The medical examiner evaluated Stryker’s heart, lungs, liver, kidneys, pancreas, and adrenal glands grossly and microscopically and did not observe any lesion that would indicate the baby was intoxicated with methanol and/or formic acid. In addition, she evaluated tissue samples of liver, skeletal muscle, and heart using an electron microscope and no specific ultrastructural abnormalities were found. Individuals who suffer from severe methanol intoxication develop damage in many organs.

For example, Verhelst *et al.* conducted a retrospective analysis of the medical records of 25 consecutive individuals admitted to the intensive care unit after severe intentional methanol poisoning. Clinical pathological signs of acute renal injury were found in 15 (60%) individuals. Acute renal impairment was defined as a serum creatinine concentration higher than 177 micro-mol/L and/or a urinary output on admission and for the first 24 hours below 0.5 ml/kg/h. Two factors contributing to renal injury could be identified: hemolysis and myoglobinuria. Analysis of proteinuria suggests that proximal tubular cells may be preferentially affected [47].

Furthermore, Hantson and Mahieu evaluated the records of 22 consecutive individuals admitted with a diagnosis of acute methanol poisoning; evidence of pancreatic damage was found in 11 (50%) patients. The abnormalities were present from admission and before ethanol therapy in 7 cases and developed after ethanol therapy in 4 cases. In addition, they evaluated a 54-year-old woman who developed acute necrotizing pancreatitis following acute methanol poisoning. She was treated by hemodialysis, ethanol infusion, and folic acid, but she died despite maximal supportive therapy from multiple organ failure 54 hours after the ingestion [48].

10. The likely source of the methanol and formic acid detected in Stryker's blood

The medical evidence described in the previous sections of this report clearly shows that Stryker did not show any sign of intoxication with methanol and death was caused by severe hyponatremia. I believe that the source of methanol (20 mg/dL) and formic acid (23.2 mg/dL) detected in Stryker's blood was contamination from the formalin fixative used in the laboratory to fix the tissues at the time of autopsy. For example, the medical examiner infused the left lung with formalin and stated that the left lung's weight was 48 g before infusion with the formalin fixative and 68.8 g with the fixative (Section 5).

The formalin fixative used contains 1 to 1.5% methanol and 3 to 4% formaldehyde as shown in Table 11 [49]. The oxidation of formaldehyde to formic acid is facilitated by formaldehyde dehydrogenase present in the red blood cells [50, 51]. For example, human blood oxidized formaldehyde (0.7 mg to 4 mL blood) to formic acid in vitro within four hours [51].

The following example illustrates how contamination of blood with formalin fixative can give the concentrations of methanol (0.2 mg/mL) and formic acid (0.23 mg/mL) detected in Stryker's blood. Ten μ L of the 10% formalin fixative contains about 0.13 mg of methanol and 0.35 mg of formaldehyde as shown in Table 11. Adding 20 μ L of the formalin fixative to one mL of blood will yield methanol concentration of 0.26 mg/mL and a formaldehyde concentration of 0.7 mg/mL. Blood can convert formaldehyde to formic acid as described above.

Table 11. Composition of a 10% neutral formalin fixative

Agent	% of total	mg/mL	mg per 10 μ L
Formaldehyde	3-4	30-40	0.3-0.4
Methanol	1-1.5	10-15	0.1-0.15
Water	94-96	940-960	9.4-9.6

11. Conclusions

The clinical data and studies described in this report revealed the following:

1) Stryker's death was caused by severe hyponatremia as indicated by his critically low level of sodium in serum and the pathological changes observed in his brain and lung.

Stryker suffered from chronic health problems that led to the development of severe hyponatremia.

2) The medical evidence clearly shows that Stryker did not show evidence of methanol and/or formic acid intoxication. I base my medical opinion on the followings clinical observations and medical studies:

a) He did not show any symptom of acute methanol poisoning during the 48 hours prior to his death.

b) The medical examiner and a neuropathologist examined Stryker's brain and spinal cord grossly and microscopically and they did not see any evidence of methanol toxicity.

c) His eyes and optic nerves were examined grossly and microscopically and did not show evidence of methanol toxicity.

d) His heart, lungs, liver, kidneys, pancreas, adrenal glands, and other tissues were examined grossly and microscopically and did not show evidence of toxicity with methanol.

e) Clinical studies showed that methanol at the level detected in Stryker's blood (20 mg/dL) did not cause severe toxicity within four hours following ingestion.

f) I believe that detecting methanol and formic acid in a single blood sample in the absence of medical data that show methanol intoxication is not sufficient to make a case for methanol intoxication. In Stryker's case, the gastric contents and tissue samples were not analyzed for the presence of methanol and formic acid as has been the protocol in many medical and legal investigations.

3) I believe that the methanol and formic acid detected in Stryker's blood resulted from the contamination of the blood with formalin used in the laboratory to fix tissues. This fixative contains 1 to 1.5% methanol and 3 to 4% formaldehyde. The oxidation of formaldehyde to formic acid is facilitated by formaldehyde dehydrogenase present in the red blood cells.

4) It is possible that there are common factors between Stryker's causes of illness and death and the family history with serious health problems.

References

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