A missed case of poisoning with arsenic

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Abstract

Christine, a 40-year-old white woman, suffered from acute gastrointestinal pain, diarrhea, malaise, and fatigue shortly after receiving oral herbal treatment and drank eight glasses of clear liquid in a clinic in California. On October 19, 2004 between 1540 and 1730, she was given Uro-well herbal supplement prescribed by her physician as a kidney-cleansing agent. Christine was transported by ambulance to the Stanford Emergency Department (SED) at approximately 1930. She was treated with activated charcoal orally and N-saline by IV. An electrocardiogram test showed that she developed sinus tachycardia. Christine's blood test was negative for alcohol and her urine test was negative for the use of illicit drugs. The treating physicians did not order screening tests for the presence of heavy metals and arsenic in blood and urine, even though, she stated that a poison might be the cause of her symptoms.

Christine was released from SED after ten hours of admission. However, she continued to suffer from abdominal pain, fatigue, vomiting, and diarrhea for several weeks. A 24 hour-urine sample was collected and analyzed for arsenic on day 26 post-her hospitalization on October 19th. It revealed a significantly high level of arsenic (270 μg arsenic per 24 hour urine collection). Christine's arsenic background level in urine was 18 μg arsenic per day. Furthermore, analysis of the Uro-well herbal supplement revealed arsenic level of 25 ppm, which is five-time, the maximum permissible level of arsenic (5 ppm) in herbs set by the American National Institute of Standards and Technology. My investigation revealed that the exposure to a toxic level of arsenic by ingestion is the likely cause for Christine's acute symptoms developed on October 19th.

Keywords: acute gastrointestinal symptoms, arsenic poisoning, arsenic in urine, kidney cleansing, Uro-well herbal supplement, sinus tachycardia.

1. **Summary of the case and findings**

A physician in California (CPh) treated Christine orally in his clinic with the Uro-well herbal supplement for kidney-cleansing on October 19, 2004. She also drank eight glasses of clear liquid between 1530 and 1730 and received the herb during that time. Christine developed acute gastrointestinal pain, diarrhea, malaise, and fatigue shortly after leaving the clinic and was transported by ambulance to the Stanford Emergency Department at approximately 1930. She was treated with activated charcoal orally and N-saline by IV. An electrocardiogram test showed that she developed sinus tachycardia.

Christine blood test was negative for alcohol and her urine test was negative for the use of illicit drugs. She was subjected for psychiatric evaluation and her exam did not reveal any mental problems. Christine was released from the hospital after ten hours of admission at Stanford. However, she continued to suffer from abdominal pain, fatigue, diarrhea, and vomiting for several weeks. A 24-hour urine sample was collected and analyzed for arsenic on day 26 post-her hospitalization on October 19th. It contained 270 μg arsenic per 24-hour urine. Furthermore, analysis of the Uro-well herbal supplement revealed an arsenic level of 25 ppm.

Christine requested that I evaluate her case to find the likely cause(s) of her acute health problem developed on October 19, 2004. My investigation revealed that the exposure to a toxic level of arsenic by ingestion is the likely cause for Christine's acute symptoms developed on October 19th. My conclusions are based on the following medical data:

(1) Christine's acute symptoms described above mimic the symptoms of acute poisoning with arsenic described in people who ingested toxic levels of arsenic [1-3]. In addition, the investigations of physicians at Stanford Emergency Department and other physicians who examined her thereafter did not identify a specific cause for Christine's illness. SED treated Christine with charcoal for ingestion of a toxic substance, which lessened the severity of her symptoms.

(2) The analysis of the Uro-well herbal supplement given to Christine on October 19th revealed an arsenic level of 25 ppm, which is five-times, the maximum permissible level of arsenic (5 ppm) in herbs set by the American National Institute of Standards and Technology [4,5]. The amount of the Uro-well herbal supplement ingested by Christine on 19th was not given.

(3) A urine analysis for arsenic was performed 26 days after her hospitalization on October 19th that revealed a significantly high level of arsenic in Christine's urine (270 μg arsenic per 24-hour). This value is 15 times her background level of arsenic of 18 μg arsenic per 24-hour. In humans, the majority of the absorbed arsenic following ingestion is excreted in the urine. The extrapolation of the arsenic level found in Christine's urine detected at 26 days after her hospitalization to October 19th indicates toxic dose of arsenic by ingestion as described in Section 3 of this report.

Furthermore, the arsenic level in the Uro-well herbal supplement is five times the maximum permissible level (MPL) that has been set by the American National Institute of Standards and Technology. Arsenic is classified as a carcinogen and a reproductive toxicant by California proposition 65 [6,7]. Sec-

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tion 25249.6 of proposition 65 states that no person in the course of doing business in California shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual, except as provided in Section 25249.10. Christine was not given any warning that the Uro-well herbal supplement contains a significant level of arsenic.

Christine's case gives a good example that shows toxicology is excluded from our current healthcare system. The physicians at Stanford Emergency Department and the physicians who examined Christine during the three weeks following her release from Stanford did not order toxicology screening tests for heavy metals and arsenic, even though, Christine stated that a poison might be the cause her symptoms. However, she was subjected for psychiatric evaluation, although, she does not have a history of mental illness or drug abuse. In addition, I have found that physicians did not consider toxic agents in their differential diagnosis in other cases that I evaluated and Christine's case is not an isolated incidence.

In the last 10 years, I evaluated many cases in the United States of individuals who suffered from the exposure of chemicals at the workplace and/or adverse reactions to medications and vaccines. I observed many common factors among these cases, these include: 1) The treating physicians ignored the claims of their patients that their illnesses were induced by exposure to chemicals and/or adverse reactions to medications even though, their case histories indicate exposure to chemicals; 2) Physicians did not do screening tests to look for certain chemicals in blood and/or urine even though these chemicals have been used in the workplace by their patients; 3) The patients were sent for psychological and/or psychiatric evaluations to check their mental fitness because they claimed that their illnesses might be induced by chemicals; 4) In chemically induced illnesses usually called idiopathic, the patients are treated with high doses of corticosteroids, other immunosuppressant agents, and/or cytotoxic drugs that resulted in serious illnesses and even death [8-13].

I believe that physicians need to include toxic agents and adverse reactions to medications and vaccines in their differential diagnosis to save lives and vital resources. We have about 2,000 chemicals as active ingredients in our prescription and nonprescription drugs and thousands of chemicals in use in our work place [8, 13]. Yet, toxicology is almost excluded from our healthcare industry. Illnesses induced by chemical agents can mimic illnesses induced by other causes such as virus, bacteria, and deficiency of vitamins and essential minerals. Physicians are unable to identify the causes of illnesses induced by chemicals if they do not do the proper screening tests for the presence of chemicals and metabolites in biological media and they lack the proper training to recognize symptoms and lesions induced by chemical agents.

2. Christine's symptoms developed after ingesting the Uro-Well herbs on October 19, 2004 and other clinical data

2.1 Christine's symptoms developed on October 19th and clinical findings

Christine visited her primary physician's clinic in California on October 19, 2004 to receive kidney-cleansing treatment prescribed by her physician (CPh). She was given a Uro-well herbal supplement along with eight glasses of clear liquid between 1540 and 1730. She developed gastrointestinal pain, diarrhea, malaise, and fatigue shortly after receiving this treatment. She was transported by ambulance to the Stanford Emergency Department (SED) at approximately 1930.

SED treated Christine with activated charcoal orally and N-saline by IV. Christine's blood test was negative for alcohol and her urine test was negative for amphetamine, barbiturates, benzodiazepines, cocaine metabolites, methadone, opiates, Phencyclidine (PCP), tricyclics, and Δ^9 Carboxy-tetrahydrocannabinol (THC). SED also took a single x-ray of Christine's abdomen, where no evidence of a radiopaque foreign body was observed.

Her examination revealed that she had a temperature of 36.1°C, blood pressure of 140/87, a heart rate of 98 b/minute, and a respiratory rate of 16 per minute. However, Christine's ECG taken at 0023 on October 20, 2004 revealed that she had sinus tachycardia, rate 103.

Christine's urine analysis performed on October 19th showed that the appearance of her urine was hazy and it contained a slight to moderate levels of blood and ketones. In addition, her blood analysis performed at 2212 on October 19th revealed that Christine's serum levels of sodium, chloride, and calcium were slightly lower than normal. Her hemoglobin level and blood lymphocyte count were also lower than normal (Table 1). Christine was released from the hospital in the early morning of October 20th.

Table 1. The results of Christine's blood analysis performed on October 19, 2004

Measurements	Values	Reference range
Sodium, ser/plasma	128L*	135-145 mmol/L
Chloride, ser/plasma	94L	96-109 mmol/L
Calcium, ser/plasma	8L	8.5-10.5 mg/dL
Hemoglobin, blood	11.5L	11.7-15.7 g/dL
Lymphocyte count, blood	0.85L	1.0-3.0 K/μL

*L: lower than reference range

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2.2 Christine's symptoms observed following her release from Stanford Hospital

Christine was released from Stanford Hospital on October 20, 2004 approximately 10 hours after her admission. However, she continued to have acute symptoms such as abdominal pain, diarrhea, and vomiting. She consulted with a physician on October 22, 2004 and her abdominal pain was 9/10. Furthermore, on November 2, 2004, Christine consulted with a second physician because of her continuous nausea and vomiting, abdominal pain and watery diarrhea. She had a very difficult time keeping food down. Her physician recorded dizziness and her heart was racing. Christine had a pulse of 120 beats/minute and she could not catch her breath.

In addition, Christine stated that she continued to have more vomiting, nausea and diarrhea, which lasted for the next four to six weeks while her insomnia got worse. Her pulse was over 110 beats per minute for 5 weeks. According to Christine's medical records from 2000 to 2002, her average pulse was 68 beats per minute. In addition, her medical records from 2003 to 2004 indicate an average pulse of 80 beats per minute. Both her lab tests and prescription records do not indicate any medications taken.

2.3 Analyses for arsenic in Christine's urine and Uro-well herbal sample

A 24-hour urine sample was collected from Christine on November 15, 2004 and was analyzed for arsenic and metals. It revealed that she had a high level of arsenic (270 μg arsenic per 24 hour urine collection). This value is equal to 15 times her background level of arsenic (18 μg arsenic per 24-hour) measured on February 24, 2005 (Table 2). Both urine collections were done without a challenge of any chelating agent such as 2,3-dimercaptopropane-1-sulfonic acid (DMPS). In addition, Christine had not eaten shellfish for several months. Her physician specifically told her in February of 2003 to get off all fish except for small fish once in a while and she followed his advice.

Furthermore, analysis of the Uro-well herbal supplement was performed by Covance Laboratories, Madsion, WI using ICP Mass Spectrometry. It revealed an arsenic level of 25 ppm. This level is five-times, the maximum permissible level of arsenic (5 ppm) in herbs set by the American National Institute of Standards and Technology [4, 5].

Table 2. The results of Christine's urine analyses for arsenic

Date of Anaysis	μg Arsenic per g Creatinine	μg Arsenic per day	Provoking Agent	Reference range (μg/g Creat.)
03/02/2003	33	40	Oral DMPS	None
11/19/2003	40	54	Oral DMPS	None
11/15/2004	210	270	None	<100
11/29/2004	57	43	Desferal (IV)	None
02/24/2005	14	18	None	<100

3. The likely cause for Christine's acute symptoms developed on October 19, 2004

Christine developed acute gastrointestinal pain, diarrhea, malaise, and fatigue shortly after receiving the Uro-well herbal treatment and drinking eight glasses of clear liquid in her physician's clinic on October 19, 2004. My review of Christine's medical records and the pertinent medical literature to her case indicates that the ingestion of arsenic is the most likely cause for her acute symptoms developed on October 19th.

I based my opinion on the following medical data: 1) Detection of significant levels of arsenic in the Uro-well herbal supplement and Christine's urine. 2) Christine's acute abdominal symptoms that developed on October 19th mimic the acute abdominal symptoms developed in individuals that ingested toxic doses of arsenic. 3) Christine developed sinus tachycardia on October 19th. Individuals who ingested toxic doses of arsenic also developed cardiac problems. 4) Christine was examined in the Emergency room at Stanford Hospital on October 19th. The Stanford resident stated "the patient may have an early acute psychotic disorder". Neuropsychiatric disturbances have also been reported in people suffered from acute arsenic poisoning.

3.1 Detection of a significant level of arsenic in the Uro-well herbal supplement

A sample of the Uro-well herbal supplement was analyzed for arsenic by Covance Laboratories, using ICP Mass Spectrometry and it contains an arsenic level of 25 ppm. This level is five-times, the maximum permissible level of arsenic (5 ppm) in herbs set by the American National Institute of Standards and Technology [4,5]. The amount of herbal supplement given to Christine is not given. The arsenic content of Uro-well was not determined prior to the treatment.

Arsenic is classified as a carcinogen and a reproductive toxicant by California proposition 65 [6,7]. Section 25249.6 of proposition 65 states that no person in the course of doing business in California shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual, except as provided in Section 25249.10. Christine was not given any warning to let her know that the Uro-well herbal supplement contains a significant level of arsenic.

3.2 Detection of a significant level of arsenic in Christine's urine

A urine sample was collected from Christine on November 15, 2004 that revealed a significant level of arsenic (270 μg arsenic per day), which is 18 times Christine's background level of arsenic measured in her urine (18 μg arsenic per day) on February 24, 2005 (Table 2). Christine stated that she had not eaten shellfish for several months prior to her urine test of November 15th. It has been known that shellfish contains organic arsenic and it is recommended that people do not eat shellfish at least 72-hour prior to giving urine sample for arsenic analysis [14]. These data indicate that the arsenic detected in Christine's urine

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on November 15th did not come from a shellfish or fish dietary source.

Christine's background level of arsenic excreted in 24-hour urine collection on February 24, 2005 was very low (18 μg arsenic per day). This value is similar to the level of arsenic detected in the urine of people whose drinking water contains less than 1 μg/L of arsenic. Kurttio *et al.* evaluated the elimination rate of arsenic in urine of nine individuals whose drinking water contained less than 1 μg/L of arsenic. They found that the geometric mean of the concentrations of total arsenic in urine of these individuals was 5 μg/L [15].

The reference range for arsenic in 24-hour urine in the general population is <100 μg arsenic per day. These data indicate that Christine's exposure to arsenic from food and water is insignificant.

Furthermore, Christine's urine value for arsenic detected on February 24, 2005 is similar to her urine level of arsenic detected in 2003 (47 μg arsenic per day) if we take in a consideration the influence of her treatment with 2,3-dimercaptopropane-1-sulfonic acid (DMPS) on the excretion of arsenic in urine. DMPS usually enhances the excretion of arsenic in urine by more than four-fold as compared to the pretreatment level as shown in the studies described below.

Aposhian *et al.* evaluated the influence of DMPS given orally on the excretion of arsenic in urine of people exposed to arsenic in the drinking water at levels of 21 to 593 μg arsenic/L. They collected urine samples before and after treating the individual with 300 mg DMPS orally. The concentrations of total arsenic in urine were increased by four-fold in two-hour urine collection following the treatment with DMPS as compared with the concentrations prior to treatment with DMPS [16]. Using the results of this study, it can be estimated that the daily excretion of arsenic in urine in Christine's case was about 12 μg arsenic per day in 2003. These data also indicate that Christine's exposure to arsenic from a dietary source is insignificant.

Furthermore in 2003, the detection of a low level of arsenic in Christine's hair also indicates that Christine did not suffer from chronic exposure to arsenic. The average concentration of arsenic detected in Christine's hair at that time was 0.058 μg arsenic per gram of hair, which is within the reference range of <0.06 μg detected in normal people. This shows that Christine did not suffer from chronic exposure to arsenic.

It has been proven that arsenic accumulates in hair. Ingested arsenic is known to be stored in sulphydryl-rich tissue like hair, nail or skin [17]. Hair analysis for arsenic was used to measure former exposures of human to arsenic [18,19]. For example, Kurttio *et al.* evaluated a group of people exposed to arsenic in drinking water (17 to 980 μg/L). They found the arsenic content of hair correlated well with past and chronic arsenic exposure; an increase of 10 μg/L in the arsenic concentration of the drinking water or an increase of 10 to 20 μg /day of the arsenic exposure corresponded to a 0.1 mg/kg increase in hair arsenic [15].

3.3 Evaluating Christine's exposure to arsenic

Christine received herbal treatment in the afternoon of October 19, 2004 at her physician's clinic. She developed acute abdominal illness following receiving this treatment and she was hospitalized within 3 hours after leaving the clinic. However, no urine analysis was performed on October 19th or shortly after to check for arsenic. Christine collected urine for arsenic analysis on November 15th (26 days post her hospitalization). Her 24-hour urinary excretion of arsenic was 270 μg.

The detection of a significant level of arsenic in Christine's urine at 26-days after her sudden illness and hospitalization on October 19th, indicates that she was exposed to a toxic level of arsenic on October 19th. The biological half-life of the ingested soluble arsenic is about 6-7 days in humans. As a result, 26 days post-exposure to arsenic is equal to approximately four biological half-lives. At four half-lives, it is estimated that about 94% of the ingested soluble arsenic has been excreted from the body in humans. The studies in humans described below explain the pharmacokinetics and metabolism of arsenic.

Upon ingestion, dissolved arsenic compounds are readily absorbed (80-90%) through the gastrointestinal tract and are distributed in the blood to the liver, kidney, lung, spleen, skin, and other tissues. Pentavalent arsenic is reduced to the trivalent (which is less toxic) form in the body. This form is then methylated in the liver to create even less toxic methylarsenic acid, which facilitates excretion of arsenic in urine. [14].

Wang *et al.* studied the pharmacokinetics and metabolism of arsenic in leukemia patients who were treated with arsenic. Each patient was injected daily with an arsenite (As (III)) solution that contained 10 mg of As(2)O(3) precursor. Speciation analysis of the patient's urine samples collected consecutively for 48 hours, encompassing two intravenous injections of arsenic, revealed the presence of monomethylarsonous acid (MMA (III)), dimethylarsinous acid (DMA (III)), monomethylarsonic acid (MMA(V)), and dimethylarsinic acid (DMA(V)). The relative proportions of As (III), As (V), MMA (V), and DMA (V) in urine samples collected 24 hours after the injections of As (III) were 27.6 +/- 6.1, 2.8 +/- 2.0, 22.8 +/- 8.1, and 43.7 +/- 13.3%, respectively. The arsenic species excreted into the urine accounted for 32 to 65% of the total arsenic injected [20].

Furthermore, Kurttio *et al.* evaluated the elimination rate of arsenic in urine of 47 people exposed to arsenic in drinking water (17 to 980 μg/L). They also measured the concentration of arsenic in the urine of nine control individuals whose drinking water contained less than 1 μg/L of arsenic. They found the excreted arsenic was associated with the calculated arsenic doses, and on average 63% of the ingested arsenic dose was excreted in urine [15].

Urinary arsenic (As) concentration is considered an important biomarker of exposure by people to arsenic present in food, drinking water, and by inhalation in the workplace [14,16,21]. It is generally considered as the most reliable indicator of recent exposure to inorganic arsenic and it is used as the main biomarker of exposure [22].

For example, Calderon et al. evaluated urinary arsenic (As) concentrations as a biomarker of exposure in a U.S. population chronically exposed to inorganic arsenic (InAs) in their drinking water. Ninety-six individuals who consumed drinking water with As concentrations of 8-620 μg/L provided first morning urine voids for up to 5 consecutive days. The study population was 56% male, and 44% were younger than 18 years of age. On one day of the study period, all voided urines were collected over a 24-hr period.

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Arsenic intake from drinking water was estimated from daily food diaries. Comparison between the concentration of As in individual urine voids with that in the 24-hour urine collection indicated that the concentration of As in urine was stable throughout the day. Comparison of the concentration of As in each first morning urine void over the 5-day study period indicated that there was little day-to-day variation in the concentration of As in urine. In addition, the concentration of As in urine did not vary by gender. These findings suggest that the analysis of a small number of urine samples may be adequate to stimulate an individual's exposure to InAs from drinking water and that the determination of the concentration of InAs in a drinking water supply may be a useful surrogate for estimating exposure to this metalloid [23].

Furthermore, Hopenhayn-Rich *et al.* conducted a large biomarker study in northern Chile of a population chronically exposed to high levels of arsenic in drinking water. The study consisted of 122 people in a town with arsenic water levels of approximately 600 μg/L and 98 participants in a neighboring town with arsenic levels in water of approximately 15 μg/L. The corresponding mean urinary arsenic levels were 580 μg/L and 60 μg/L [24].

Also in 2004, Meza *et al.*, evaluated the excretion of arsenic in urine of people as a biomarker for their exposure to arsenic in drinking water. Study subjects were from four towns in Mexico with different arsenic concentrations in their drinking water. Arsenic exposure was estimated through water intake over 24 hours. Arsenic excretion was assessed in the first morning void urine [25].

They found that the town of Esperanza with the highest arsenic concentration in water had the highest daily mean intake of arsenic through drinking water (65.5 μg/day). Positive correlation between total arsenic intake by drinking water/day and the total arsenic concentration in urine ($r = 0.50$, $P < 0.001$) was found. Arsenic excreted in urine ranged from 18.9 to 93.8 μg/L. These people had the highest geometric mean value of arsenic in urine, 65.1 μg/L, and it was statistically significantly different from those of the other towns ($P < 0.005$) [25].

3.4 Acute symptoms observed in people following ingestion of toxic levels of arsenic

Christine suffered from acute symptoms shortly after receiving an oral herbal treatment in her physician's clinic On October 19, 2004. These acute symptoms include gastrointestinal pain, diarrhea, malaise, fatigue, and sinus tachycardia, and an early acute psychotic disorder. These are similar to those symptoms induced by the ingestion of toxic dose of arsenic in people. It has been reported that human symptoms of arsenic poisoning include nausea, vomiting, and diarrhea [14].

Ratnaike also stated that acute arsenic poisoning is associated initially with nausea, vomiting, abdominal pain, and severe diarrhea. Encephalopathy and peripheral neuropathy were also reported. Arsenic exerts its toxicity by inactivating up to 200 enzymes, especially those involved in cellular energy pathways and DNA synthesis and repair [26].

Furthermore, Campbell and Alvarez reported that the diagnosis of acute arsenic poisoning should be considered in any patient with severe gastrointestinal complaints. Signs and symptoms include nausea, vomiting, colicky abdominal pain and profuse, watery diarrhea. Hypotension, fluid and electrolyte disturbances, mental status changes, electrocardiographic abnormalities, respiratory failure and death can result.

Treatment includes gastric emesis or lavage, chelation therapy, electrolyte and fluid replacement, and cardiorespiratory support. They also stated that quantitative measurement of 24-hour urinary arsenic excretion is the only reliable laboratory test to confirm arsenic poisoning [27].

Vantroyen *et al.* reported a case of a 27-year-old woman who ingested 9000 mg arsenic trioxide (As2O3). Her symptoms were gastrointestinal cramps, vomiting, diarrhea, EKG changes and disturbed liver function tests [28].

In addition, Cullen *et al.* reported a pediatric case of acute arsenic ingestion treated initially with British antilewisite (BAL) and D-penicillamine (DP), and later with dimercaptosuccinic acid (DMSA). A 22-month-old girl ingested 1 oz 2.27% sodium arsenate and developed immediate vomiting and diarrhea. The patient was presented to a community emergency department with the following vital signs: blood pressure 96/72 mm Hg, pulse 160 beats/min, respirations 22 breaths/min. She was pale and lethargic. Gastric lavage was performed, and an abdominal X-ray was normal. She continued to have gastrointestinal symptoms and received 3 mg/kg BAL. Sinus tachycardia persisted, with her heart rate increasing to 200 beats/min [29].

In 12 hours, she was asymptomatic and was started on oral DP. On day 1, 24-hour urine arsenic was 4,880 μg/L. She remained asymptomatic and was discharged on day 6 on oral DP. She did well except for a rash that could have been a side effect of DP. On day 8, when the day 5 24-hour urine arsenic level was returned at 650 μg/L, the patient was readmitted and started on DMSA. After 4 days on DMSA, the 24-hour urine arsenic level was 96 μg /L. The white blood cell count and renal and hepatic function remained normal. The excretion half-life was approximately 2.5 days, which is at least 2 to 3 times faster than the spontaneous excretion half-life expected in adults [29].

Furthermore, Stephanopoulos *et al.* evaluated a case of 22-month-old boy who ingested approximately twice the estimated lethal dose of arsenic trioxide (As (2)O(3)) ant bait. Initially, he developed signs of acute hemodynamic compromise with tachycardia, hypertension, gastrointestinal symptoms, and poor urine output. He became lethargic with muscle weakness and was somnolent [30].

He was stabilized with fluid resuscitation, placed on a sodium bicarbonate intravenous drip, and treated with intramuscular dimercaprol (British anti-Lewisite), 5 mg/kg every 6 hrs for 3 days. When the British anti-Lewisite and the sodium bicarbonate drip were discontinued, oral meso 2,3-dimercaptosuccinic acid (Succimer) was administered three times a day for 5 days and thereafter twice daily until the urine arsenic concentration decreased below 50 μg/L [30].

3.5 Cardiac problems observed in people who ingested a toxic dose of arsenic

Ingestion of toxic doses of arsenic has been known to cause a cardiac disturbance. Christine's electrocardogram (EKG) taken at 0023 on October 20, 2004 revealed that she had sinus

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tachycardia, rate 103. Her heart rhythm was normal on October 22, 2004. My review of Christine's medical records revealed that she did not suffer from tachycardia prior to October 19, 2004. Table 3 shows a summary of Christine's cardiac exam history.

Tachycardia was also observed in a 22-month-old boy who ingested approximately twice the estimated lethal dose of arsenic trioxide (As (2)O(3)) ant bait [30]. In addition, Cullen et al. reported a pediatric case of acute arsenic ingestion. A 22-month-old girl ingested 1 oz 2.27% sodium arsenate. She developed tachycardia with a heart rate increasing to 200 beats per minute. She was treated initially with British antilewisite (BAL). In 12 hours, she was asymptomatic and was started on oral D-penicillamine (DP). On day 1, 24-hour urine arsenic was 4,880 µg/L [29].

Furthermore, Ohnishi et al. evaluated the cardiac toxicities resulting from arsenic trioxide therapy in eight patients with relapsed or refractory acute promyelocytic leukemia. Arsenic trioxide, 0.15 mg/kg of body weight, administered daily by a 2-hour infusion for a maximum of 60 days. Their hearts were continuously monitored with ambulatory electrocardiography. Five individuals (63%) achieved complete remission. During induction therapy with arsenic trioxide, prolonged QT intervals were observed in all patients. Ventricular premature contractions were noticed during 8 of 12 courses of therapy. Four individuals developed non-sustained ventricular tachycardia and required treatment with antiarrhythmic agents [31].

In addition, Little et al. reported two cases of arsenic poisoning causing torsade de pointes. Marked prolongation of the QT-U interval and the rarely observed phenomenon of T-U wave alternans were also demonstrated. Thus, arsenic intoxication may be complicated by prolongation of the QT-U interval and torsade de pointes. T-U wave alternans occurs in the presence of a long QT-U interval and may be an electrocardiographic warning sign of torsade de pointes [32].

Table 3. Christine's cardiac exam results (2000-2004)

Exam date	Description of findings
08/26/2000	Regular rate and rhythm without murmurs, rubs, or gallops
07/21/2001	ECG: Normal sinus rhythm, rate 76
11/14/2001	Regular rate and rhythm without murmurs, rubs, or gallops
11/04/2002	Regular rate and rhythm without murmurs, rubs, or gallops
02/11/2003	Regular sinus rhythm, no murmurs
10/19/2004	ECG: Sinus tachycardia, rate 103
10/22/2004	Regular rate and rhythm without murmurs, rubs, or gallops

3.6 Neuropsychiatric disturbances observed in people ingested toxic dose of arsenic

On October 19, 2004, a Stanford resident did a psychiatric evaluation of Christine. Her medical records do not indicate a history of manic or impulsive behavior, hallucinations, suicidality or homicidality. According to the psychiatrist, Christine was alert and oriented and told an internally consistent story. However, despite her clinically observed physical symptoms including watery diarrhea, the psychiatric resident stated "the patient may have an early acute psychotic disorder, rule out delusional disorder, as the delusion may be non-bizarre." Neuropsychiatric disturbances have been reported in people suffering from acute arsenic poisoning.

Liu *et al.* reported neuropsychiatric disturbances caused by arsenic poisoning in 28 individuals. The incidence occurred in 32.2% of all the arsenic poisoning patients. These individuals were classified into three types according to their clinical symptoms. The neurologic type constituted 46.4%, mental type 21.4%, and mixed type 32.1% of the patient, respectively. Various abnormalities were found in electroencephalogram (EEG), electromyogram (EMG), and electrocardogram (EKG) examination. The EMG was still abnormal in most of the individuals after treatment for three months. The results showed that arsenic poisoning may cause neuropsychiatric disturbances [33].

3.7 Influence of the treatment given on the toxicity of arsenic in Christine's case

Christine drank eight glass of liquid with the Uro-well herb on October 19th. Christine was treated with activate charcoal orally at Stanford Hospital and IV fluid. I believe that the use of activated charcoal helped in reducing the toxicity of arsenic in Christine's case. Activated charcoal helped in preventing the absorption of some of the ingested arsenic from the gastrointestinal tract.

Kamijo *et al.* reported a case of a 23-year-old male pharmacist who ingested 1040 mg arsenic trioxide (788 mg trivalent arsenic, 13 mg/kg). After 7 asymptomatic hours, frequent vomiting and diarrhea occurred. Fearing death from shock, he drank 5 L of water over 5 hours. He was brought to the hospital with the chief complaint of constricted vision about 20 hours after ingestion; the major abdominal symptoms had already subsided. Despite a lethal plasma arsenic level on admission, all toxic symptoms including hepatic dysfunction, erythematous dermal eruption, and peripheral neuropathy improved during his hospital stay with no treatment except for dimercaptopropanol [34].

Furthermore, Mathieu *et al.* reported a case of an acute suicidal intoxication with a high dose of arsenic (10 g of sodium arsenate) and survived. Treatment included gastric lavage, oral charcoal and supportive measures. Hemodialysis was performed immediately and repeated over the next day. BAL therapy was prescribed only on the second day. Cardiovascular collapse, anuria and hepatic disturbance recovered in a few days then the individual was discharged on the 15th day [35].

Heinrich-Ramm *et al.* also reported case of a young man who tried to commit suicide by ingesting about 0.6 g of arsenic trioxide and survived due to the treatment with chelating agents. He received immediate therapy with dimercaptopropanesulfonic acid (DMPS) after his delivery into the hospital. In the first urine voiding in the clinic, the total arsenic concentration was 215 mg/L, which fell 1000-fold after 8 days of DMPS therapy. The patient left the hospital after a 12-day treatment with an antidote [36].

Also Dittrich *et al.* evaluated a case of attempted suicide by ingestion of 4.8 g As2O3 (more than 20 times the estimated lethal dose) and survived due to the treatment with chelating agent. Absorption of arsenic caused elevated urinary levels over

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5 days. BAL treatment was started within three hours after arsenic ingestion. The individual did not develop any signs of polyneuropathy or other clinical changes [37].

4. Conclusions

The medical data presented in this report indicate that the ingestion of a toxic level of arsenic is the likely cause for Christine's acute symptoms developed on October 19, 2004. This case represents an excellent example of demonstrating that toxicology is excluded from our current healthcare system. There are no medical or technical reasons to prevent the physicians at Stanford Hospital and other physicians who examined Christine on October 19th and the three weeks thereafter from performing screening tests for arsenic and heavy metals poisoning. In this case, Christine stated to her physicians that she suspected poisoning. Also, her acute symptoms mimic the symptoms of individuals acutely intoxicated with arsenic by ingestion. Physicians need to include toxic agents in their differential diagnosis of causes of illness to reduce patient discomfort and save lives.

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