Thin White Line

Professionals in law enforcement believe they are a thin blue line of restraint holding society back from barbarism. The kinds of issues that involve police and prosecutors may seem a long way from the white lab coats of academia, so figure the intelligentsia, because their neighborhoods do not have problems. No fighting here. No losers living in the lobby. Yet one of the most credentialed white lab-coated academics in the nation has recently been convicted of murder, purportedly using a common lab chemical for a murder weapon. How could this happen?

For approximately twenty years, Robert Ferrante was a Professor of Neurology, Pathology and Psychiatry at the Boston University School of Medicine, with prior appointments at Harvard Medical School and the Massachusetts General Hospital. Robert had a very distinguished career and a long list of publications in neuroscience, even with therapy projects in ALS and Huntington's Disease. He met his wife, Autumn Klein in 1995 and they subsequently worked together publishing highly regarded findings in neuroscience and clinical neurology. Robert Ferrante and Autumn Klein moved to Pittsburgh in 2011 to advance Autumn's career. Their plans involved expanding their family with another child, although conceiving became difficult. Autumn was diagnosed with a mitochondrial dysfunction of her oocytes. From Robert and Autumn's own research, and through consultation with their own IVF specialist, Autumn began supplementing her diet with a daily dose of 10grams of creatine monohydrate. Through their research, Robert and Autumn believed that creatine would increase Autumn's chances of having another child. Other published evidence showed this to be ab effective treatment.

This creatine is the same unregulated food supplement taken by millions of people around the world, typically in association with sports training and body building. As readers in the academic community know, being unregulated means that manufacturers of the substance are not obligated to perform toxicity, metabolic or patient diagnostic tests. Anyone can consume as much creatine any time they want. Any manufacturer can make and market creatine with quality guidelines falling under food safety, not pharmaceutical regulations.

Robert Ferrante had used creatine made in Germany for many years in his research, and selected it for it high purity. Degraded, or lower grade creatine, and creatine past its shelf life may contain significant amounts of impurities and contaminants, including fragments with variations on the carbon-nitrogen bond arrangement, including classes of cyanogens. Autumn took the purer form of creatine for her own use.

After fifty days, Autumn collapsed suddenly and died two days later. In the emergency room, she was diagnosed with a lethal cardiac dysrhythmia. Because she did not respond well to treatment, a toxicology screen was performed, including a cyanide test sent to Quest Diagnostics as a last resort.

The result came back from Quest as a positive, measuring a lethal amount of cyanide quantified at an astounding 3.4mg/kg. Good medical practice demanded a second opinion, so a second sample, drawn just 30minutes after the first one was sent to National Medical Services (NMS Labs) a specialty lab in cyanide analysis, which used a different method from Quest. It came back with cyanide levels of 0.3mg/kg, a little high but still in the normal range and consistent with levels in people known to be supplementing with creatine. A third test was performed by the Medical Examiner's office, using blood samples from the medical transplantation group that harvested Autumn's organs for donation. In a test that yielded merely positive or negative results without quantification, the finding was a negative.

Clearly, the results were conflicted, and a third independent laboratory should have been employed by the Medical Examiner to measure cyanide confirming either Quest or NMS. This was not done. Reproducibility is a

basic principle of science, with truth unable to be declared until two independent methods arrive at the same conclusion. This did not happen in the diagnosis of Autumn Klein. Instead, supposed experts simply picked the result they wanted.

Two lines of thinking among law enforcement ultimately led to Robert Ferrante's conviction of murder: The later tests perhaps showed lower cyanide, so they figured, because it was all dialysed away by treatment in the ER (related to the half-life of the drug under dialysis), and Robert Ferrante had purchased cyanide for his research in the same week as his wife died. The measured amount of cyanide in the purchased bottle did not match the weight stated on the container, so this was also deemed circumstantial, but lab personal who shared the facilities actively worked on a project involving cyanide, and as such, already had an open bottle available in the lab space and had been consuming it steadily as the project progressed. The public may be surprised to learn that cyanide is a common lab reagent, and plans for its use in Robert Ferrante's stem cell project were discussed among numerous personnel.

Despite the dramatic results from Quest, Autumn's symptoms were mysterious to the medical staff attending upon her. At trial, all medical experts called by prosecution and defense testified that Autumn did not experience classic cyanide symptoms. Doctors tended toward considering formaldehyde or alcohol poisoning, ordering tests that all returned negative before Quest reported cyanide. According to the results from Quest, Autumn had a lethal level of cyanide in her blood, typically expected to cause death within minutes, yet she survived for several hours before being put on life support measured, ultimately taking two days to die. Upon admission at the emergency room, she was not vomiting and her brain showed no bleeding. She was conscious and not convulsing. Her skin color was described alternatively as normal or grayish, yet cyanide is infamous for the red-violet hue it bestows upon the skin of the face and extremities. When cyanide is ingested, it causes burning and bleeding in the gastro-intestinal tract, sometimes with blood-filled foaming at the mouth. At autopsy, however, Autumn Klein's stomach and esophagus were declared normal. In total, she exhibited zero symptoms of cyanide poisoning. Her liver and kidneys were sufficiently normal to be successfully transplanted into two separate recipients. The only abnormality noted at autopsy concerned Autumn's heart. It showed an anatomic alteration consistent with a conduction abnormality and arrhythmia.

In June 2000, in Virginia, Chuck Fleming consumed excessive quantities of creatine mixed into Gatorade, and died three days later. Chuck Fleming's blood tested positive for methanol, and his wife was sentenced to 30 years imprisonment for his murder, based on the circumstantial evidence of a wiper fluid bottle found in their garage. Like Autumn Klein, Chuck Fleming's symptoms did not match well to classic methanol presentation. He exhibited no drunken behavior, had no eye damage and did not respond to ethanol dialysis, with the supposed methanol pharmacokinetics being completely mismatched to predicted half-life under treatment. Chuck Fleming consumed a dose about ten times that of Autumn Klein, in a shorter period of time. Despite this difference, the key symptoms presented by Autumn Klein and Chuck Fleming are alike: lactic acidosis, tachycardia, respiratory distress and end-stage brain dysfunction and hemorrhage. These symptoms can be presented in a range of poison responses, but are not typical of cyanide nor methanol poisoning.

One of the unintended consequences of creatine being classified as a food instead of a drug, is that adverse events are not followed nor systematically recorded by the FDA or medical community. Creatine may be benign in some individuals and toxic in others, pr at least some people may be especially sensitive to dosage Bulletin boards on body builder websites are replete with stories of toxic events, yet the professional community, including academics, operate under the assumption that the prevailing marketing claims are correct: *That creatine is natural and generally considered safe.*

Are we sure about that? No-one is responsible for comprehensive toxicology studies and not surprisingly, no publications exist reporting maximum tolerated dose (MTD) or the lethal dose 50% (LD50), the dose at which half the mice die. Doctors operate under the assumption that the creatine molecule cyclizes into creatinine, which is actively transported across the kidney by a number of drug transporters, a class of very important clearance pumps. About 2g of creatinine are excreted every day like this in a normal adult, but little thought is given to where the excess might go, if creatine supplementation exceeds this transport rate of if the pumps are defective. It is widely known that elevated creatinine is an indicator of poor kidney health but the issue of whether elevated creatinine is causative in this renal damage is unknown.

Peer-review publications that have trickled from curious academics actually show something quite disturbing. Excess creatinine not transported into the urine is metabolized into urea, methylamine and formaldehyde. These chemicals can further react with each other to form paraformaldehyde and dimethylamine. So while creatine itself might be safe, its metabolites can include toxic substances. Creatine can be a "pro-toxin" in a similar way to a "pro-drug."

In 2014, Diane Fleming filed a Writ of Actual Innocence with the Virginia Appeals Court, based on these discoveries about the metabolism of creatine. In the Writ of Actual Innocence for Diane Fleming, these toxic metabolites, together with an overdose quantity of creatine (130g in 24hrs) are cited as directly responsible for Chuck Fleming's death. Whether these metabolites directly killed Autumn Klein is not clear, since her consumption quantities were much smaller, but what is sure is that if Autumn Klein consumed creatine, then these metabolites should have been present in her blood, as they should in Chuck Fleming's blood. Yet no diagnostic test picked them up. Or did they?

Chuck Fleming's blood alcohol test was performed on a micro GC column without a mass spectrometer. The observed peak was deduced to be methanol due to position on a chromatogram. Diane Fleming's writ of actual innocence calls for retesting of the Gatorade bottles still in evidence storage from June 2000, this time with mass spectrometry. The defense predicts that the Gatorde bottles into which everyone admits Chuck mixed creatine monohydrate that had previously tested positive for methanol, will now actually be reported as containing dimethylamine and paraformaldehyde.

The cyanide test on Autumn Klein's blood performed at Quest Diagnostics used a pyridine reagent made by LabChem. Prosecution star witness, Les Edinboro testified that it reacted with "cyanide in all its forms," including thiocyanate, the major metabolite of cyanide and the vague concept of "cyanogens," Meanwhile, NMS Labs used a method that was specific for thiocyanate, the metabolite. This is considered a better test because cyanide has a very short half-life in blood, while thiocyanate is more stable and long-lived.

Professor Ferrante's expert witness Dr. Richard Middleberg testified that the Quest reagent was non-specific and the LabChem Operations Manager confirmed directly to the author in writing in August 2015, that the reagent would indeed react with dimethylamine, a predicted metabolite of creatine, leading to a false positive for cyanide.

Of course, both cyanide and dimethylamine could have been present in Autumn Klein's blood, but it is important that only one of the three cyanide tests returned positive, and this is the one that cross-reacts with a predicted metabolite. The prosecution attempted to claim that the thiocyanate was all gone from the samples sent to NMS Labs because of the heroic dialysis efforts of the MD team, but the second blood sample was drawn just 30minutes after the first, making an absurdity of the prosecution's claim.

At a very minimum, it seems the Pittsburgh Chief Medical Examiner has missed some critical controls in declaring Autumn Klein's death to be solely due to cyanide poisoning. Autumn Klein's death cannot be conclusively and uniquely associated with cyanide on the basis of the existing medical evidence, and the charges against Robert Ferrante are therefore without foundation. Meanwhile, the roles and baseline levels of creatine metabolites in Autumn Klein's decline and diagnosis are unaddressed.

The thin blue line may have drawn its mark with Robert Ferrante now serving a life sentence without the possibility of parole, but his conviction fails the test of science. It is on the wrong side of the thin white line of experimentally-verified truth, at least until the creatine metabolites are accounted for and their lack of interference in the pyridine-based cyanide assay is verified. (unlikely)

Carol Gebert PhD
Co-founder of Woodland Biosciences, and,
Expert Witness for Diane Fleming and Robert Ferrante

The missing controls are:

(a) To spike human blood samples with creatinine, mono-methylamine (MMA), dimethylamine (DMA), paraformaldehyde, urea and other known creatine metabolites and send to Quest Diagnostics for a Conway-method cyanide assay using the pyridine reagent.
(b) To retest any frozen blood samples still remaining from Autumn Klein, by GC/MS and LC/MS to identify known creatine metabolites, and to perform comparative mass balances of these findings to those from Quest Diagnostics' first assay results. Alternatively, examine MS data from the blood alcohol and formaldehyde tests already performed on Autumn Klein's samples.

Do you know Professor Robert Ferrante?
Write to him!
Here is how:

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or you can go to http://www.jpay.com/ to register for jail email.
(You can send email, but Bob cannot respond by email, so send him a physical return address.)
select the state of Pennsylvania
Inmate# LW6933
You have to buy stamps.