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CASE REPORT

Brian D. Andresen,[1] *Ph.D.; Armando Alcaraz,*[1] *M.S.; and Patrick M. Grant,*[1] *Ph.D.*

The Application of Pancuronium Bromide (Pavulon) Forensic Analyses to Tissue Samples from an "Angel of Death" Investigation

ABSTRACT: The case report of a serial killer who worked at several hospitals as a respiratory therapist is presented. The suspect was initially labeled a benevolent Angel of Death who ended the suffering of elderly patients through mercy killing. However, his subsequently declared motive for homicide was very different from other similar cases in medical settings. The application of new analysis techniques for the detection of pancuronium bromide in a series of aged exhumation tissues gave positive results and led to the resultant conviction of the therapist.

KEYWORDS: forensic science, aged exhumation tissues, pancuronium bromide (Pavulon), GC/MS, solid-phase extraction (SPE), liquid chromatography-electrospray mass spectrometry (HPLC-ES-MS/MS), Angel of Death

A number of historic homicides have been investigated in which medical professionals were ultimately proven responsible. However, it is often very difficult to recognize homicide in a healthcare environment, identify a victim, or determine how a patient was killed. A number of past examples have been reported.

Jane Toppan, a private nurse, was responsible for a number of deaths in the early 1900's (1). She was employed in many homes in New England for over two decades and administered lethal doses of morphine and atropine, killing more than 31 patients. America's first "Angel of Death," she was found guilty at trial in 1902. However, it was believed that she had actually murdered somewhere between 70–100 victims. She was judged insane and remanded to a state asylum in Massachusetts, where she died in August 1938 at the age of 84.

Genene Jones was born in 1951 and chose nursing as a profession. She was active in Texas hospitals from an age of 27–31 and was responsible for the deaths of many children, all of whom were injected with lethal drugs (2). She was apparently motivated by the attention and notoriety she received while trying to nobly resuscitate the ill children. She was ultimately brought to justice in 1984 and sentenced to 99 years in prison. The exact number of her victims remains unknown to this day.

Donald Harvey was a nurse who found satisfaction in tissue-sample analyses in the morgue. He would joke with the hospital staff about "getting rid of patients" using morphine, cyanide, and arsenic. Harvey performed (in his own words) "mercy killings" from the early 1970s–1987, when he was finally arrested (3). He was convicted of 34 deaths, but is believed to have actually murdered 87 victims.

[1] Forensic Science Center, Livermore National Laboratory, Livermore, CA.
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Michael Swango was a physician who may have poisoned and murdered as many as 60 patients under his care during staff positions in Ohio, Massachusetts, Virginia, South Dakota, New York, and Zimbabwe (4). At these locations, colleagues became ill and patients died. He appeared motivated by an obsession with the control that he exercised over the lives of his patients. In 1998, he was charged with killing five patients in a hospital in Zimbabwe, where he had been employed from 1994–1996. Arraigned in 2000, he eventually confessed and pled guilty to fatally poisoning three patients in 1993 at a New York hospital. He was also convicted of another murder in Ohio. In a plea arrangement, he was sentenced to life in prison without the possibility of parole.

Beverley Allitt, a nurse in Great Britain, was thought to have suffered from both Munchausen Syndrome and Munchausen-by-Proxy syndrome. She was responsible for the deaths of many children in her care (5). She would inject an overdose of insulin to induce shock, or use other medications to induce cardiac arrest. She then received praise and attention for being the first to attempt resuscitation of her victims. However, in 1993 Allitt was convicted and sentenced to 13 life terms for murder and attempted murder.

Dr. Harold Shipman was convicted of 15 counts of murder in England in 2001 (6). Mental illness induced by the death of his mother may have been the reason for his actions. It is estimated that he killed nearly 300 of his older female patients by lethal injection.

In these examples, administration of a lethal drug overdose via injection was often the preferred method because the discovery of medical malpractice leading to homicide is minimal. It is often very difficult to investigate a potential victim because of cremation, or because the remains were buried for a number of years prior to examination. Additionally, serious illnesses in a medical setting can easily mask real causes of death, allowing responsible individuals continued access to patients for long periods of time without any criminal activities being discovered. If an end-stage illness leading to death appears normal, an autopsy is seldom requested

by the attending physician, further minimizing the probability of discovering homicide. Furthermore, highly potent drugs can be administered quickly, without a patient's knowledge. The patient may then subsequently die after healthcare worker has left the room, eliminating any obvious cause-and-effect association.

This is a brief case report on an investigation in which such activities were successfully performed over many years prior to discovery, and on the resultant police inquiry into the magnitude of the problem. Patients who died unexpectedly were identified, exhumed after interment of several years, and re-autopsied. In this work, new analytic techniques were applied to the autopsy samples to aid the investigation of an illicit drug used for hospital homicides.

Case Background

In 1988, a male subject told a female friend in confidence that he was attending school to become a respiratory therapist to ". . . help people and put those who are suffering out of their misery" (7). The individual subsequently became a licensed practitioner and began working as a therapist at a number of hospitals in the Los Angeles, California area. He was employed for approximately 9 years, and during this time, a number of unlawful incidents were witnessed by hospital workers, including: closure of patient breathing tubes, possession of controlled drugs, suspicious injections in patient IV lines, and candid admissions to other respiratory therapists that he had administered lethal drugs. Amazingly, other colleagues actually obtained lethal drugs, provided them to him, and then observed while he committed murder.

The male therapist was often working night shifts with little supervision, and while on duty, he managed many patients. Some of his eventual victims were very ill, some were recuperating from illness or injury, while others had recovered sufficiently to be able to soon leave the hospital. In 1998, one staff member finally reported to hospital administrators the suspicion that an unusual number of deaths were occurring at night, and on the floors where the subject worked. An internal hospital review was performed, and it was concluded that no data were statistically correlated to any unusual patient deaths at the facility.

The concerned hospital worker then notified the police and related the same apprehensions. The male therapist was subsequently detained, questioned, and arrested on March 11, 1998. In a preliminary interview with detectives, he confessed to killing 100–200 patients. In a subsequent, lengthy interview, the therapist again confessed that he had killed many patients, but had mentally suppressed their names due to guilt feelings. He claimed to have overdosed selected patients by injection with either pancuronium bromide (Pavulon) or succinylcholine chloride (SCC), and to have expedited the deaths of other patients by other means (e.g., shutting off oxygen supplies). However, shortly after these admissions, he recanted his confession. He was then necessarily released after 48 hours because of the lack of any direct physical evidence to support the accusation and confession. The therapist next elected to participate in interviews with various news and television programs, where a benevolent "Angel of Death" descriptor was coined by the media. On these television shows, the male subject declared that his earlier admissions were the result of his suicidal depression and were actually untrue.

Methods

Law Enforcement Investigation

Search warrants were then executed, and an inspection of his work locker discovered packaged syringes. The search of his residence revealed additional syringes and a vial of the drug Versed, a powerful sedative/hypnotic, with syringe puncture marks evident in the septum top. After analysis of the remaining liquid and an estimate of the quantity of missing Versed, investigators concluded that sufficient drug had been removed to provide a lethal dose.

Soon after the search warrants had been executed, the defendant contacted one of the police investigators regarding the return of some of his property. The investigator met the male therapist at a restaurant, and during this conversation, the subject denied completely that he had been complicit in any hospital homicides. He also verbally threatened the coworker who had brought the concerns of hospital deaths to the attention of the authorities, and stated that the entire investigation was a police conspiracy. Following this meeting, the suspect remained free for more than two years while an extensive investigation was conducted.

During the investigation, a considerable amount of circumstantial information was uncovered. However, tangible forensic results were necessary to proceed with legal prosecution. Habeas Corpus guidelines were imposed, and the suspect remained free because no specific victims had been identified, nor were patient deaths linked to any drugs proven to be in his possession.

Consequently, a task force was formed to uncover facts and information, and an extensive review of relevant hospital records of health-care facilities that had employed the therapist was undertaken. Conducted over 1998–1999, the Glendale Police Department task force scrutinized the records of all patients who had died at these institutions and had not been cremated. Following medical reviews of hundreds of patients and interviews with many health-care providers to determine which had not been administered SCC or pancuronium bromide as part of their medical regime, the task force then identified 20 patient deaths that appeared most suspicious. In May of 1999, the County Coroner exhumed the bodies for autopsy, with the aim to conduct subsequent toxicologic analyses of tissues and fluids to detect the presence (or absence) of pancuronium bromide. Chemical analyses of selected post-mortem tissue specimens from these autopsies occurred between June-December 1999. The sole focus of the forensic effort was an answer to a single question from the Los Angeles County District Attorney: "Were detectable quantities of pancuronium bromide present in any of these exhumed tissue samples?"

Patients and Lab Protocols

The backgrounds of the 20 patients selected from a list of >100 suspicious deaths are summarized in Table 1. The deceased had been buried in variety of wooden, metal, or pressboard caskets and had been interred in a concrete crypt below ground. Water from cemetery sprinkler systems was present in each casket, and all caskets were infested with insects.

Tissue, soil, and liquid samples were delivered to the Livermore Forensic Science Center (FSC) on the day after each exhumation and autopsy. All samples were personally transported to the FSC by Glendale P.D. personnel, logged into the FSC chain-of-custody system, and assigned an internal FSC number for cross-reference. Four redundant levels of access control were maintained over the samples at all times.

At the time of sample acquisition by the Coroner, each tissue was divided into "A" and "B" subsets. All samples were sealed with tape and locked in a freezer when not under analysis. Only the A samples were analyzed by the FSC, while the B sample-sets were secured in a locked freezer for archival purposes.

The 20 exhumation sample-sets included soil from the burial sites as local environmental exemplars. All such controls were analyzed

TABLE 1—*Patient background information.*

Patient Number	Date of Birth	Date of Death	Age	Days in Hospital Prior to Death	Time of Death	Reason for Hospitalization	Death Certificate	Pancuronium Detected
99-03041	7/17/06	8/28/97	91	6	0505	Dehydration, renal failure, urosepsis, cererbrovascular accident	Cardiopulmonary Arrest Due to Stroke	No
99-03042	09/28/28	08/05/97	68	2	0401	Hypertension, Liver Cancer, Ascites	Cardiopulmonary Arrest	No
99-03043	01/01/22	08/15/97	73	11	2013	Possible cererbrovascular accident and urinary tract infection, hypertension	Cardiopulmonary Arrest	No
99-03044	01/01/21	12/30/96	75	3	0440	Congestive hear failure, pneumonia	Cardiopulmonary Arrest	Yes
99-03045	20/12/22	12/08/97	75	2	0330	Pneumonia and hypoxemia caused by high levels of digoxin	Respiratory Failure and Cardiopulmonary Arrest	No
99-30346	02/20/07	08/28/97	90	7	0535	Sepsis, severe dehydration, and kidney failure	Cardiopulmonary Arrest	No
99-03047	05/18/10	08/15/97	87	10	0550	Chronic obstructive pulmonary disease and status asthmaticus	Cardiopulmonary Arrest	Yes
99-03048	09/07/15	07/24/97	82	13	0330	Lung infiltrate	Cardiac Arrest, Seizure, Bacterial infection	No
99-03049	11/7/39	7/28/97	58	6	2205	Hypoxemia, congestive heart failure, metastatic colon cancer, drug toxicity	Cardiopulmonary Arrest with Sinus Bradycardia	No
99-03050	4/30/20	8/28/97	77	2	0635	Hyponatremia, Thrombocytopeniz, Lymphoma and rash	Pulmonary Embolus and Cardiopulmonary Arrest	No
99-03051	09/14/12	8/28/97	85	11	0512	Stroke, aspiration pneumonia, depression and mental retardation	Cardiopulmonary Arrest	Yes
99-03052	02/23/21	01/07/97	76	11	0756	Respiratory tract infection and bronchospasms, chronic asthma	Cardiopulmonary Arrest	No
99-03053	06/25/69	02/22/97	28	2	0350	Acute lymphoblastic leukemia, severe headache, CNS disturbance	Cardiopulmonary Arrest	No
99-03054	04/24/10	10/09/96	86	13	2250	Abdominal pain	Cardiopulmonary Arrest	No
99-03055	04/14/09	01/22/97	88	3	0112	Chronic pulmonary disease with severe Asthmatic Bronchitis	Cardiopulmonary Arrest	Yes
99-03056	01/20/06	05/24/97	91	4	0940	Seizure disorder, organic brain syndrome, urosepsis, pulmonary disease	Cardiopulmonary Arrest	No
99-03057	05/26/06	10/24/97	91	2	0425	Right hemiplegia and pressure ulcers	Cardiopulmonary Arrest	No
99-03058	08/27/14	01/04/97	83	3	2110	Pneumonia, chronic pulmonary disease, and coronary artery disease	Cardiopulmonary Arrest	Yes
99-03059	08/11/19	01/02/97	78	4	0715	Pneumonia with chronic pulmonary disease, multiple sclerosis, reflux disease	Cardiopulmonary Failure	Yes
99-03360	12/26/23	08/2097	74	6	0001	Advance head and neck carcinoma	Cardiopulmonary Arrest	No

TABLE 2—*Tissue and fluid analyses—identification of pavulon.*

Specimen Number	Lung	Kidney	Arm Vein	Gall Bladder	Bladder Tissue	Chest Blood and Fluid	Pericardial Fluid	Heart Tissue and Blood	Liver	Stomach Content	Thigh Muscle	Aorta Blood	Brain	Soil	Embalming Fluids	Other
99-03041	− Θ	− Θ		− Θ	− Θ			− Θ	−							
99-03042	− Θ	− Θ							−							
99-03043	− Θ	− Θ							−							
99-03044	t ⊕	+ ⊕	⊕	x	⊕	Θ	x	+ ⊕	+ ⊕	x	⊕	x	Θ	Θ	Θ	Θ[1]
99-03045	− Θ	− Θ														
99-30346	− Θ	− Θ														
99-03047	+ ⊕	t u	u	u	t ⊕	x	u	+ ⊕	+ ⊕	u	u	Θ	⊕	Θ	Θ	t[2] u[2]
99-03048	− Θ	− Θ							−							
99-03049	− u	− Θ						−	−							
99-03050	− Θ	− Θ														
99-03051	+ ⊕	− Θ	+ u	t	+ ⊕	x	x	t Θ	t Θ	x	+ ⊕	−	+ ⊕	Θ	Θ	−[1] −[2]
99-03052	− Θ	− Θ							−							
99-03053	− Θ	− Θ							−							
99-03054	− Θ	− Θ														
99-03055	+ ⊕	+ ⊕	t	+	t	+	t	+ ⊕	+ ⊕	t	+	+	+	Θ	Θ	−[1] +[3]
99-03056	− Θ	− Θ							−							
99-03057	− Θ	− Θ							−							
99-03058	+ ⊕	+ ⊕	t	x	−	x	x	+ ⊕	+ ⊕	+	t	t	−	Θ	x	
99-03059	+ ⊕	+ ⊕	−	+	+	+	x	t Θ	+ ⊕	x	t	+	+	Θ	Θ	−[1] −[2]
99-03360	− Θ	− Θ							−							

+ = Screened positive by GC-MS.
− = Screened negative by GC-MS.
t = Trace diagnostic GC-MS ions at levels 2–9 times background.
x = no sample, 1 = Crypt water, 2 = Bladder fluid, 3 = Abdominal blood clot.
⊕ = Confirmed by μHPLC-ESI-MS/MS.
Θ = Negative by μHPLC-ESI-MS/MS.
u = Unconfirmed by μHPLC-ESI-MS/MS.

in tandem with exhumed tissue samples, clotted blood, and urine specimens. Samples of crypt water were also obtained from some of the burial sites. They were filtered and processed as well through the entire analysis procedure with the exhumed tissue samples. Solvent blanks and control-tissue samples were likewise analyzed in a manner identical to the questioned specimens.

Most of the exhumed bodies had been treated with several different types of embalming fluid. Therefore, commercial embalming fluids, identical to those used prior to the burials, were obtained and processed along with the exhumation tissues and fluid samples.

Results and Forensic Observations

The exhumed specimens were from patients who died suspiciously over 1996–1997, and the number of primary (and archival) samples in each set ranged from 10–19. Several of these tissue-sample sets were extensively decomposed. Some also contained high levels of embalming fluids, dyes, and formaldehyde, while one exhumation contained numerous parasitic flukes. Analyses for pancuronium were performed on extracts from postmortem tissues and fluids, control samples from the exhumed bodies, soil above the caskets, water in the burial crypts, and embalming-fluid samples. Analyses of all blank and control samples for pancuronium were negative.

Samples were processed for pancuronium following a protocol developed for extracting, concentrating, and identifying the drug (8). The initial screening efforts focused on the detection and confirmation of pancuronium in lung and kidney tissues. These tissue samples were chosen because they would have been highly perfused with blood at the time of death. Pancuronium was judged detected and confirmed when the prescreen of tissue extracts by pyrolysis GC-MS, followed by subsequent μHPLC-ESI-MS/MS, were both positive for pancuronium (8). The results of these experiments indicated that 6 of the 20 patients had detectable levels of pancuronium in their tissues (see Table 2). Although the kidney data from patients 99-03047 and 99-03051 were $<10\times$ instrumental background, other tissues (e.g., brain) from those patients assayed positive for pancuronium above this threshold. Although the electrospray MS/MS data from the analysis of lung tissue from patient 99-03049 hinted at trace levels of pancuronium, it could not be detected and confirmed in any other tissues from this sample set.

To confirm the effectiveness of the GC-MS screening procedure, an acetic acid/water extraction of sample 99-03053-6A (lung tissue) was spiked with pancuronium at a concentration of 5 ng/μL and reanalyzed. (Sample-set 99-03053 had previously assayed negative for pancuronium.) The analytic protocol then indicated the presence of pancuronium in this sample, validating detection of the thermal-degradation compound and application of m/z 340 mass–chromatogram plots for screening purposes (8).

The ESI-MS/MS mass spectrum of pancuronium is very specific. The doubly charged molecular ion, m/z 286, generates a unique MS fragmentation pattern. However, to fully exclude false-positive data possibly generated by other compounds in the tissues and fluids, the medical records of all exhumed patients were further reviewed at the FSC. Specifically, any therapeutic drugs administered to the pancuronium-positive patients were evaluated. Thus, administered drugs noted in the patient records that had molecular weights or other characteristics that could potentially generate false-positive MS data were also analyzed. The results of these assessments indicated that the administration of these therapeutic drugs did not warrant any further concern to the investigation at hand. Therefore, to a reasonable scientific certainty, false-positive μHPLC-ESI-MS/MS

analyses for pancuronium could not be generated by the drugs known to be administered to these six patients.

Conclusion

Based solely on these analytic results, the respiratory therapist was rearrested. A plea-bargain arrangement allowed him to avoid the death penalty, and he subsequently received six life sentences without the possibility of parole.

In contrast to previous, historic homicides in health-care settings, where emotional trauma, mental illness, or revenge criteria were causative factors, this case report provides a different motivation of possible interest to psychological profilers: when asked by investigating officers the true reason for murdering his victims, his reply was ". . . to reduce the workload." An "Angel of Death" label was therefore most inappropriate for this particular individual, and his actions provide yet another motivational factor for the use of lethal drugs in a health-care environment. Health-care professionals and law-enforcement investigators should therefore be cognizant of such lesser motives during investigations of any future incidents.

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Additional information and reprint requests:
Patrick M. Grant
Forensic Science Center
LLNL, L-231
Livermore, CA 94550
E-mail: patgrant@llnl.gov