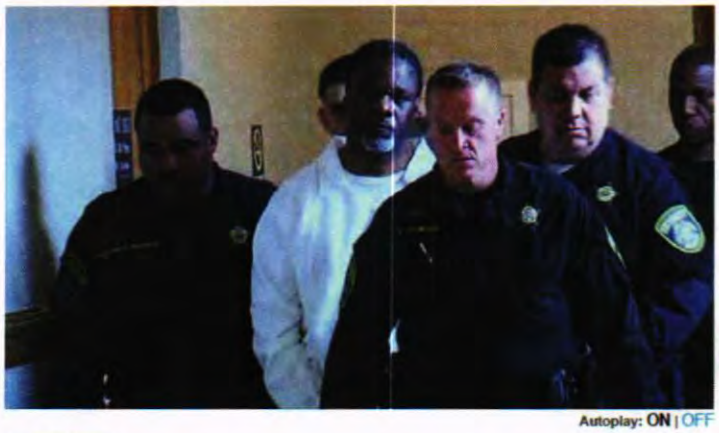
EXHIBIT 1



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Apr 25, 8:33 AM EDT

ARKANSAS CONDUCTS NATION'S 1ST DOUBLE EXECUTION SINCE 2000

BY ANDREW DEMILLO AND KELLY P. KISSEL
ASSOCIATED PRESS

VARNER, Ark. (AP) – After going nearly 12 years without executing an inmate, Arkansas now has executed three in a few days - including two in one night.

Jack Jones and Marcel Williams received lethal injections on the same gurney Monday night, just about three hours apart. It was the first double execution in the United States since 2000.

While Jones, 52, was executed on schedule, shortly after 7 p.m., attorneys for Williams, 46, convinced a federal judge minutes later to briefly delay his execution over concerns about how the earlier one was carried out. They claimed Jones "was moving his lips and gulping for air," an account the state's attorney general denied, but the judge lifted

her stay about an hour later and Williams was pronounced dead at 10:33 p.m.

In the emergency filing, Williams' attorneys wrote that officials spent 45 minutes trying to place an IV line in Jones' neck before placing it elsewhere. It argued that Williams, who weighs 400 pounds, could have faced a "torturous" death because of his weight.

Intravenous lines are placed before witnesses are allowed access to the death chamber.

An Associated Press reporter who witnessed the execution said Jones moved his lips briefly after the midazolam was administered, and officials put a tongue depressor in his mouth intermittently for the first few minutes. His chest stopped moving two minutes after they checked for consciousness, and he was pronounced dead at 7:20 p.m.

Asked why Jones' lips moved, Arkansas Department of Correction spokesman Solomon Graves said he understood that the inmate was apologizing to the department director, Wendy Kelley, and thanking her for the way she treated him.

Williams was already in the death chamber when the temporary stay was issued. He was escorted out of the chamber and used the restroom, then was brought back in after the stay was lifted.

Initially, Gov. Asa Hutchinson scheduled four double executions over an 11-day period in April. The eight executions would have been the most by a state in such a compressed period since the U.S. Supreme Court reinstated the death penalty in 1976. The state said the executions needed to be carried out before its supply of one lethal injection drug expires on April 30.

Besides the two executions Monday, Arkansas put to death one other inmate last week and has a final one scheduled for Thursday. Four others have been blocked.

Before last week, Arkansas hadn't had an execution since 2005 or a double execution since 1999.

Jones, who'd argued that his health conditions could lead to a painful death, gave a lengthy last statement. His final words were: "I'm sorry."

"I hope over time you can learn who I really am and I am not a monster," he said in the roughly 2-minute statement.

Williams declined to make a final statement.

Jones was sent to death row for the 1995 rape and killing of Mary Phillips. He strangled her with the cord to a coffee pot.

He was also convicted of attempting to kill Phillips' 11-year-old daughter and was convicted in another rape and killing in Florida.

Jones said earlier this month that he was ready for execution. He used a wheelchair and he'd had a leg amputated in prison because of diabetes.

Williams' "morbid obesity makes it likely that either the IV line cannot

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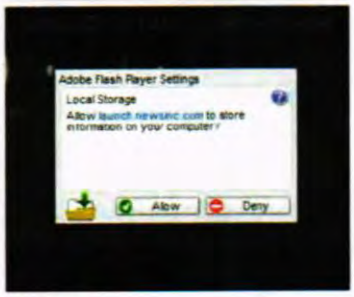

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be placed or that it will be placed in error, thus causing substantial damage (like a collapsed lung)," his attorneys wrote in an earlier court filing asking justices to block the execution.

Both men were served last meals on Monday afternoon, according to Graves, the corrections department spokesman. Jones had fried chicken, potato logs with tartar sauce, beef jerky bites, three candy bars, a chocolate milkshake and fruit punch. Williams had fried chicken, banana pudding, nachos, two sodas and potato logs with ketchup, Graves said.

In recent pleadings before state and federal courts, the inmates said the three drugs Arkansas uses to execute prisoners - midazolam, vecuronium bromide and potassium chloride - could be ineffective because of their poor health.

Williams weighed 400 pounds, was diabetic and had concerns that the execution team might not be able to find a suitable vein to support an intravenous line.

The poor health of both men, their lawyers claimed, could make it difficult for them to respond during a consciousness check following a megadose of midazolam. The state shouldn't risk giving them drugs to stop their lungs and hearts if they aren't unconscious, they have told courts.

The last state to put more than one inmate to death on the same day was Texas, which executed two killers in August 2000. Oklahoma planned a double execution in 2014 but scrapped plans for the second one after the execution of Clayton Lockett went awry.

Arkansas executed four men in an eight-day period in 1960. The only quicker pace included quadruple executions in 1926 and 1930.

Williams was sent to death row for the 1994 rape and killing of 22-year-old Stacy Errickson, whom he kidnapped from a gas station in central Arkansas.

Authorities said Williams abducted and raped two other women in the days before he was arrested in Errickson's death. Williams admitted responsibility to the state Parole Board last month.

"I wish I could take it back, but I can't," Williams told the board.

In a letter earlier this month, Jones said he was ready to be killed by the state. The letter, which his attorney read aloud at his clemency hearing, went on to say: "I shall not ask to be forgiven, for I haven't the right."

Including Jones and Williams, nine people have been executed in the United States this year, four in Texas, three in Arkansas and one each in Missouri and Virginia. Last year, 20 people were executed, down from 98 in 1999 and the lowest number since 14 in 1991, according to the Death Penalty Information Center.

Associated Press writers Jill Bleed contributed to this report from Little Rock.

Follow Andrew DeMillo at www twitter.com/ademillo and Kelly P. Kissel at www.twitter.com/kisselap

EXHIBIT 2

2 killers executed hours apart

By Eric Besson , Lisa Hammersly , John Moritz Twitter

This article was published today at 4:30 a.m.

PHOTO BY STATON BREIDENTHAL

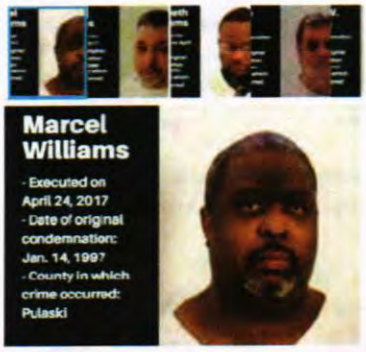
Inmates Marcel Williams and Jack Jones were put to death Monday night at the Cummins prison in the nation's first double execution in a day since 2000

EXECUTIONS: In-depth look at 7 men whose deaths Arkansas scheduled

GRADY -- In the nation's first double execution since 2000, Arkansas delivered heart-stopping doses of lethal drugs Monday night to death-row inmates Jack Jones Jr., 52, and Marcel Williams, 46.

Jones was pronounced dead at 7:20 p.m., 14 minutes after the execution began, prison officials said.

The convicted murderer moved his lips for about two minutes after the first drug entered his body at 7:06 p.m., according to witness Andrew DeMillo of The Associated Press. It wasn't clear whether the inmate was trying to speak, because the chamber microphone was



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Arkansas executions

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7:04 P.M.

The curtains to the execution chamber opened. An intravenous line was placed prior to the curtains opening. Jones began a lengthy last statement.

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Arkansas murder victim's daug...

turned off after his final statement, DeMillo said.

Jones' consciousness was checked at 7:11 p.m., and his chest rose and fell until about 7:13 p.m.. DeMillo said.

Officials don't administer the second and third drugs in the three-drug injection process until the inmate is determined to be unconscious.

In interviews afterward, DeMillo and two news media witnesses reported no obvious signs of suffering or pain.

But a federal court filing submitted shortly afterward described Jones' execution as "torturous," with the inmate "moving his lips and gulping for air" more than five minutes after the sedative drug, midazolam, was administered.

The filing by Williams' attorneys asked U.S. District Judge Kristine Baker to postpone Williams' execution.

In response, the state attorney general's office said the filing was "inaccurate" and that claims of Jones moving his lips and gasping were "unsupported by press accounts or the accounts of other witnesses."

Baker's postponement delayed Williams' execution for about two hours as she reviewed the case and held a hearing by telephone. After she declined to halt the execution, the curtains of the death chamber opened at 10:15 p.m, according to media witnesses. Two IVs appeared to be hooked up.

Prison staff started the first drug at 10:16 p.m. Williams closed his eyes. Witnesses saw deep breathing. By 10:19, his head rolled to the side. After a consciousness check at 10:21, an executioner moved toward another person and mouthed the words, "I'm not sure," according to witness and AP reporter Kelly Kissel.

At 10:24, Williams' breathing appeared to stop and he grimaced. He was pronounced dead at 10:33 p.m.

Arkansas has executed three inmates in five days at the Cummins prison unit at Grady, about 30 miles southeast of Pine Bluff. The first was convicted killer Ledell Lee, 51, on Thursday night.

Gov. Asa Hutchinson initially scheduled eight executions over 11 days, an unprecedented

Governor's spokesman comme...

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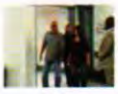

Mary Phillips' husband, James Phillips (from left), son Jesse James Phillips and daughter Lacey Phillips Seal prepare to speak Monday after the execut...

Death-penalty protester Randy Gardner (left) embraces Gina Grimm, the daughter of executed inmate Jack Jones, as a bell tolls nearby in a protest area...

rate since the United States reinstated the death penalty in 1976.

His plan captured attention across the U.S. and in countries that ban the death penalty. Time.com on Monday described the effort as "Arkansas' controversial attempt to thin its death row in quick succession."

Court stays and Arkansas Board of Parole decisions, however, have postponed four of the eight scheduled executions. One more inmate and convicted murderer, Kenneth Williams, is set to die this month, on Thursday.

Late Monday, after hearing accounts from state Department of Correction witnesses, Hutchinson called the executions "flawless," according to spokesman J.R. Davis.

Monday in the execution chamber, Jones gave his final statement calmly, witnesses said, apologizing to the family of his victim.

A White County jury recommended death for Jones for the 1995 rape and murder of 34-year-old Mary Phillips in the Bald Knob accounting office where she worked.

Jones also beat Phillips' 11-year-old daughter Lacey so badly that police at first thought she was dead, too. Mary Phillips' husband and Lacey's father, James Phillips, was at the prison to witness the execution.

Jones had told the Parole Board he was ready to die for his crimes, rather than spend more years on death row.

"Well, I just want to let the James family and Lacey know how sorry I am," the inmate said Monday night. "I can't believe I did something to her. ... I hope over time you could learn who I really am, and I am not a monster. There was a reason why those things happened that day. I am so sorry, Lacey. Try to understand I love you like my child."

In a handwritten final statement Jones gave to his attorney, Jeff Rosenzweig, the inmate said he dedicated his life in prison to becoming a better person, referencing his practice of Buddhism and study of physics.

"I met the right people and did the right things," the statement said. "There are no words that would fully express my remorse for the pain that I caused."

Lacey Phillips Seal told reporters she didn't want to discuss Jones' last words.

"There's definitely a different mood in the air right now," she said. "More tension and a little less tension in different ways. ... I'm glad it's done. ... I'm glad that chapter is closed."

Rosenzweig said he witnessed Jones' mouth open during the execution about three to five times from 7:10 p.m. to 7:11 p.m. He equated it to a "fish with its mouth open and then chomping on bait."

"He did not appear to be talking," Rosenzweig said. "He did not appear to have anything else moving other than his mouth."

Jones did not appear to suffer, Rosenzweig said, though he cautioned that he's not trained for subtle movements that would indicate Jones experienced pain.

Jones and Williams both sought to halt their executions on grounds that their poor health put them at greater risk for botched executions under Arkansas' three-drug injection method.

Jones appealed to the nation's highest court that a prior case determining whether to re-sentence him was flawed.

The inmate's lawyer has argued that Jones' bipolar mental illness wasn't properly presented during trial. The inmate was also physically and sexually abused as a child, family members said.

Jones received a last meal between 3 and 4 p.m. Monday of three pieces of fried chicken, potato logs with tartar sauce, jerky bites, three Butterfinger candy bars, a chocolate milkshake with Butterfinger pieces, and fruit punch, Department of Correction spokesman Solomon Graves said.

Shortly after 6 p.m., the U.S. Supreme Court rejected Jones' last two appeals.

Williams was convicted in the 1994 rape and murder of 22-year-old Stacy Errickson of Jacksonville. He and Jones each had spent more than 20 years on death row.

Williams had ordered a last meal Monday afternoon of three pieces of fried chicken, potato logs with ketchup, banana pudding, two Mountain Dews and nachos with chili, cheese and jalapeno peppers.

At 7:45 p.m, the U.S. Supreme Court rejected what appeared to be his last two pending court appeals, and Department of Correction officials took steps to start his execution.

But Williams' attorneys were filing documents with the U.S. District Court in Little Rock headlined in red type: "Unconstitutional execution imminent." The lawyers asked for an immediate stay of execution based on problems they saw with Jones' lethal injection.

Williams was on the gurney in the execution chamber Monday night when Baker issued a stay, witnesses said. He was allowed to go to his holding cell and use the restroom. He remained there until the stay was lifted.

A clemency petition to the Parole Board said Williams was physically and sexually abused as a child, with his mother facilitating sexual encounters between him and older women in exchange for money.

"On at least one occasion, Marcel's mother put a pot of water on to boil, heated up extension cords in the water, and then beat him, naked, with the cords until he was covered gashes," the petition says. "His cousins watched in horror as he fled the house, still naked and bleeding."

Baker rejected Williams' filing of an unconstitutional execution shortly before 9:30 p.m.

When prison officials asked for last words, Williams shook his head and made no other response.

The family of his victim, Errickson, declined to comment.

Less than 30 minutes after Williams was pronounced dead, at 10:51 p.m. Monday, a pair of black hearses left the prison, witnesses said.

'EMOTIONAL ROLLER COASTER'

Family of Jones and his victim were among the nearly two dozen protesters outside the Cummins prison gates Monday. Among them were Jones' sister Lynn Scott and children of James Phillips.

Zia Authier, a stepdaughter of James Phillips, said she and others came to support the Phillips family.

Jones' execution is "what was set for the trial, and this is what the Phillips family expects. So I'm hoping that for my family's sake, once this is all over and done with, they'll be at peace," she said before the execution was carried out.

Phillips' son-in-law Robby Jones, no relation to the inmate, said after Jones was dead: "It's been an emotional roller coaster. We're ready as a family to move on."

Anti-death penalty protesters were joined by Episcopalian priests who later prayed with Jack Jones' daughter, Gina Grimm.

At 7 p.m., when protesters rang the death toll, Grimm held Randy Gardner, a Utah resident whose brother was the last to die in the United States by firing squad.

Scott sat in the passenger seat of a car, praying and looking at the last pictures she took with her brother, just days before.

"I was letting him know that I would be right here until the end," she said. "It was a piece of him, and it was my way ... of saying goodbye."

Scott flew in from Raleigh, N.C., on Thursday and saw him for the last time Sunday. Her brother was still in good spirits and was truly at peace, she said.

She said she asked Jones to keep a promise before she left him Sunday.

"I wanted him to promise me that when he was on that table that he did not focus on those people behind the glass viewing him as a monster and anticipating what they were hoping and praying for on their end," she said, "that [instead] he would be thinking of me, that I'm right here and that I'm loving him till the end."

About 50 people protested the execution outside the governor's mansion Monday evening, holding flickering white candles and praying before the execution of Jones.

The announcement of his execution led many of them to tears. But Cackie Upchurch, a theologian for the Catholic Diocese of Little Rock, said she didn't believe her efforts are for naught.

"I think the fact that the entire nation is watching us and wondering what kind of barbaric things we're doing down here tells us that there is a swell against the death penalty across the country -- not in Arkansas and not in several states across the South," Upchurch said. "I am a proud Arkansan. I love my state and I love the South. But we're wrong on this."

The plan for eight executions over 11 days was unprecedented in Arkansas since at least September 1913, according to Department of Correction records.

The compressed schedule was necessary, prison officials said, not only because the state's supply of a sedative required for the three-drug lethal injection protocol, midazolam, was set to expire, but because most drug manufacturers refuse to sell their products for executions. Shortages of midazolam and the other two drugs have slowed executions nationwide.

Despite the hurried pace Hutchinson set, death-row inmates Don Davis and Bruce Ward received temporary stays April 17 on the basis that a pending U.S. Supreme Court case might apply to their convictions.

Another inmate awaiting death, Stacey Johnson, who has claimed innocence, was spared Thursday so lower courts could decide whether to order new DNA testing on evidence in his case.

A federal judge also granted a break to Jason McGehee, originally scheduled for execution this Thursday, on grounds that Arkansas could not kill him on that date without running afoul of the proper clemency process. The state Parole Board recommended Hutchinson grant McGehee a more lenient sentence despite recommending death for the other seven inmates.

After Monday's executions, 30 inmates, all men, remain on Arkansas' death row.

Information for this article was contributed by Hunter Field, Aziza Musa and Michael R. Wickline of the Arkansas Democrat-Gazette *and Brandon Riddle and Jillian Kremer of Arkansas Online.*

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AGG says... April 25, 2017 at 6:25 a.m.

Heartbreaking and sobering on all accounts. How tragic for the families of the victims. How sad it is for the perpetrators whose lives' courses ran amok for a host of reasons. The sobering reality is innocence was defended last night in Arkansas as it should have been. The message has been delivered: Do not commit rape and murder in Arkansas.

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drs01 says... April 25, 2017 at 7:54 a.m.

Heartbreaking that the family of the victims had to endure YEARS of fruitless appeals by do-gooders and public defenders.
Three down and .....

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titleist10 says... April 25, 2017 at 7:59 a.m.

You murder another human being you must pay the price

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TravisBickle says... April 25, 2017 at 9:32 a.m.

Finally Arkansas is in the news for something positive!!

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EXHIBIT 3

Arkansas executions: 'I was watching him breathe heavily and arch his back'

Arkansas on Monday . Jacob Rosenberg witnessed the murderer Marcel Williams being put to death

Jacob Rosenberg in the Cummins Unit, Arkansas

Tuesday 25 April 2017 08.36 EDT

At 9.34pm we entered the execution chamber. I passed through a door with a large sign on its front showing two letters, "EC", and took a seat among a few rows of chairs that faced four large rectangular windows. Some lights were on, but it was mostly dim. A black curtain was drawn behind the windows in front of us.

Behind that curtain, strapped to a gurney in an even smaller room, was Marcel Williams.

In Arkansas, we do not get to see the placement of the IV for lethal injection. So, from the time we entered until the curtain opened, I saw nothing. We just stared forward at those windows, waiting for them to reveal Williams, 46, who was sent to death row for

the 1994 rape and killing of 22-year-old Stacy Errickson, whom he kidnapped from a gas station.

We had done this earlier in the night, when a last-minute stay had us waiting in the chamber for over an hour. During that time, we later learned, Williams had been strapped down on the gurney. Now, as then, with the stay lifted, I simply looked at the black curtain, knowing almost nothing about what was happening to the prisoner.

The curtain created a reflection of the room behind me, like a mirror. I could see other witnesses, and myself, fidget.

At 10.16pm, after 32 minutes of IV placement, the curtain opened.

Light from fluorescent bulbs cast a strange yellow glow in the room in front. Marcel Williams's eyes looked right up at the ceiling. He was on a gurney, tied down. His head was locked in place and the right side of his body was facing us, the viewers. He said no final words.

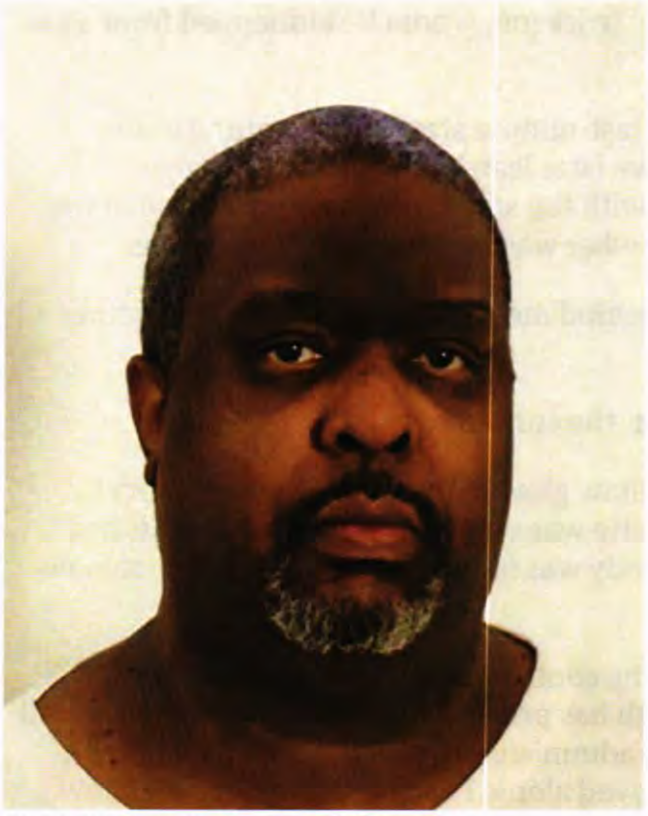
At this point, the first lethal injection drug - the controversial sedative midazolam, whose expiration date at the end of this month has prompted Arkansas's unprecedented wave of judicial killings - was supposed to be administered. No one announced that a drug was being given . The process simply moved along. I watched and tried to follow.

His eyes began to droop and eventually closed (the right one lingered slightly open throughout). His breaths became deep and heavy. His back arched off the gurney as he sucked in air.

I could not count the number of times his body moved in such a way, rising off the gurney.

Procedure dictates that five minutes after the introduction of midazolam there should be no movements. But, at 10.21pm, Williams was still breathing heavily and moving. The man in the room checked his pulse and touched his eyes and said something. (The audio was cut off for us.)

At this point, it is likely another dose of midazolam was given. I cannot be sure it was administered. I was watching him breathe heavily and arch his back and then the breathing began to shallow out. By 10.24pm, Williams looked completely still.



Marcel Williams. Photograph: UPI / Barcroft Images

The first consciousness check was clearly at 10.21pm, and then it seems the breathing subsided, but the situation became confusing as the official continually checked Williams by touching his hands and face. At 10.27pm, the official ran a finger across Williams's eyelids again. Was this the second consciousness check? Did they determine Williams was unconscious? Would the second drug be administered now?

These questions are crucial because the next drug was a paralytic, which stops all movement.

I do not know when the second drug, which would mask all pain, was administered. I did not see the IV placed. The audio was cut so I could not hear whether he was moaning, and I could not see how many times each drug was administered - meaning, even as a witness, I could not say if Marcel Williams felt pain or what happened during his death by the midazolam three-drug protocol.

The process is designed to feed me details as a viewer that suggest peaceful passing. But this will not have been the experience of Marcel Williams.

Protocol ensures that by the time the potassium chloride, which stops the heart and can be excruciatingly painful, is administered, even if the prisoner feels pain, the viewer will not see it. The paralytic is in place.

Near 10.31pm, they switched off the IVs. The man who had been checking for consciousness pulled out a stethoscope and put it to Williams's heart. He called in a coroner. I remember seeing Williams, there on the gurney, not moving.

And then, the one detail you can't obfuscate. That nothing can hide. The time of death was 10.33pm.

Jacob Rosenberg is a reporter with the Arkansas Times, which is also publishing a version of this article.

EXHIBIT 4

DECLARATION OF JAMIE GIANI

1. I am an Assistant Federal Public Defender with the Capital Habeas Unit in Little Rock, Arkansas. Marcel Williams was a client of our office.
2. I was present at Cummins from about 2:40 until after 11:00 PM on April 24, 2017. I visited with Marcel prior to his execution and then witnessed the execution itself.
3. During this time, and particularly during the execution itself, I took notes as to what was going on, marking down exact times whenever possible. The following timeline is taken from my notes and accurately reflects my recollection of what happened on April 24, 2017:

- 2:40 Arrived at prison with Scott; told only Scott was approved to go back, but that even he could not go back right now
- 4:44 After repeated requests to see our clients, to no avail, and without being given any good reason, I attempted to call Lee Rudofsky's cell phone from the deputy warden's office. It went to voicemail.
- 4:45 I call Judge Baker's chambers to let her know we were not being allowed to see our clients at this crucial time and we had been waiting two hours. While we were on the phone, Major Cyr informed us that they would now take Scott and Jeff back. Scott and Jeff left the deputy warden's office to visit the clients.
- 5:40 Scott returned, and I was driven to the death house.
- 5:45 Began my visit with Marcel
- 6:40 They came to take Jack Jones to be executed.
- 7:00 Marcel was given clean, pressed, execution whites and told to put them on by 7:30. No shoes – socks only.
- 7:20ish Father Harris administered last rites to Marcel.

- 7:50ish The Emergency Response Team in full riot gear came to take Marcel out of his cell. I asked if I could hug him goodbye. They said no. So I reached through the bars, squeezed his hand, and said goodbye. Father Harris and I were escorted out. White vans with witnesses arrived, and Scott was brought over from the garment factory. We waited to be told when to go into the witness room.
- 8:03 We sat down in the witness room. We were the last to be seated as the attorneys. We were seated in the back row by the door so that we could stand to see if we needed. There were three rows of seats ahead of us, packed in a tight room, facing four large windows covered on the inside by a black curtain. The door to the execution chamber was to the right of the windows. Light and movement of feet could be seen through a slight crack. Lights in the witness room were dimmed. Witnesses sat quietly. 9 men and one woman were citizen witnesses; 2 men and 1 woman were media; 2 male chaplains; Scott and myself. An officer stood in the passageway in front of the execution door with another female ADC employee.
- 8:16 I hear the phone ring in the execution chamber.
- 8:17 We are told there is a 20-minute stay from the courts. Wendy Kelley opened the door from the execution chamber and asks Will Jones (citizen witness) to step out. I stepped out and called John Williams. I eventually rejoined the others in the witness room after a brief conversation to determine what was happening (there was movement in Jones's execution and they were asking for a stay of Marcel's before Judge Baker).
- 8:28 Scott left to call John. I remained in the witness room (with no watch or clock). During the following 20 minutes, we hear muffled talking coming from the execution chamber. I can discern what sounded like Marcel's voice and Wendy Kelley's voice. I overhear the female ADC employee talking with officer saying Jones kept talking after his last words

and media is saying we turned the mic off too early (maybe her name is Shelly?). Loud laughter comes from execution chamber – clearly Marcel. "Shelly" whispers "That's Marcel in there laughing." Marcel laughs several times, and I continue to hear voices. Officer asks "Shelly" if "we need to take these witnesses back out." "Shelly" makes a call on her cell phone and is apparently told not to take the witness out. I believe I hear Marcel say "Seriously. Go look it up." And another loud laugh. Continue to hear Marcel and what sounds like Wendy Kelley's voice.

- 8:49 Hear a knock inside the execution chamber
- 8:50 Hear jangling inside execution chamber – something happening with shackles.
- 8:56 Scott still outside; continue to hear some talking in execution chamber but can't discern voices; witness room is quiet.
- 8:59 "Shelly" makes another phone call – still no word; Banging sound in execution chamber; witnesses begin to stand up and stretch.
- 9:04 It seems to be quieter in the execution chamber
- 9:10 Officer and "Shelly" step into vestibule for about ten seconds and close door; everything is quiet; the air kicks on
- 9:17 The main door to the outside opens and all witnesses are taken back out. I'm feeling hopeful. I ask if Marcel is back in the cell. Father Harris and I would like to go see him.
- 9:20 Father Harris and I are escorted back to Marcel's cell, passing what appears to be the IV team on the way in. Marcel said that he had been strapped down for quite a while but that he eventually said he had to go to the bathroom if they were going to be there a while. They then brought him to the bathroom and Wendy Kelley told them to just let him stay in the cell until the stay was lifted. He still had his ankle straps on. He said that

they had tried to start on IV but had not actually stuck him yet. He said he had been in the cell for maybe about 15 minutes. I told him we were not sure the stay would hold.

- 9:25 They came back in and said the stay was lifted. Same procedure with the riot gear and a rushed second goodbye. This one would be the last.
- 9:32 We were again seated in the witness room, and the officer knocked on the door to let the execution chamber know we were present and seated. Dexter Payne is also in the room now.
- 9:43 Hear talking from execution chamber – I believe it's Marcel and Wendy Kelley; rolling noise
- 9:45 "Shelly" makes quick phone call to say "be careful with that curtain." Don't know what she was talking about. I had not noticed any issues with curtain.
- 9:55-56 Continue to hear people talking in low voices in the execution chamber; otherwise everything is quiet
- 9:59 Drawer-like noise and shackles noise from execution chamber
- 10:04 Dexter Payne shows "Shelly" something on his cell phone
- 10:09 More talking from execution chamber – sounds something like "do not cover it up."
- 10:14 A banging sound and jangling from execution chamber
- 10:15 Hear a male's voice from execution chamber – don't think it's Marcel's
- 10:16 Knocking sound in execution chamber; after 45 minutes of sitting in the witness room, the curtains are suddenly opened and light comes pouring in from the execution chamber. Marcel is lying with his right side facing us, his right arm extended out, strapped down, towards the witness room. The designee stands by Marcel's head on Marcel's right side, at times slightly obstructing the view. I see tubes going to the crook of Marcel's right elbow as well as his right wrist. I see no tubes going anywhere else on

his body. Marcel is asked if he has any last words; he slightly shakes his head no and says nothing. The sound feed from the execution room is turned off. Marcel's body is covered with a sheet, but his right arm is visible. There is some sort of board-type strap across his chest and his arms and hands are strapped down. His legs and feet are not visible. His head is squeezed between a yellow, vice-type contraption but limited movement of his head is still possible as evidenced by his ability to indicate he had no last words. The medication is started.

- 10:17 Marcel's eyes close. He is breathing very hard. His chest visibly rises up and down in hard, almost jerky motions.
- 10:18 Hard breathing continues; Marcel turns his head slightly.
- 10:19 After only two minutes, designee begins checking Marcel's neck, touches his arm and hand. Not clear if this is part of the consciousness check.
- 10:20 Hard breathing continues. Designee touches Marcel's right fingers; I hear loud talking coming from outside.
- 10:21 Marcel's head moves; hard breathing continues; Designee places pulse ox on Marcel's right middle finger
- 10:22 Designee touches Marcel's eyelashes and speaks into his ear (not loudly enough to be heard in witness room where I was standing); Marcel's head turns; hard breathing continues; Designee touches Marcel's hand and removes pulse ox (it is never replaced)
- 10:23 Marcel's breathing visibly slows; I no longer see the sheet moving.
- 10:24 Designee checks Marcel's right wrist
- 10:25 Marcel coughs
- 10:26 Designee again brushes Marcel's eyelashes and touches his hand and arm
- 10:27 Designee just keeps looking at Marcel; his face appears to show concern

- 10:28 Marcel's right eye (I cannot see his left) opens slightly; I can see movement of his eyeball
- 10:29 I continue to see eye movement
- 10:30 Designee continues to just look at Marcel at this point
- 10:31 Designee brushes Marcel's eyelashes; the right eye is still open; Designee takes out a stethoscope and puts it on Marcel's neck and chest; appears to listen for breathing.
- 10:32 Designee says I think we need to call the coroner (this was actually audible even without the audio being on); Coroner comes in and uses his stethoscope to briefly check Marcel
- 10:33 Time of death is announced; Wendy Kelley reads proclamation.

4. I kept waiting for the consciousness check to be completed. I never saw the designee make any affirmative indication that Marcel was not conscious, and in fact, there was eye movement until at least 3 minutes before the coroner was called. I did not think they had even pushed the second or third drugs yet, so I was shocked when the coroner was called. I saw no sternum rub or pinch. It certainly was not clear how the consciousness decision was made – if, in fact, it ever was.

I swear that the foregoing is true and correct to the best of my knowledge under penalty of perjury under the laws of the United States and the State of Arkansas.

4/25/17

Date

Jamie Giani

EXHIBIT 5

Declaration of Joel Zivot, M.D., F.R.C.P. (C)

I, Joel Zivot, hereby declare:

1. I received my Doctor of Medicine from the University of Manitoba, Canada, in 1988. From 1989 to 1993, I was a resident in Anesthesiology at the University of Toronto, Department of Post Graduate Medical Education, and from 1993 to 1995, I completed an additional residency in Anesthesiology and a Fellowship in Critical Care Medicine at the Cleveland Clinic Foundation, Department of Anesthesiology in Cleveland, Ohio.

2. I hold an active medical license from the State of Georgia and have held unrestricted medical licenses in Ohio, the District of Columbia, Michigan, and the Canadian provinces of Ontario and Manitoba. I also hold an active license to prescribe narcotics and other controlled substances from the federal Drug Enforcement Administration.

3. I hold board certification in Anesthesiology from the Royal College of Physicians and Surgeons of Canada and the American Board of Anesthesiology. I am also board certified in Critical Care Medicine from the American Board of Anesthesiology.

4. I have served as the Medical Director of the Cardio-Thoracic Intensive Care Unit and the Fellowship Director for Critical Care Medicine at Emory University Hospital. I am an Associate Professor of Anesthesiology and Surgery at the Emory University School of Medicine and an adjunct Professor of Law at Emory University Law School.

5. I have practiced anesthesiology and critical care medicine for twenty-two years, and, in that capacity, I have personally performed or supervised the care of more than 42,000 patients. My resume is included as Attachment 1.

6. I am, by reason of my experience, training, and education, an expert in the fields of anesthesiology and critical-care medicine. The opinions that follow

are within my field of expertise and are stated to a reasonable degree of medical and scientific certainty unless otherwise noted. Ethical requirements prohibit my participation in lethal injection. The opinions below express my medical opinion regarding the risks of the lethal-injection procedure to be used against Kenneth Williams. These opinions are not and should not be construed as an attempt to assist the state in developing a better way to perform executions.

7. Counsel for Kenneth Williams retained me to review witness accounts of the State of Arkansas's recent executions and to determine if Mr. Williams has any medical conditions that would cause a unique and particular danger of significant pain and suffering during the State's planned lethal injection of him on April 27, 2017. I have reviewed pertinent medical records for Mr. Williams, and I performed a physical examination of him.

8. I have reviewed the State's lethal-injection protocol entitled "Attachment C." I previously authored a declaration setting forth my concerns that the lethal-injection protocol is insufficient to anesthetize any prisoners against the pain of the second and third drugs and lacks safeguards to prevent a tortuous death or sub-lethal injury. My concern was that the pain of death as a result of the lethal injection protocol set forth in "Attachment C" far exceeds any pain that might be associated with a natural death. That declaration is included here as Attachment 2.

9. I have also reviewed publicly reported accounts of the April 24, 2017, executions of Jack Jones and Marcel Williams using the Arkansas lethal injection protocol. These accounts provide important information regarding how the midazolam protocol works in action.

10. Based on the accounts of the April 24 executions, my physical exam of Kenneth Williams, and my review of his medical records, it is my opinion that the State's lethal injection protocol, if performed against Mr. Williams, will

cause him extreme pain and suffering due to his unique medical conditions and in light of the manner in which Arkansas is performing executions under its protocol.

11. Witness accounts of Jack Jones's execution on April 24, 2017, indicate that the lethal injection team unsuccessfully attempted for 45 minutes to place a central line before eventually placing two intravenous lines. These events reflect that the execution team lacks the necessary medical skill to do these tasks competently. In order to be certain that these intravenous starting events occur without needless and excessive pain, it will be necessary to allow observation by knowledgeable individuals, not otherwise under the employ of the ADC. Obviously, in a medical setting, failing to place a central line or taking so long to place an IV would not accord with any minimum standard of care.

12. Witness accounts also indicate that, after injection of midazolam, Mr. Jones was moving his lips, speaking to Corrections Director Kelley, and/or gulping for air. As an anesthesiologist who has administered anesthesia to many thousands of patients in my career, I can state that such actions and movements are not consistent with general anesthesia or "unconsciousness" and instead reflect the inability of midazolam to induce general anesthesia or relieve pain.

13. Witness accounts of Marcel Williams's execution on April 24, 2017, indicate that, when an execution team member checked Mr. Williams's consciousness after injection of the midazolam, "the executioner moved toward another person and mouthed the words, 'I'm not sure,'" according to multiple witnesses. Mr. Williams continued arching his back and moving during this time. Three minutes later Williams's breathing stopped, and he grimaced. These events reflect that the executioners lack the medical skill and

experience to perform a reliable consciousness check. Further, the fact that Marcel Williams continued moving after the midazolam injection and grimaced when his breathing stopped – likely upon the administration of the paralytic vecuronium bromide – clearly indicates that he was not under general anesthesia and was not insensate to pain at the time.

14. Striking in both executions is what cannot be seen. The ADC does not allow a clear unobstructed vantage point to view the fullness of the execution. Reports by witnesses that claim to have seen no obvious suffering are utterly insufficient as verification that excessive pain and suffering did not occur. The inmates are strapped down, from head to toe to fingertips and large movements are therefore impossible even for those that have not received any of the execution drugs. A pulse oxymeter was applied to Marcel Williams for unclear reasons. At some point, the pulse oxymeter was removed and not reapplied. This device is in no way a monitor of consciousness although the ADC has claimed it would provide some form of an aid in this question. It speaks further to a lack of technical understanding on the part of ADC.

15. This information demonstrates that, in practice, Arkansas's lethal injection protocol causes condemned prisoners to experience significant pain and suffering, and that the State's lethal injection team lacks the ability and experience to perform its functions competently.

16. I evaluated Kenneth Williams on March 23, 2017, at the Varner Supermax Unit in Grady,

Arkansas. Mr. Williams is a thirty-eight-year-old African-American man with several noteworthy medical issues. Mr. Williams suffers from sickle cell trait, erythrocytosis, and brain dysfunction with a history of brain injury. He was also diagnosed with Lupus in 2013.

17. Sickle cell trait is a blood condition that in this country is found primarily among African-Americans. Sickle cell trait is inherited genetically. When one parent has sickle cell trait, there is a fifty percent chance that the child will inherit the trait. If both parents have sickle-cell trait, three in four children will inherit the trait. and one of those three will also develop sickle cell disease.

18. Sickle cell disease is a lifelong medical condition that causes significant pain and serious health problems. The disease causes a chronic shortage of functioning red blood cells, which are required to deliver oxygen throughout the body. The damaged cells can also cause blood clotting and associated problems such as stroke. Red blood cells that contain the abnormal hemoglobin protein pathognomonic for sickle cell disease will alter shape from a normal spherical bi-concave appearance to a crescent or sickled shape. This occurs whenever the red blood cells afflicted with the abnormal hemoglobin molecule are exposed to low oxygen.

19. Persons with sickle cell trait, as opposed to full-blown sickle cell disease, are not usually symptomatic, and they typically can lead normal lives. However, people with sickle cell trait can develop "sickle crises," in which the symptoms of sickle cell disease manifest under conditions where their bodies – and their red blood cells in particular – are placed under significant strain. This can occur as the result of intense exercise, being in high altitude/low oxygen conditions, or other activities like scuba diving. When a tourniquet is applied to the arm or leg of a person with sickle prone cells, the resulting fall in oxygen to the limb in question can initiate a cascade of sickling cells. Sickled cells are ineffective oxygen carriers and the sickled red cell clump is associated with progressive organ failure as a consequence of obstructive vascular emboli. Impaired blood flow will necessarily result in

inadequacy of circulation and uneven distribution of the chemicals set for execution.

20. Arkansas's lethal injection protocol, when administered to Kenneth Williams, is likely to provoke a "sickle crisis." The administration of midazolam will at first cause a fall in blood oxygen and cause red cell sickling. Once paralysis is achieved by vecuronium, the further inexorable fall in blood oxygen will only serve to further lead to a severely painful sickle crisis.

21. Mr. Williams's brain damage and Lupus diagnosis will also likely cause significant pain and suffering during administration of the lethal injection drugs. Brain injury and Lupus are independently associated with significantly increased risk of seizure and associated complications. There is a substantial likelihood that the injection of midazolam will provoke such a response in Mr. Williams.

22. Alone and in combination, each of Mr. Williams's medical conditions will complicate the State's "one size fits all" execution procedure and lead to severe pain and suffering for him. After the State injects Mr. Williams with vecuronium bromide, however, most or all of the manifestations of his extreme pain and suffering will not be discernible to witnesses. Vecuroniumbromide is a paralytic that will prevent movement of all major muscle groups in his body and prevent him from breathing, but it will not reduce his pain or affect his consciousness in any way. The only discernable reason for including vecuronium bromide in Arkansas's lethal injection procedure is to cloak from the execution team and other witnesses the extreme pain and suffering that Mr. Williams will endure.

I certify that the facts set forth above are true and correct to the best of my personal knowledge, information, and belief, subject to the penalty of perjury, pursuant to 28 U.S.C. § 1746.

April 25, 2017

Date

Joel Zivot, M.D., F.R.C.P.(C)

EXHIBIT 5
ATTACHMENT 1

EMORY UNIVERSITY SCHOOL OF MEDICINE
CURRICULUM VITAE

Revised: April 2017

1. Name: *Joel B. Zivot, MD, FRCP(C)*

2 Office Address.,
1364 Clifton Road, Atlanta, GA 30322
Telephone: (404) 686-4411
Fax: (888) 980-5928

3 E-mail Address: *Jzivot@emory.edu*

4 Citizenship
American, Canadian

5. Current Titles and Affiliations

a Academic Appointments.

1. Primary Appointments:
Associate Professor, Department of Anesthesiology

2 Joint and Secondary Appointments:
Associate Professor, Department of Surgery

3 Other academic appointments
Adjunct Professor Emory School of Law
Adjunct Professor, Emory University Institute of Liberal Arts

b. Other Administrative Appointments:

Medical Advisor Southern Center for Human Rights, Atlanta, Georgia

6 Previous Academic and Professional Appointments.

-Fellowship Director, Critical Care Medicine, Department of Anesthesiology, Emory University School of Medicine, Jan 2013-January 2016
- Medical Director, 4A/5A, EUH (February 2013 –June 2015)
- Medical Director, 11S, EUHM (June 2010-February 2013)
- Associate Professor, Department of Anesthesiology, University of Manitoba, Winnipeg, Manitoba, Canada, 2007-2010
Member, Academic Promotions Committee, University of Manitoba, Faculty of Medicine, Winnipeg, Manitoba, Canada, 2009
-Member of selection committee, Physician Assistant Program, The University of Manitoba, Winnipeg, Manitoba, Canada, 2008
- Member, Accreditation Review Committee-Anesthesiologist Assistants, Commission on Accreditation of Allied Health Education Programs (ARC-AA), 2008
- Assistant Professor, Department of Anesthesiology and Critical Care Medicine, George Washington University Hospital, District of Columbia, USA, 2005-2007

-Program Medical Director, Master of Science in Anesthesiology, Case Western Reserve University School of Graduate Studies, Cleveland, Ohio, USA, 2000-2005
- Assistant Professor of Anesthesia, Surgery, and Intensive Care, University Hospitals of Cleveland, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA, 1998-2005
- Director Critical Care Medicine Fellowship, Department of Anesthesiology, University of Michigan Medical Center, Ann Arbor, Michigan, USA, 1996-1998
- Assistant Professor, Department of Anesthesiology and Critical Care Medicine, University of Michigan Medical Center, 1995-1998

7 Previous Administrative and/or Clinical Appointments:

-Medical Director, Cardio-thoracic ICU, Intensive Care Cardiac Sciences Program, Winnipeg Regional Health Authority, Winnipeg, Manitoba, Canada, 2007-2010
-Medical Director, CTICU, George Washington University Hospital, Washington, DC, 2005-2007
-Co-Medical Director, Surgical Intensive Care Unit, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio, USA, 2002-2005
-Director, Post Anesthesia Care Unit, Department of Anesthesiology, University of Michigan Medical Center, Ann Arbor, MI, 1995-1998

8 Licensures / Boards.

-Licentiate, Medical Council of Canada, 1989-present
-License, Controlled Substance, Drug Enforcement Agency, 1995-present
-License, Michigan State Medical Board, 1995-2000
-License, Ohio State Medical Board, 1998-2012
-Fellow, American College of Chest Physicians, 2000-2010
-License District of Columbia Medical Board, 2005-present
-License, College of Physicians and Surgeons of Manitoba, 2007-2011
-License, Georgia Composite Medical Board, 2010-present

9. Specialty Boards:

-Fellow, Royal College of Physicians of Canada, 1993-present
-Diplomat, Anesthesiology, American Board of Anesthesiology, 1995-present
-Diplomat, Critical Care Medicine, American Board of Anesthesiology, 1995-present
-Fellow, American College of Chest Physicians, 2000-2010
-Testamur in basic peri-operative trans-esophageal echocardiography, National Board of Echocardiography, 2010-present

10 Education:

-University of Manitoba, Winnipeg, Manitoba, Canada, 1980-1983
-University of Toronto, Toronto, Ontario, Canada, 1984
-Doctor of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada, 1988

11 Postgraduate Training.

-Rotating Internship, Mount Sinai Hospital, University of Toronto, Department of Post Graduate Medical Education Toronto, Canada, 1988-1989
-Residency, Anesthesiology, University of Toronto Department of Anesthesiology, Dr David McKnight, Toronto, Canada, 1989-1993
-Residency, Anesthesiology, Cleveland Clinic Foundation, Department of Anesthesiology, Dr. Armin Schubert, Cleveland, Ohio, United States, 1993-1994
-Fellowship, Critical Care Medicine, Cleveland Clinic Foundation, Department of Anesthesiology, Dr. Marc Popovich, Cleveland, Ohio, United States, 1994-1995

-Masters of Bioethics, Emory Center for Ethics, Dr. Toby Schonfeld, program director, 2012-present, expected graduation spring 2017

12. Committee Memberships:

a. National and International:

-American Society of Anesthesiology, Committee on Ethics, 2011-present
-American Society of Anesthesiology, Care Team Committee, 2007-2009
-Society of Critical Care Medicine, Committee on Ethics, 2011-present
-Society of Critical Care Medicine, Patient and Family Satisfaction Committee, 2013-present
-Society of Cardiovascular Anesthesiology, Committee on Ethics, 2012-2013
-Society of Critical Care Anesthesiologists, Graduate Education Committee 2013-present

b. Regional and State:

-President, Cleveland Society of Anesthesiology, 2001-2002
-President Elect, DC Society of Anesthesiology, 2006-2007

c. Institutional

-EUHM Committee on Ethics, 2011-present
-EUHM Pharmacy and Therapeutics Committee 2011-present
-EUHM Executive Critical Care Committee 2010-present
-EUHM CAUTI and CLABSI prevention committee 2010-present
-EUH Executive Pharmacy Committee 2012-present
-EUH Antibiotic Utilization Subcommittee 2012-present
-EUH Resuscitation Committee 2013-present
-EUH Difficult Airway ad-hoc group 2013-2014
-EUH Executive Critical Care Committee 2013-present
-Department of Anesthesiology Residency Review Committee2013-present
-EUH/EUHM CTS Quality Committee, 2012-present

13. Peer Review Activities

a. Manuscripts:

-Canadian Journal of Anesthesiology, (manuscript reviewer), 2013

-Critical Care Medicine, (manuscript reviewer), 2014-2015

-Mayo Clinic Proceedings, (manuscript reviewer), 2015-

b. Grant reviewer

- Reviewed grant applications for The Emory Georgia Tech Healthcare Innovation Program (HIP), (HIP-ACTSI-GSU) Seed grant

b. Conference Abstracts:

i. National and International:

-American Society of Anesthesiology, 2012

Abstract Review Committee and poster session moderator

ii Regional

-Midwestern Anesthesia Resident Conference, 2001-2003
Abstract reviewer

14 Consultantships:

-Merck Pharmaceuticals, physician advisory board, 2005-2007
-Consultant for Wireless EKG Monitor, 2004-2005
-Masimo Corporation, product design and physician advisory board, 2013-present
-Doximity, physician advisory committee. 2014-present

15 Honors and Awards:
-Robert B. Sweet Clinical Instructor of the Year, University of Michigan, Department of Anesthesiology, 1997

-Outstanding Clinical Instructor of the Year. Case Western Reserve University, Master of Science in Anesthesiology Program, 1999

-Clinical Instructor of the Year, University Hospitals of Cleveland, Department of Anesthesiology, 2000

-Outstanding Clinical Instructor of the Year, Case Western Reserve University, Master of Science in Anesthesiology Program, 2001

-Meritorious Service Award, American Academy of Anesthesiologist Assistants, 2003

This award was given to me for academic work as the medical director of the Masters in Science of Anesthesiology at Case Western Reserve University and also advocacy for scope of practice, and committee work to improve the relationship between the American Society of Anesthesiology and American Academy of Anesthesiologist Assistants.

-Quality and Patient Safety Award, University Health Systems Consortium, 2002

This award was given by University Health System Consortium for various quality benchmark projects when I was the co-medical director of the Cardio-thoracic Intensive Care Unit at University Hospitals of Cleveland

-Distinguished service by a Physician Award, American Academy of Anesthesiologist Assistants, 2005

This award was given to me for work with the American Academy of Anesthesiology Assistants annual meetings where I served as a speaker on multiple locations and also developed and hosted an annual Jeopardy game competition between all of the Masters of Science in Anesthesiology schools around the country

-District of Columbia Annual Patient Safety Award, District of Columbia Department of Health, 2006

This award was given by the District of Columbia Department of Health for quality improvement work done when I was the medical director of the cardio-thoracic intensive care unit at George Washington University Hospital. I developed several collaborative quality projects between cardio-thoracic surgery and critical care medicine.

-*Presidential Citation, Society of Critical Care Medicine, 2013*

This award was given to me for work done within the Society of Critical Care Medicine that included writing a book chapter, service on 2 society committees, and moderating an o- line debate about the topic of end of life decisions in patients with implanted mechanical cardiac support devices.

16. Society Memberships:

-American Academy of Anesthesiologist Assistant, 2005-present
-American College of Chest Physicians, 2000-2007
-American Medical Association, 1995-2000
-American Medical Association (reactivated), 2010-present
-Society of Critical Care Anesthesiologists, 1995-present
-American Society of Anesthesiologists, 1993-present
-Canadian Anesthesiologist Society, 2007-present
-District of Columbia Society of Anesthesiologists, 2006-2007
-International Anesthesia Research Society, 1996-2000
-International Extra-Corporeal Life Support Organization, 1997-2005
-Ohio Society of Anesthesiologists, 1993-2005
-Society of Critical Care Medicine, 1995-present
-Manitoba Medical Society, 2007-2010
-Canadian Medical Association, 2008-2012
-Georgia Society of Anesthesiologists, 2010-present
-Society of Cardiovascular Anesthesiologists, 2010-present
-Society of Academic Anesthesiology Associations, 2013-present
-Medical Association of Georgia, 2016-

17. Organization of National or International Conferences:

"On the Ethics of Drug Shortages" June 2012, Jointly with the American Society of Anesthesiology and the Emory Center for Ethics

a. Administrative Positions: *Director, Meeting Planning Committee*

b. Sessions as chair: *Overall conference chair*

18. *Research Focus:*

Medicine, moral theory, rhetoric, semantics, end of life, physicians and vulnerable populations. Physician participation in lethal injection. Ethogram to study conflict in the operating room. Human factors in critical care decision-making and biological variability. Developed economic model explaining the national generic drug shortages. Studied Propofol wastage in the operating room.

19. Grant Support:

a. Active Support:

1. Other: *Team Based Science (TBS) grant from the Department of Anesthesiology for Evaluation of conflict in the operating room, $20,000.00*
2. *The Emory Georgia Tech Healthcare Innovation Program (HIP), (HIP-ACTSI-GSU) Seed grant, $25,000.00, for "Managing Conflict and Error in the Operating Room". Awarded July 2014.*

b. Previous Support
$20,000.00 from the American Society of Anesthesiology to plan the meeting "On the Ethics of Drug Shortages". June 2012

20. Clinical Service Contributions

-Medical director of 11S ICU (EUHM) and 4A/5A ICU (EUH)

I created and chaired a joint protocol development group with Critical Care Medicine, Surgery, Nursing, and Respiratory Therapy with the purpose of improving quality metrics in critical care medicine. This group accomplished several things including a blood conservation strategy for post-operative cardiac surgery patients, intra-aortic balloon pump removal, DVT and GI prophylaxis and the beginning of an atrial fibrillation management protocol. I also wrote and helped implement a rapid extubation protocol for EUH and EUHM cardiac surgery patients.

-Hospital Committee involvement

I was involved in several Emory committees that addressed a broad range of issues. (see 12 c)

-GME involvement, Fellowship Director, Critical Care Medicine, Department of Anesthesiology

I am the fellowship director for critical care medicine. I developed the first joint Anesthesiology-Emergency Medicine critical care medicine fellowship at Emory and I am expanding the number of fellows who will also be trained to assist in providing overnight coverage for airway management at EUH. Overnight airway coverage has been a project of the EUH emergency airway committee on which I am a member. My ongoing conflict project has been embraced by Emory Healthcare Office of Quality and they are also contributing to the funding and management of the project on an ongoing basis.

21. Community Outreach:

Community Service

International
-St. Petersburg, Russia, 2002, 2004
Home visits to community members who were unable to travel to see a physician

Regional
-Hurricane Katrina Medical Response Team, 2005
-Emory 500 Atlanta Motor Speedway Health Tent Volunteer, 2010

Media

Op-Ed:

-"Baby's status as human is on trial" Op-Ed, Feb 19, 2010, Winnipeg Free Press, 2010
-"Why I am for a moratorium on lethal injections" Op-Ed, Dec 15, 2013, USA Today, 2013
-"The Slippery Slope from Medicine to Lethal Injection" Op-Ed, May 2, 2014 TIME, 2014

Interviews:

Anesthesiology News,2002
-Anesthesiologist Assistants

The Medical Post, 2009

-*Waiting for Cardiac Surgery*

The Health Report, CJOB 68 AM, Winnipeg, Canada, 2010
-*Cardiac Critical Care*
-*End of Life in the ICU*
-*VIP syndrome*

Inside the Black Box, WREK 91.1 FM, Atlanta, Georgia, 2011
-*Biting the Bullet: The Technology of Anesthesia*

National Public Radio WABE 90.1 FM Atlanta, Georgia, 2011
-*Physicians and the death penalty*
-*Drug shortages*
Georgia Public Broadcasting, Atlanta GA, 2012
-*Drug shortages reaching critical levels*
Medpage Today, 2013
-*No Advantage for Fresh Blood in ICU Transfusions*
-*Meningitis Outbreak: Suspicion needed for nausea complaints*
-*Drug Shortages spark use of compounders*
Medscape Medical News, 2013
-*GPOs to Blame for Drug Shortages, Says Physicians Group*
Medpage Today, 2014
-*Cruel and Unusual Punishment*
-*Lethal Injection: a cruel, painful, terrifying execution*
Miami Herald, 2014
-*Doctor speaks out on use of untested drugs in capital punishment*

The New York Times, 2014
-*Timeline describes frantic scene at Oklahoma execution*

The Washington Post, 2014
-*Florida's Gruesome Execution Theater*
-*Another execution gone awry. Now what?*

CNN with Sanjay Gupta, 2014
-*Dr. Zivot. Lethal injection not humane*

Amicus on State with Dahlia Lithwick, 2015
-*Botched protocols*

Huffington Post, 2015
-*Oklahoma wants to reinstate the gas chamber and experts say it's a bad idea*
Time, 2015
-*The harsh reality of execution by firing squad*

CNN, 2017
-*Executions put physicians in unfair dilemma (Opinion)*
-*Gorsuch grapples with death: a physician's viewpoint (Opinion)*
Medpage Today, 2017
-*Op-Ed. Neil Gorsuch and Assisted Suicide*

22. Formal Teaching

a. Medical Student Teaching:

i. *Discovery Project "Propofol wastage in the ICU" Medical student Mina Tran, 2012-2013, contact hours 4 hrs/week*
ii. *Serve as teacher and mentor for medical students in anesthesiology and critical care medicine 2010-present, contact hours 3 hrs/week*
iii. *Instructor for Fundamental Critical Care Support (FCCS) training course for medical students, 2012-present, contact hours 1 hr/week*
iv. *Forge Medical Student Innovation Group, Mentor, contact hours: 0.5 hrs/week*

b Graduate Programs:

1. Training Programs:
Instructor in the Masters of Science in Anesthesiology program. I developed the first critical care medicine rotation for all of the students and also a series of didactic lectures on the topic of critical care medicine the included "Critical Care Medicine", "Heart Failure", and "Acid-Base Disorders"

2 School of Law:
*Co-chief instructor of **LAW 819-002, "Law, Medicine and Human Rights"**, a 2 credit hour seminar taught in the fall 2016 semester in the Emory School of Law*

3. Residency Programs:
Served as instructor for residents in anesthesiology, emergency medicine, and surgery in the area of critical care medicine. I also sit on the residency review committee for the Department of Anesthesiology. Lecture topics "Septic shock", "Thyroid disease in critical care", "Mechanical heart support", "Pulmonary artery catheters" "Heunstics and biases in clinical reasoning", "delirium and agitation in critical illness", "biological variability".

c Other Categories
I give regular lectures on a variety of critical care topics for respiratory therapy including "capnography" and "paralytics". I lecture students in the Emory critical care NP/PA program and also regular critical care lectures to the NP/PA practitioners in critical care. I teach those students how to read chest X-rays. I am invited to lecture in the Emory School of Law on the topic "Physician Assisted Suicide".

Emory Tibet Science Initiative:
I taught biology to Buddhist monks at Drepung Loseling Monastery in Southern India in June 2015. This initiative is a result of an invitation from His Holiness, The Dalai Lama, to bring science education to the education of the monks and represents the first time in 700 years that the curriculum has changed. I spent 2 weeks at the monastery teaching for 6 hours per day including microscopy lab teaching. I worked with a series of translators.

23. Supervisory Teaching:

a Residency Program.
Fellowship director, Critical Care Medicine, Department of Anesthesiology 2013-present. I am chiefly responsible for the education and training of the critical care fellows in the Department of Anesthesiology. In addition to a multitude of critical care topics, I assist the fellows in abstract writing for a national critical care meeting, grand rounds for the Department of Anesthesiology and a quality improvement project for Graduate Medical Education Day that occurs annually in June.

b Other:
I completed a summer internship at the Southern Center for Human Rights and also teach law students on the topic of lethal injection.

c Emory University, Institute of the Liberal Arts, Interdisciplinary Studies
Thesis advisor and honors thesis committee member for student Katy Mayerson for the project: ***"Transcultural Pathways and the Literary Imagination:*** *The Francophone Footprint in Imperial Russia and Postcolonial Africa"*

24. Lectureships, Seminar Invitations, and Visiting Professorships:

"The Case of Samuel Golubchuk: Lessons about end-of-life decision-making?"
A debate between Doctors Joel Zivot and Adrian Fine
Wednesday, 18 March, 2009, 12h30-13h30. The Centre for Professional and Applied Ethics, The University of Manitoba, Winnipeg, Manitoba

"Cardiac output after the Pulmonary Artery Catheter" American Academy of Anesthesiologist Assistants Annual Meeting. Clearwater, Florida, April 2009

"End of Life in the ICU", Canadian Hospice Palliative Care Conference Annual Meeting, Winnipeg, Manitoba, Canada. October 2009

"Reductions in wait times for cardiac surgery may be harmful", poster presentation. Canadian Cardiovascular Society Annual Meeting, Edmonton, Alberta, Canada, October 2009

"Biological Variability" American Society of Anesthesiology, 2009-(I formed a panel to discuss biological variability. My panel consisted of an anesthesiologist, a mathematician, and a physicist.)

"End of life in the ICU: When the patient and doctor disagree..." Province wide health care ethics grand rounds, St. Boniface Research Centre, Winnipeg, Manitoba, Canada. January 2010

"Mostly dead is slightly alive, the problem with the dying process" Center for Ethics, Emory University, 2011.

"Anesthesiology Jeopardy!" American Academy of Anesthesiologist Assistants Annual Meeting, 2006, 2007, 2008, 2009, 2010, 2011

"Queuing Theory: Applications for Anesthesiology" American Academy of Anesthesiologist Assistants Annual Meeting, Destin, Florida, 2011

"Cardiac Anesthesia: Mostly we have it wrong" American Academy of Anesthesiologist Assistants Annual Meeting, Destin, Florida, 2011

"End of life in the ICU: When the patient and doctor disagree" American Academy of Anesthesiologist Assistants Annual Meeting, Destin, Florida, 2011

"Sedating the difficult patient" 5th Annual Southeastern Critical Care Summit. Emory University, Atlanta, GA. March 2012

"End of Life Care" IMPACT 2012 American Academy of Physician Assistants Annual Meeting, Toronto, Canada, June 2012

"Biosimilars, where do we stand?" Georgia Bio and the Georgia Association of Healthcare Executives. September 2012, Atlanta, Georgia

"Drug Shortages" Visiting Professor. Rutgers Business School, Newark, New Jersey, November 2012.

"Deactivating a permanent cardiac device is not physician assisted death", Pro-con debate Webinar. Society of Critical Care Medicine, November 2012

"Drug shortages: The invisible hand of the Market" New Horizons in Anesthesiology, Vail, Colorado, February 2013

"Hey Anesthesia is a compliment, not an insult: the case for protocols" New Horizons in Anesthesiology, Vail, Colorado, February 2013

"Pro/Con: Death Panels in End of Life Care" New Horizons in Anesthesiology, Vail, Colorado, February 2013

"Hockey Violence and Killer Apes: Conflict Management in the Operating Room" New Horizons in Anesthesiology, Vail. Colorado, February 2013

"Drug Shortages, a failed market" American Society of Anesthesiology Legislative Conference Annual Meeting, April 2013, Washington, DC

"Lethal injection in the death penalty", Georgia Law Society and the Southern Center for Human Rights, Atlanta, Georgia, July 2014

"Identifying and managing futile care in the ICU", 10th Annual South Easter Critical care Summit, May 2016, Atlanta, Georgia

"Capital Punishment and Lethal Injection", Georgia State School of Law, Atlanta, Georgia, September 2016

"The Ethics of Drug Pricing", GEM annual meeting, Georgia Society of Ophthalmology, February 2017

"Burnout: don't thank me for normal work", American Academy of Anesthesiologist Assistants annual meeting, March 2017

"Too sick to be executed" American Academy of Anesthesiologist Assistants annual meeting, March 2017

25. Invitations to National or International Conferences:

University of Richmond Law Review, Allen Chair Symposium, 2014.
"The Death Penalty in the United States".

Yale Law School, March 2015
"Lethal injection"

The Fordham Law Review, Fordham Law School, February 2016
"Criminal Behavior and the Brain. When Law and Neuroscience Collide"

American College of Correctional Physicians
Fall Educational Conference
October 2016
Las Vegas, Nevada
"Physician participation in executions: A discussion of the Ethical Challenges and the Pros and Cons, a pro-con debate between Dr. Carlo Muso and Dr. Joel Zivot

"Prescribing Price: The Ethics, Science, and Business of Drug Development and Pricing"
Panelist
Emory Conference Center, November 2016
Atlanta, Georgia
Emory Center for Ethics

"The First International Emory Tibet Symposium: Bridging Buddhism & Science
Drepung Loseling Monastery
Karnataka State, India"
Panelist: What is life and what are its origins?

26. Bibliography

a. Published and Accepted Research Articles (clinical, basic science, other) in Refereed Journals

*Perera ER, Vidic DM, **Zivot J** "Cannal resection with two high frequency jet ventilation delivery systems" Canadian Journal of Anesthesia Jan 1993; 40(1):59-63 PMID: 8425245*

***Zivot JB**, Hoffman WD. "Pathological effects of endotoxin". New Horizons. May 1995; 3(2):267-75. PMID:7583168*

*Popovich MJ, Lockrem JD, **Zivot JB**. "Nasal bridle revisited: an improvement in the technique to prevent unintentional removal of small-bore naso-enteric feeding tubes". Critical Care Medicine. March 1996; 24(3):429-31. PMID. 8625630*

*Kumar K, Zarychanski R, Bell DD, Manji R, **Zivot J**, Menkis AH, Arora RC; Cardiovascular Health Research in Manitoba Investigator Group. "Impact of 24-hour in-house intensivist on a dedicated cardiac surgery intensive care unit". Ann Thorac Surg. 2009 Oct;88(4):1153-61 doi: 10.1016/j athoracsur 2009 04.070*

***Zivot JB**. "The Case of Samuel Golubchuk", AJOB Volume 10, Issue 3 March 2010, pages 56 – 57 doi 10.1080/15265160903681890*

*AbdulRazaq A. H. Sokoro, PhD., **Joel B. Zivot**, . MD, FRCPC, Robert E. Ariano, PharmD, FCCM "Neuroleptic malignant syndrome versus Serotonin syndrome: the search for a diagnostic tool?" Ann Pharmacother. 2011 Sep;45(9):e50.doi. 10.1345/aph. 1P787. Epub 2011 Aug 30.*

*When patient and doctor disagree. **Zivot JB**. CMAJ 2012,Jan 10;184(1):76-6. doi: 10 1503/cmaj. 112-2008*

***Zivot JB**. "Anesthesia does not reduce suffering at the end of life", Crit Care Med. 2012 Jul; 40(7):2268-9 doi: 10.1097/CCM.0b013e31824fc12b.*

***Zivot JB**, "The absence of cruelty is not the presence of humanness: physicians and the death penalty in the United States". Philos Ethics Humanit Med. 2012 Dec 3;7(1):13. doi: 10.1186/1747-5341-7-13.*

*Mazzeffi, M, **Zivot J**, Buchman T, Halkos M, "In hospital mortality after cardiac surgery: patient characteristics, timing, and association with postoperative length of intensive care unit and hospital stay". Ann Thorac Surg 2014 Apr;97(4):1220-5. doi: 10.1010/j.athoracsur 2013. 10.040. Epub 2013 Dec 21*

***Zivot JB**. "The withdrawal of treatment is still treatment". Can J Anesth 2014; Oct;61(10):895-8*

***Zivot J**, "Lethal injection: the states medicalize execution" 49 U. Rich. L. Rev. 711 (2015)*

***Zivot J**, "Elder care in the ICU: Spin bravely?" Crit Care Med 2015 July;43(7):1526-7*

*Jones LK, Jennings BM, Goetz RM, Haythorn KW, **Zivot JB**, de Waal FB "An Ethogram to Quantify Operating Room Behavior" Ann Behav Med. 2016 Jan 26. [Epub ahead of print]*

***Zivot J**, Arenson K, "Lessons learned from physician participation in lethal injection: Is Carter v. Canada a death knell for medical self-regulation?" Can J Anaesth 2016 March;63(3):246-251*

***Zivot JB**. "Elderly patients in the ICU: Worth it, or not?" Crit Care Med 2016 April;44(4):842-3*

*Moll V, Ward CT, **Zivot JB**, "Antipsychotic-Induced Neuroleptic Malignant Syndrome after Cardiac Surgery" AA Case Rep. 2016 July 1, 7 (1): 5-8*

***Zivot J**, "Too Sick to be Executed: Shocking Punishment and the Brain" November 2016 Vol 85, pp 697-703, Fordham Law Review*

b. Examination Activities:

Committee Member, 2005, National Anesthesiologist Assistant Certification Examination Development Committee

Question writer, 2005, Critical Care Medicine, National Board of Medical Examiners

Question reviewer, 2015, American Board of Anesthesiology-Maintenance of Certification in Anesthesiology (MOCA), Critical Care Medicine

c. Book Chapters:

*Bojan Paunovic MD, FRCPC[1], Rizwan Manji MD, PhD, FRCSC[2], Rakesh Arora MD, PhD, FRCSC[3], Johan Strumpher MD, FRCPC[3], Rohit Singhal MD, FRCSC[2], **Joel Zivot MD, FRCPC[4]**, and Eric Jacobsohn MBChB, MHPE, FRCPC[5] "Diagnosis and Management of Sepsis and Septic Shock in the Cardiac Surgical Patient" Society of Cardiovascular Anesthesiology Monograph, March 2010*

***Zivot, JB**, "What Are Advance Directives?" Critical Care Ethics: A Practice Guide, Third Ed Copyright 2014 Society of Critical Care Medicine.*

d. Other Publications:

***Zivot J**, Hoffman W, Lockrem J, Esfandiari S, Bedocs N, Vignali C, Popovich M "Changes in gastric intramucosal pH are not predicted by therapeutic changes in conventional hemodynamic variables for septic surgical patients". Critical Care Medicine 23(1) Supplement A:107, Jan 1995*

*Webster J, Thomson V, **Zivot J**. "Excessive endotracheal tube cuff pressures are common but are not clinically significant". Anesthesiology 87(3 Suppl) A984, 1997*

*Bloch, MG, **Zivot JB** "Successful transplantation of liver and kidney allografts from a donor maintained on veno-arterial extracorporeal membrane oxygenation". Anesthesia and Analgesia, 94(25 Supplement) S104, Feb 2002*

***Zivot J**, Polemenakas A, Aggarwall S, Rowbottom J "Differential lung capnography after single lung transplant". Critical Care Medicine 30(12) Supplement A90 December 2002*

*Voltz D, **Zivot J**, "Changes in the Bispectral Index during Deep Hypothermic Circulatory Arrest." Society of Critical Care Medicine Annual Meeting, San Francisco, California, January 2003*

*Ravas R, **Zivot J**, "Blood conservation; Designing a better blood bag", Department of Anesthesiology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio, Midwestern Anesthesia Resident Conference (MARC), Chicago, Illinois, March 2003*

*Hacker L, **Zivot J** "Local anesthetic spread for skin infiltration", Department of Anesthesiology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio, Midwestern Anesthesia Residents Conference, Chicago, Illinois, March 2003*

*Falk S, **Zivot J**, "Post-operative Sidenafil for pulmonary hypertension following mitral valve repair" 17th Asia Pacific Conference on Diseases of the Chest, Istanbul, Turkey, August 2003*

*Aggarwal S, **Zivot J**, "New onset anterior spinal artery syndrome after lumbar drain removal" Department of Anesthesiology, University Hospitals of Cleveland, Case Western Reserve*

University, Cleveland, Ohio, Midwestern Anesthesia Residents Conference, Rochester, Minnesota, March 2004

*Stetz J, **Zivot J**, "Dextromethorphan masquerading as phencyclidine" Department of Anesthesiology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio, Midwestern Anesthesia Residents Conference, Rochester, Minnesota, March 2004*

*Petelenz K, **Zivot J**, "Bilateral BIS monitoring in unilateral brain injury", Department of Anesthesiology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio, Midwestern Anesthesia Residents Conference, Chicago, Illinois, March 2005*

*Arora RC, Zarychynski R, Bell D, **Zivot J**, Lee J, Kumar K, Zhang L, Menkis A "The Manitoba Model of Post-Operative Cardiac Surgery Intensive Care" The Cardiac Sciences Program, St Boniface Hospital and the University of Manitoba, Winnipeg, Canada. Toronto Critical Care Meeting, October 2007*

*K Kumar, R Zarychanski, DD Bell, **J Zivot**, J Lee, R Manji, A Menkis, RC Aurora, "The Impact of the Manitoba Model of 24 hour in-house intensivist on a dedicated cardiac surgery ICU" Canadian Cardiovascular Society Annual Meeting, Toronto, Ontario, Canada, October 2008*

Fergusson DA, Hébert PC, Mazer CD, Fremes S, MacAdams C, Murkin JM, Teoh K, Duke PC, Arellano R, Blajchman MA, Bussières JS, Côté D, Karski J, Martineau R, Robblee JA, Rodger M, Wells G, Clinch J, Pretorius R; BART Investigators. "A comparison of aprotinin and lysine analogues in high-risk cardiac surgery". N Engl J Med. 2008 May 29;358(22):2319-31. Epub 2008 May 14. Erratum in: N Engl J Med. 2010 Sep 23;363(13):1290

*M Rivet, S Chartrand, G Henry, ICCS Nurses, RC Aurora, DD Bell, A Menkis, **J Zivot**, RA Manji, on the GRACE, GRACE2 Investigators, "Bunk Beds in the ICU - Can Two Cardiac Surgery Patients Occupy One ICU Bed?" Canadian Cardiovascular Society Annual Meeting, Toronto, Ontario, Canada, October 2008*

*RA Manji, E Jacobsohn, D Bell, RK Singal, **J Zivot**, A Menkis " Delirium and bed management in the cardiac surgery ICU" Canadian Cardiovascular Society Annual Meeting, Edmonton, Alberta, Canada, October 2009*

*RA Manji, D Bell, C Shaw, C Moltzan, P Nickerson, AH Menkis, **J Zivot**, E Jacobsohn Management Suggestions for Cardiac Surgery Patients with a Positive Heparin Induced Thrombocytopenia (HIT) ELISA. Canadian Cardiovascular Society Annual Meeting, Edmonton Alberta, Canada, October 2009*

*RA Manji, E Jacobsohn, **J Zivot**, H Grocott, Alan Menkis, Prolonged in-hospital wait times does not affect outcomes for urgent coronary artery bypass surgery, Canadian Cardiovascular Society Annual Meeting, Edmonton, Alberta, Canada, October 2009*

***J Zivot**, RA Manji, E Jacobsohn, H Grocott, A Menkis, Reductions in wait times for cardiac surgery may be harmful, Canadian Cardiovascular Society Annual Meeting, Edmonton, Alberta, Canada, October 2009*

*RA Manji MD PhD FRCSC MBA, E Jacobsohn MBChB FRCPC, H Grocott MD FRCPC, **J Zivot** MD FRCPC, AH Menkis DDS MD FRCSC, Longer in-hospital wait times does not affect outcomes for urgent coronary artery bypass grafting surgery, American Heart Association Annual Meeting, Orlando, Florida, November 2009*

***Zivot, JB**, "When the patient and the doctor disagree: end of life in the ICU" (poster presentation) American Society of Anesthesiology Annual Meeting, San Diego, California, October 2010*

***Joel Zivot, MD,** "A cure in search of a disease, comments on: From an Ethics of Rationing to an Ethics of Waste Avoidance". N Engl J Med. 2012. 366:1949-1951. May 24 2012*

*Mazzeffi, Halkos, **Zivot** "Timing and characterization of post-cardiac surgery in-hospital mortality" Society of Critical Care Annual Meeting Society of Critical Care Annual Meeting, Jan 2013*

Nearnu, Halkos, **Zivot** *"Right Ventricular Laceration During Closed Chest Compression in a Cardiac Surgical Patient" Society of Critical Care Annual Meeting: Jan 2013*

Caridi-Scheible, **Zivot**, *Paciullo, Connor "Successful treatment of pulmonary-renal syndrome secondary to p-ANCA vasculitis using ECMO with Argatroban", Society of Critical Care Medicine Annual Meeting, San Francisco, CA. Jan 2014*

EXHIBIT 5
ATTACHMENT 2

DECLARATION OF JOEL ZIVOT, MD

1. I received my Doctor of Medicine from the University of Manitoba, Canada, in 1988. From 1989–1993, I was a resident in Anesthesiology at the University of Toronto, Department of Post Graduate Medical Education, and from 1993–1995, I completed an additional residency in Anesthesiology and a Fellowship in Critical Care Medicine at the Cleveland Clinic Foundation, Department of Anesthesiology in Cleveland, Ohio.
2. I hold an active medical license from the State of Georgia and have held unrestricted medical licenses in Ohio, the District of Columbia, Michigan, and the Canadian provinces of Ontario and Manitoba. I also hold an active license to prescribe narcotics and other controlled substances from the federal Drug Enforcement Administration (DEA).
3. I hold board certification in Anesthesiology from the Royal College of Physicians and Surgeons of Canada and the American Board of Anesthesiology. I am also board certified in Critical Care Medicine from the American Board of Anesthesiology.
4. I have served as the Medical Director of the Cardio-Thoracic Intensive Care Unit and the Fellowship Director for Critical Care Medicine at Emory University Hospital. I am an Associate Professor of Anesthesiology and Surgery at the Emory University School of Medicine and an adjunct Professor of Law at Emory University Law School.
5. I have practiced anesthesiology and critical care medicine for 22 years, and, in that capacity, I have personally performed or supervised the care of more than 42,000 patients.
6. I am, by reason of my experience, training, and education, an expert in the fields of anesthesiology and critical care medicine. The opinions that follow are within my field of

expertise, and are stated to a reasonable degree of medical and scientific certainty unless otherwise noted. I believe that my ethical duties prevent the participation in lethal injection. The opinions below express my medical opinion regarding the risks of the lethal injection procedure designed by the state and should not be construed as an attempt to assist the state in developing a better way to perform executions.

7. At the request of counsel, I reviewed Arkansas's lethal injection procedure, titled "Attachment C." Based on the review of that document, and my medical training and experience, I offer the following opinions.

8. The state of Arkansas uses a three-drug protocol involving Midazolam, Vecuronium Bromide, and Potassium Chloride.

9. The use of Midazolam is an inappropriate drug for lethal injection. In a surgical setting it is used as a sedative and in combination with other drugs. It is not used on its own to induce general anesthesia and is not capable of rendering a patient unaware or insensate to pain. The company that created Midazolam never contemplated that it would be used in the execution of prisoners.

10. Midazolam is prepared as a liquid and the solution is rendered at a pH of 2.5-3.5 Strong acids like Midazolam risk precipitation when mixed with weak acids or bases. The pH of normal saline is 5-6 and the mixing of Midazolam with normal saline runs the real risk of the formation of a salt precipitate. This precipitate compound will risk the obstruction of the intravenous preventing any further drug administration. Midazolam precipitate is pharmacologically inactive and will lower the total amount of Midazolam delivery in a completely unpredictable fashion.

11. Midazolam injection in large doses as contemplated in the Arkansas lethal injection protocol has been associated with paradoxical hyper-reactivity reactions. This paradoxical reaction will be seen as intense agitation and movement. In this state, increasing the dose of Midazolam will only further exacerbate this agitation.

12. Vecuronium Bromide is a paralytic that, when administered, blocks the capacity of movement in a particular group of muscles known as skeletal muscles. Paralytics act only on skeletal muscles and have no effect on smooth or cardiac muscle. The inability to breathe as a consequence of Vecuronium induced muscle paralysis would be akin to the experience of suffocation. A person would still have the desire and need to breathe but would be completely unable to do so. Midazolam will not in any way block the sensation for the need to breathe.

13. Potassium, available as Potassium Chloride, is a naturally occurring element necessary for normal bodily functions in a number of human physiological systems. Of importance here is the effect of Potassium Chloride on the heart. As potassium rises outside of the heart cell, depolarization is increasingly blocked until a point at which the heart cell is essentially held in place and cannot contract. At his point, the heart ceases to function in any capacity. The lack of heart muscle contraction causes the blood pressure to drop. The lack of blood flow, which carries oxygen to each cell in the body, ceases and progressive and rapid multi-organ failure ensues. Potassium Chloride, when injected into the body, produces an intense burning sensation of the veins. Midazolam is not a pain reliever in any dose and is insufficient to prevent the experiencing of burning by the prisoner.

14. As a general matter, my review of the protocol shows that the execution process involves multiple complex tasks that, to be done without risking serious injury to the prisoner, require a high-level of skill and training.

15. I am aware the Arkansas Department of Correction has a supply of Midazolam that lists the expiration date as April 2017. My understanding of expiration dates and drug potency is based on my years of medical training and practice. An expiration date is an estimate of the date at which the drug manufacturer expects that the drug will either change or transform into something that 1) loses its efficacy or 2) becomes poison. As a practitioner, I would not use a drug in the month at which it is stated to expire. I do not feel confident that it can be relied upon to perform its expected function.

16. Arkansas's lethal injection protocol calls for the preparation of syringes at a different location in advance of the execution. In my opinion, this practice creates a needless risk of contamination or degradation of the chemicals. An ampule of Midazolam, or any other sterile injectable compound, is sterile while it is in the ampule. As soon as the seal is broken, it is no longer sterile. In my practice, I would insert the syringe into the ampule, draw the solution into the syringe, and inject it immediately. The delay used by the protocol creates the risk that the drug will be mislabeled, contaminated, and at increased risk of falling out of solution as a precipitate.

17. Setting of IVs is crucial to the successful delivery of a substance into the circulatory system. Multiple or unsuccessful attempts to set an IV can cause perforations in the veins and infiltration of the tissue surrounding the vein. When this happens, the substance that was meant to circulate throughout the body will instead pool in the tissue and not reach the systems of the body necessary for it to have its intended effect.

18. Insertion of a central line is a complicated medical procedure that is not done by nurses, or EMTs. A physician's assistant may insert a central line under the supervision of a physician. The central line accesses the circulatory system through a large vein in the neck, chest, or groin. The vein accessed through a central line is not visible to the eye through the skin. In order to safely place a central line in a clinical setting, I would use an ultrasound machine and a central line kit. The lethal injection protocol allows for the placement of a central line with no way of determining where the prisoner's vein is and no clear expertise within the personnel of the execution team. Blindly stabbing at the neck, chest, or groin could hit an artery or a nerve, causing pain and blood loss. A misplaced central line may be hard to verify and an individual placing this line may be under a false impression that the line is properly positioned. In a clinical setting, a follow up chest x-ray is required prior to using a central line that has been placed in the chest to verify the proper placement and rule out the presence of a collapsed lung. Such lung collapse when occurring can lead to a tension pneumothorax that can be in itself fatal. Death in this circumstance would be as a consequence of suffocation and cardiovascular collapse.

19. The amount of liquid Midazolam called for in the protocol is roughly a third to a half of the volume of liquid in a standard Styrofoam cup. The plan calls for it to be injected in two syringes. The syringes will have to be quite large. Pushing that amount of liquid out of such a large syringe creates a great amount of pressure at the point where the liquid exists the syringe. A vein can only withstand so much pressure. When a large amount of fluid runs into a vein, especially at a rapid rate, the vein can rupture. In a clinical setting 2-4 mg would normally be administered over a minute. The Arkansas lethal injection

protocol intends to inject 10-20 times this quantity over the same length of time. A real danger exists to vein patency and serious pain on injection. In a clinical setting, in order to modulate the speed of the injection, and prevent rupture, I would sit by the side of the patient and look at their vein while I was plunging the drug. I understand that the Arkansas lethal injection procedure calls for the person plunging the syringe to be in a separate room from the inmate. Viewing a vein through a window will not allow a person to have adequate sight of the vein in order to prevent rupture and properly modulate the injection.

20. The protocol purports to require that the inmate be determined to be "unconscious" after the administration of the Midazolam. "Unconscious" is an exceedingly vague term in scientific circles. The protocol does not provide any guidance to the execution team to judge whether the prisoner is "unconscious." General anesthesia is not same thing as "unconsciousness." General anesthesia is a state in which a person can undergo noxious stimuli and 1) does not experience it in the moment and 2) does not recall it. In contrast, a person can be seemingly unresponsive and still experiencing stimulus. Certain noxious stimuli will lift a person from what might at first glance appear to be a state of unresponsiveness. Many people have had the experience of not being awoken by their alarm clock but hearing the alarm clock in their dreaming state. An outside observer would have no way of knowing that the sleeping person was hearing the alarm clock. This example shows that simple observation is insufficient to determine levels of anesthesia and has no capacity to confirm the sort of unresponsiveness contemplated by the lethal injection protocol.

21. An anesthesiologist is as much of an expert in consciousness as you can find. However, neither I, nor my peers, would ever attempt to assess anesthetic level by visual inspection alone. In a hospital setting, I would not give the okay for a surgeon to cut a patient just by looking at them. Instead, I use equipment to measure physiological signs such as heart rate, blood pressure, brain activity, before allowing painful procedures to proceed. In addition, it is important to continually monitor anesthetic depth as it is dynamic. There may be subtle physiological changes in the body that show that a person is reacting to painful stimuli. For example, if the heart rate increased from 60 bpm to 70 bpm, that would be a signal that I may need to give additional medicine. The protocol provides for no modification based on inmate signs and symptoms after the 500 mg of Midazolam has been injected. The well-known ceiling effect of Midazolam renders additional dosage completely superfluous.

22. It is my professional opinion that because the protocol uses a sedative rather than an anesthetic, fails to use personnel trained in assessing anesthetic depth, fails to instruct the personnel on signs of consciousness, and fails to provide equipment necessary to judge anesthetic depth, there is a serious risk that the prisoner will be able to feel and experience the injection and the effects of the Vecuronium Bromide and Potassium Chloride.

23. I have a great concern that the protocol does not provide a plan for resuscitation or antidote of the chemicals in the event that the execution fails. Based on my training and experience, I expect that the prisoner will never reach general anesthesia with the injection of Midazolam. I think a likely scenario is that after the first injection of the Vecuronium Bromide the prisoner will move, gasp, or otherwise show signs of

awareness. If this happens, and the Vecuronium Bromide is not reversed, the prisoner will suffocate. Vecuronium Bromide does have an antidote, Sugammadex. A safeguard in the event that the prisoner shows any signs of movement that will indicate awareness or "consciousness" would be an injection of Sugammadex.

24. It is also possible that the Midazolam may need to be reversed. Midazolam on its own is not a fatal drug, but it can cause airway collapse or cause confusion and lack of awareness in the patient that would cause them to fail to clear their own airway and choke. Midazolam can be reversed with Flumazenil.

25. Potassium Chloride can also be reversed through the sequential injection of insulin, D-50 (dextrose and water), and calcium chloride.

26. In order to maximize the effects of the antidotes, the prison would also need to have on hand qualified personnel to start life-saving measures and have immediately available oxygen and a mask, an Ambu bag, a nerve stimulator to measure the degree of neuromuscular blockage, cardiac monitoring, pulse oxymeter and a blood pressure cuff. If the inmate is a diabetic, the prison would also need equipment and medicine to measure and treat abnormal blood sugar.

I swear that the foregoing is true and correct to the best of my knowledge under penalty of perjury under the laws of the United States and the State of Arkansas.

March 24, 2017

Date

Joel Zivot, M.D.

EXHIBIT 6

Nitrogen Induced Hypoxia as a Form of Capital Punishment

Michael P. Copeland, J.D.

Thom Parr, M.S.

Christine Papas, J.D., Ph.D.

East Central University

Executive Summary

At the request of Oklahoma State Representative Mike Christian, the authors of this study researched the question of whether hypoxia induced by nitrogen gas inhalation could serve as a viable alternative to the current methods of capital punishment authorized under Oklahoma law. As per the above, this study does not express an opinion on the wider question of whether Oklahoma should continue to administer capital punishment in general. The scope of this study is limited to the assumption that capital punishment will continue to be administered in Oklahoma, and given that assumption, analyzing whether hypoxia via nitrogen gas inhalation would be an effective and humane alternative to the current methods of capital punishment practiced in Oklahoma law.

This study was conducted by reviewing the scientific, technical, and safety literature related to nitrogen inhalation.

The study found that:

1. An execution protocol that induced hypoxia via nitrogen inhalation would be a humane method to carry out a death sentence.
2. Death sentence protocols carried out using nitrogen inhalation would not require the assistance of licensed medical professionals.
3. Death sentences carried out by nitrogen inhalation would be simple to administer.
4. Nitrogen is readily available for purchase and sourcing would not pose a difficulty.
5. Death sentences carried out by nitrogen inhalation would not depend upon the cooperation of the offender being executed.

Accordingly, it is the recommendation of this study that hypoxia induced by the inhalation of nitrogen be offered as an alternative method of administering capital punishment in the State of Oklahoma.

The views expressed in this study are solely those of its authors and do not necessarily reflect those of the university at which we are affiliated.

Introduction

Nitrogen is an inert gas that at room temperature is colorless, odorless, and tasteless. It is the most common gas in the earth's atmosphere, comprising 78.09% of the air that humans breathe on a regular basis.

When combined with the normal 20.95% oxygen found in the atmosphere, nitrogen is completely safe for humans to inhale. However, an environment overly enriched in nitrogen will lack the appropriate level of oxygen necessary for human survival and will thus lead to hypoxia and rapid death. (U.S. Chemical Safety and Hazard Investigation Board, 2003, p. 1).

Nitrogen hypoxia has been suggested as a means of administering capital punishment in the popular media on previous occasions. For example, in1995 the National Review featured an article by Stuart Creque titled *Killing With Kindness: Capital Punishment by Nitrogen Asphyxiation (1995)*. Creque's article was written in response to a 9th Circuit U.S. District Court decision that California's gas chamber was an unconstitutionally cruel and unusual punishment. The article suggested nitrogen could provide a simple and painless alternative to the gas chamber that would require no elaborate medical procedures to administer.

The idea of administering capital punishment via nitrogen hypoxia resurfaced more recently in a Tom McNichol Slate magazine article titled *Death by Nitrogen (2014)*. The article was inspired by the stay of execution issued by the U.S. Supreme Court for a Missouri man facing execution via lethal injection. Again, the author suggested nitrogen induced hypoxia as a painless alternative to traditional methods of execution, adding that it offered the additional benefits of requiring no medical training to administer and lacked any of the supply issues that exist with lethal injection.

The capital punishment protocols cited that utilize nitrogen to administer a death sentence do not actually rely on the nitrogen itself to bring about death. Nitrogen simply displaces the oxygen normally found in air and it is the resulting lack of oxygen which causes death. Without oxygen present, inhalation of only 1-2 breaths of pure nitrogen will cause a sudden loss of consciousness and, if no oxygen is provided, eventually death. (European Industrial Gases Association, 2009, p. 3).

Since nitrogen has not previously been used for capital punishment there is a lack scientific literature that specifically addresses its performance for that purpose. However, there have been medical experiments which involved human subjects breathing pure nitrogen until they became unconscious. Beyond those experiments, most of the data related to nitrogen induced hypoxia comes from documented suicides in humans and research in high altitude pilot training.

> *Author's Note: in some cases the lay press will inadvertently refer to hypoxia as asphyxiation. This is technically inaccurate in this context, as asphyxia is the inability to breathe in oxygen and the inability to exhale carbon dioxide. Hypoxia is the pathology related to the inability to intake oxygen even though one may still be able to exhale carbon dioxide. As will be seen later, the ability to exhale carbon dioxide is critical to the proposed method of execution, as it prevents the acidosis normally associated with asphyxiation.*

Medical Literature

The adult brain uses about 15 per cent of the heart's output of oxygenated blood (Graham, 1977, p.170). Hypoxia is the condition of having a lower-than-normal amount of oxygen in the blood. Anoxia is an extreme form of hypoxia in which there is a complete absence of oxygen in the blood (Brierley, 1977 p.181). If the supply of oxygen in the blood is reduced

below a critical level it will result in a rapid loss of consciousness and eventually irreversible brain damage will occur (Graham, 1977, p.170).

A complete immediate global loss of oxygen to the brain, (a scenario in which no residual oxygen in the lungs or blood is delivered to the brain), will result in a loss of consciousness in eight to ten seconds, and a loss of any electrical output by the brain will occur a few seconds later. The heart may continue to beat for a few minutes even after the brain no longer functions (Brierley, 1977 p.182).

Ernsting (1961) performed a study on human volunteers that hyperventilated on pure nitrogen gas. The subjects performed the test multiple times, varying the length of time they inhaled the nitrogen. When the subjects inhaled nitrogen for eight-to-ten seconds they reported a dimming of vision. When the period was expanded to fifteen-to-sixteen seconds, the subjects reported some clouding of consciousness and impairment of vision. When the tests were expanded to seventeen-to-twenty seconds, the subjects lost consciousness. There was no reported physical discomfort associated with inhaling the pure nitrogen. (p. 295)

Unlike asphyxiation, hypoxia via the inhalation of nitrogen allows the body to expel the carbon dioxide buildup that is normally associated with the respiratory cycle. This helps prevent a condition known as hypercapnia - an accumulation of carbon dioxide in the blood. The result of this buildup of carbon dioxide is respiratory acidosis - a shifting of the ph levels in the blood to become more acidic. This is the pathology many people associate with suffocating. Some of the symptoms of respiratory acidosis are expected to be present in cases of asphyxiation, but not expected to be present under pure hypoxia are anxiety and headaches, (Merrick Manuel, 2013).

Suicide Data

Perhaps one of the greatest testaments to both the humanity of nitrogen induced hypoxia as well as the ease of administration is its rapidly gaining popularity as a self-selected means of suicide. Suicide by hypoxia using an inert gas is the most widely promoted method of human euthanasia by right-to-die advocates (Howard, M.O. et. al., 2011, P. 61).

The trend toward using an "exit bag" filled with an inert gas such as nitrogen or helium likely started with a publication of *Final Exit: The Practicalities of Self Deliverance and Assisted Suicide for the Dying*. The authors of the publication sought to identify methods of death that were swift, simple, painless, failure-proof, inexpensive, non-disfiguring and did not require a physician's assistance or prescription (Howard, M.O. et. al., 2011. p 61).

This method of suicide is indeed simple. It involves a clear plastic bag fitted over the head, two tanks filling the bag with helium via vinyl tubing, and an elastic band at the bottom of the bag to prevent the bag from slipping off the head. The parts needed to create the bag are inexpensive and available locally without prescription (Howard, M.O. et. al., 2011. p 61-62).

Reports of deaths observed via this method suggest that it is painless. Jim Chastain, Ph.D. President of the Final Exit Network of Florida described the process this way:

> In the several events I have observed the person breathes the odorless, tasteless helium deeply about three or four times and then is unconscious. no gagging or gasping. Death follows in 4-5 minutes. A peaceful process.

Derek Humphrey, current chair of the Final Exit advisory board is quoted as saying:

> In the approximate 300 cases which have been reported to me there has never been mention of choking or gagging. When I witnessed the helium death of a friend of mine it could not have been more peaceful (Final Exit, 2010).

However, it should be noted that deviations from the above protocols have not always been as successful. When masks were placed over the face (instead of using bags of helium over

the head) it has been reported some problems have occurred. This is typically a result of the mask not sealing tightly to the face, resulting in a small amount of oxygen being inhaled by the individual. This extends the time to become unconscious and extends the time to death. This may result in purposeless movements by the decedent (Ogden et al, 2010. p 174-179).

Research on High Altitude Pilot Training

A great deal of research on the effects of hypoxia on human beings comes from aerospace medicine. Pilots that fly at high altitudes are subject to becoming hypoxic if their cabins lose air pressure. Altitude hypoxia has similar effects as the hypoxia one gets from breathing inert gases although it is caused by the inability of the lungs to absorb the oxygen in the air rather than a lack of oxygen in the air.

The Federal Aviation Administration (2003, p. 11) states:

> Hypoxia is a lack of sufficient oxygen in the body cells or tissues caused by an inadequate supply of oxygen, inadequate transportation of oxygen, or inability of the body tissues to use oxygen. A common misconception among many pilots who are inexperienced in high-altitude flight operations and who have not be exposed to physiological training is that it is possible to recognize the symptoms of hypoxia and to take corrective actions before becoming seriously impaired. While this concept may be appealing in theory, it is both misleading and dangerous for an untrained crew member. Symptoms of hypoxia vary from pilot to pilot, but one of the earliest effects of hypoxia is impairment of judgment. Other symptoms can include one or more of the following:
> (1) Behavioral Changes (e.g. a sense of euphoria).
> (2) Poor coordination.
> (3) Discoloration in the fingernails (cyanosis).
> (4) Sweating.
> (5) Increased breathing rate, headache, sleepiness, or fatigue
> (6) Loss or deterioration of vision
> (7) Light-headedness or dizzy sensations and listlessness.
> (8) Tingling or warm sensations.

Indeed, hypoxia has caused several airline accidents which are often fatal. The onset of hypoxia is typically so subtle that it is unnoticeable to the subject. The effects of hypoxia are often difficult to recognize. (Federal Aviation Administration, 2014, Ch. 8-1-2 (A) 5)

Attempts to train pilots to notice hypoxia are conducted using a hyperbaric chamber to simulate high altitudes. Often a trainee will be asked to remove his or her mask and perform simple tasks. At low levels of hypoxia, trainees typically feel little more than euphoria and a sense of confidence. At higher levels of hypoxia, trainees will quickly become unconscious. Time of useful consciousness at altitudes above 43,000 is 5 seconds (Federal Aviation Administration, 2003, p. 13).

Findings

Based on the review of the literature related to hypoxia induced by inert gases, this study makes the following findings:

1. An execution protocol that induced hypoxia via nitrogen inhalation would be a humane method to carry out a death sentence.
2. Death sentence protocols carried out using nitrogen inhalation would not require the assistance of licensed medical professionals.
3. Death sentences carried out by nitrogen inhalation would be simple to administer.
4. Nitrogen is readily available for purchase and sourcing would not pose a difficulty.
5. Death sentences carried out by nitrogen inhalation would not depend upon the cooperation of the offender being executed.
6. Use of nitrogen as a method of execution can assure a quick and painless death of the offender

Finding 1. An execution protocol that induced hypoxia via nitrogen inhalation would be a humane method to carry out a death sentence.

Rationale:

As an inert gas, nitrogen is odorless, colorless, tasteless and undetectable to human beings. It is 78% of the air we breathe on a daily basis, and thus there is little chance that any subject would have an unusual or allergic reaction to the gas itself.

Because the subject is able to expel carbon dioxide, the anxiety normally associated with acidosis in asphyxiation would not be present.

The literature indicates after breathing pure nitrogen, subjects will experience the following: within eight-to-ten seconds the subjects will experience a dimming of vision, at fifteen-to-sixteen seconds they will experience a clouding of consciousness, and at seventeen-to-twenty seconds they will lose consciousness. There is no evidence to indicate any substantial physical discomfort during this process.

There is a possibility that subjects will feel euphoria prior to losing consciousness and a slight possibility they will feel a tingling or warm sensation. After the subjects are unconscious, it should be expected some of the subjects will convulse. Most electrochemical brain activity should cease shortly after loss of consciousness, and the heart rate will begin to increase to varying degrees until it stops beating 3 to 4 minutes later. Observed suicides involving inert gas hypoxia are described as peaceful, so long as caution is taken to eliminate the possibility of the subject inadvertently receiving supplemental oxygen during the process. Inert gas hypoxia is considered such a humane and dignified process to achieve death that it is recommended as a preferred method by right-to-die groups.

Finding 2. Death sentence protocols carried out using nitrogen inhalation would not require the assistance of licensed medical professionals.

Rationale:

The administration of a death sentence via nitrogen hypoxia does not require the use of a complex medical procedure or pharmaceutical products. The process itself, as demonstrated by those who seek euthanasia, requires little more than a hood sufficiently attached to the subject's head and a tank of inert gas to create a hypoxic atmosphere.

While a state execution would likely have a more elaborate mechanism to create hypoxia, nothing in the process would require specialized medical knowledge or the use of regulated pharmaceutical products. Accordingly, except for the pronouncement of death, the assistance of licensed medical professionals would not be required to execute this protocol.

Finding 3. Death sentences carried out by nitrogen inhalation would be simple to administer.

Rationale:

When considering a substitute method of capital punishment it is important to consider more than just what happens if everything goes according to protocol. The likelihood of mishaps must also be considered, as well as the consequences that would flow if those mishaps should occur.

Because the protocol involved in nitrogen induced hypoxia is so simple, mistakes are unlikely to occur. Oxygen and nitrogen monitors may be placed inside the contained environment to insure the proper mixes of gas are being expelled into the bag and inhaled by the subject.

However, the protocol should be careful to prevent the possibility of oxygen entering into the hood, as that can prolong time to unconsciousness and death, as well as increase the possibility of involuntary movements by the subject.

The risks to witnesses are minimal, as any potential leak of the nitrogen would not be harmful in a normally ventilated environment.

Finding 4. Nitrogen is readily available for purchase and sourcing would not pose a difficulty.

Rationale:

Nitrogen is utilized harmlessly in many fields within United States industries. Nitrogen is used in welding, hospital and medical facilities, cooking, and used in the preparation of liquid nitrogen cocktails. Nitrogen is used as a process to extend the life of food products such as potato chips. Nitrogen is used in doctor's offices to remove skin tags as well as other procedures. Accordingly, sources of nitrogen to be used for administering a death sentence should be easy to find and readily available for purchase for such purpose.

Finding 5. Death sentences carried out by nitrogen inhalation would not depend upon the cooperation of the offender being executed.

Rationale:

Some forms of capital punishment require the offender to submit or comply to some degree in order to assure an efficient and humane method of execution. With proper protocol and utilizing such devices as a restraint chair, nitrogen inhalation can be administered despite the presence of a non-compliant offender. The use of nitrogen can be used by non-medical personnel and a delivery system can be designed to ensure the execution is carried out without issue.

Conclusion

As per the above, it is the recommendation of this study that hypoxia induced by the inhalation of nitrogen be offered as an alternative method of administering capital punishment in the State of Oklahoma.

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Appendix D

Death by Nitrogen: Will This New Method of Execution Save the Death Penalty?

Sign In | Sign Up

Death by Nitrogen

If lethal injection falls out of favor, death penalty states could turn to a new method: nitrogen gas.

By Tom Scocca

Justice Samuel Alito issued an order halting the execution of a Missouri inmate.

Photo by Bob Levey/Getty Images

On Wednesday night, the Supreme Court stopped an execution by lethal injection. The condemned Missouri man, Russell Bucklew, says he has a medical condition affecting his veins, that would make the injection cause hemorrhaging—and make him feel like he's choking on his own blood. The court took the unusual step of intervening at the last minutes, when every other court had turned Bucklew down, and also of sending the case back to the lower courts to decide whether to hold a hearing about Bucklew's claim.

The Supreme Court ruled in 2008 that Kentucky's three-drug protocol for carrying out lethal injections was constitutional, but there's no question that the method looks pretty suspect in the wake of Clayton Lockett's apparently painful, botched execution in Oklahoma last month. Not so long ago, though, this was the method that represented progress. Hanging. Firing squad. The guillotine. The electric chair. The gas chamber. Lethal injection. Every age seems to feature a new and improved method of capital punishment, billed as more efficient and humane. The spectacle of Lockett's death, and the Supreme Court's hesitation, shines a spotlight on the latest idea—death by nitrogen.

As long as there's a will to kill criminals, someone will come up with an improved form of capital punishment.

The new proposed method, known as nitrogen asphyxiation, seals the condemned in an airtight chamber pumped full of nitrogen gas, causing death by a lack of oxygen. Nitrogen gas has yet to be put to the test as a method of capital punishment—no country currently uses it for state-sanctioned executions. But people do die accidentally of nitrogen asphyxiation, and usually never know what hit them. (It's even possible that death by nitrogen-gas is mildly euphoric. Deep-sea divers exposed to an excess of nitrogen develop a narcosis, colorfully known as "raptures of the deep," similar to drunkenness or nitrous oxide inhalation.)

You can oppose the death penalty and still see the merit in making executions more humane. As Sean Dang and Dahlia Lithwick argued in *Slate*, opponents of the death penalty inadvertently have made lethal injection less safe, by forcing prison officials into using inferior methods and substandard drug providers. As the states struggle to obtain drugs, such as pentobarbital, for lethal injections because of an export ban by the European Union, lethal injection has been turned from a method of execution into a medical experiment.

Proponents say that death by nitrogen, by contrast, adheres to the constitutional prohibition against cruel and unusual punishment. The condemned prisoner would detect no abnormal sensation breathing the odorless, tasteless gas, and would not undergo the painful experience of suffocation, which is caused by a buildup of carbon dioxide in the bloodstream, not by lack of oxygen.

In late April, Louisiana Department of Corrections Secretary James LeBlanc suggested to a state legislative committee that Louisiana should look into using nitrogen gas as a new method of execution, since lethal injection has become so contentious. "It's become almost impossible to execute someone," LeBlanc complained to the Louisiana House Administration of Criminal Justice Committee.

"Nitrogen is the big thing," LeBlanc told the committee. "It's a painless way to go. But more time needs to be spent [studying] that." The committee instructed LeBlanc to do some research on the subject and "report back" to the committee. Louisiana has delayed a pending execution. "I'm not taking anything off the table," says state Rep. Joseph R. Lopinto III, chairman of the state's Administration of Criminal Justice Committee. "If someone says nitrogen gas is the way to go, then we can debate that and do it if need be."

As long as 32 states have capital punishment on the books, there should be a less reliably cruel method of execution than lethal injection. "If we're going to take a life, then we should do it in the most humane, civilized manner as is possible," says Lawrence Gist II, an attorney and professor of business and law at Mount St. Mary's College. "Right now, nitrogen is the best of the available options."

Gist, a death penalty opponent, runs a website dedicated to promoting nitrogen asphyxiation for state-sanctioned executions. Polling suggests the public could get behind the idea. In a recent NBC News poll, 1 in 3 people said that if lethal injections are no longer viable, executions should be scrapped altogether. But many others were open to alternative methods of putting prisoners to death. About 20 percent opted for the old version of the gas chamber (which traditionally used hydrogen cyanide to kill), 18 percent for the electric chair, 12 percent for death by firing squad, and 8 percent for hanging.

Nitrogen gas, unlike the lethal drugs that states have relied on, is widely available. The gas is used extensively in industrial settings, from aerospace to oil and gas production. "Lethal injection is just fine if you can get the pentobarbital," says Kent Scheidegger, legal director of the Criminal Justice Legal Foundation, a group that favors capital punishment. "But if that's not available, an alternative like nitrogen gas would work."

Top Comment

I always thought that people who voluntarily went to witness a cyanide gas chamber execution were morons. You have to have a special kind of faith in window caulking. More...

-Pete R

Join In

In contrast to lethal injection, no medical expertise would be needed to introduce nitrogen gas into a sealed chamber. The gas chamber itself is technology that has been around since the 1920s. In fact, three states—Arizona, Missouri, and Wyoming—still authorize lethal gas as a method of execution (depending on the choice of the inmate, the date of the execution or sentence or the possibility that lethal injection is held unconstitutional).

The last gas chamber execution in the U.S. was in 1999—the method fell out of favor because hydrogen cyanide is a poison causing suffering that lasts 10 minutes or longer. Lethal injection, of course, was supposed to be painless and better. What if it's not? That's the question the Supreme Court now finally seems to be returning to. The history of capital punishment suggests that as long as there's a will to kill criminals, someone will come up with an improved way. The new tool in the executioner's bag may turn out to be nitrogen, a better way to carry out a gruesome task.

Tom McNichol is a writer in San Francisco.

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alt.suicide.methods

Killing with kindness - capital punishment by nitrogen asphyxiation (too old to reply)

Philbert 9 years ago

http://www.findarticles.com/p/articles/mi_m1282/is_n17_v47/ai_17374449

Capital punishment needn't be cruel or unusual -- especially if you use nitrogen asphyxiation to put people to sleep.

LAST October, Judge Marilyn Hall Patel of the 9th U.S. District Court ruled that execution in California's gas chamber is a form of cruel and unusual punishment, the first ruling ever by a state or federal judge to invalidate a method of execution on Eighth Amendment grounds. She noted that the evidence showed that the condemned man might remain conscious for several minutes, experiencing the emotions of 'anxiety, panic, terror,' as well as 'exquisitely painful muscle spasms' and 'intense visceral pain.'

On its face, Judge Patel's ruling applies only to the gas chamber, but every method of execution in current use involves toxic chemicals or physical trauma to induce death -- and every method can go awry. An ideal hanging snaps the condemned man's neck cleanly; a botched one either strangles him slowly or severs the head entirely from the body. A firing squad that misses its mark leaves the condemned man conscious as he bleeds to death. In the electric chair, according to eyewitness accounts, some condemned men have literally been cooked until their flesh was charred and loosened from the bone; some had sparks and flame emanating from their cranial-cap electrodes.

Besides society's concern for the condemned man's physical suffering, all of these methods implicitly require an executioner to inflict some degree of trauma upon the condemned Concern for the executioner's conscience drives such customs as loading one of the guns for a firing squad with a blank cartridge, so that each member of the squad can imagine that his will be the non-lethal shot. And with lethal injection, the executioner's use of skills and procedures normally devoted to life-saving poses ethical questions for medical caregivers.

Given these defects, abolitionists will presumably press to have each of these methods declared 'cruel and unusual.' The intended result of these efforts is to make the death penalty unconstitutional in practice, even if it remains constitutional in theory.

It is in fact possible to conceive of a method of execution that would cause neither pain nor physical trauma, require no medical procedure (other than pronouncing death), and use no hazardous chemicals. A case of accidental

death suggests such a method.

Early in the Space Shuttle program, a worker at Kennedy Space Center walked into an external fuel tank (a vessel nearly as big inside as a Boeing 737) to inspect it. He was not aware that it had been purged with pure nitrogen gas to prevent oxygen in the air from corroding its interior. Since nitrogen is the major component of ordinary air, pure nitrogen has no distinctive feel, smell, or taste; the worker had no indication that anything was out of the ordinary. After walking a short distance into the tank, he lost consciousness and collapsed. A co-worker, not realizing that his collapse had an external cause, ran in to aid him and succumbed also. By the time other workers realized what was happening, the two men were dead.

More recently, a bizarre accident involving nitrogen killed two people in the Bay Area. They had stolen from a hospital a gas cylinder containing what they thought was laughing gas. However, the cylinder contained not the anaesthetic nitrous oxide but pure nitrogen. When the two men stopped their car to partake of their booty, the nitrogen gas displaced the air in the car, leaving them without oxygen. Had they had any indication of the problem, they could have saved their lives simply by opening the car doors.

These deaths were similar in cause to a relatively common drowning accident known as shallow-water blackout, mentioned specifically in certification classes for recreational scuba diving. When a person is skin diving (that is, without scuba gear), his bottom time is limited by how long he can hold his breath. Occasionally, a skin diver will attempt to lengthen the time he can stay under by hyperventilating before a dive. Unfortunately, this can lead to his losing consciousness underwater, sometimes only a few feet before reaching the surface.

THE connection between nitrogen asphyxiation and shallow-water blackout lies in human respiratory physiology. When you hold your breath, you begin to develop a powerful urge to breathe. This is caused not by the depletion of oxygen from your body, but by the buildup of carbon dioxide in your bloodstream, which changes the pH of the blood. The ambitious skin diver "blows off" most of the carbon dioxide in his bloodstream when he hyperventilates; as a result, he notices the urge to breathe much later than he normally would, at a point when his blood oxygen is dangerously low. If his blood oxygen falls too low before he reaches the surface, he blacks out and drowns. Because the Kennedy Space Center workers continued to exhale carbon dioxide with each breath, neither of them noticed an unusual urge to breathe, even though they were completely deprived of oxygen.

Nitrogen asphyxiation is a unique way to die. The victim is not racked by a choking sensation or a burning urge to breathe, because as far as his body

knows, he is breathing normally. Carbon dioxide is not building up in his bloodstream, so he never realizes that anything is wrong, nor does he experience any discomfort; he simply passes out when his blood oxygen falls too low.

Nitrogen asphyxiation is therefore a perfect method of execution. It uses a cheap and universally available working medium that requires no special environmental precautions for its storage and disposal. Its first symptom is loss of conscious sensation, a primary goal in a humane execution. It involves no physical trauma, no toxic drugs; the executed man's organs will even be suitable for donation, a factor cited in a recent stay of execution for a Georgia killer.

Assuming that the prisoner's guilt has been sufficiently proved, nitrogen asphyxiation is perhaps the most gentle way to deal with him. A condemned man awaiting death by nitrogen asphyxiation would experience no more pain or suffering than he created in his own mind.

nubbins 9 years ago

```
x-no-archive:yes

Maybe even go out laughing.

- nubbins -
```


Philbert 9 years ago

> *Post by nubbins*
> x-no-archive:yes
> Maybe even go out laughing.
> - nubbins -

```
You're thinking of nitrous oxide aka laughing gas. The article is about
nitrogen.
```

nubbins 9 years ago

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x-no-archive:yes
```

> *Post by Philbert*
> > *Post by nubbins*
> > Maybe even go out laughing.

> You're thinking of nitrous oxide aka laughing gas. The article is about nitrogen.

You are absolutely correct, sir. I was not paying due attention. Gets me in trouble in class all the time. Who would mind if a doctor diagnosed onychomycosis as cryptorchidism, really? Details, details.

- nubbins -

d*@hotmail.com** 9 years ago

Awesome article. I think you just solved the puzzle for me. Thank you.

Philbert 9 years ago

Google nitrogen suicide for a lot of stuff. Basically people find that euthanising animals works pretty well using nitrogen, plus it's safe to use
unless it's in a very high concentration.

Rabbits don't like nitrogen because they have adaptive traits for living in
holes where nitrogen can build up, unlike other animals and humans.

On 4/6/06 3:25 PM, in article

> *Post by d***@hotmail.com*
> Awesome article. I think you just solved the puzzle for me. Thank you.

slunky 9 years ago

Thanks for finding an article on it. I've been saying it for weeks, and was starting to wonder if I had just imagined it or what.

-
-slunky

Cesar 9 years ago

Thanks for the great post and it was interesting and informative. I have concern that when the death penalty is ruled out as cruel and inhumane, it leaves the potential that the prisoners on death row could at some point get release and re-enter society. When prisons become too full, it can be ruled that a certain amount of prisoners be released early. In the years to come, laws could change and see a prisoner sentenced to death instead getting a life sentence of 20 years then getting out. Of course, it would help those that were wrongly convicted in the first place.

Jimmy 9 years ago

EIGA

HAZARDS OF INERT GASES AND OXYGEN DEPLETION

IGC Document 44/09/E

Revision of IGC Doc 44/00/E

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IGC Doc 44/09/E

EIGA

HAZARDS OF INERT GASES AND OXYGEN DEPLETION

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Table of Contents

1 Introduction

EIGA is very concerned about the accidents that industrial gas companies and users of inert gases continue to report each year, where the direct cause has been lack of oxygen resulting in asphyxiation. EIGA identified that existing information on the hazards of inert gases was not sufficiently directed at the users who were most at risk. This document sets out the essential information that is necessary to prevent asphyxiation accidents involving inert gases.

2 Scope and purpose

It is intended that this document is used as a training package suitable for supervisors, line managers, direct workers and users wherever inert gases are produced, stored, used, or where oxygen depletion could otherwise occur.

This document has 4 parts:

The main document is intended for line managers and supervisors and gives the background of the subject, the typical description of oxygen deficiency accidents and the recommended rescue preparations to be in place in case of accident.

Appendix A is a simplified summary of the main document, designed to be reproduced as a pamphlet for sharing with workers and end users.

Appendix B gives an introduction to rescue considerations from normally accessible rooms, confined spaces or pits and trenches.

Appendix C lists some actual accidents that have taken place in recent years, which can be used as examples to underline the potentially fatal hazards of inert gases.

Appendix D gives an example of a warning sign or poster to highlight the hazards of inert gases and asphyxiating atmospheres.

3 Definitions

Asphyxiation: the effect on the body of inadequate oxygen, usually resulting in loss of consciousness and/or death. This is also known as suffocation or anoxia.

Asphyxiant: any material which reduces the amount of available oxygen either by simple dilution or by reaction.

Inert gas: A gas that is not toxic, which does not support human breathing and which reacts little or not at all with other substances. The common inert gases are nitrogen and the rare gases like helium, argon, neon, xenon and krypton.

Flammable gas: a gas whose major hazard is flammability. Note that all flammable gases also act as asphyxiants.

User: for the purpose of this document this term covers any individuals, companies or other organisations that make use of the products sold by industrial gas companies. Users may be, but are not necessarily, customers.

4 General Information about Inert Gases and Oxygen Depletion

In spite of the wealth of information available, such as booklets, films and audio-visual aids, there are still serious accidents resulting in asphyxiation caused by the improper use of inert gases or by oxygen depletion. It is therefore absolutely essential to draw attention to the hazards of inert gases and oxygen depletion. Accidents due to oxygen depleted atmospheres are usually very serious and in many cases fatal.

Although carbon dioxide is not an inert gas, most of the information in this document is applicable as it too will cause oxygen depletion. However, the specific hazards and physiological effects of carbon dioxide are more complex than those of inert gases. This document does not cover these aspects. (See IGC Doc. 67 "CO2 cylinders at user's premises" for more details about the additional hazards of carbon dioxide).

4.1 Oxygen is essential for life

Oxygen is the only gas that supports life. The normal concentration of oxygen in the air we breathe is approximately 21 %. Concentration, thinking and decision-making are impaired when the oxygen concentration falls only slightly below this norm. These effects are not noticeable to the affected individual.

If the oxygen concentration in air decreases or, if the concentration of any other gases increase, a situation is rapidly reached where the risks of asphyxiation are significant. For this reason any depletion of oxygen below 21 % must be treated with concern.

Asphyxia – Effect of O_2 Concentration (from NL/77 Campaign against Asphyxiation)

O_2 (Vol %)	Effects and Symptoms
18-21	No discernible symptoms can be detected by the individual. A risk assessment must be undertaken to understand the causes and determine whether it is safe to continue working.
11-18	Reduction of physical and intellectual performance without the sufferer being aware.
8-11	Possibility of fainting within a few minutes without prior warning. Risk of death below 11%.
6-8	Fainting occurs after a short time. Resuscitation possible if carried out immediately.
0-6	Fainting almost immediate. Brain damage, even if rescued.

***WARNING**: The situation is hazardous as soon as the oxygen concentration inhaled is less than 18 %.*
With no oxygen present, inhalation of only 1-2 breaths of nitrogen or other inert gas will cause sudden loss of consciousness and can cause death.

4.2 Inert gases give no warning

It is absolutely essential to understand that with inert gases such as nitrogen, argon, helium, etc., asphyxia is insidious - there are no warning signs!

- Inert gases are odourless, colourless and tasteless. They are undetectable and can therefore be a great deal more dangerous than toxic gases such as chlorine, ammonia, or hydrogen sulphide, which can be detected by their odour at very low concentrations.
- The asphyxiating effect of inert gases occurs without any preliminary physiological sign that could alert the victim. Lack of oxygen may cause vertigo, headache or speech difficulties, but the victim is not capable of recognising these symptoms as asphyxiation. Asphyxiation leads rapidly to loss of consciousness – for very low oxygen concentrations this can occur within seconds.

4.3 Inert gases act quickly

In any accident where the supply of oxygen to the brain is affected, prompt emergency treatment is critical. Proper medical treatment (resuscitation) if given quickly enough can prevent irreversible brain damage or even death in some instances.

Furthermore, and this is often poorly understood, the emergency rescue procedure to save the victim must be carefully thought out in advance to avoid a second accident, where members of the rescue

team can become victims. Unplanned interventions resulting in the fatalities of would-be rescuers are sadly not unusual.

4.4 The ambiguity of inert gases

Everyone, particularly customers, must be aware of the ambiguity of the expression "inert gas" (sometimes called "safety gas", when it is used to prevent fire or explosion), whereby an "inert gas" is often perceived, understood and wrongly taken to be a harmless gas!

4.5 Watchfulness with regard to inert gases and oxygen depletion

Considering the hazards mentioned above, it is essential to provide all those who handle or use inert gases (gas company personnel as well as customers) with all the information and training necessary regarding safety instructions. This includes the means of prevention and procedures to be respected to avoid accidents, as well as planned rescue procedures to be implemented in the event of an accident.

5 Some typical situations with inert gas and/or oxygen depletion hazards

5.1 Confined or potentially confined spaces and enclosures

Confined, restricted or enclosed spaces are particularly dangerous situations where an inert gas may be normally present (inside a process vessel), may have accumulated (from leaks or vents) and/or because the space has not been adequately vented or purged, and/or the renewal of air is poor or ventilation is inadequate.

Examples of such spaces include:

- Confined spaces: tanks, vessels, reservoirs, the inside of "cold boxes" of liquefaction equipment, cold storage rooms, warehouses with fire suppressant atmospheres, etc.
- Enclosures: analyzer or instrument cabinets, small storage sheds, temporary/tented enclosures, or spaces where welding protective gas is used, etc

The precautions required for safe access by personnel will be different in each of these cases as explained in Appendix B.

5.2 The use of inert cryogenic liquids

It is to be noted, that the use of inert cryogenic liquids such as nitrogen or helium is accompanied by two primary hazards:

- The fluids are very cold (-196°C for nitrogen and -269°C for helium) and can cause serious cold burns on contact with the skin.
- Once vaporised both products will generate a large volume of cold inert gas (e.g. 1 litre of liquid nitrogen will yield 680 litres gaseous product) that will displace ambient air, causing oxygen deficiency and may accumulate in low points.

In processes where cryogenic liquids are handled and vaporisation takes place, special care must be taken to avoid situations where personnel are exposed to oxygen deficiency. These may be in rooms which people regularly enter or work in.

Examples of such spaces include:

- The internal rooms of a building where cryogenic liquid cylinders/dewars are filled and/or stored,
- Laboratory rooms,
- Elevators (lifts) used for transport of dewars.
- Rooms where liquid nitrogen food freezers are operated. (Tunnel, cabinet)
- Rooms where Magnetic Resonance Imaging (MRI) scanner or other liquid helium cooled equipment is used
- Rooms in which cryogenic de-flashing equipment is operated.

Notes: Due to the extremely low temperature of liquid helium a secondary hazard may exist where the product is flowing through hoses or pipes. In this case it is possible for the components of air to liquefy on the outside of the hose/pipe, possibly leading to pooling of liquid containing levels of enriched oxygen. [See Ref. 7].

5.3 Areas near where inert gases are vented or may collect

The risk of asphyxiation can arise, even outdoors, in the vicinity of:
- Gas leaks
- Vent exhausts
- Outlet of safety valves and rupture disks
- Openings of machines in which liquid nitrogen is used for freezing
- Blind flanges
- Near manways/access to vessels or purged enclosures (e.g. ASU cold boxes, electrical enclosures)

Any cold gas or heavier-than-air gas will travel or "flow" – often unseen - and collect even outdoors, in low spaces such as:
- Culverts
- Trenches
- Machine pits
- Basements
- Elevator (lift) shafts

Similarly and just as dangerously lighter-than-air gases (e.g. helium) will rise and collect in unventilated high points such as:
- Behind false ceilings
- Under a roof

5.4 Use of inert gas instead of air

Planned Use
In many workplaces, there are often compressed inert gas distribution networks that are used for process applications, safety or instrumentation purposes, e.g. inerting/purging of reactors or using nitrogen as a pressure source to operate pneumatic equipment (such as jackhammers) or as instrument fluids.

Additionally, nitrogen is often used as either a backup to, or substitute for, an instrument air system. Where it is used as a backup supply in case of instrument air compressor failures it is quite common to find a nitrogen supply connected to an air supply by means of isolation valves. It must be appreciated that most pneumatically operated instruments vent continuously and that the vented nitrogen may accumulate in poorly ventilated control panels/cubicles or plant rooms. This can present a serious asphyxiation risk. Where nitrogen is used temporarily to substitute for compressed air in this way, it must be done under strictly controlled conditions such as a permit to work, and all relevant personnel shall be informed.

Improper Use
In situations where piped breathing systems exist there is always the potential for employees, who are insufficiently trained or not familiar with the systems, to connect the breathing apparatus to a nitrogen system with fatal results. Such systems must be clearly marked and ideally the breathing air system should have a dedicated connection type not used elsewhere in the premises.

5.5 Dangers of improper inhalation (abuse) of inert gases

There has been increased of reporting and presentations in TV-programmes on the careless approach and dangerous misuse of breathing in gases such as helium and other inert rare gases. The media reports in particular trivialise the effects of inhaling helium to achieve a very high-pitched voice. Inhalation of helium can lead to unconsciousness, cessation of breathing and sudden death.
[See Ref. 6 for more information]

6 Hazard mitigation and preventive measures

6.1 Information, training

All persons who handle or who use inert gases shall be informed of:
- Safety measures that should be adopted when using gases.
- The hazard represented by the release of inert gases in to the working space and the potential for oxygen depletion.
- Procedures to be observed should an accident occur.

This information and training should be systematically and periodically reviewed in order to ensure that it remains up to date and appropriate for the hazards identified.

6.2 Proper installation and operation

Equipment for the manufacture, distribution or use of inert gas must be installed, maintained and used in accordance with:
- All applicable regulations.
- The recommendations of the supplier
- Industrial gas industry standards and codes of practice

Newly assembled equipment for inert gas service must undergo a proof test and be leak-checked using suitable procedures.

Each inert gas pipeline entering a building should be provided with an easily accessible isolation valve outside the building. Ideally such valves should be remote activated by push buttons or other safety monitoring equipment.

Discontinued inert gas lines shall be physically disconnected from the supply system when not in use.

At the end of each work period, all valves that isolate the inert gas should be securely closed to avoid possible leakage between work periods.

6.3 Identification and safeguarding of potentially hazardous areas

Measures should be taken to identify potentially hazardous areas, or restrict access to them, e.g.
- Warning signs should be displayed to inform of an actual or potential asphyxiation hazard (An example is shown in Appendix D). The warning sign should be associated with measures to prevent unauthorised entry to the areas.
- Temporary or permanent barricades, for example physical lock on vessel manway or barricades around temporary excavations.
- Communication to site personnel to ensure awareness and understanding.

6.4 Ventilation and atmospheric monitoring for inert gases and oxygen deficiency

Typically there are three situations where the need for ventilation or atmospheric monitoring must be assessed in order to avoid asphyxiation accidents from inert gases and/or oxygen depletion:

6.4.1 Ventilation/ monitoring of rooms which people regularly enter or work in

Examples in this category would include:
- Rooms containing inert gas pipelines with possible leaks such as compressor houses, control rooms (with control/analyser panels).
- Rooms where inert cryogenic liquid is used or stored (see 5.2 above)

Building/room size, ventilation capacity, system pressures, etc. must be determined for each specific case. The following guidelines can be applied to ventilation system design:
- Ventilation must be continuous while the hazard exists. This can be achieved by interlocking the ventilation system with the process power supply.

- Ventilation system design should ensure adequate air flow around the normal operating areas.
- Good engineering practice indicates a minimum ventilation capacity of 6-10 air changes per hour.
- The use of devices to indicate correct system operation, such as:
  - Warning lights
  - "Streamers" in the fan outlet,
  - Flow switches in the suction channels (monitoring should not rely only upon secondary controls such as "power on" to the fan motor).
- Exhaust lines containing inert gases shall be clearly identified, and should be piped to a safe, well ventilated area outside the building, away from fresh air intakes.
- Consideration should be given to the use of workplace atmospheric monitoring, e.g. personal oxygen analyser or an analyser in the work area, location to be based on assessment of the areas described in 5.3.
- People working in or entering the area shall be aware of action required in event of alarms from atmospheric monitors or loss of ventilation.

6.4.2 Ventilation/ monitoring prior to entry into confined spaces or enclosures

As described in 5.1 above, these spaces would include enclosures or vessels which:
- Are not routinely entered and
- Are known to have contained inert gas or
- May contain inert gas or low concentration of oxygen
- Any vessel not known and verified to contain atmospheric air.

In these cases the following guidelines apply to prepare a safe atmosphere prior to entry:
- Sources of inert gas must be isolated from the space or enclosure by positive blinds or by disconnection of lines. Never rely only on a closed valve.
- The vessel or enclosure must be adequately purged with air (i.e. remove the inert gas and substitute with air).
  - It is necessary to have at least 3 complete air changes within the enclosure involved.
  - Purging shall continue until analysis confirms that the quality of the vessel atmosphere is safe for personnel entry. If there is any doubt that effective purging has taken place, the analysis should be made in the interior of the vessel by taking a sample at several locations by probe, or if this is not possible, by a competent person using a self contained breathing apparatus.
  - The purge system must ensure turbulence for adequate mixing of air and inert gas to take place (to avoid "pockets" of dense or light inert gases remaining or to avoid "channelling" of gases due to inadequate purging).
  - Removal of argon or cold nitrogen from large vessels and deep pits can be difficult due to the relatively high density of the gas compared with air. In that case the gas should be exhausted from the bottom of the space.
  - Ventilation should never be carried out with pure oxygen, but exclusively with air.
- Another method of removing inert gases is to fill the vessel with water and allow air to enter when the water is drained off.
- Oxygen content of the atmosphere in the enclosure/vessel shall be monitored continuously or repeated at regular intervals.
- Consideration should also be given to the use of personal oxygen monitors.

Where a safe atmosphere cannot be created and confirmed, then the task must only be performed by competent personnel provided with a positive breathing air supply.

6.4.3 Ventilation/monitoring for entry into other spaces where inert gases may be present

This type of confined space is one that has any of the following characteristics:
- Limited opening for entry and exit
- Unfavourable natural ventilation

Examples are listed in sections 5.1 and 5.3 and include;
- Underground works
- Trench/pit deeper than 1 metre
- Small rooms where gases are stored but not designed for continuous worker occupancy.

In the majority of these cases the presence of inert gases is not anticipated when entering such spaces. However, the one essential safeguard in all cases is to sample the atmosphere in the room, enclosure, trench, pit, etc. for oxygen prior to any entry. Where appropriate a continuous fixed point monitoring device should be used.

The fact that an oxygen deficient atmosphere is not normally expected is the greatest danger.

6.4.4 Notes on purging requirements

The guidance for air changes, mentioned in section 6.4.2, is valid where nitrogen is the inert gas involved because its density is very near to that of air and oxygen.

If the gas to be purged has a density very different from the density of air, such as helium, argon or carbon dioxide, etc. the ventilating air may not adequately mix and the purge may be inadequate.

For inert gases of this type the volume of gas to be displaced (air changes) must be at least 10 times that of the volume involved. The preferred method of removal of very dense gases (e g argon or cold nitrogen vapour) is to suck out the gas from the bottom of the space.

In the presence of toxic or flammable gases, it is mandatory to perform an additional analysis of the gases present in the confined space, before entry of personnel. For obvious reasons, the measurement of only the oxygen content is not sufficient in this case. All other dangerous toxic or flammable gases must also be analysed.

In the specific case of flammable gases, a nitrogen purge must be used first to prevent any explosion risk and then subsequently purge with ventilating air.

6.5 Testing of oxygen content

Historically, the need to check that an atmosphere is respirable has been considered to be of the greatest importance. In the past, simple means were employed, such as, for example, the lighted candle or the canary bird.

Currently, various types of oxygen analysers are available, which are often reliable and simple and to operate. The selection of the type of apparatus depends on the nature of the work in the place to be monitored (presence of dust, temperature and humidity, multiple detectors, portable equipment, etc.).

- Oxygen analysers are critical equipment and must be properly maintained and calibrated in order to sufficiently reliable. It is also important to ensure that fixed and portable detectors are properly positioned to measure a representative sample of the atmosphere.
- A simple way check to confirm that an oxygen analyser is operating properly before use is to measure the oxygen content of the open air (21 %). This check should be part of the work permit requirements.
- All oxygen analysers should be fitted with an alarm device to indicate possible defects (e.g. low battery).
- The minimum safe oxygen concentration for entry into a space that is being controlled or measured because of the risk is 19.5 % oxygen. There are applications with oxygen concentrations below 19.5 % where entry is permitted provided that further precautions are taken in accordance with proper risk assessment and national regulations (e.g. fire suppression). [See Ref 4]

6.6 Work permit

For certain types of work, safety instructions and a special work procedure must be set up in the form of a work permit, this particularly relates to any form of confined space entry. [See Ref 8]
This procedure is necessary during work carried out by subcontractors in air separation cold boxes, or where vessel entry is required.

It is important that a work permit procedure deals with the detailed information that must be given to involved personnel before the start of work. This information should include contractual conditions together with documented risk assessments, procedures and the training of site workers.

6.7 Lock-out Tag-out procedure

To ensure any sources of inert gas have been properly isolated, the implementation of a stringent, formal lock-out and tag-out procedure is necessary before safe entry into a confined space.

6.8 Protection of personnel

The type of work to be performed, the layout of the premises and the assessment of potential rescue scenarios will determine the provision of additional protective measures. This additional protection should include organisational measures and/or safety equipment such as:

- Fixed or personal oxygen monitoring equipment
- The wearing of a harness so that the worker can be easily and rapidly taken out of an enclosed space in the case of an emergency. Preferably, this harness is to be connected to a hoist to facilitate removing the victim. (In practice, it is extremely difficult for one person to lift up another person in the absence of a mechanical aid of some kind.)
- The provision of an alarm system in case of an emergency.
- The wearing of a self contained breathing apparatus (not cartridge masks, which are ineffective in a case of lack of oxygen).
- In the case of work inside a confined space, a standby person should be placed on watch outside the space/vessel.
- Having a self contained breathing apparatus on stand by.
- The wearing of other personal protective equipment such as safety boots, hard hat, goggles or gloves, depending on the hazards of the location and task.

7 Confined space entry

The employer has an overriding duty to ensure that tasks in confined spaces with potentially hazardous atmospheres are performed without entry whenever this is practical. Only if it there is no practical alternative shall people be required to enter confined spaces.

Any entry into a confined space or enclosure with a potentially hazardous atmosphere shall be carefully controlled and have:

- A written method statement for the work to be undertaken with the space.
- A documented risk assessment for performing this task in this particular vessel.
- Formal, stringent lock-out and tag-out procedures.
- An assessment of potential scenarios where rescue may be required.
- An emergency (rescue) plan to deal with any possible accident scenario related to entry in to the enclosure or vessel.
- Rescue personnel and equipment should be available as required by the rescue plan.
- Trained and competent personnel in roles of; entrant, stand-by watch, rescue team (where required) and supervisor/permit issuer.
- A safe work permit issued and signed before entry is allowed.

This document is not a detailed procedure for confined space entry, but focuses on the considerations which are important where there is an actual or potential hazard from inert gases or oxygen deficiency.

8 Rescue and first-aid

Awareness training in the hazards of inert gases and oxygen deficient atmosphere is of vital importance for everyone who might enter a space or who might discover and affected person in a space with potentially asphyxiant atmosphere, in order to prevent subsequent fatalities as result of "unplanned rescue" attempts.

Training in rescue work is fundamental since quickly improvised rescue without the formality of a procedure, often proves to be ineffective, if not catastrophic, i.e. the rescue worker lacking foresight becomes a second or even a third victim. This is one of the most common causes of multiple fatalities in cases involving asphyxiation.

8.1 Basic rules

If a person suddenly collapses and no longer gives any sign of life when working in a vessel, a partially enclosed space, a trench, a pit, a small sized room, etc., it MUST be assumed that the person may lack oxygen due to the presence of an inert gas (which is, as mentioned, odourless, colourless and tasteless).

WARNING: the discoverer must assume that his life is at risk entering the same area!

The risk is that the rescuer will become the second victim, which obviously must be avoided at all costs. Ideally he should raise an alarm and call for assistance so that a prepared rescue can be carried out.

Rescuers intent on saving a possible asphyxiation victim should only do so if they have the necessary equipment, have been suitably trained, have proper assistance and support.

8.2 Rescue plan elements

The method of rescue will be determined by the access to particular space. If practical a non-entry rescue is preferred. Appendix B lists the considerations which should be given to rescue plans from three different situations:

- Rescue from normally accessible rooms
- Rescue from Confined Spaces
- Rescue from pits, trenches or excavations

In each case the Rescue plan must have elements which address:

- How the alarm is raised
- Identification of possible rescue scenarios (not only for low oxygen effects)
- Any scenarios in the surrounding work place which may or may not require immediate exit from the space (e.g. site evacuation in event of fire elsewhere)
- Stand-by watch trained to keep visual and verbal contact with the entrant and to ensure the entrant exits the space if symptoms of oxygen deficiency are suspected or observed
- Any assistance which may be needed/given from outside the space to help entrant escape from the space, without further entry.
- Re-checking/confirmation of atmosphere prior to rescue
- Manpower and equipment required to move unconscious person from that space
- Provision of first aid/medical treatment (e.g. resuscitation and/or oxygen treatment) inside the space if necessary
- Safe access by rescue and/or medical personnel if necessary
- How to make the space safe/prevent further injury after the rescue.

8.3 Equipment

A successful rescue action may need some of the following equipment. The actual needs must be assessed as part of the rescue plan and made available and accessible during the confined space work:

- A portable audible alarm devices, e.g.; personal horn, whistle, klaxon etc. to alert nearby people that assistance is required.
- Telephone or radio at the work site so that an alarm can be raised in event of problems
- A safety belt or harness connected to a line
- Mechanical aid such as pulley, hoist, to extract the victim.
- Possibly a source of air or oxygen to ventilate the confined space, such as:
  - A compressed air hose connected to the plant compressed air network,
  - A ventilation device.

- Additional oxygen monitors for rescue team for re-checking conditions inside the space
- Positive pressure breathing air supply. This may be an externally fed breathing air system or self-contained breathing apparatus (SCBA).
  WARNING: *Cartridge masks for toxic gases are not suitable as they do not replenish missing oxygen.*
- A resuscitation kit supplied with oxygen for the victim. In general, such a kit includes a small oxygen cylinder, a pressure regulator, an inflatable bag, and a mask to cover both the nose and mouth of the victim.
- Stretcher to carry injured person out of the space, away from work place and/or to ambulance.

It should be noted that any equipment identified as necessary to carry out an emergency rescue from a confined space should be defined on the basis of a full risk assessment and the emergency plan developed from it. Where this equipment is not available, a rescue should not be undertaken.

8.4 Rescue training

Where an emergency plan considers that a rescue is to be performed, it is recommended that there is an annual programme of training including practical rescue drills. It is also a good practice to consider a rescue exercise before start of confined space work.

8.5 First Aid

Where there is a potential hazard from inert gases/oxygen deficiency it is advisable to have personnel available who are formally qualified to give first aid and/or perform resuscitation in the event of an accident. The simplest first aid treatment for someone suffering from effects of oxygen deficiency is to bring the affected person into fresh air – as long as it safe to do so!

In most countries additional training is required so that first aiders are qualified to provide Oxygen as medical treatment for anoxia and other conditions.

9 Conclusions

There are two essential points to remember related to oxygen deficiency accidents involving inert gases:

- Accidents resulting from oxygen deficiency due to inert gases happen unexpectedly and the reactions of personnel may be incorrect. To avoid this, all personnel who may work with, or may be exposed to, inert gases must have routine awareness training in respect of the hazards of these gases.
- Accidents involving asphyxiant atmospheres are always serious, if not fatal. It is absolutely necessary to carry out both regular and periodic awareness training sessions for all personnel, as well as rescue drills.

10 References

[1] CGA document SB-2 2007 Oxygen-Deficient Atmospheres

[2] EIGA Asphyxiation campaign documents 2003 – including Dangers of Asphyxiation leaflet; Oxygen Deficiency training presentation and Newsletter 77/xx

[3] Oxygen deficiency hazards. Video tape EIGA, 1997

[4] EIGA Position Paper PP-14: Definitions of Oxygen Enrichment/Deficiency Safety Criteria – August 2006.

[5] US Chemical Safety and Hazard Investigation Board website Video Room www.csb.gov

[6] EIGA position Paper PP-24: Abuse of Gases

[7] IGC Doc 004 Fire Hazards of Oxygen and Oxygen Enriched Atmospheres

[8] IGC Doc 040 Work Permit Systems

Appendix A: Summary for operators

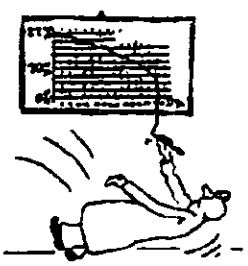
1 Why do we need oxygen?

OXYGEN IS ESSENTIAL FOR LIFE

WITHOUT ENOUGH OXYGEN WE CANNOT LIVE

When the natural composition of air is changed, the human organism can be affected or even severely impaired.

If gases other than oxygen are added or mixed with breathing air, the oxygen concentration is reduced (diluted) and oxygen deficiency occurs.



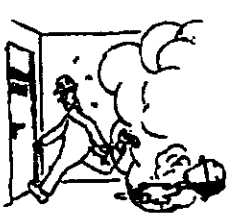
If oxygen deficiency occurs due to the presence of inert gases (e.g. nitrogen, helium, argon, etc.) a drop in physical/mental efficiency occurs without the person's knowledge; at about 11 % oxygen concentration in air (instead of the normal 21 % concentration) fainting occurs without any prior warning.

Below this 11 % concentration there is a very high risk that death due to asphyxiation will occur within a few minutes, unless resuscitation is carried out immediately!

See also EIGA Safety Newsletter **NL/77 Campaign against Asphyxiation**

2 Causes of oxygen deficiency

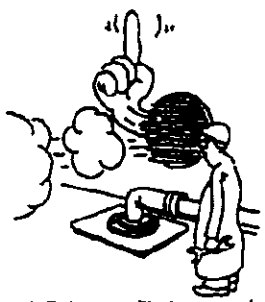
a) When liquefied gases (such as liquid nitrogen, liquid argon, or liquid helium) evaporate, one litre of liquid produces approximately 600 to 850 litres of gas. This enormous gas volume can very quickly lead to oxygen deficiency unless there is adequate ventilation.



b) In the event of gases other than oxygen leaking out of pipe work, cylinders, vessels, etc., oxygen deficiency must always be expected. Checks should be made periodically for possible leaks.

Spaces with limited or inadequate ventilation (e.g. vessels) must not be entered unless air analysis has been made, safe conditions are confirmed and a work permit has been issued.

c) If work has to be carried out in the vicinity of ventilation openings, vent pipes or vessel man ways for example, personnel must be prepared to encounter gases with low oxygen concentration or without oxygen at all being discharged from these openings.



d) Oxygen deficiency will always arise when plant and vessels are purged with nitrogen or any other inert gases.

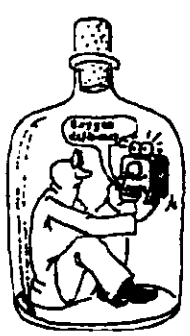
3 Detection of oxygen deficiency

HUMAN SENSES CANNOT DETECT OXYGEN DEFICIENCY

Measuring instruments give an audible or visual alarm of oxygen concentration and can indicate the oxygen content.

These instruments should always be tested in the open air before use.

If the presence of toxic or flammable gases is possible, specific instruments should be used.



4 Breathing equipment

Breathing equipment must be used in situations where oxygen deficiency has to be expected and which cannot be remedied by adequate ventilation.

Cartridge gas masks necessary for use in the presence of toxic gases (such as ammonia, chlorine, etc.) are useless for this purpose.

Recommended types of breathing equipment are:
- Self contained breathing apparatus using compressed air cylinders;
- Full-face masks with respirator connected through a hose to a fresh air supply.

NOTE:

- It should be born in mind that when wearing these apparatus, particularly with air filled cylinders, it might sometimes be difficult to enter manholes.
- Periodic inspection of the correct functioning of the equipment shall be carried out in accordance with local regulations.
- Users shall be trained and shall practice handling of the equipment regularly.

5 Confined spaces, vessels, etc.

Any vessel or confined space where oxygen deficiency is expected and which is connected to a gas source shall be disconnected from such a source:

By the removal of a section of pipe; or
by inserting a blanking plate before and during the entry period.

Reliance on the closure of valves alone might be fatal.

A space or vessel should be thoroughly ventilated, and the oxygen content shall be measured periodically before and during entry period.

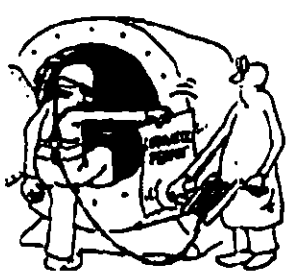
If the atmosphere in such a vessel or space is not breathable, a qualified person shall use breathing equipment.

Permission to enter such a space shall be given only after the issue of an entry permit signed by a responsible person

As long as a person is in a vessel or confined space, a watcher shall be present and stationed immediately outside of the confined entrance.

He shall have a self-contained breathing apparatus readily available.

The person inside the confined space to facilitate rescue shall wear a harness and rope. The duty of the watcher should be clear y defined. A hoist may be necessary to lift an incapacitated person.

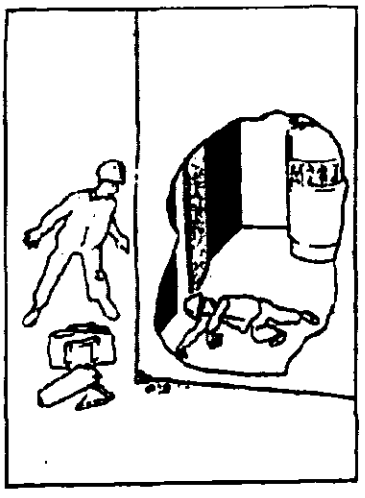


6 Emergency Measures

In the event of a person having fainted due to oxygen deficiency, he can only be rescued if the rescue personnel are equipped with breathing apparatus enabling them to enter the oxygen deficient space without risk.

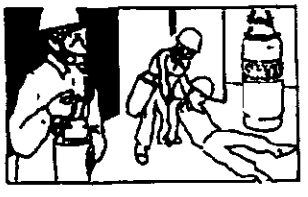
Remove the patient to the open air and administer oxygen without delay from an automatic resuscitator if available or supply artificial respiration. Guidelines and instructions for resuscitation can be obtained from the European Resuscitation Council (Internet Homepage: www.erc.edu).
Continue until patient revives or advised to stop by qualified medical personnel.

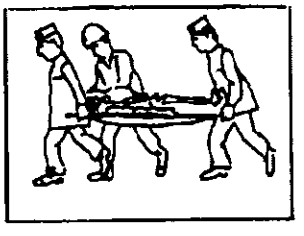
Appendix B1: Rescue considerations from normally accessible rooms



Planned Rescue Scenario:
If work is undertaken on inert gas or cryogenic liquid systems within an enclosed room it is suggested that:

- The entrant carries a personal oxygen monitor in addition to any fixed systems as the oxygen concentration may vary within the room if ventilation is absent or inadequate for the leak rate.
- The atmosphere within the space is checked before entry
- A stand-by watch is posted outside the space, to keep visual and verbal contact with the entrant and to ensure the entrant leaves the room unaided in case of early symptoms of oxygen deficiency
- The stand-by watch can raise an alarm by telephone or radio on event of problems
- The stand-by watch has Self Contained Breathing Apparatus (SCBA) ready so that he can safely enter the enclosed room to go to the assistance of, or to extract the victim if necessary.
- Unless a plan is in place so that the entrant can be safely removed by the standby-watch alone, then the rescue team should have been warned of the confined space entry work in progress, and be ready with Self Contained Breathing Apparatus (SCBA) and other equipment so that they can safely enter the Confined space to go to the assistance of, or to extract the victim if necessary.
- Plans have been made to obtain treatment/assessment from qualified medical personnel for the victim as soon as possible after he is retrieved from the room.



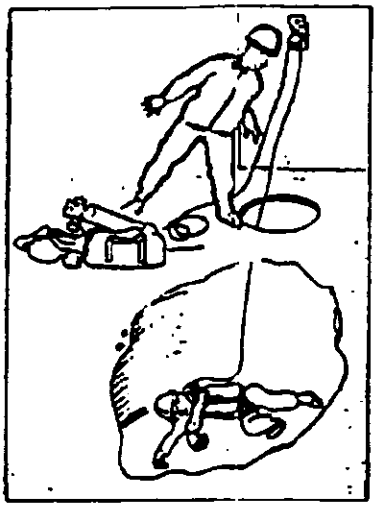


Unplanned Rescue Scenario:
If a person is found collapsed in a room where there is a potential inert gas leak / oxygen deficient atmosphere, then the discoverer must assume that his life is at risk entering the same area. He should raise an alarm and call for assistance so that a prepared rescue can be carried out.

ONLY if the collapsed person can be reached, from outside the room should any consideration be given to extracting the victim from the space and bringing him out to fresh air and medical attention.

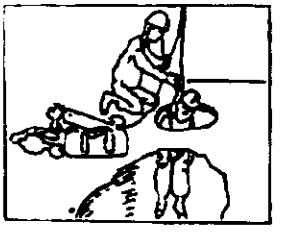
IF the victim has collapsed as a result of an oxygen deficient atmosphere and been there for any length of time it is very likely that he is dead and the discoverer's life is risked in vain.

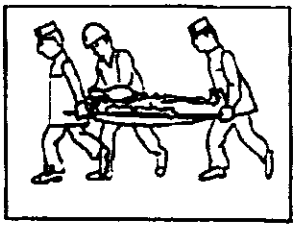
Appendix B2: Rescue considerations from Confined Spaces



Planned Rescue Scenario:
If work is undertaken within a Confined Space such as a vessel or a difficult access space, with potential inert gas/ oxygen deficient atmosphere, it is essential that:

- The atmosphere within the space is made safe, ventilated and checked before entry
- The entrant carries a personal oxygen monitor.
- If practical the entrant wears a body harness with life line, so that he can be removed from the space by persons outside. A hoist or other mechanical aid may be needed
- A stand-by watch is posted outside the space, to keep visual and verbal contact with the entrant and to ensure the entrant exits the Confined Space if symptoms of oxygen deficiency are suspected or observed
- The stand-by watch can raise an alarm to call a trained rescue team by telephone or radio on event of problems
- The rescue team should have been warned of the confined space entry work in progress, and be ready with Self Contained Breathing Apparatus (SCBA) and other equipment so that they can safely enter the Confined space to go to the assistance of, or to extract the victim if necessary.
- The stand-by watch should never enter the Confined Space.
- Plans have been made to obtain treatment/assessment from qualified medical personnel for the victim as soon as possible after he is retrieved from the room.



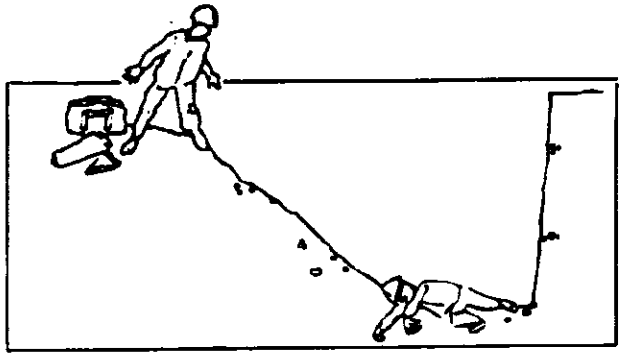


Unplanned Rescue Scenario:
All Confined Spaces shall be closed or barricaded to prevent unauthorised access. There should be no possibility for uncontrolled entry into the Confined Space, so the "unplanned rescue" situation should not occur!

If however a person is found collapsed in a Confined Space where there is a potential inert gas / oxygen deficient atmosphere, then the discoverer must assume that his life is at risk entering the same area. He must raise an alarm and call for assistance so that a prepared rescue can be carried out.

If the victim has collapsed as a result of an oxygen deficient atmosphere and been there for any length of time it is very likely that he is dead and the discoverer's life is risked in vain.

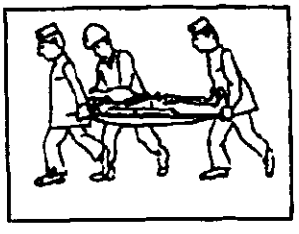
Appendix B3: Rescue considerations from pits, trenches



Planned Rescue Scenario:

If work is undertaken in an excavation, trench, pit, or other open spaces with potential inert gas / oxygen deficient atmosphere, it is strongly recommended that:

- The atmosphere within the space is checked before entry
- The entrant carries a personal oxygen monitor, as the oxygen concentration may vary within the space if there is limited fresh air circulation.
- A stand-by watch is posted outside the space, to keep visual and verbal contact with the entrant and to ensure the entrant exits the area unaided if symptoms of oxygen deficiency are suspected or observed.
- The stand-by watch can raise an alarm to call a trained rescue team by telephone or radio on event of problems.
- The stand-by watch has Self Contained Breathing Apparatus (SCBA) ready IF it is practical for him enter the enclosed room to go to the assistance of, or to extract the victim alone. OR
- The rescue team should have been warned of the confined space entry work in progress, and be ready with Self Contained Breathing Apparatus (SCBA) and other equipment so that they can safely enter the space to extract the victim if necessary
- Plans have been made to obtain treatment/assessment from qualified medical personnel for the victim as soon as possible after he is retrieved from the room.



Unplanned Rescue Scenario:
If a person is found collapsed in a trench, pit or other space where there is a potential inert gas leak / oxygen deficient atmosphere, then the discoverer must assume that his life is at risk entering the same area. He should raise an alarm and call for assistance so that a prepared rescue can be carried out.

IF the victim has collapsed as a result of an oxygen deficient atmosphere and been there for any length of time it is very likely that he is dead and the discoverer's life is risked in vain.
In addition it will often require several people to remove a victim from these kinds of spaces.

Appendix C: Accidents involving oxygen deficiency

The following list highlights real accidents recorded by EIGA, some of them very recent. The list illustrates how essential it is to regularly draw the attention of our personnel, as well as that of our customers, to the hazards of inert gases and oxygen deficiency.

1. A new pipeline in a trench was being proof tested with nitrogen. A charge hand entered the trench to investigate the cause of an audible leak. He was overcome by nitrogen and died.

2. A workman was overcome by lack of oxygen after entering a large storage tank, which had been inerted with nitrogen. Two of his workmates, who went to his aid, without wearing breathing equipment, were also overcome and all three died.

3. A man was overcome on entering a steel tank which had been shut up for several years. The atmosphere inside the tank was no longer capable of supporting life due to removal of oxygen from the air by the rusting of steel.

4. A worker from a contractor company had to carry out welds inside a vessel. The vessel had been under a nitrogen blanket, but was ventilated with air before work started. In order to be on the safe side, the welder was asked to wear a fresh air breathing mask. Unfortunately a fellow worker connected the hose to a nitrogen line and the welder died from asphyxiation.

   This accident happened because the nitrogen outlet point was not labelled and had a normal air hose connection.

5. Welding work with an argon mixture was performed inside a road tanker. During lunchtime the welding torch was left inside the tank, and as the valve was not properly closed, argon escaped. When the welder re-entered the tank, he lost consciousness, but was rescued in time.

   Equipment that is connected to a gas source, except air, must never be left inside confined spaces during lunch breaks, etc. Merely closing the valves is not a guarantee against an escape of gas. If any work with inert gas is carried out in vessels, etc. take care with adequate ventilation or the use of proper breathing equipment.

6. A driver of a small-scale liquid nitrogen delivery service vehicle was making a delivery. He connected his transfer hose to the customer-installed tank, which was situated in a semi-basement. After he had started to fill, one of the customer's employees told him that a cloud of vapour was forming around the tank. The driver stopped the filling operation and returned to the area of the tank to investigate. On reaching the bottom of the stairs, he collapsed, but fortunately he was seen by one of the customer's staff that managed to put on breathing apparatus, go in and drag the man to safety. The driver fully recovered.

   Unknown to the driver, the bursting disc of the storage tank had failed prior to the start of his fill and as soon as he started filling, nitrogen escaped in the vicinity of the storage tank. The oxygen deficient atmosphere overcame him when he went down to investigate without wearing his portable oxygen monitor, which would have warned him of the oxygen deficiency. The installation had been condemned and was no longer being used. Not only was the tank situated in a semi-basement, but the relief device was also not piped to a safe area.

7. During a routine overhaul of an air separation plant, a maintenance technician had the task of changing the filter element on a liquid oxygen filter. The plant was shut down and a work permit was issued each day for each element of work. In spite of these precautions, the technician collapsed when he inadvertently worked on the filter after it had been purged with nitrogen. The fitter collapsed apparently asphyxiated by nitrogen. All efforts to revive him failed.

8 At a cryogenic application, the equipment pressure relief valve located on the equipment inside the building opened because the pressure in the storage tank outside increased above the setting of the equipment pressure relief valve. Personnel about to enter the room the next morning were warned by the frosted appearance and did not enter.

9. A customer was supplied with 2 low temperature-grinding machines, which were located in the same area in the factory. The customer installed a joint nitrogen extraction system between the two machines. One machine was switched off for cleaning while the other machine was left running. One of the operators who had entered the unit for cleaning fell unconscious and was asphyxiated before help arrived. The linked extraction system had allowed exhausted nitrogen from the operating machine to flow into the unit to be cleaned.

10. A driver was fatally asphyxiated during commissioning of a nitrogen customer station. The customer station tank was located in a pit that was not recognized as a confined space by the design team, distribution operation team or the driver. The driver was sent to do the commissioning by himself.
During the commissioning the driver made a mistake in opening the liquid supply line valve, instead of the gas vent valve, for purging and cool down of the tank. It is believed he did not immediately notice the valving error partially due to a modified manifold that allowed gas to vent from an uncapped drain in the liquid supply line. When the driver opened the valve gas started venting as would normally occur except from the wrong location. Once he noticed that liquid rather than gas venting, he went into the pit to correct the valving error. At this point he walked into a nitrogen rich/oxygen deficient atmosphere.

11. A group of workers were routinely working at the in-feed end of a tunnel freezer. As the temperature of the tunnel was approaching the desired set point, a new operator noticed that there was a cloud of N_2 gas coming out at exit end of the freezer. He suddenly increased the speed of the scroll fan in order to remove the gas from exit to product entrance. The exhaust and scroll fans were running on manual mode. As a result, the N_2 cloud moved to product entrance and five workers who were working around the loading table passed out. Fortunately, there were no serious injuries and all of them returned to work after taking a rest.

12. On an ASU still in commissioning phase three painters from a sub-subcontractor were working on a ladder to complete external painting works on nitrogen/water tower. To complete the painting of top tower section a wooden plank was put across the exhaust section to atmosphere. One painter climbed on the plank, surrounded by the nitrogen stream, and fell off inside the tower. The two other painters rushed from the ladder to the plank to rescue their team mate. Both collapsed into the tower as well. The three painters died before they could be rescued.

13. An experienced contractor was used to purge a natural gas pipeline, 0.5m diameter 10 km long, with nitrogen before start-up. When one contractor employee and two customer employees entered the remotely located chamber, they were asphyxiated and later found dead in the chamber. Two blind flanges were leaking and the oxygen monitor was not used.

14. A customer nitrogen tank, volume 10 m^3, on a PSA plant was to be inspected by the competent body. The inspector entered the tank and lost consciousness immediately. Two persons from the gas company participating in the inspection managed to bring the inspector out without entering the tank. The inspector recovered.

15. A liquid CO_2 tank was installed. The tank should be purged with air but mistakenly the hose was connected to nitrogen. The tank manhole was situated 4 m above ground. For reasons unknown, a contract employee brought a ladder, entered the tank and was asphyxiated. Previously that morning employees had been told not to enter the tank before the atmosphere was officially checked.

16. Employee stepped into a control cubicle where the instrument air was temporarily replaced with N2 during shutdown. The green light outside the door was on indicating safe atmosphere. As soon as he stepped into the cubicle his personal O_2 monitor alarmed indicating 18% O_2 or less. After exiting safely he opened the door and when O_2 level was OK, checked the fan. The ventilation fan was not running. The light was wrongly wired.

17. The perlite in a storage tank under erection had to be emptied by a contractor company, familiar with this job. During this work one of the workers fell down in the perlite, depth approximately 3m, and was asphyxiated.

18. During the cleaning and painting maintenance of the internal and external surfaces of a water tank, one operator suffered anoxia due to nitrogen being used to purge the vessel instead of air. Two employees tried to rescue the victim and fainted. These two operators were rescued and transported to hospital for intensive care however the original operator died.

19. During the installation of a new LIN phase separator on LIN pipe work at a customer site, a technician went into the roof space. His personal oxygen-monitoring device began to alarm immediately, indicating low oxygen levels. The technician left the roof space immediately and informed the customer. Later in the same week, the customer owned food-freezing machinery was operating, and a project engineer measured concentrations far below 19% in the production room. He left the room, asked all subcontractors to stop work and leave the room, and informed the customer. Investigation showed that the customer had not connected the exhaust ducting to the food-freezing machine that they owned and installed. The exhaust pipes ended in the attic space, not being extended to the atmosphere. Customer had "bridged" the alarm/trip output so LIN supply would not be shut off by low O_2 concentrations.

20. An experienced site employee wanted to take some photographs to add to a report concerning production problems relating to problems with leaks in the argon condenser. In the control room he asked a Contractor to accompany him to take photographs of equipment in the cold box. One hour later the two men were found unconscious in a manhole access to the cold box. Emergency authorities were called and declared the two men dead.

21. Two people on a customer's site were asphyxiated and died whilst attempting to unblock a pipe, using Argon gas in a confined space. The use of Argon gas in this application is not authorised. The incident took place in a sump 2 metres below ground level, which is used to drain water from a nearby trench.

22. An air compressor that provided instrument air to an acetylene plant and for breathing air failed. A back-up nitrogen supply from a liquid cylinder was connected to the piping system to replace the function of the air compressor. An operator put on a full respiratory face mask to load Calcium Carbide into the hopper and inhaled nitrogen. He died.

Appendix D: Hazard of inert gases sign

DANGER OF DEATH

Potential Asphyxiating Atmosphere

Safety Bulletin

U.S. Chemical Safety and Hazard Investigation Board

HAZARDS OF NITROGEN ASPHYXIATION

No. 2003-10-B | June 2003

Introduction

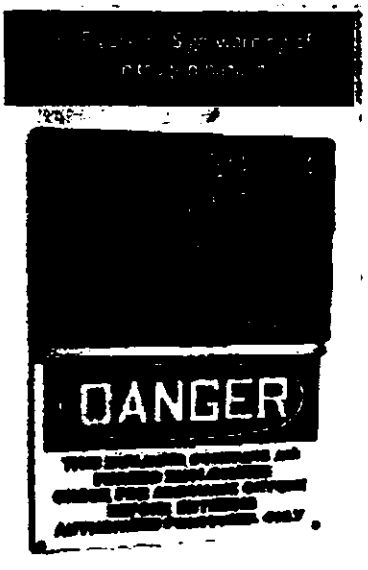
Every year people are killed by breathing "air" that contains too little oxygen. Because 78 percent of the air we breathe is nitrogen gas, many people assume that nitrogen is not harmful. However, *nitrogen is safe to breathe only when mixed with the appropriate amount of oxygen.*

These two gases cannot be detected by the sense of smell. A nitrogen-enriched environment, which depletes oxygen, can be detected only with special instruments. If the concentration of nitrogen is too high (and oxygen too low), the body becomes oxygen deprived and asphyxiation occurs.

This Safety Bulletin is published to bring additional attention to the continuing hazards of nitrogen asphyxiation.[1]

- Nitrogen is widely used commercially. It is often used to keep material free of contaminants (such as oxygen) that may corrode equipment, present a fire hazard, or be toxic.
- Nitrogen asphyxiation hazards in industry resulted in 80 deaths from 1992 to 2002. These incidents occurred in a variety of facilities, including industrial plants, laboratories, and medical facilities, almost half involved contractors.
- Good practices and awareness of hazards minimize the risk of nitrogen asphyxiation (Figure 1).

Many incidents reviewed by CSB were caused by inadequate knowledge of the hazard or inadvertent use of nitrogen rather than breathing-air delivery systems.



This bulletin focuses only on the hazard of asphyxiation, though nitrogen also presents cryogenic and high-pressure hazards.

Commercial Uses of Nitrogen

One of the most important commercial uses of nitrogen is as an inerting agent to improve safety. Nitrogen is inert under most conditions (i.e., it does not react with or affect other material).

It is often used to keep material free of contaminants, including oxygen—which can corrode equipment or present a fire and explosion hazard when in contact with flammable liquids or combustible solids. In such cases, a flow of nitrogen is maintained in a vessel to keep oxygen out. Nitrogen is also used to purge air from equipment prior to introducing material, or to purge flammable or toxic material prior to opening equipment for maintenance.

In industrial and commercial settings where a nitrogen-enriched environment may present a hazard, such as when using supplied air or working in or around spaces that are confined,

[1] In 1998, the U.S. Chemical Safety Board (CSB) investigated a nitrogen asphyxiation incident that occurred in Hahnville, Louisiana. As part of that investigation, CSB reviewed the prevalence of asphyxiation incidents.

precautions must be taken to ensure that sufficient oxygen is provided to personnel.

* Nitrogen is safe to breathe only when mixed with the appropriate amount of oxygen.

Effects of Oxygen-Deficient Atmosphere

Nitrogen is not a "poison" in the traditional sense. It presents a hazard when it displaces oxygen, making the atmosphere hazardous to humans. Breathing an oxygen-deficient atmosphere can have serious and immediate effects, including unconsciousness after only one or two breaths. The exposed person has no warning and cannot sense that the oxygen level is too low.

The Occupational Safety and Health Administration (OSHA) requires employers to maintain workplace oxygen at levels between 19.5 and 23.5 percent. As shown in the table on page 3, the human body is adversely affected by lower concentrations.

As the oxygen concentration falls below 16 percent, the brain sends commands to the breathing control center, causing the victim to breathe faster and deeper. As the oxygen level continues to decrease, full recovery is less certain. An atmosphere of only 4 to 6 percent oxygen causes the victim to fall into a coma in less than 40 seconds. Oxygen must be administered within minutes to offer a chance of survival. Even when a victim is rescued and resuscitated, he or she risks cardiac arrest.

* In industrial and commercial settings where a nitrogen-enriched environment may present a hazard, . . . precautions must be taken to ensure that there is sufficient oxygen in the atmosphere.

* Nitrogen . . . presents a hazard when it displaces oxygen.

Statistics on Nitrogen Asphyxiation

From reported data for the United States, CSB identified 85 nitrogen asphyxiation incidents that occurred in the workplace between 1992 and 2002. In these incidents, 80 people were killed and 50 were injured.[1]

Profile of Affected Industries and Activities

Of the 85 incidents reported, 62 percent occurred in chemical plants and refineries, food processing and storage facilities, metal and manufacturing operations, and other industrial, maritime, and manufacturing sites, including nuclear plants.

Approximately 13 percent of the incidents involved maintenance

[1] Data sources for the CSB review include regulatory agencies, media reports, technical publications, and contacts with safety personnel; however, only those incidents that were reported and accessible are represented. Although the summary data reported above are not all-inclusive, the numbers clearly indicate that nitrogen asphyxiation presents a serious hazard in the workplace. Statistical analysis is based on available, limited information.

CSB Safety Bulletins offer advisory information on good practices for managing chemical process hazards. Case studies provide supporting information. Safety Bulletins differ from CSB Investigation Reports in that they do not comprehensively review all the causes of an incident.

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Effects of Oxygen Deficiency on the Human Body

Atmospheric Oxygen Concentration (%)	Possible Results
20.9	Normal.
19.0	Some unnoticeable adverse physiological effects
16.0	Increased pulse and breathing rate, impaired thinking and attention, reduced coordination.
14.0	Abnormal fatigue upon exertion; emotional upset, faulty coordination, poor judgment.
12.5	Very poor judgment and coordination, impaired respiration that may cause permanent heart damage, nausea, and vomiting.
<10	Inability to move, loss of consciousness, convulsions, death

SOURCE: Compressed Gas Association, 2001.

* CSB identified 85 nitrogen asphyxiation incidents that occurred in the workplace between 1992 and 2002 . . . 80 people were killed and 50 were injured.

activities, such as railcar and tank truck cleaning, painting, maintenance, and repair. These incidents are categorized as "maintenance" because incident reports do not include enough information on the type of industrial setting; they could have occurred at manufacturing sites, which would increase the 62 percent estimate above.

Likewise, trenches and manholes—not specifically identified as being in manufacturing facilities—account for about 14 percent of the incidents. The remainder of the incidents occurred in laboratories and miscellaneous industries, such as medical and transportation.

The data show that employees and contractors alike are victims of asphyxiation. Of the 85 incidents reviewed, 42 involved contractors, including construction workers;

* Of the 85 incidents reviewed, 42 involved contractors, including construction workers; these 42 incidents account for over 60 percent of the fatalities.

* . . . 130 workplace fatalities and injuries occurred from breathing nitrogen-enriched air. Over 60 percent of these victims were working in or next to a confined space.

these 42 incidents account for over 60 percent of the fatalities.

Causal Information

From the CSB data, a combined total of 130 workplace fatalities and injuries occurred from breathing nitrogen-enriched air. Over 60 percent of these victims were working in or next to a confined space.[3,4]

One characteristic of a confined space is its capability to contain an atmosphere that may be totally different from outside air. Confined spaces in manufacturing sites typically include equipment such as reactors, vessels, tanks, and boilers. Other such spaces are railcars, trenches, and areas accessible by manholes.

[3] "Next to a confined space" means that a person's breathing zone is affected by the atmosphere emanating from the space. The person may be standing in the immediate area but not actually in the space.

[4] According to OSHA, a confined space can be entered to perform work, has limited means of egress, and is not designed for continuous employee occupancy. A "permit-required confined space" includes a space that contains or has the potential to contain a serious safety or health hazard, such as a hazardous atmosphere.

Failure to Detect Oxygen-Deficient Atmosphere

Failure to detect an oxygen-deficient (nitrogen-enriched) atmosphere was a significant factor in several incidents.

In the data evaluated for this study, 67 of the 85 incidents involved circumstances where personnel were in or around a confined area—such as a railcar, room, process vessel, or tank (Figure 2)—and nitrogen was initially present in high levels or later collected in the area. These incidents accounted for 62 fatalities and 33 injuries. In each of the 67 incidents, personnel failed to detect elevated levels of nitrogen and take appropriate precautions.

When fatalities and injuries occurred in "open areas" (including areas with ventilation, laboratories, buildings, and outside in the vicinity of equipment), the hazard of asphyxiation was not expected and personnel were typically caught off guard. In some cases, personnel unknowingly created a nitrogen-enriched atmosphere by mistakenly using nitrogen instead of air to flush equipment prior to entry. In either situation, inadequate knowledge of the hazard and failure to detect additional nitrogen resulted in a fatal concentration of gas.

* When fatalities and injuries occurred in "open areas" . . . the hazard of asphyxiation was not expected and personnel were typically caught off guard.

Mix-Up of Nitrogen and Breathing Air

Confusing nitrogen gas with air and problems with breathing-air delivery systems accounted for 12 of the 85 incidents, and approximately 20 percent of fatalities.

The data provide examples of workers inadvertently using nitrogen instead of air because of interchangeable couplings on lines and poor or nonexistent labeling.

In one incident, a worker mistakenly used nitrogen instead of air to purge a confined space. An inert atmosphere was unexpected and undetected. One worker was killed, and a colleague also died while attempting rescue. In another case, workers inadvertently connected the hose for their breathing-air respirator to a pure nitrogen line.

* In one incident, a worker mistakenly used nitrogen instead of air to purge a confined space . . . In another case, workers inadvertently connected the hose for their breathing-air respirator to a pure nitrogen line.

Fatalities and Injuries During Attempted Rescue

One of the most difficult issues concerning hazardous atmosphere emergencies is the human instinct to aid someone in distress. Approximately 10 percent of fatalities from the CSB data were due to attempts to rescue injured persons in confined spaces.

* Approximately 10 percent of fatalities from the CSB data were due to attempts to rescue injured persons in confined spaces.

Asphyxiation Hazards Outside Industry and Effect on General Public

Asphyxiation hazards may also be present outside industry, especially among people who use breathing air, such as firefighters, divers, and medical patients. Statistics on these types of incidents are difficult to collect and are not included in this bulletin, though one such case is summarized below.

Selected Case Studies

Failure to Recognize Asphyxiation Hazards Near Confined Spaces

Employee Dies After Partially Entering a Nitrogen-Purged Tank

Two coworkers and the victim were cleaning filters in a hydrogen purifying tank. The tank was partly purged with nitrogen to remove internal dust particles. The victim used a lift to access the *external* area of the upper tank, which was fitted with a manway. As he leaned into the tank opening, his coworkers noticed that he was not responding to their communication. They found the victim unconscious, and he later died as a result of oxygen deficiency.

Employee Overcome While Testing Atmosphere

An operator was conducting a flammable gas test on a tower feedline that discharged into a low-pressure flare gas header. The test was required for a hot work permit to take flash photos.

The chief operator issued a work permit that required a supplied-air respirator. Two contractor pipefitters wore respirators and removed the safety valve. The operator, however, wore no respiratory protection. After climbing the scaffold, he was overcome by nitrogen gas from the open flare line before he could complete atmospheric sampling.

The operator backed away, turned, and slumped to his knees. He was disoriented and briefly lost consciousness. An investigation concluded that the incident was due to elevated levels of nitrogen gas that had inadvertently entered the flare system.

Inadequate Monitoring of Atmosphere

Contractor Asphyxiated Inside Tank Car

White mineral oil in a tank car at an oil refinery was offloaded by injecting nitrogen gas into the car. An employee of a railcar cleaning company was asphyxiated while cleaning the nitrogen-filled tank car.

Corrupt Breathing Air Supply

Two Laborers/Painting Contractors Asphyxiated

Two painting contractors were abrasive-blasting tubes inside a boiler at a chemical plant. They each wore supplied-air respirators connected to a 12-pack cluster of compressed air cylinders. Another subcontractor monitored the work outside the confined space.

Work proceeded normally throughout the night shift; however, at 3:00 am, the attendant got no response after repeatedly sounding the air horn. When another contractor employee was sent into the boiler to assess the situation, he found the two men lying on opposite ends of the scaffolding.

When the plant health, safety, and environmental department tested the compressed air 12-pack, they found that it contained less than 5 percent oxygen. The "air" had been manufactured with too low a

concentration of oxygen. (Note: This fatal incident prompted OSHA to issue a safety alert on the batch of breathing air.)

Mix-Ups Between Nitrogen and Air

Three Employees Asphyxiated In Coating Tank

The atmosphere inside a coating tank was tested and ventilated the day before work was to be performed. On the following day, a contractor entered the tank to clean it and collapsed. Two plant employees entered to attempt rescue, but they were also overcome.

The tank had been ventilated with what was thought to be compressed air but was actually nitrogen. The atmosphere was not tested prior to beginning work. All three men were asphyxiated.

Employee Killed by Overexposure to Pure Nitrogen

A contractor planned to use an air-powered hammer to chip residue from a furnace in an aluminum foundry. He wore an airline respirator. Of two compressed gas lines with fittings, one was labeled "natural gas" and the other had an old paper tag attached with "air" handwritten on it. However, this line actually contained pure nitrogen.

A splitter diverted one part of the gas stream to the air hammer and the other part to the airline respirator. Once the respirator was in place, the worker breathed pure nitrogen and was asphyxiated.

Four Killed and Six Injured in Nursing Home

A nursing home routinely ordered large pure oxygen compressed gas cylinders for residents with respiratory system diseases. The supplier mistakenly delivered one cylinder of pure nitrogen with three cylinders of oxygen; a nursing home maintenance employee mistakenly accepted the nitrogen tank.

Another maintenance employee took this cylinder, which had a nitrogen label partially covering an oxygen label, to connect it to the oxygen supply system. The tank was fitted with nitrogen-compatible couplings. The employee removed a fitting from an empty oxygen cylinder and used it as an adapter to connect the nitrogen tank to the oxygen system. Four deaths and six injuries occurred as a result of pure nitrogen being delivered to the patients.

Good Practices for Safe Handling of Nitrogen

Implement Warning Systems and Continuous Atmospheric Monitoring of Enclosures

The atmosphere in a confined space or small enclosed area may be unfit for breathing prior to entry, or it may change over time, depending on the type of equipment or work being performed. Recognizing this hazard, good practice calls for continuous monitoring of a confined space to detect oxygen-deficient, toxic, or explosive atmospheres. The entire confined space should be monitored — not just the entry portal.

* The atmosphere in a confined space or small enclosed area may be unfit for breathing prior to entry, or it may change over time . . .

Warning and protection systems include flashing lights, audible alarms, and auto-locking entryways to prevent access. Such devices, if properly installed and

maintained, warn workers of hazardous atmospheres. Personal monitors can measure oxygen concentration and give an audible or vibration alarm for low oxygen concentrations.

* Good practice calls for continuous monitoring of a confined space to detect oxygen-deficient, toxic, or explosive atmospheres.

Ensure Ventilation With Fresh Air

Because the atmosphere of a confined space or small/enclosed area often changes during the course of work, it is essential to maintain continuous forced draft fresh-air ventilation before the job begins through to completion. Areas with the potential to contain elevated levels of nitrogen gas should be continuously ventilated prior to and during the course of the job.

Ventilation is also required in rooms and chambers into which nitrogen may leak or vent. In a few of the study cases, people who were simply working close to the nitrogen-containing confined space, room, or enclosure were asphyxiated.

Systems must be in place to properly design, evaluate, and maintain ventilation systems. A warning system will alert workers of a dangerous atmosphere. Personnel should be trained on how to properly respond and evacuate in the event of failure of the system.

Implement System for Safe Rescue of Workers

Rescue may be necessary in the event of continuous monitoring, ventilation failure, or another emergency condition. The ability to immediately retrieve immobilized workers is a critical component of confined space entry preplanning.

* It is essential to maintain continuous forced draft fresh-air ventilation before the job begins through to completion.

One method is to attach a body harness and lifeline to personnel entering confined areas. This procedure also benefits potential rescuers because they do not have to enter the confined area to retrieve the victim. However, when a worker enters a pipeline, some furnaces, ducts, or other narrow-diameter confined spaces, pulling on a line attached to a body harness may cause the person to bunch up and become stuck inside.

Depending on the situation, wristlets or anklets attached to a lifeline and a retrieval mechanism allow the confined space attendant to pull the person out by the arms or legs. The attendant and rescue personnel should be available at all times. Rescuers must have an effective system to communicate with personnel inside enclosures. No one should enter a dangerous atmosphere without proper personal protective equipment.

The last measure of defense requires personnel to actually enter the confined area to retrieve the victim. This approach should be used only when personnel are appropriately trained, have donned rescue equipment, and have dependable breathing air.

Approximately 10 percent of fatalities from the survey data occurred to personnel attempting rescue. These deaths could have been prevented if a reliable retrieval system was in place. Such a system would also prevent many entry worker fatalities because it provides for quickly removing the worker from a dangerous atmosphere to a safe one.

Ensure Uninterrupted Flow and Integrity of Breathing Air

Breathing air must be supplied when workers enter environments where oxygen is or may become deficient. Workers may use either a self-contained breathing apparatus (SCBA) or an airline respirator, which consists of a long hose connecting a breathing air supply to the respirator or hood.

Because a worker using an airline respirator does not control the

* Breathing air must be supplied when workers enter environments where oxygen is or may become deficient.

source of supply, air may suddenly or inadvertently be interrupted. For example, a power failure may stop an air compressor, the air supply may simply run out, or the supply hose may become twisted or obstructed (e.g., by a vehicle). When supplied air is used, facility management systems must protect against interruption of airflow and provide alternate sources of power for the compressors.

A comprehensive management system includes the following:

- Continuous monitoring of air supply.
- Routine inspection and replacement of supplied-air hoses.
- Restriction of vehicular traffic in the area of supply hoses.

When using supplied air, a worker should carry a small backup cylinder (escape pack)—attached to a different supplied-air system—with enough breathing air to last 5 to 10 minutes.

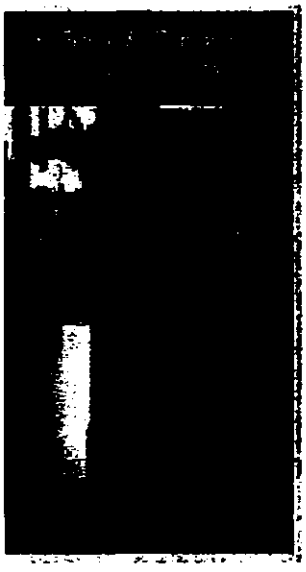
Breathing air is manufactured either by purifying and compressing air or by mixing nitrogen and oxygen to the appropriate ratio. A breathing-air compressor and its hoses should be specifically manufactured for and dedicated to breathing-air systems. The compressor should have a moisture trap, an oil trap, and a carbon monoxide sensor and alarm. When breathing air is manufactured by mixing nitrogen and oxygen, the pressure of the cylinders during filling must be known to ensure that the correct amounts are mixed. The final product must be tested to ensure its integrity.

Prevent Inadvertent Mix-Up of Nitrogen and Breathing Air

To prevent interchanging compressed nitrogen with compressed industrial grade air or compressed breathing-quality air, specific fittings should be used for each cylinder. Cylinders for nitrogen, industrial grade air, and breathing-quality air have distinct, incompatible fittings that cannot be cross-connected.

* Personnel should understand that the fittings are *intended* to be incompatible to ensure safety.

Personnel should understand that the fittings are *intended* to be incompatible to ensure safety. Cylinders should be clearly labeled; typical cylinders are shown in Figure 3. Labels on piping systems, compressors, and



fittings are additional reminders of which gas is contained inside. Color coding also helps to identify systems.

Develop and Implement Comprehensive Training Programs

The good practices for safe handling of nitrogen, described above, are effective only if personnel are trained on the importance of the following:

- Use of ventilation systems, retrieval systems, and atmospheric monitoring equipment—both how to use them and how to determine when they are not working properly.
- Dangers of nitrogen-enriched atmospheres and the systems to

prevent interchanging breathing air and nitrogen.

- Implementing good hazard communication, which includes safe handling of air and nitrogen delivery systems.
- Mandatory safety practices and procedures for entry into confined spaces, such as permits, providing an attendant, monitoring, ventilating, rescue, and contractor oversight.
- Precautions when working around equipment that may contain elevated levels of nitrogen.
- The reason for special fittings on compressed gas cylinders.
- Proper use of air supply equipment.

Training should cover new and revised procedures for confined space entry, and establish measurements for employee proficiency. Contractors as well as employees should be trained.

* Contractors as well as employees should be trained.

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Experimental hypoxic brain damage

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The majority of hypoxic episodes that result in histologically proven damage in the human brain cannot be adequately defined in physiological terms. They are usually accidents so that basic information such as the precise duration of a cardiac arrest or the blood pressure and heart rate during a period of severe hypotension is very rarely available. In such cases, neuropathological descriptions, however exhaustive, may well explain the final neuropsychiatric status of the patient but can at best indicate only tentatively the nature of the episode itself.

The experimental approach is justified if it can indicate whether damage of a particular type in neurones and in white matter is or is not a direct consequence of a particular hypoxic stress adequately delineated in physiological terms.

At the outset it must be recalled that the energy for the normal functioning of the central nervous system is derived from the oxidative metabolism of glucose. A deficiency of oxygen or glucose will impair function and if severe and protracted enough will lead to irreversible brain damage. Interruption of the oxygen supply produces the most rapid impairment of brain function. Thus consciousness is lost about 10 sec after circulatory arrest. Abrupt anoxia exemplified by inhalation of an inert gas or sudden decompression to an altitude above 50 000 ft leads to loss of consciousness after a slightly longer interval (17-20 sec). This rapid loss of consciousness in instances of profound hypoxia may well be responsible for the widely held view that enduring brain damage may begin soon after consciousness is lost.

Types of hypoxia

Before considering the relationships between the known neuropathological patterns in the human brain that are ascribed to hypoxia and their apparent counterparts in the brains of experimental animals, it will be useful to classify the several types of hypoxia. However, it will be shown that there is no justification for the assumption that each type of hypoxia can, *per se*, give rise to brain damage. The original classification of Barcroft (1925) must be modified in the light of subsequent information from human and experimental animals sources as follows:

1 ISCHAEMIC
Blood flow is arrested in the brain as a whole or in the territory of a single artery.

2 OLIGAEMIC
A reduction in blood flow in the brain as a whole or within the territory of a single artery may occur as a result of a greatly reduced cardiac output or major systemic hypotension from any cause.

3 ANOXIC
The arterial oxygen tension is 0 mm Hg. It occurs if inert gases are inhaled, if there is total obstruction of the upper respiratory tract or in the event of sudden exposure to an altitude greater than 50 000 ft (the combined tensions of water vapour and carbon dioxide within the pulmonary alveoli then exceed the ambient pressure and no oxygen can enter the lungs).

4 HYPOXIC
There is some reduction in a pO_2 short of anoxaemia. This occurs in chronic pulmonary disease and in congestive heart disease; when the inspired oxygen is diluted by an inert gas (as in some anaesthetic accidents) and also in exposures to altitudes less than 50000 ft.

5 ANAEMIC
There is some reduction in the amount of circulating haemoglobin available for combination with oxygen. It can occur after severe haemorrhage, in severe hypochromic anaemia but the commonest apparent cause of anaemic brain damage is carbon monoxide intoxication.

6 HISTOTOXIC
This implies the poisoning of oxidative enzymes within neuronal mitochondria. Cyanide and azide are examples.

7 HYPOGLYCAEMIA
A deficiency of the principal substrate, glucose, *per*

se can also give rise to ischaemic cell change even if the level of arterial oxygenation is normal.

The previous contributors to this section of the Symposium have defined the nature and time course of ischaemic cell change and have pointed out that it is the principal neuronal response to all types of hypoxia in the brains of rodents as well as in those of primates including man. In this survey of the brain damage attributable to hypoxia in all its forms, only the patterns of distribution of ischaemic cell change will be considered with emphasis on the contributions from experimental studies.

1 Ischaemic

Arrest of circulation within a single brain artery results in an infarct which can range in size from the 'total territory' in an anatomical sense to a small volume of tissue close to the point of arterial occlusion. Where the cortex of cerebrum or cerebellum is concerned the extent of infarction is determined by the level of systemic blood pressure at and after the instant of occlusion and, in particular, by the functional efficiency of the leptomeningeal vessels that anastomose with the cortical branches of neighbouring arteries. If these anastomotic systems and the major arteries in the neck and the circle of Willis are normal, the cortical infarct will be small. If one or both are the site of occlusive vascular disease, the infarct will be larger.

It must be borne in mind that the basal ganglia and the internal capsule, in particular, are supplied by end-arteries (penetrating or ganglionic branches of the major cerebral arteries). Occlusion of an arterial trunk proximal to the ganglionic branches produces an infarct in these deeply placed regions of grey and white matter even in the healthy experimental primate. Evidently the retrograde flow of blood from leptomeningeal anastomoses into the arterial stem may never enter all its ganglionic branches or, if it does so, it may be too little and too late to avert irreversible tissue damage. Thus, for example, division of the middle cerebral artery close to its origin from the internal carotid artery in the baboon leaves the sensory and motor cortex intact and cortical infarction is confined to some portion of the insula. A variable hemiparesis involves only the contralateral face and upper limb and its neuropathological basis has been shown to lie entirely within white matter, ie, in the genu and supralentiform portions of the internal capsule, where after a survival of three years there is a sharply circumscribed cystic infarct (Symon and Brierley, 1976). The limited neurological deficit and the small, deeply placed infarct that follow division of the middle cerebral artery in a healthy experimental primate are sharp reminders that such 'models' cannot provide two of the most important factors in the aetiology of 'stroke' in man. These are some impairment in cardiac function (leading to some reduction in cerebral blood flow) and some degree of occlusive vascular disease. These factors, singly or together, account for the extension of the infarct into the centrum semi-ovale and even into the whole of the anatomical cortical territory. It follows, that in the human brain, ischaemic necrosis in some portion of an arterial territory can seldom be explained satisfactorily without careful examination of the myocardium, the coronary arteries and the major arteries of the neck and brain.

Overall or global arrest of the brain circulation leads to a loss of consciousness in eight to 10 sec and the EEG is isoelectric a few seconds later. Respiration fails at about the same time while the heart may continue to beat for a matter of minutes. Neuropathological descriptions of the consequences of circulatory arrest (including 35 personal cases) provide the best examples of the involvement of the 'selectively vulnerable' regions of the brain in hypoxia. Frequently, little of the cerebral cortex is normal but damage is usually greater in the posterior half of each cerebral hemisphere, in the floors of sulci rather than over the crests of gyri and in the third, fifth and sixth layers rather than in the second and fourth. Certain portions of the hippocampus (zones h.1—Sommer sector—and h.3-5,—endfolium) are vulnerable as are the Purkinje cells of the cerebellum. Many sensory nuclei in the brain stem are vulnerable in the infant and young child (Ranck and Windle, 1959; Brierley, 1965, 1976).

Where circulatory arrest has been studied in the experimental animal, it is important to recognize that earlier studies were concerned to define the maximum period of arrest of the cerebral circulation beyond which some degree of irreversible brain damage would occur. Attempts to define such a 'threshold' have been reviewed by Hoff *et al* (1945), Meyer (1963) and Brierley (1976). The general conclusion from these studies has been stated by Schneider (1963) as follows: 'A complete revival without neurological or histological damage cannot be brought about after a complete stop of brain circulation of more than four to five min duration'.

In contrast to the experiments summarized above, certain recent studies have attempted to define a much greater period of circulatory arrest after which there can be some evidence of recovery in at least a neurophysiological sense and histological examination can show that some parts of the brain are normal. Thus Hossmann and Sato (1970) claimed that '... unequivocal signs of neuronal recovery can be detected after complete ischaemia of more than one

hour's duration'. Hirsch *et al* (1975) failed to confirm these results and attributed 'recovery' after such protracted ischaemia in the experiments of Hoesmann and Sato (1970 and subsequent studies) to the protective effects of anaesthesia and the progressive fall in temperature that must occur in the isolated head during such periods of time.

It must be emphasized that experimental studies of the effects of circulatory arrest (or any other form of hypoxia) on the brain, whether directed towards the definition of a 'threshold' for a particular hypoxic stress or to the capacity for recovery after an extended period of the same stress, have clinical relevance only if spontaneous respiration has been resumed in the unmedicated animal, and detailed neurological assessments, together with serial recordings of the EEG, have been made during an adequate period of survival. All these are essential for a meaningful appraisal of 'recovery'. Finally, after *in-vivo* perfusion-fixation of the brain, neuropathological examination of the brain must be comprehensive. Unfortunately clinico-pathological studies according to such standards have not yet been reported in support of the claim that 'recovery' of the central nervous system can occur after periods of circulatory arrest far in excess of those hitherto accepted as 'critical' where the inception of minimal brain damage is concerned.

2 Oligaemic hypoxia

A reduction of blood flow in a single artery of the human brain is usually due to a combination of systemic hypotension and occlusive disease in the vessel itself. If flow is sufficiently impaired the outcome will be an infarct involving grey and white matter. Such a local reduction in flow can only be inferred if thrombosis and embolism can be excluded. There are, as yet, no experimental models of this particular situation.

Global oligaemia implies some reduction in the overall flow of blood through the brain. Experimental studies in the Rhesus monkey have shown that, if arterial oxygenation remains normal, cerebral perfusion pressure (mean arterial blood pressure – venous sinus pressure) must be reduced to 25 mm Hg for at least 15 min before brain damage is produced (Brierley *et al*, 1969; Meldrum and Brierley, 1969). However, it was only possible to damage the brain if the profound hypotension was continued beyond the point of apnoea when mechanical ventilation was required in order to maintain a normal arterial oxygen tension. These experiments clearly demonstrated that in the healthy spontaneously breathing primate, global oligaemia *per se* is unlikely to lead to brain damage if respiration does not fail. In these monkeys, typical ischaemic neuronal alterations were not evenly distributed in the cerebral cortex but were restricted to the arterial boundary zones of the cortex of the cerebrum and also of the cerebellum. They were variable in the basal ganglia. The pysiological basis of lesions along arterial boundary zones has been discussed by Zülch and Behrend (1961) and by Meldrum and Brierley (1971). When perfusion pressure falls below 45-50 mm Hg the capacity of the vascular bed to maintain a constant cerebral blood flow (autoregulation) is lost (there is then maximum vasodilatation) and flow becomes directly dependent upon perfusion pressure. The reduction in flow is greatest in the vessels most remote from the arterial stem, ie, at the boundary of each arterial territory.

In the clinical situation, a reduction in brain perfusion pressure while arterial oxygenation remains normal is virtually confined to the technique of hypotensive anaesthesia with controlled ventilation and then only when perfusion pressure through the brain is lowered by excessive head-up tilt (Brierley and Cooper, 1962). The two additional factors that may result in brain damage after a period of relatively moderate hypotension are some degree of hypoxaemia and some element of occlusive disease in the extra- and/or intracranial arteries. The frequency of these two factors in addition to the reduction in brain blood flow due to the initial systemic hypotension is largely responsible for the fact that ischaemic damage along arterial boundary zones of the cortex of cerebrum and cerebellum is the commonest neuropathological outcome of hypoxia in all its forms. It is important to appreciate that no experimental model permitting the introduction and control of oligaemia, hypoxaemia and partial vascular occlusion is yet available.

Previous contributors to this section of the Symposium have emphasized that this 'boundary zone' pattern of brain damage can only be identified if blocks for histological examination are selected with an awareness of the anatomical distribution of the cortical arteries of cerebrum and cerebellum.

3 Anoxic

Anoxia, induced by breathing pure nitrogen, has been studied in human volunteers by Gastaut *et al* (1961) and Ernsting (1963). After a few seconds the EEG shows low voltage activity at 11 to 13 c/s and consciousness is lost at 17 to 20 sec. In experimental animals, longer periods of nitrogen breathing lead, after an initial hyperventilation, to slowing of respiration, bradycardia and a falling blood pressure. Apnoea occurs at about the third minute while blood pressure is still appreciable (5-20 mm Hg) at

the fifth minute (Swann and Brucer, 1949). In the Rhesus monkey, the responses to nitrogen breathing are similar and if mechanical ventilation is begun soon after the 'last breath', the blood pressure rises, spontaneous respiration is resumed and the EEG, previously isoelectric, returns to normal. Subsequent neuropathological examination reveals no brain damage (Brierley and Meldrum, unpublished observations). Evidently the period of anoxaemia and of secondary circulatory impairment is too brief to lead to ischaemic neuronal alterations so that it must be concluded that pure anoxic anoxia cannot produce brain damage.

4 Hypoxic

In spontaneously breathing experimental animals, including primates, the minimal level of arterial oxygen tension that does not lead to early apnoea and cardiac failure is about 20 mm Hg. At this level the cerebral vascular bed is fully dilated, the cerebral A-V oxygen difference is reduced (due to reduced oxygen consumption and increased blood flow) but the EEG is normal. This precarious state can be disturbed by a slight fall in perfusion pressure and the immediate decline in the EEG is evidence of some reduction in cerebral blood flow. This may occur as a consequence of a period of cardiac arrhythmia. A progressive fall in heart rate and blood pressure together with slowing of respiration herald the cardio-respiratory crisis that sets the limit to the period during which the organism can tolerate this level of hypoxia. Where the circulatory failure is concerned the final bradycardia and falling blood pressure may not be a direct effect of hypoxia on the myocardium but a consequence of the stimulation of chemoreceptors in the carotid bodies or brain stem (Cross *et al*, 1963). As blood pressure continues to fall respiration ceases and the EEG becomes isoelectric at about the same time. Adequate resuscitation commenced soon after the 'last breath' can, as after anoxic anoxia, allow the heart to recover, spontaneous respiration to be resumed and the EEG to return to normal. Brain damage is rarely seen and only when there has been a prolonged period of cardiac impairment and an even longer period of isoelectric EEG (Brierley, Prior, Calverley, and Brown—unpublished results). Brain damage in such animals consists of ischaemic neuronal alterations along the arterial boundary zones of the cerebrum and cerebellum and sometimes in the basal ganglia. This pattern of damage, indistinguishable from that seen after oligaemic hypoxia, underlines the fact that systemic hypoxaemia can only bring about brain damage through the medium of a secondary reduction in perfusion pressure.

In the human subject exposed to hypoxia not severe enough to bring about failure of respiration and the heart, the initial increase in cerebral blood flow may be so restricted by occlusive vascular disease in the arteries of the brain and/or neck that ischaemic brain damage may ensue.

5 Anaemic

There is no convincing evidence that a simple reduction in circulating haemoglobin due to severe hypochromic anaemia (iron-deficient or haemolytic) or to haemorrhage can result in brain damage. Carbon monoxide intoxication remains the sole example of anaemic hypoxia (due to the formation of stable carboxyhaemoglobin) that can be associated with ischaemic cell change and also with damage in white matter. The pathology in the human brain has been reviewed by Meyer (1963), Lapresle and Fardeau (1966) and Brierley (1976). Ischaemic alterations may be seen in the vulnerable regions of the cortex of cerebrum and cerebellum and of the hippocampus. Necrosis in the globus pallidus is not invariable (Meyer, 1928; Lapresle and Fardeau, 1967) and damage in white matter varies considerably.

The presence of some element of perfusion failure in the genesis of, at least, the cortical damage was suggested by the report of Poursines *et al* (1956). A woman, aged 33 years, lived 26 days after attempted suicide with illuminating gas. In her brain, laminar necrosis was distributed along arterial boundary zones but information concerning respiratory and cardiac functions early in the survival period was lacking. The case of Neubuerger and Clarke (1945), dying 13 days after carbon monoxide poisoning, exhibited patchy myocardial infarction suggesting a direct effect of carbon monoxide on the myocardium.

Among experimental studies, that of Lewey and Drabkin (1944) in the dog was important because, after intermittent exposures to carbon monoxide for up to 11 weeks the electrocardiograms were abnormal and the brain damage was considered to be similar to that seen in man but was not described in detail. Further details of electrocardiographic abnormalities were presented by Ehrich *et al* (1944). Recently Ginsberg *et al* (1974) exposed 19 Rhesus monkeys to 0·2 or 0·3 per cent carbon monoxide for 60 to 325 min with a carboxyhaemoglobin level of 72 to 77 per cent throughout. Cardiac arrhythmias and some degree of hypotension were common but the EEG was only intermittently isoelectric. Grey matter damage (globus pallidus and hippocampus) was seen in less than a fifth of the brains while white matter was abnormal in the majority. Apparently the degree of intoxication was not sufficient to produce the

more extensive grey matter damage so often seen in the human brain.

Further confirmation of a direct effect of carbon monoxide on the heart was provided by Hodjati *et al* (1976) who irrigated the cerebral circulation of one dog from one carotid artery of a donor animal. A mean carboxyhaemoglobin level of 52 per cent in the donor animal led to bradycardia, hypotension and its death in 10 to 15 min. All the recipients survived.

6 Histotoxic

Cyanide, the best known cause of histotoxic hypoxia, acts by inhibiting cytochrome oxidase in mitochondria while the oxygen tension and content of arterial blood remain normal. The few human cases with delayed death and evidence of brain damage have been reviewed by Brierley (1976). There was loss of neurones in cerebral cortex and cerebellum and a single case showed haemorrhagic necrosis in each globus pallidus. Hyperaemia and haemorrhages occurred in white matter.

Numerous experimental studies have suggested that cyanide, in any form and administered by any route, can damage neurones and myelin sheaths. In the first experimental study (Meyer, 1933) subcutaneous injections of potassium cyanide in dogs and rabbits produced typical ischaemic alterations in cerebral cortex, globus pallidus, hippocampus and cerebellum. White matter damage was most marked in the corpus callosum. Subsequent studies were more concerned with white matter damage because of its apparent similarity to the plaques of multiple sclerosis. However, the report of Levine and Stypulkowski (1959) was noteworthy because it suggested that grey matter damage in the rat brain after the administration of cyanide was largely due to concomitant ischaemia and hypoxic hypoxia. Brierley *et al* (1976) gave sodium cyanide to rats by intravenous infusion. There was full physiological monitoring in an anaesthetized group and restricted monitoring in the unanaesthetized remainder. White matter, particularly the corpus callosum, was damaged in six of 19 animals and grey matter additionally in only one. In the latter animal bradycardia, epileptic seizures and hypotension were particularly marked and it was concluded that the neuronal damage was brought about through the medium of the secondary effects of cyanide on the circulation. In a recent study in *M mulatta* (Brierley *et al*, 1977) sodium cyanide was given by intravenous infusion. The effects of the infusion on respiration, heart rate, blood pressure, blood gases and the EEG were monitored in the lightly anaesthetized animals. Brain damage was seen in four of 11 animals. It involved white matter in all four but ischaemic cell change was restricted to the striatum of a single animal. In the latter there had been a period of bradycardia, hypotension and raised central venous pressure. It was concluded that in the lightly anaesthetized and spontaneously breathing Rhesus monkey, as in the rat, there is no evidence for the entity of hypoxic neuronal damage of purely histotoxic type.

7 Hypoglycaemia

Hypoglycaemic damage in the human brain is usually associated with irreversible coma and Meyer (1963) stated that the neuropathological findings '. . . closely resemble those which occur in other types of anoxia'. Most of the selectively vulnerable regions may be involved but with a tendency to spare the globus pallidus and cerebellum. Although hypoglycaemic coma may be associated with cardiovascular disturbances and epileptic seizures the ability of hypoglycaemia *per se* to produce ischaemic damage in physiologically monitored experimental primates has been demonstrated only recently.

Kahn and Myers (1971) and Myers and Kahn (1971) studied the long-term effects of insulin-induced hypoglycaemia in Rhesus monkeys. Blood glucose fell to 20 mg/100 ml after one and a half to three h and was maintained at this level for four to 10 h with normal blood oxygenation. In seven of 11 animals there was neuronal loss with a gliomesodermal reaction in striatum, cerebral cortex and hippocampus.

In order to define the earliest neuronal alterations due to insulin-induced hypoglycaemia, lightly anaesthetized Rhesus monkeys received insulin intravenously while EEG, EKG, heart and respiratory rates were recorded and blood gas tensions, pH and glucose content were measured at intervals (Meldrum *et al*, 1971). When blood glucose was below 20 mg/100 ml for more than two h and the brains were fixed by perfusion, typical ischaemic cell change (from the stage of microvacuolation) was seen in the cortex and occasionally in striatum, hippocampus and cerebellum. Thus a major deficiency in substrate alone can produce the same type of neuronal damage as a deficiency of oxygen.

Conclusion

It will be evident from this brief review that ischaemic cell change is the cytopathological common denominator in all types of hypoxia. Nevertheless there is no pattern of its distribution specific for each category with the exception of circulatory arrest (global ischaemia) and pure hypoglycaemia after both of which ischaemic neuronal alterations may occur

uniformly within the 'selectively vulnerable' regions of the brain. In the remaining categories of hypoxia, ie, oligaemic, anoxic, hypoxic, histotoxic and probably anaemic (carbon monoxide), an initially pure hypoxic stress in the intact and spontaneously breathing animal gives rise, sooner or later, to terminal secondary impairments of respiration and particularly of circulation. In the healthy experimental animal, however, it is only rarely that the associated period of reduced cerebral blood flow is long enough to cause brain damage but not too long to preclude recovery. In such instances, brain damage consists of a concentration of ischaemic cell change along the arterial boundary zones.

Experimental studies have shown that the terminal hypoxic cardio-respiratory deterioration or crisis consists of a slowing of respiration to the point of apnoea with a fall in blood pressure and in heart rate (but the heart may continue to beat long after the 'last breath'). There is a more or less parallel decline in EEG background activity and an isoelectric state is reached at about the time of the 'last breath'. There is no evidence to suggest that systemic hypoxia of any type can lead to brain damage unless the EEG has been isoelectric for an appreciable period. In the paralyzed and mechanically ventilated animal exposed to systemic hypoxia, initial hyperventilation as well as the 'last breath' cannot occur and the duration of hypoxia may be considerably prolonged. For this reason 'thresholds' for brain damage defined in such preparations must be applied with considerable caution to the spontaneously breathing experimental animal and to man.

There is now ample evidence to show that in the intact healthy, and spontaneously breathing animal tolerance to hypoxia is limited by the respiratory and circulatory systems and not by the intrinsic energy reserves of the brain itself. If effective resuscitation is begun soon after the 'last breath' the EEG will return and the brain will be undamaged. Thus a depression of central nervous system function up to and some time after the 'last breath' and the appearance of transiently isoelectric EEG need have no structural consequences.

The relative frequency of all degrees of ischaemic damage in the human brain after hypoxic episodes does not, however, necessarily imply a greater susceptibility of the brain itself. The existence of a single type of hypoxia in human patients is rare. It should be stressed that several types of hypoxia, each constituting a relatively mild stress can, in combination, produce brain damage. The additional factors most probably responsible for the increased extent and frequency of brain damage in man are twofold. Preexisting cardiac disease will impair the capacity to maintain a high level of blood flow through a cerebral vascular bed initially fully dilated by hypoxia. It will also impair the rapid restoration of normal cerebral blood flow after any terminal cardio-respiratory crisis. Secondly, preexisting occlusive disease in the arteries of brain and neck and any impairment of the normal reactivity of the smaller cerebral vessels will further reduce cerebral blood flow during and after hypoxia.

In conclusion, experiments in physiologically monitored, spontaneously breathing animals can show that hypoxia gives rise to an integrated series of responses in the respiratory and circulatory systems and in the nervous system itself. Initially these serve to maintain brain function and respiration in particular. Ultimately these compensatory cardio-respiratory responses may fail. Experiments have also shown that where the human brain is concerned the commonest cause of damage must be sought in some failure of brain perfusion.

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THE EFFECT OF BRIEF PROFOUND HYPOXIA UPON THE ARTERIAL AND VENOUS OXYGEN TENSIONS IN MAN

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The partial pressure of oxygen in the alveolar gas may be reduced either by decreasing the total pressure of the environment or by replacing the oxygen normally present in the inspired air by an inert gas. The severe anoxia induced by rapid decompression from 565 to 155 mm Hg absolute, whilst breathing air, may be terminated by the delivery of 100% oxygen to the respiratory tract. The effects of such brief profound anoxia upon the alveolar and arterial gas tensions and upon the central nervous system have been studied extensively (Ernsting & McHardy, 1963; Ernsting, Gedye & McHardy, 1960; Ernsting, 1962). The effect of the resultant severe but short-lived arterial hypoxaemia upon the supply of oxygen to various organs of the body is of considerable interest. The oxygen content of the venous blood flowing from a region reflects the balance between the supply of oxygen to it and its metabolic oxygen consumption. Continuous measurements of the oxygen content of the venous blood flowing from several regions have been made in subjects exposed to brief but profound hypoxia. In the experiments described in this paper a short period of overventilation, nitrogen being used as the inspired gas, was employed in place of rapid decompression to induce hypoxia. This method allowed more extensive observations to be made than were considered practical in a decompression chamber.

METHODS

Induction of hypoxia. Three healthy men, aged from 23 to 28 years, were used. The subject lay on a couch and breathed through a valve box, to the inlet of which two taps were connected in series. The side arm of the tap next to the box was open to the atmosphere. One arm of the second tap was connected to a demand valve which was supplied with nitrogen, whilst the other arm was connected to a second demand valve supplied with oxygen. Before the experiment was started the hoses between the two demand regulators and the second tap were purged with the gas delivered by the corresponding regulator. The dead space between the two taps was purged with nitrogen to ensure that 100% nitrogen was delivered directly the first tap was operated. During each rest period the first tap was positioned so that the subject breathed air. Nitrogen was administered by instructing the subject to expire maximally at the end of a normal expiration, and at this instant the first tap was turned so that the subject breathed from the demand valve which supplied nitrogen.

During the period of breathing nitrogen the subject was instructed to breathe as deeply as possible at a rate of about 20 breaths per minute. After 7–20 sec over-ventilation with nitrogen the first tap was returned to its original position so that air was breathed again. At the same time the subject was told to cease over-breathing.

Respired gas tensions. The partial pressures of oxygen and carbon dioxide in the gas passing the subject's lips were recorded continuously in all the experiments by means of a respiratory mass spectrometer (Fowler & Hugh-Jones, 1957). Preliminary studies showed that the output of the instrument was linearly related to the partial pressure of each of these gases. The delay between a sudden change of partial pressure of either at the sampling tip and the beginning of the response of the recording pen motor was 0·2 sec and 90% of the total response occurred in a further 0·1 sec. Calibrations employing gas mixtures of known composition were performed at intervals throughout each experiment. Over a 30 min period no significant change occurred in the sensitivity of the instrument. The pulmonary ventilation was recorded in some of the experiments by collecting the expired gas in a recording Tissot spirometer.

Blood sampling. In separate experiments blood was sampled continuously from various sites in the cardiovascular system. Blood was obtained from the brachial artery and the femoral vein through a Cournand needle introduced into the vessel after local analgesia had been produced with 2% lignocaine. A catheter was introduced into the right side of the heart through a large-bore needle which had been inserted into a vein in the antecubital fossa. The position of the catheter was determined during its introduction by recording the pressure at the tip by means of a strain-gauge pressure transducer. The catheter was advanced until its tip lay in the pulmonary artery. Blood flowing through the internal jugular vein was sampled by means of a radio-opaque catheter which was introduced into a vein which had been exposed through an incision in the right antecubital fossa. This catheter was advanced under direct fluoroscopic control with the subject's head held against his left shoulder. The catheter entered the right internal jugular vein and was placed so that its end lay above the level of the tip of the right mastoid process. When in place, the patency of the Cournand needle or the intravascular catheter was maintained when sampling was not in progress by a flow of sterile physiological saline (NaCl 0·9 g/100 ml.), approximately 2 ml./min containing heparin (200 i.u./100 ml.).

Recording of blood oxygen saturation and pH. The blood from the intravascular needle or catheter flowed through a tubular cuvette oximeter (Fig. 1) and was then diluted 1:10 with neutral physiological saline to which heparin had been added (Sherwood-Jones, Robinson & Cooke, 1960). The diluted suspension of blood was then passed through a microflow-glass-electrode–calomel-reference-electrode system. The saline reservoir and microflow-electrode system were immersed in a water-bath which was maintained at 38° C. The flow of blood and the desired dilution of the blood with saline were produced by means of a two-cylinder pump with a single piston, the velocity of which could be varied. The pump was constructed so that the cross-sectional area of one cylinder, which was charged with saline, was 10/11 of that of the other cylinder into which the mixture of saline and blood was drawn after it had passed through the glass-electrode system. In all the experiments a blood sampling rate of 20 ml./min was used.

The outputs of the oximeter amplifier and of the pH meter were fed on to two of the pen motors of a recorder. Preliminary experiments showed that the output of the oximeter amplifier was linearly related to the oxygen saturation of the blood flowing through the cuvette. At the beginning and end of each period of recording the output of the oximeter was calibrated by drawing a fully saturated sample of blood and a second sample of a known degree of unsaturation through the cuvette. A linear relation was also found between the pH of the blood and the output of the pH meter. The output of the latter was calibrated at intervals by using two phosphate buffers (pH 6·84 and 7·60). The time course of the response of the entire measuring system to a sudden change in the oxygen saturation and pH of the blood entering the sampling system was determined at the end of each experiment.

When sampling was required the drip of heparinized saline was turned off and the speed of the sampling pump was increased until blood was withdrawn at 20 ml./min. Sampling was continued for 1 min before the subject breathed nitrogen and was maintained until all the disturbances produced by the procedure had subsided.

Electroencephalogram (e.e.g.) and electrocardiogram (e.c.g.) recording. In many of the experiments the e.e.g. was recorded. Two pairs of saline pad electrodes were placed on the scalp over the frontal and occipital regions of the left side of the head. The potential changes from each pair of electrodes were amplified and recorded at a high paper speed. In addition, lead II of the e.c.g. was recorded.

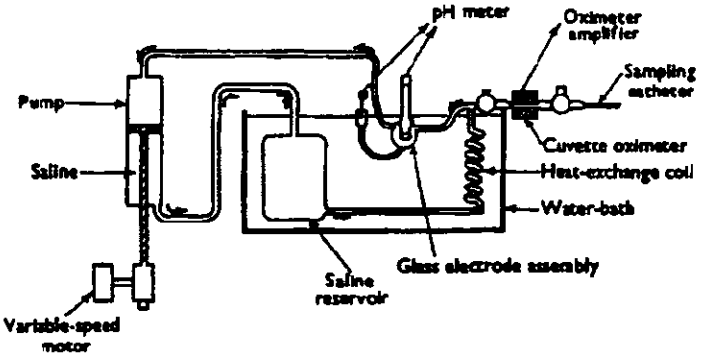

Fig. 1. Apparatus for the continuous measurement of the oxygen saturation and pH of blood. Blood is drawn into the apparatus through a catheter and then it passes through the cuvette oximeter. Saline at 38° C driven by the pump in the direction indicated by the arrows mixes with the blood and the diluted blood flows through the pH electrode assembly back to the pump.

Arterial pressure and calf blood flow. The arterial blood pressure was recorded through a Riley needle by means of an unbonded strain-gauge pressure transducer which was filled with physiological saline containing heparin. The needle was connected to the transducer by means of a 3 cm length of polyethylene tubing with an internal diameter of 1 mm. Preliminary measurements demonstrated that the complete recording system faithfully reproduced the magnitude and phase of sinusoidal pressure fluctuations at frequencies of up to 20 c/s. The Riley needle was inserted into the brachial artery and the transducer was placed on the same horizontal plane as the tip of the needle. The output of the amplifier connected to the transducer, which was fed to one channel of the recorder, was calibrated by means of a mercury manometer before and after each series of measurements. Blood flow through the calf was measured by means of venous occlusion plethysmography, with a mercury-in-rubber strain gauge (Whitney, 1953) to measure changes in the circumference of the calf. The lower limb was supported so that the lower border of the calf was just above the horizontal level of the sternal angle. The circulation to the foot was occluded by means of a cuff placed around the ankle, which was inflated to 250 mm Hg 1 min before the calf blood-flow measurements were started. The venous outflow from the calf was obstructed for 5 sec of every 10 sec period by inflating the cuff placed around the lower part of the thigh to between 30 and 40 mm Hg. The exact pressure used in the venous cuff was adjusted at the beginning of each experiment so that the circumference of the calf increased at a constant rate during each collection period. The output of the gauge was calibrated while it was in position by producing a known reduction of its length. The circumference of the calf at the level at which the gauge was fixed was measured at the end of each experiment.

In all the experiments the subject was carefully observed during and following the period of over-ventilation with nitrogen. If any severe disturbance of consciousness or respiration occurred, oxygen was administered.

RESULTS

Effect upon consciousness. The increase of pulmonary ventilation achieved by each subject during nitrogen breathing was measured from the spirometer records. The mean pulmonary ventilation of the three subjects was increased to 80 l./min at b.t.p.s. during the period of over-ventilation. When the duration of over-ventilation with nitrogen was greater than 8–10 sec the subject reported a transient dimming of vision. In the experiments in which nitrogen breathing was carried out for 15–16 sec the subject experienced some general clouding of consciousness and impairment of vision. Vision was frequently lost in these experiments for a short period. In the few experiments in which nitrogen was breathed for 17–20 sec unconsciousness supervened and was accompanied on most occasions by a generalized convulsion. The duration of the interval between the start of over-ventilation with nitrogen and the onset of symptoms was 12–14 sec.

End-tidal gas tensions. A typical record of the partial pressures of oxygen and carbon dioxide in the gases flowing through the mouth-piece is presented in Fig. 2. The end-tidal oxygen tension fell very rapidly when the subject commenced over-ventilation with nitrogen. It reached a value of less than 10 mm Hg at the end of the third expiration and remained below this level until air was inspired after 16 sec of nitrogen breathing. During the over-ventilation period the end-tidal carbon dioxide tension also fell rapidly. With the restoration of air breathing and the cessation of over-breathing the end-tidal oxygen and carbon dioxide tensions rose gradually to regain their control values. Each of the three subjects over-ventilated, whilst breathing nitrogen for a period of 15–16 sec on six separate occasions. The time course of the changes of the end-tidal tensions of oxygen and carbon dioxide has been measured for each of these 18 experiments and mean curves for each of these variables are presented in Fig. 3.

Arterial blood oxygen saturation and pH. Blood was sampled from the brachial artery of each subject on three separate occasions during which the subject over-ventilated with nitrogen for 16 sec. The records of the response of the entire system to a sudden change in the composition of blood at the tip of the Cournand needle showed a mean delay of 0·7 sec to the beginning of the response of the pen motor recording oxygen saturation and a further 0·9 sec elapsed before 90 % of the total response had occurred. The corresponding times for the response of the pH recording system were 1·4 sec and 2·0 sec respectively. Corrections for these delays in response were applied to the recorded values of oxygen saturation and pH. A

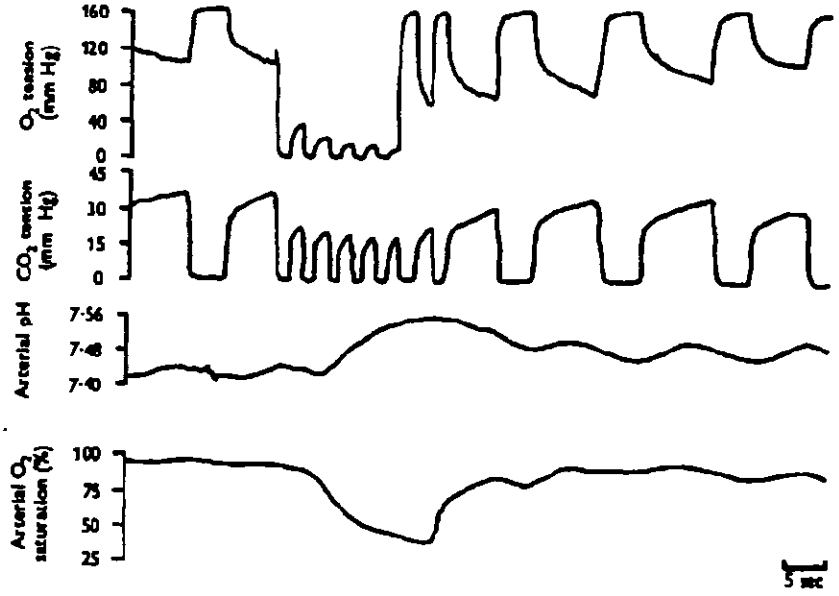

Fig. 2. Respiratory gas tensions and systemic arterial oxygen saturation and pH before, during and after 16 sec over-ventilation with nitrogen. The tensions of oxygen and carbon dioxide were recorded at the lips, whilst the blood was sampled continuously from the brachial artery. Delay time of oxygen saturation record, 0·7 sec of pH record, 1·5 sec.

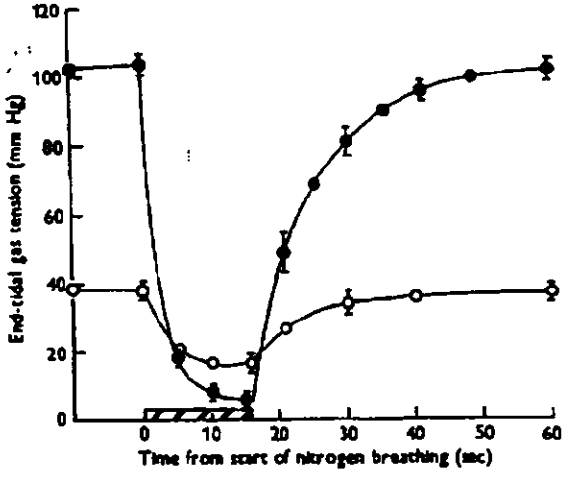

Fig. 3. Effect of over-ventilation with nitrogen upon end-tidal tensions of oxygen (●) and carbon dioxide (○). Each point represents the mean of eighteen values from three subjects; each bar represents ± 1 S.E. of the mean. The period of over-ventilation with nitrogen is indicated by the hatched bar.

typical experimental record of the arterial oxygen saturation and pH is presented in Fig. 2. The arterial oxygen saturation and hydrogen-ion concentration began to fall 4–5 sec after the commencement of nitrogen breathing and both fell very rapidly at first and then more slowly until air breathing was started again at 16 sec. The oxygen saturation then increased rapidly whilst the pH gradually returned to its control value. The mean time courses of the changes of arterial oxygen saturation and pH have been calculated for the nine experiments and these values together with their standard errors are shown in Fig. 4.

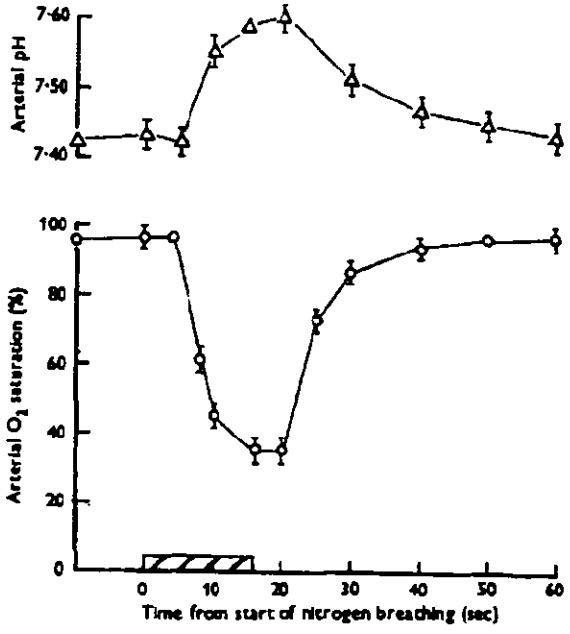

Fig. 4. Effect of over-ventilation with nitrogen upon arterial oxygen saturation (O) and arterial pH (Δ). Each point represents the mean of nine values from three subjects; each bar represents ± 1 S.E. of the mean.

Venous blood oxygen saturation and pH. Blood was sampled from the femoral vein, the pulmonary artery and the right jugular bulb on separate occasions in each of the subjects. The delay in the response of the recording systems was lengthened considerably when intravascular catheters were employed. On none of these occasions did any significant change of pH occur during the period of nitrogen breathing. The mean time courses of the oxygen saturation of the venous blood drawn from these three sites are presented in Fig. 5.

Electroencephalogram changes. The resting e.e.g. shows no specific electrical activity and no change occurred in any experiment until 15–18 sec after the beginning of the period of over-ventilation with nitrogen. When nitrogen over-breathing was carried out for 8–12 sec low voltage

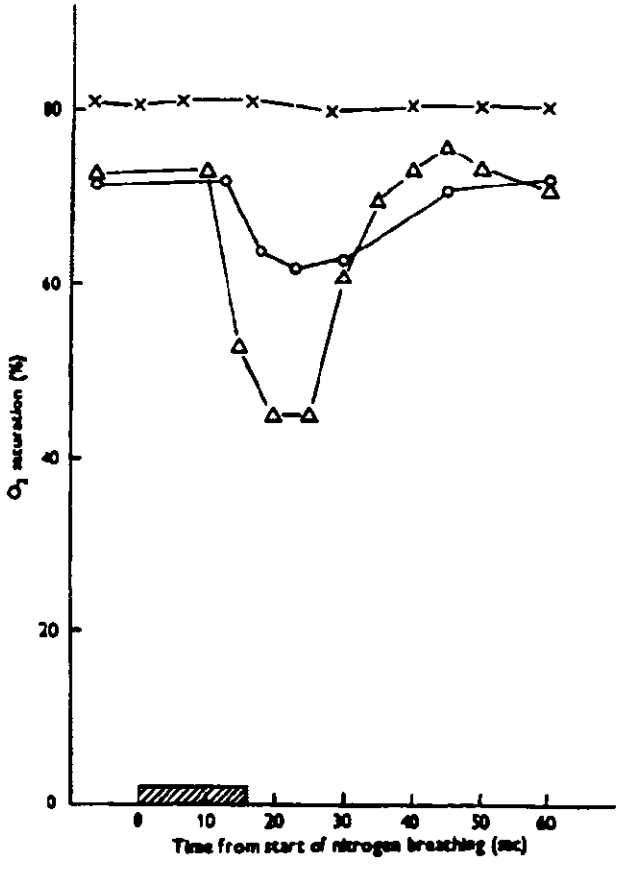

Fig. 5. Effect of over-ventilation with nitrogen upon the oxygen saturation of blood flowing through the femoral (x) and internal jugular (△) veins and the pulmonary artery (○). Each point represents the mean of three values obtained from three subjects.

activity at 11–13 c/s appeared in both channels of the e.e.g. 15 sec after the beginning of the procedure and persisted for 7–9 sec. When the duration of nitrogen over-ventilation was extended to 15–16 sec, similar changes arose in the e.e.g. but they persisted for slightly longer. Occasionally the

11–13 c/s activity was replaced by high-voltage 2–4 c/s activity, which appeared 4–6 sec after the beginning of the change of the e.e.g. This slow activity generally persisted for 4–6 sec. When nitrogen breathing was extended to 18–20 sec the initial fast, low-voltage activity was always replaced by high-voltage 2–4 c/s activity after 5 sec, which lasted for about 10 sec. Control experiments in which a subject over-ventilated for a similar period whilst breathing air produced no change of e.e.g. activity.

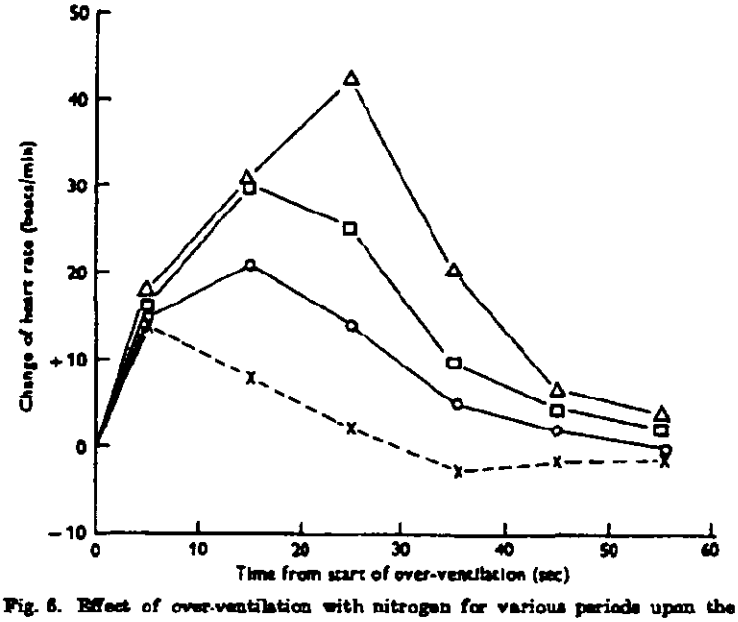

Fig. 6. Effect of over-ventilation with nitrogen for various periods upon the heart rate. △, nitrogen for 17 sec; □, nitrogen for 11 sec; ○, nitrogen for 8 sec; ×, air for 15 sec. Each point represents the mean of three values obtained from three subjects.

Cardiovascular changes. The period of over-ventilation with nitrogen produced a transient acceleration of the heart rate. This commenced at the beginning of the period of over-ventilation and reached a maximum about 30 sec later. The magnitude of the increase varied directly with the duration of the nitrogen over-ventilation. The mean changes of the heart rate for the three subjects when they over-ventilated with nitrogen for various periods are presented in Fig. 6. There were no consistent changes in the shape of the e.c.g. in these experiments. In one subject, however, there was a transient flattening of the 'T' wave, which started 5 sec after the beginning of the nitrogen over-ventilation and persisted for 10 sec. In

several experiments the subjects over-ventilated whilst breathing air. This caused a relatively small and transient increase of heart rate which had subsided 10 sec after the end of the over-ventilation period (Fig. 6).

The period of over-ventilation produced marked respiratory variations of the arterial blood pressure. The mean and pulse pressure were both increased during the deep expiratory efforts and decreased during each inspiration. The mean blood pressure was increased by about 20 mm Hg during the period of over-breathing. Directly the subject ceased over-ventilation the arterial pressure fell and reached a minimum after some 15 sec from the beginning of nitrogen breathing. The minimal value was less than the mean blood pressure before the over-ventilation period. The fall of mean pressure was accompanied by a reduction of the pulse pressure. It was followed by a secondary rise of pressure and an increase of pulse pressure, both of which reached a maximum at about 30 sec after the beginning of the period of over-ventilation with nitrogen. In all, two separate periods of over-ventilation with nitrogen were studied for each of the three subjects and the mean values of arterial pressure before, during and after the period of over-ventilation with nitrogen are presented in Fig. 7. The blood flow through the calf was calculated from the rate at which the circumference of the part increased during each venous-congestion period (Whitney, 1953). The mean value for the calf blood flow obtained in twelve separate periods of over-ventilation with nitrogen in the three subjects are shown in Fig. 7. The flow of blood into the calf was increased during the period of over-ventilation, following which it returned to the resting level, to increase again between 20 and 40 sec after the beginning of over-ventilation.

DISCUSSION

Preliminary experiments in which the subjects over-ventilated with nitrogen for various periods showed that unconsciousness supervened if the duration of this procedure exceeded 16–17 sec. In the majority of these experiments, therefore, the period of over-ventilation with nitrogen was limited to 16 sec. This period of nitrogen over-breathing produced only a transient disturbance of the e.e.g. The low-voltage 8–13 c/s activity was generally associated with a transient dimming of vision and could not be distinguished from that produced by closure of the eyelids. Further, apart from a transient flattening of the 'T' wave on one occasion, no significant change was seen in the e.c.g., although only a standard limb lead (II) was recorded. In view of these findings it was considered that the degree of hypoxia induced by over-ventilation with nitrogen for 15–16 sec was within acceptable limits for resting subjects.

The concentration of oxygen in the gas contained within the respiratory tract at the beginning of the nitrogen breathing period was reduced very rapidly by the very large voluntary increase of pulmonary ventilation. The reduction of the lung volume to a minimum before the first breath of nitrogen was taken decreased the quantity of oxygen to be washed out. The combination of these two manoeuvres resulted in a very rapid fall of end-tidal oxygen tension to 10 mm Hg after 8 sec of over-ventilation. The rate of rise of the end-tidal oxygen tension following the cessation of nitrogen over-ventilation and the return to breathing air was considerably less than the rate at which it had fallen. This difference reflects the reduction of alveolar ventilation associated with the resumption of a more normal breathing pattern.

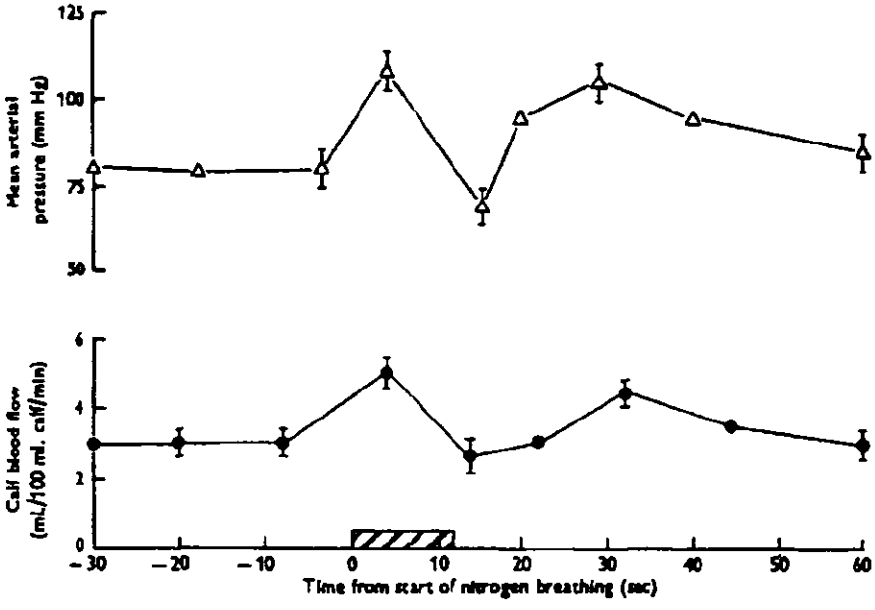

Fig. 7. Effect of over-ventilation with nitrogen upon the mean systemic arterial pressure (△) and the blood flow through the calf (●). The results are from three subjects, each pressure point representing the mean of six values whilst each blood flow point is the mean of twelve values; each bar depicts ±1 s.e. of the mean value.

Arterial oxygen saturation and pH

The delay of 4–5 sec between the beginning of nitrogen breathing and the reduction of the oxygen saturation of the brachial artery blood was a reflexion of the circulation time from the pulmonary capillaries to the sampling point in the systemic arterial tree. A similar delay occurred

between the restitution of air breathing and the subsequent increase of the arterial oxygen saturation. The reduction of the end-tidal oxygen tension to below 10 mm Hg was associated with an arterial oxygen saturation of less than 40 %. The increase of the pH of the arterial blood was related to the fall of the alveolar carbon-dioxide tension and the reduction of the blood oxygen saturation (Christiansen, Douglas & Haldane, 1914). The mean increase of the arterial pH produced by the over-ventilation amounted to 0·18 unit. This gave a calculated value for the minimal arterial carbon-dioxide tension of 22·5 mm Hg as compared with the observed end-tidal value of 17 mm Hg. The changes of arterial oxygen tension produced by over-breathing with nitrogen have been calculated from the simultaneous measurements of the oxygen saturation and pH of the arterial blood by means of standard oxygen dissociation curves (Dill, 1944). The mean time course of the oxygen tension for all the experiments is presented in Fig. 8. together with the curve for the end-tidal oxygen tension. During over-ventilation the end-tidal oxygen tension may be taken as representative of the mean alveolar tension of this gas. When allowance is made for the 4 sec delay between the change of alveolar gas composition and the resultant change of the oxygen tension of the arterial blood at the sampling point, it is apparent that the arterial oxygen tension fell in the same manner as the alveolar oxygen tension until this was less than 16 mm Hg. Beyond this point the systemic arterial oxygen tension was consistently greater than that of the alveolar gas until air breathing was restored. There was a statistically significant difference ($P < 0{\cdot}01$; $n = 9$) between the oxygen tensions of the arterial blood and of the alveolar gas for the last 7 sec of the period of nitrogen breathing. The oxygen tension of the mixed venous blood during nitrogen breathing was between 35 and 40 mm Hg (Fig. 9), and hence the oxygen tension of the alveolar gas was less than that of the blood entering the pulmonary capillaries for nearly the whole period of nitrogen over-ventilation. During this procedure, therefore, there was a reversal of the normal oxygen-tension gradient between the alveolar gas and the mixed venous blood. Since the oxygen saturation of the systemic arterial blood was considerably less than that of the mixed venous blood, oxygen must have passed from the blood flowing through the pulmonary capillaries into the alveolar gas during the latter part of the nitrogen-breathing period. Such a reversal of the normal direction of passage of oxygen across the alveolar capillary membrane has been demonstrated following rapid decompression to high altitude (Luft, Clamann & Adler, 1949; Ernsting & McHardy, 1960) and during rapid ascent following a breath-holding dive to a water depth of 60–100 ft. (18–30 m; Rahn, 1963). In both these situations the oxygen tension of the alveolar gas is reduced rapidly below that of the mixed venous blood.

Venous pH and oxygen saturation

The absence of any detectable change of the pH of the blood sampled from the three venous sites following the period of over-ventilation with nitrogen demonstrated the marked carbon dioxide buffering power of the peripheral tissues and the rapid diffusibility of this gas. The constancy of the venous pH was unexpected, since the reduction of the oxygen saturation of the venous blood would of itself have produced an increase of pH (Christiansen *et al.* 1914). At a constant carbon-dioxide tension the greatest increase of pH due to this mechanism, associated with the decrease of

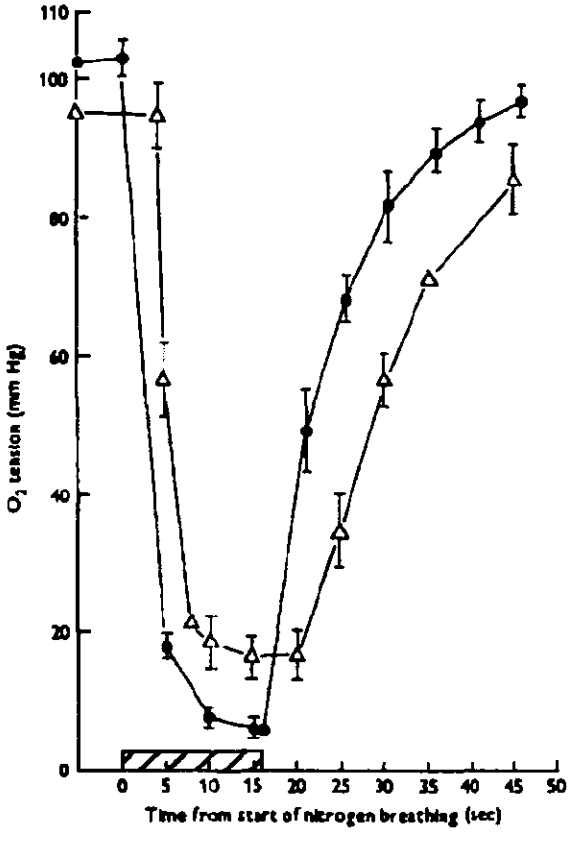

Fig. 8. Effect of over-ventilation with nitrogen upon end-tidal oxygen tension (●) and systemic arterial oxygen tension (△). Each point represents the mean of eighteen end-tidal values and nine arterial values. Each bar denotes ± 1 S.E. of the mean value.

oxygen saturation of the cerebral venous blood by 27 % was calculated to be of the order of 0·012 unit. The over-all sensitivity of the system used for the measurement of the pH of the venous blood was such, however, that a change of this magnitude might not have been detected.

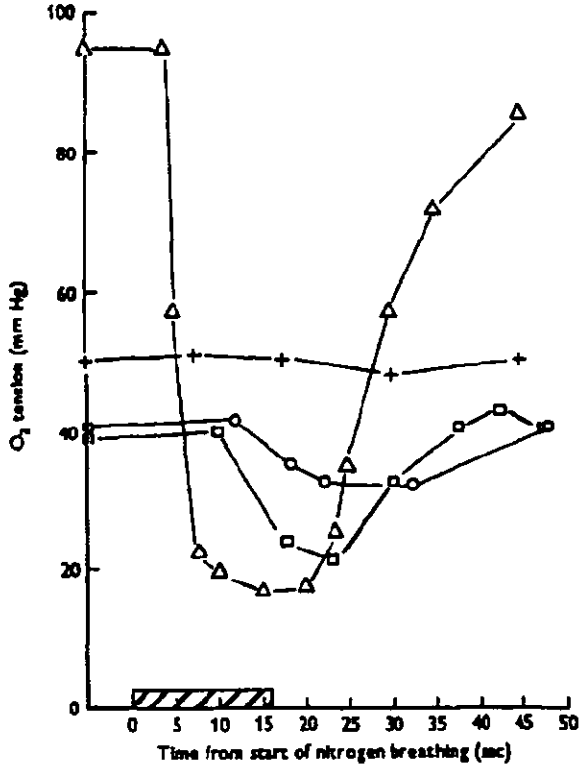

Fig. 9. Effect of over-ventilation with nitrogen upon the oxygen tension of the systemic arterial (△), femoral venous (+), internal jugular (□) and pulmonary arterial (○) blood. Each point represents the mean of the values obtained from three subjects.

The pattern of the reduction of the oxygen saturation of the venous blood produced by the period of nitrogen breathing varies markedly with the site of sampling (Fig. 5). The oxygen content of the jugular venous blood was the first to change and it exhibited the greatest reduction and the most rapid recovery. In contrast the oxygen saturation of the femoral venous blood started to fall last, was reduced by the smallest amount and recovered the most slowly. Mixed venous blood showed changes which

were intermediate between those of the jugular and femoral venous bloods. The maximal fall of the oxygen saturation of the femoral venous blood was half that which occurred in the blood sampled from the pulmonary artery, whilst the maximal reduction of the oxygen content of the jugular blood was more than twice the latter. The changes of the oxygen tension of the blood sampled from these venous sites have been calculated from the measured values of oxygen saturation and pH and the mean curves are presented in Fig. 9, together with the mean curve for the arterial oxygen tension. It is apparent that during the period of severe hypoxia the oxygen tension of the blood flowing from the lower limbs, the brain and the whole body was greater than that of the arterial blood flowing into these regions.

Cardiovascular effects of profound hypoxia

The limited measurements made in this study demonstrate that the period of over-ventilation with nitrogen produced significant changes in the cardiovascular system. The control experiments in which the subject over-breathed with air make it possible to distinguish two phases in the cardiovascular response. First, during the period in which the pulmonary ventilation was increased there was a moderate rise of heart rate and the arterial pressure and calf blood flow were raised (Fig. 7). Immediately the over-ventilation ceased the arterial pressure and calf blood flow returned to their resting values. These changes occurred when either air or nitrogen was breathed. When the over-breathing was performed with nitrogen the rise of heart rate persisted for considerably longer and there was a secondary increase of arterial pressure and calf blood flow. These secondary changes were absent when air was substituted for nitrogen and were due, therefore, to the severe hypoxia induced by the nitrogen. Throughout each experiment the calf blood flow was directly proportional to the mean systemic arterial pressure. Thus the observed changes of calf blood flow were a result of the concomitant changes of arterial pressure. The secondary changes which occurred after over-ventilation with nitrogen were probably the result of an increase of cardiac output and of systemic arteriolar constriction which were produced reflexly by chemoreceptor stimulation. It is apparent that the arterioles of the calf did not contribute to this vasoconstriction, and the most probable sites for the increase of peripheral resistance were the splanchnic and cutaneous circulations. The rise of the oxygen saturation of the jugular venous blood above the control value when air breathing was restored (Fig. 5) suggests that there was an increase of the over-all cerebral blood flow at this time. In the steady state moderate arterial hypoxaemia, even when accompanied by hypocapnia, is known to produce a dilatation of the cerebral vessels (Kety &

Schmidt, 1948). The rate at which the cerebral vasodilatation develops when arterial hypoxaemia is induced suddenly is not known, but the present experiments suggest that the cerebral vessels respond to a fall of arterial oxygen tension within 20 sec.

Pulmonary gas exchange in profound hypoxia

The arterial oxygen-tension values derived in this study demonstrated that during over-ventilation with nitrogen the oxygen tension of the arterial blood was significantly greater than that of the alveolar gas. The time for which this state existed was only 7–8 sec, although during this period the rates of change of alveolar and arterial oxygen tensions were relatively slow. Furthermore, this length of time is large relative to the average transit time of 0·73 sec (Roughton, 1945; Roughton & Forster, 1957) for a red cell through the pulmonary capillaries lining ventilated alveoli. It would appear, therefore, that the observed difference between systemic arterial and alveolar oxygen tensions cannot be accounted for on the basis of the short period for which the condition existed. Such a difference could be produced by the presence of either a shunt of venous blood into the systemic arterial tree or a higher tension of oxygen in the blood leaving the pulmonary capillaries than in the alveolar gas. Mixed venous blood flowing into the systemic arterial tree without having transversed the capillaries of ventilated alveoli would raise the oxygen tension of the systemic arterial blood above that of the alveolar gas. The effect of the normal quantity of venous admixture upon the arterial oxygen tension would be insignificant, because of the relative steepness of the blood-oxygen dissociation curve over the range concerned here. If, however, the proportion of the cardiac output perfusing ventilated alveoli was reduced during nitrogen breathing, this effect could become significant. In order for this mechanism to account for the total observed oxygen-tension gradient the venous-arterial shunt would have to amount to at least half of the total cardiac output. There is at present no evidence in favour of such a degree of shunting during severe hypoxia. It would appear probable, therefore, that the tension of oxygen in the blood leaving the pulmonary capillaries is considerably greater than that in the alveolar gas during over-ventilation with nitrogen.

Since no measurements were made of the rate of gaseous exchange during the period of over-ventilation with nitrogen it is impossible to examine quantitatively the factors affecting the exchange of oxygen between the pulmonary capillary blood and the alveolar gas. It is of value, however, to compare the effects of over-ventilation with nitrogen with those produced by moderate hypoxia in the steady state. Thus, Lilienthal, Riley, Proemmel & Franke (1946) found that at an alveolar

oxygen tension of 46 mm Hg at rest the difference between the tensions of oxygen in the alveolar gas and the systemic arterial blood amounted to 9·1 mm Hg. They calculated that under these circumstances the oxygen tension of the mixed venous blood was 19 mm Hg less than that of the alveolar gas and that the oxygen tension of the blood leaving the pulmonary capillaries was about 8 mm Hg less than that of the alveolar gas. Although in the nitrogen over-ventilation experiments the oxygen tension gradient between the alveolar gas and the mixed venous blood was reversed, it was of the same order as that which existed in the experiments performed by Lilienthal *et al.* (1946). Furthermore, the mean difference between the oxygen tensions of the arterial blood and the alveolar gas obtained in the present study, which amounted to 11 mm Hg, was only slightly greater than that found in moderate hypoxia by Lilienthal *et al.* (1946). The arterial–alveolar oxygen-tension difference observed in nitrogen over-ventilation experiments was probably due, therefore, to a mechanism analogous to that which was deduced by Lilienthal *et al.* (1946) to be responsible for the existence of an alveolar to end-pulmonary capillary blood-oxygen tension difference in moderate hypoxia. The limited rate at which oxygen was transferred from chemical combination in the pulmonary blood into the alveolar gas under the circumstances which existed in the nitrogen-breathing experiments gave rise to a large oxygen-tension difference between the blood leaving the pulmonary capillaries and the alveolar gas.

Exchange of oxygen between blood and peripheral tissues in profound hypoxia

The reduction in the rate at which oxygen is carried to a part caused by a short period of arterial hypoxaemia depends upon the degree and duration of the desaturation of the arterial blood and the arterial flow to the part. In the resting state the total blood flow to the brain is over twice that to the lower limbs. Thus in the present experiments the deficit of the oxygen supply to the brain was twice that to the lower limbs. The effect of such a deficit in the oxygen supply to a region upon the oxygen content of the blood flowing from it will be determined in part by the relation between the magnitude and nature of its oxygen store and its metabolic oxygen consumption. Where the available oxygen store is small in relation to the oxygen uptake, the venous oxygen saturation will be reduced to a greater extent than when the store is large in relation to the oxygen consumption. Quantitatively the most important oxygen store is that contained by the blood, and the greater proportion of this resides in the small and large veins. Muscle possesses in addition a specific oxygen storage mechanism in the form of oxymyoglobin. The amount of oxygen stored in this manner in man is, however, relatively small (Drabkin, 1950)

and the oxygen tension in muscle must be reduced below 10 mm Hg before a significant proportion of the oxygen held in this form is liberated (Hill, 1936). Finally, all tissues contain oxygen in simple physical solution, although quantitatively this store is relatively small. The brain, in contrast to the lower limbs and the body as a whole, has a high arterial inflow, a high oxygen consumption and a small oxygen store. For a specified transient arterial hypoxaemia all these factors tend to produce a greater fall of the oxygen saturation in the jugular blood than in the blood flowing from the lower limbs.

The pattern of the fall of the saturation of venous blood caused by a transient arterial hypoxaemia will be modified by changes of blood flow into the region and of the capacity of its vascular bed. In the present experiments there were transient changes of calf blood flow during and after the period of hypoxaemia. There was also evidence which suggested that the cerebral blood flow changed, although no direct measurements of this quantity were made. If an increase of blood flow occurred during the period of hypoxaemia, the deficit of the oxygen supply would have been increased. If, however, the increase of blood flow did not occur until the arterial oxygen saturation was rising, it would have produced a more rapid recovery of the venous oxygen saturation, or even a rise to above the control value. Although no direct measurements of the capacity of the vessels of the calf were made, it was noted that the volume of this region was decreased by the period of over-ventilation with nitrogen. Eckstein, Hamilton & McCammond (1958) have shown that the reflex reduction of the distensibility of the capacity vessels produced by over-ventilation is in part due to the hypocapnia and in part a result of the intrathoracic pressure changes associated with the over-ventilation. Such a reduction of the blood content of the calf would have tended to increase the venous desaturation produced by the arterial hypoxaemia.

During the period of over-ventilation with nitrogen, the oxygen tension of the arterial blood was reduced to 20–30 mm Hg below that of the venous blood normally flowing from the regions studied. Thus the oxygen tension of the arterial blood during this period was lower than the mean capillary oxygen tension (Barcroft, 1938) which existed before nitrogen breathing was commenced. Furthermore, during the period of profound hypoxaemia the oxygen tension of the blood flowing from the regions under investigation was greater than that of the arterial blood perfusing them. Although the oxygen content of the blood leaving the tissue capillaries was probably raised by admixture with the blood already present in the venules and veins of the part, it is apparent that during the period of severe hypoxaemia the oxygen tension of the capillary blood was markedly reduced. Thus the diffusion of oxygen into the various tissues from the blood flowing through

them was severely reduced by the period of hypoxia. Indeed, in some areas, especially those with a relatively high capillary blood flow, the capillary oxygen tension may have been reduced below that of the surrounding tissues, so that oxygen actually diffused into the blood as it flowed through them. Thus direct measurements of the oxygen tension of the grey matter of the cerebral cortex in animals breathing air have given values of the order of 18-25 mm Hg (Cater, Garattini, Marina & Silver, 1962), whilst in the present experiments the arterial oxygen tension was reduced to about 17 mm Hg. The effect of a given reduction of the rate at which oxygen diffuses into a tissue upon the cellular oxygen tension will depend upon the relation between the cellular oxygen consumption and the extravascular oxygen store. There is considerable evidence that the cellular oxidative enzyme systems will continue to function normally until the local oxygen tension is reduced to below 5 mm Hg (Keilin, 1930). Thus the cellular metabolic oxygen uptake will probably remain unchanged until severe hypoxia is induced. In the brain, where the only extravascular oxygen store is oxygen dissolved in tissue fluid, and the metabolic oxygen uptake is high, sudden arterial hypoxaemia will produce a very rapid fall of the cellular oxygen tension.

In the present series of experiments it was found that unconsciousness ensued if over-ventilation with nitrogen was continued for longer than 17 sec. A more rapid fall of arterial oxygen tension can be produced by sudden reduction of the environmental pressure to below 140 mm Hg whilst air is breathed. Thus in one series of experiments in which the arterial oxygen tension was reduced to below 20 mm Hg in about 1 sec, unconsciousness ensued 8 sec after the induction of arterial hypoxaemia (Ernsting *et al.* 1960). The delay between a sudden occlusion of the cerebral circulation and loss of consciousness in man also amounts to between 7 and 8 sec (Rossen, Kabat & Anderson, 1943). Thus the time which elapses between a sudden reduction of the arterial oxygen tension to below 20 mm Hg and the onset of unconsciousness is very similar to the interval which occurs between sudden occlusion of the cerebral circulation and loss of consciousness. Kety (1950) has calculated that at any one moment the total oxygen content of the brain and of the cerebral capillary blood is about 7 ml. Thus at the normal level of cerebral oxygen consumption the oxygen tension of the brain following cessation of the supply of this substance would be reduced to zero in about 8 sec. These results suggest that when unconsciousness supervenes following the sudden induction of severe cerebral hypoxia the cellular oxygen tension in many regions of the brain will be virtually zero. This conclusion is in close agreement with the results of calculations made by Thews (1962) with respect to hypoxia of slow onset. His calculations suggest that when the arterial oxygen tension is

reduced to the level which produces unconsciousness, the oxygen tension of the neurones which are furthest from their vascular supply will be of the order of 2–4 mm Hg.

SUMMARY

1. Brief profound hypoxia was induced by voluntary over-ventilation whilst breathing nitrogen. Unconsciousness ensued when this procedure was performed for longer than 16 sec. Voluntary over-ventilation with nitrogen for 16 sec reduced the end-tidal oxygen tension to below 10 mm Hg for 8 sec.

2. Continuous recordings were made of the systemic arterial oxygen saturation and pH during 16 sec of nitrogen over-ventilation. The calculated minimal arterial oxygen tension was 16 mm Hg. There was therefore a reversal of the normal alveolar-arterial oxygen tension difference.

3. The oxygen saturation and pH of venous blood flowing through the jugular bulb, the femoral vein and the pulmonary artery were recorded continuously. The oxygen tension of the jugular blood exhibited the most rapid and most profound reduction when nitrogen was breathed. The femoral-vein oxygen tension exhibited only a very transient and slight fall, whilst the oxygen tension of the blood flowing through the pulmonary artery exhibited a moderate fall.

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Pathology of hypoxic brain damage in man

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The energy requirements of the brain demand amongst other things adequate supplies of oxygen and glucose. These are provided by the functions of respiration and circulation. Neurons are particularly susceptible to hypoxia since they have an obligative, aerobic, glycolytic metabolism. The adult brain receives about 15 per cent of the cardiac output, or as expressed in terms of blood flow, about 45 ml/100 g/minute in the adult and about twice as much in children (McIlwain, 1966). The respiratory quotient of the brain is almost unity and glucose is the principal source of energy by oxygenation. If the supply of oxygen or glucose is reduced below a critical level consciousness is lost after a few seconds and irreversible brain damage may occur if the 'hypoxia' is more prolonged.

Physiology

The supply of oxygen to the brain depends on the cerebral blood flow (CBF) and the oxygen content of the blood. Cerebral blood flow in turn depends on the cerebral perfusion pressure (CPP) which is defined as the difference between the mean systemic arterial pressure (SAP) and the cerebral venous blood pressure. Blood flow to the brain shows a remarkable capacity for remaining constant, only hypercapnia, hypoxia and extreme hypotension affecting it to any marked extent. The preservation of CBF in response to changes in arterial blood pressure is brought about by autoregulation which can be defined as the 'maintenance of a relatively constant blood flow in the face of changes in perfusion pressure' (Harper, 1972). The mechanism of this autoregulation is still uncertain but it appears to be lost or at least severely impaired in a wide range of acute conditions producing brain damage (Bruce *et al*, 1973; Harper *et al*, 1975). Thus there are many situations in which cerebral autoregulation may be impaired before an episode of hypoxia. The level of CPP at which brain damage is produced is not known in man but in the presence of normal autoregulation the critical level of SAP is about 50 mm Hg (Harper, 1972). In primates with a normal PaO_2 it would appear that brain damage does not occur until the CPP falls to less than 25 mm Hg (Brierley *et al*, 1969).

The energy state of the brain may also be severely reduced in the presence of normal supplies of oxygen and glucose by substances which poison the oxidative enzymes of nerve cells. These considerations form the basis of the various categories of brain hypoxia (Brierley, 1976; Adams, 1976).

Categories of brain hypoxia

1 STAGNANT

(a) Ischaemic is due to local or generalized arrest of blood supply; (b) oligaemic is due to local or generalized *reduction* in blood supply.

2 ANOXIC AND HYPOXIC

(a) Anoxic, an absence of oxygen in the lungs which leads to tissue anoxia; (b) hypoxic, a reduced oxygen tension in the lungs which leads to tissue hypoxia.

3 ANAEMIC

Anaemic is where there is insufficient haemoglobin in the blood to carry the oxygen in chemical combination.

4 HISTOTOXIC

Histotoxic is due to poisoning of neuronal respiratory enzymes.

5 HYPOGLYCAEMIC

Hypoglycaemic is due to a deficiency of the substrate glucose.

6 FEBRILE CONVULSIONS AND STATUS EPILEPTICUS

Hypoxic brain damage

Hypoxic brain damage may occur in any situation where there is an inadequate supply of oxygen or glucose to nerve cells. It is therefore a potential hazard to any patient subjected to general anaesthesia, a severe episode of hypotension, cardiac arrest, status epilepticus, carbon monoxide or

barbiturate intoxication and hypoglycaemic coma. The eventual degree of clinical recovery will be determined by whether or not satisfactory resuscitation can be achieved before permanent brain damage ensues. Crises of this kind are not uncommon in clinical practice but the central question as to 'what duration of anoxia or ischaemia defines the watershed between recovery of the tissue and extensive permanent injury?' has not been critically defined in man (Plum, 1973). Reasons for this include the lack of precise physiological data about a patient's cardiovascular and respiratory status at the time of a crisis since the immediate priority is resuscitation, and the inadequate neuropathological examination of the brains from fatal cases.

Postmortem examination of patients with severe hypoxic brain damage is usually carried out under warrant by the forensic pathologist who often feels obliged to slice the unfixed brain in the mortuary. Under these conditions it is impossible to recognize recent hypoxic brain damage up to and including frank cerebral infarction even when subsequent histological examination shows severe and extensive neuronal necrosis. When the brain has been properly dissected after adequate fixation (up to three weeks' immersion in buffered 10 per cent formol saline) an infarct of about 18 to 24 hours' duration may just be recognizable but even an experienced neuropathologist may fail to identify extensive diffuse hypoxic brain damage if it is less than some three to four days' duration (figs 1 and 2). The extent and severity of hypoxic brain damage can be identified and its distribution analysed only by the microscopical examination of many large, bilateral and representative sections of the brain.[1] It is, however, often possible to establish that a patient has suffered hypoxic brain damage on the basis of a more restricted histological examination provided that the pathologist knows that certain parts of the brain are selectively vulnerable and is familiar with the cytological and histological appearances of ischaemic nerve cell change.

The identification of ischaemic cell change is made difficult in the human brain because of the frequent occurrence of histological artefact. The commonest artefacts are 'dark cells', 'hydropic cells' and 'perineuronal and perivascular spaces' (Cammermeyer, 1961). They are due partly to postmortem handling and to the slow penetration of fixative. Studies in experimental primates and in selected human material have shown that there is an identifiable process, namely ischaemic cell change, which is the neuropathological common denominator in all types of hypoxia.

The earliest histological stage of recent hypoxic neuronal damage in experimental animals is perfusion-fixed material is microvacuolation (Brown and Brierley, 1966; Brierley *et al*, 1971a and b; Meldrum and Brierley, 1973). This rather subtle histological change is difficult to identify in human material so that perhaps the earliest incontrovertible evidence in man of hypoxic brain damage is the second stage, ie, ischaemic cell change. The cell body and nucleus are shrunken and become triangular in shape. The cytoplasm, which usually still contains microvacuoles, stains intensely with eosin and from bright blue to dark mauve with the very useful Luxol fast blue/cresyl violet technique (Adams and Miller, 1970); the nucleus stains intensely with basic aniline dyes. The succeeding stage of ischaemic cell change with incrustations is characterized by

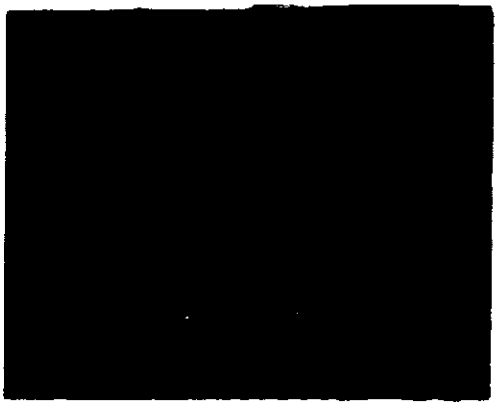
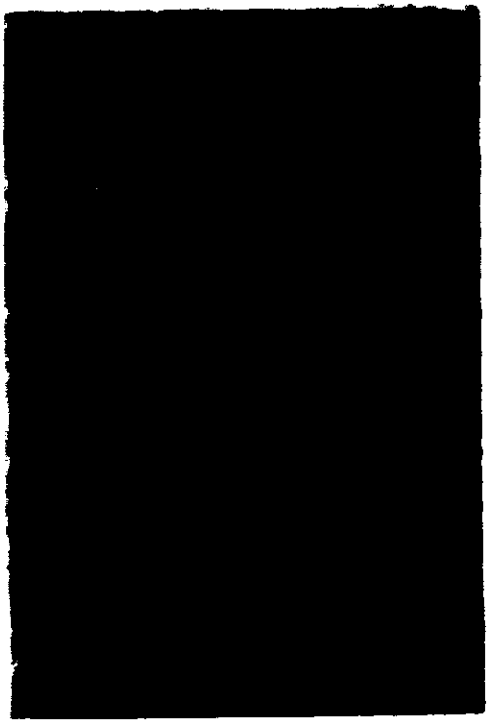


Fig 1 *Coronal section of brain from patient who survived 48 hours after cardiac arrest. There are no macroscopic abnormalities.*

Fig 2 *Same patient as in figure 1. Note subtotal ('laminar') necrosis of the third, fifth and sixth cortical layers with relative sparing of the second and fourth layers (darker staining). Cresyl violet.* × 4.



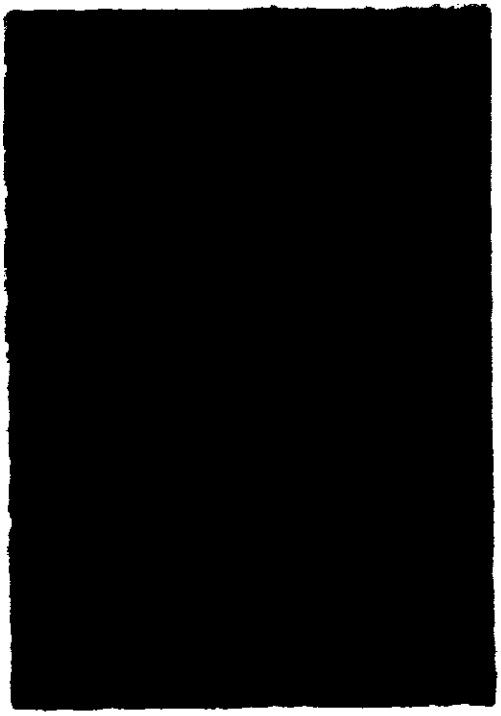


Fig 3

Fig 4

Fig 3 *Bottom: normal cortex. H and E × 500. Top: Ischaemic cell change. The nerve cells are small and triangular and contain hyperchromatic nuclei (arrows). The cytoplasm is intensely eosinophilic. There is also some disintegration of the neuropil. H and E × 500. Top inset: Ischaemic cell change with incrustations. Note the granules on the surface of the cell. H and E × 500.*

Fig 4 *Homogenising cell change. Note the Purkinje cells with swollen homogeneous cytoplasm and hyperchromatic nuclei (arrows). Cresyl violet. × 300.*

further shrinkage of the nerve cell cytoplasm and the development of small, relatively dense granules lying on or close to the surface of the nerve cell (fig 3). Finally the neuron undergoes homogenizing cell change when the cytoplasm becomes progressively paler and homogeneous and the nucleus smaller. This type of change is most commonly seen in the Purkinje cells (fig 4) of the cerebellum. The time course of ischaemic cell change is relatively constant for neurons according to their size and site so that the interval between a hypoxic episode and death if between two and 18 to 24 hours can be assessed with reasonable accuracy. If the patient survives for more than 24 to 36 hours more advanced changes occur in neurons, and early reactive changes appear in astrocytes, microglia and endothelial cells. After a few days the dead nerve cells disappear and reactive changes become more intense, including the formation of lipid phagocytes, even though the latter may not appear if damage is restricted to neuronal necrosis. When survival is for more than a week or so the damaged tissue becomes rarefied due to loss of myelin and there is a reactive gliosis. Collagen and reticulin fibres are also laid own, the whole appearing as a glio-mesodermal reaction.

The differing susceptibility of nerve cells to hypoxia has been known for many years. According to Jacob (1963), 'in general the nerve cells are the most sensitive followed by oligodendroglia and astrocytes while the microglia and the cellular elements of the vessels are the least vulnerable'. Recent work suggests that local metabolic rather than vascular factors largely determine the pattern of selective vulnerability (Brierley, 1976).

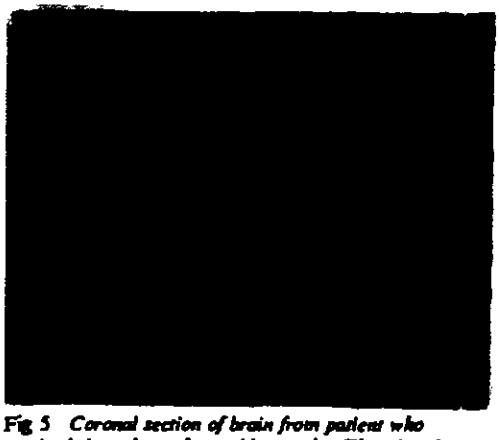


Fig 5 *Coronal section of brain from patient who survived three days after sudden stroke. There is a large recent swollen infarct in territories of left middle and anterior cerebral arteries. Part of the infarct is 'anaemic' and part is 'haemorrhagic'. Note the asymmetry of the lateral ventricles, the displacement of the midline structures to the right, the supracallosal hernia to the right (black arrow) and deep grooving (white arrows) along the line of bilateral tentorial herniae.*

Fig 6 *Recent infarction in cerebral cortex. There is irregular pallor (infarction) of staining of the affected areas. H and E × 15·6.*

I STAGNANT HYPOXIC BRAIN DAMAGE

This is divided into two main types, viz, ischaemic and oligaemic.

Ischaemic

If the blood flow through an artery is arrested, eg by thrombus or an embolus, an infarct will develop within part or the whole of the distribution of the occluded vessel. The earliest macroscopic change is swelling of the infarct and its edges may be just discernible in the fixed brain within 12 to 18 hours. The lesion may be 'haemorrhagic' or 'anaemic' (fig 5) and at an early stage there is irregular, blotchy pallor of the affected cortex (fig 6). A sharp

Fig 7 *Recent infarction in white matter. There is a sharply defined border between the abnormal (pale) and normal white matter. H and E × 40.*

and often very irregular line of demarcation between normal and abnormal myelin also appears early, the abnormal myelin staining palely (fig 7). A large infarct may swell sufficiently to constitute a space-occupying mass within 24 to 48 hours (Adams, 1966) resulting in tentorial herniation with secondary distortion of the mid-brain and infarction in the medial occipital (calcarine) cortex. The necrotic tissue is ultimately removed and replaced by a rather shrunken and cystic gliomesodermal scar.

A generalized arrest of blood flow to the brain is most commonly the result of cardiac arrest. This is usually a complication of some surgical procedure under general anaesthesia. Milstein (1956) estimated that about 300 deaths in the United Kingdom were caused by cardiac arrest related to surgery but by 1970 the number of such deaths had dropped to 100

Fig 8a *Normal right Ammon's horn to compare with figure 8b.*

Fig 8b *Right Ammon's horn. Necrosis in the Sommer sector is seen macroscopically.*

Fig 9a *Normal right Ammon's horn. To compare with figure 9b. The arrows delineate the Sommer sector. Cresyl violet.* × 9.

Fig 9b *Right Ammon's horn showing recent selective neuronal necrosis of Sommer sector (between arrows) and in endfolium. Cresyl violet.* × 9.

per annum in England and Wales (Wylie, 1975), the difference in mortality being attributed to better methods of resuscitation.

If cardiac arrest is of abrupt onset and occurs in a patient at normal body temperature, complete clinical recovery is unlikely if the period of arrest is more than five to seven minutes (Brierley, 1972). A short period of cardiac arrest combined with periods of reduced cerebral perfusion pressure before or after the arrest may be as important as the duration of complete arrest (Miller and Myers, 1972) and may lead to accentuation of the ischaemic damage in the arterial boundary zones (Brierley, 1976).

If death occurs within 24 to 36 hours of the arrest, the brain, apart from a variable degree of swelling, may appear normal externally and on section even after adequate fixation. Within 36 to 48 hours it is sometimes possible to identify laminar or patchy discolouration in the depths of sulci, particularly in the posterior halves of the brain and selective necrosis in the Sommer sector of the Ammon's horn (fig 8a and b). Microscopy reveals diffuse neuronal necrosis with a characteristic pattern of selective vulnerability. Ischaemic damage is commonly greater within sulci than at the crests of gyri and is maximal in the third, fifth and sixth layers of the parietal and occipital lobes (fig 2). In the Ammon's horn the Sommer sector and endfolium are the most vulnerable (fig 9a

and b). These changes are sometimes associated with necrosis of the baso-lateral portion of the amygdaloid nucleus. The pattern of damage in the basal ganglia is less constant and tends to be most frequent in the outer halves of the head and body of the caudate nucleus, and in the outer half of the putamen. Damage in the globus pallidus may occur in all types of hypoxia but is especially common in carbon monoxide intoxication. Primary hypoxic damage in the thalamus is most common in the anterior, dorsomedial and ventro-lateral nuclei. In the cerebellum there is characteristically diffuse necrosis of Purkinje cells. Damage to the brain stem nuclei tends to be more severe in infants and young children than in adults.

Patients with severe diffuse brain damage due to cardiac arrest rarely survive for more than a few days (Bell and Hodgson, 1974) but occasionally they may remain alive in a persistent vegetative state for up to six months or longer (Brierley *et al*, 1971; Jennett and Plum, 1972). With increasing survival, the necrotic tissue is replaced by a gliomesodermal scar. When this occurs there may be an appreciable reduction in the weight of the brain and evidence of atrophy of both the cortical gyri and cerebellar folia. In coronal slices ventricular enlargement may be considerable. Whereas the cortex of the parietal and occipital lobes will be reduced to a thin band of discoloured tissue, often with a line of cleavage between it and the underlying white matter, that of the frontal and temporal lobes may appear essentially normal. While the parahippocampal gyri are usually normal, the hippocampi may show the features of Ammon's horn sclerosis. Even when cortical necrosis is severe and survival is for only a few weeks the thalami may appear grossly normal. Eventually evidence of retrograde degeneration will be seen in the corresponding thalamic association nuclei (fig 10).

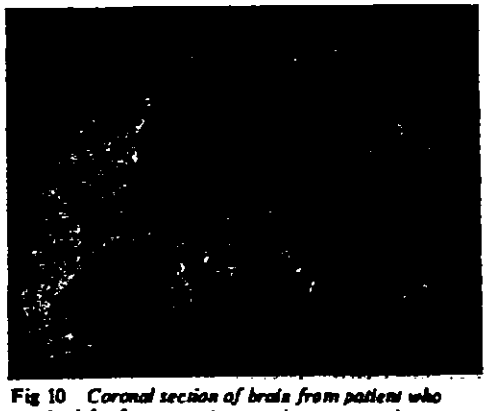


Fig 10 *Coronal section of brain from patient who survived for four years in a persistent vegetative state after cardiac arrest. The cortex is greatly narrowed and there is gross essentially symmetrical enlargement of the ventricles. The Ammon's horns and the thalami are also small.*

Oligaemic

Because of autoregulation a moderate fall in cerebral perfusion pressure does not lead to a reduction in cerebral blood flow. However, when vasodilatation is maximal, autoregulation ceases and the cerebral blood flow will fall parallel to the perfusion pressure. Oligaemic brain damage due to systemic arterial hypotension conforms to one of three patterns (Adams *et al*, 1966), of which the first two types are the most common.

1 Ischaemic damage is concentrated along the boundary zones between the arterial territories of the cerebral cortex and in the cerebellum (fig 11). If the lesions are large and of several days' duration they can be recognized macroscopically provided that the brain is cut in the coronal plane (fig 12a). They vary in size from foci of necrosis in the cortex to large, wedge-shaped lesions extending from the cortex almost to the angle of the lateral ventricle. In the cortex, damage is most frequent and most severe in

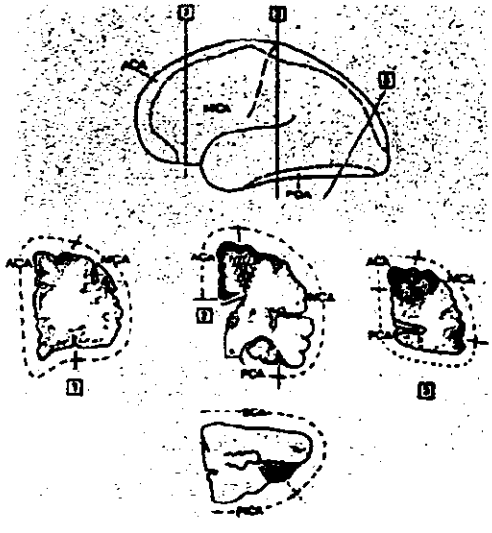


Fig 11 *Diagram to show arterial boundary zones in cerebral and cerebellar hemispheres. The right cerebral hemisphere is shown at three levels, viz, 1 = frontal, 2 = mid-temporal and 3 = occipital. Each boundary zone is stippled. ACA = anterior cerebral artery, MCA = middle cerebral artery, PCA = posterior cerebral artery, SCA = superior cerebellar artery and PICA = posterior inferior cerebellar artery.*

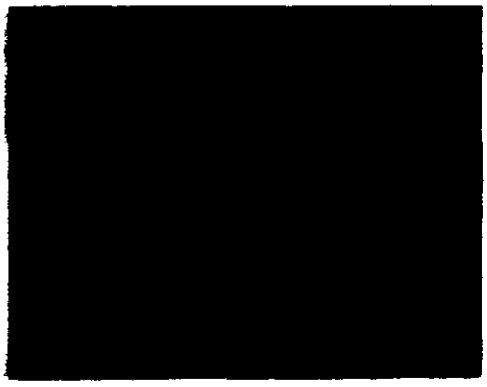


Fig 12a

Fig 12a *Coronal section of brain from patient who survived for 17 days after a myocardial infarct. Note focally haemorrhagic infarcts (arrows) in the boundary zones between the anterior and middle cerebral arterial territories, and between the middle and posterior cerebral arterial territories. Compare distribution of lesions with figure 11.*

Fig 12b *Same case as illustrated in figure 12a. Slices of cerebellar hemispheres to show dually haemorrhagic infarcts at dorsal angle of each hemisphere, ie, in the boundary zones between the superior and posterior inferior cerebellar arterial territories. Compare with figure 11.*

Fig 12b

the parieto-occipital regions, ie, in the common boundary zone between the territories of the anterior, middle and posterior cerebral arteries: it decreases towards the frontal pole along the intraparietal and the superior frontal sulci, ie, between the anterior and middle cerebral arterial territories, and towards the temporal pole along the inferior temporal gyrus, ie, between the middle and posterior cerebral arterial territories. The lesions are usually asymmetrical and may be unilateral, the pattern of ischaemic damage often being determined by atheroma and variations in the calibre of the vessels forming the circle of Willis. In the cerebellum the boundary zone between the territories of the superior and posterior inferior cerebellar arteries lies just beneath the dorsal angle of each hemisphere (fig 12b). There is variable involvement of the basal ganglia particularly in the head of the caudate nucleus and the upper part of the putamen. The Ammon's horn and brain stem are usually not involved. While infarction in the cortical boundary zones may occur in the absence of ischaemic lesions in the basal ganglia and cerebellum the converse is not common.

On the basis of clinical evidence (Adams *et al*, 1966; Adams, 1974) and experimental studies on primates (Brierley *et al*, 1969) this type of brain damage appears to be caused by a major and abrupt episode of hypotension followed by a rapid return to a normal blood pressure. It is often seen after a conscious patient has collapsed as a result of a sudden reduction in cardiac output, viz, due to ischaemic heart disease, and it may occur in the anaesthetized subject during dental or neurosurgical procedures, particularly in the sitting position (Brierley, 1970). More recently it has been described following the use of methylmethacrylic bone cement (Adams *et al*,

1972), in patients undergoing emergency treatment with antihypertensive agents (Graham, 1975) and in patients dying from blunt head injury (Graham *et al*, 1975). Because of the precipitate decrease in arterial pressure there is a transient failure of autoregulation and a severe reduction in CBF in the regions most removed from the parent arterial stems, ie, the boundary zones.

2 Ischaemic damage is generalized in the cortex of the cerebrum and cerebellum, is minor or absent in the hippocampi and is often severe in the thalami. The number of reported cases is small (Brierley and Cooper, 1962; Adams *et al*, 1966) but it would seem that this type of damage appears to be associated with hypotension of a relatively slow onset but of long duration.

3 Ischaemic damage is generalized in the cortex of the cerebrum and cerebellum but with variable accentuation along the arterial boundary zones. The hippocampi are usually spared and there is patchy damage in the basal ganglia. This type of damage appears to be associated with the abrupt onset of hypotension which is responsible for the accentuation of damage within the boundary zones followed by a sustained period of less severe hypotension which causes the diffuse damage.

2 ANOXIC AND HYPOXIC BRAIN DAMAGE

These terms imply that the blood leaving the lungs is either devoid of or has a greatly reduced oxygen content. Hypoxaemia of this severity will occur if there is obstruction of the air passages, after the inhalation of inert gases and in aviation accidents producing decompression. Even though it is still widely believed that brain damage can result from a simple reduction in the oxygen content of arterial blood, there is a lack of critical physiological data about cases purporting to show a correlation between neurological dysfunction and brain damage ascribed to the hypoxaemia. Indeed there is good experimental evidence in Rhesus monkeys and in baboons (Brierley, 1972) that the severity of the hypoxia required to produce brain damage also produces myocardial depression and a reduction in cardiac output. Thus, Brierley concluded that hypoxic hypoxia can produce brain damage only through the medium of a secondary depression of the myocardium, the pattern of damage being similar to that of oligaemic hypoxic brain damage as described above.

3 ANAEMIC BRAIN DAMAGE

This occurs classically in carbon monoxide poisoning. The neurological complications of carbon monoxide poisoning are many (Garland and Pearce, 1967) but there is not a combination of neurological and psychiatric symptoms that can be regarded as the specific consequences of such poisoning since similar symptoms and signs may be encountered after cardiac arrest, hypoglycaemia, etc.

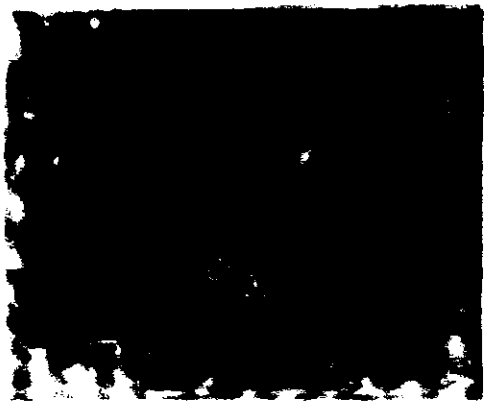


Fig 13 *Carbon monoxide poisoning. There is infarction of the superior pole of the globus pallidus (arrow). Celloidin section—myelin stain. × 1·6.*

When death occurs within a few hours after poisoning, the organs display the pink/red colour characteristic of carboxyhaemoglobin. When survival is for 36 to 48 hours, the brain shows evidence of congestion, and petechiae are frequently seen in the white matter and the corpus callosum. Although there is a particular predilection for infarction of the globus pallidus in carbon monoxide poisoning (fig 13), there is also neuronal necrosis in other selectively vulnerable regions such as the Ammon's horn and the cerebral and cerebellar cortex.

Changes in the white matter are a common and often conspicuous neuropathological consequence of carbon monoxide poisoning. Damage to white matter tends to occur, particularly in patients who develop delayed signs of intoxication after a period of relative normality following acute poisoning.

Recent experimental work in the Rhesus monkey (Ginsberg *et al*, 1974) has underlined the importance of systemic circulatory factors in the production of brain damage, the concentration of damage in the white matter possibly being due to a combination of a toxic effect of carbon monoxide together with a moderate reduction in blood flow and perhaps an additional acidosis.

4 HISTOTOXIC BRAIN DAMAGE

The histotoxic effects of the cyanide ion and sodium azide are due to the inhibition of cytochrome oxidase. In acute intoxication death ensues rapidly from respiratory failure. In such cases the brain shows

hyperaemia and multiple petechial haemorrhages. In longer surviving cases necrosis has been identified in the lentiform nucleus and in the cortex of the cerebrum and cerebellum (Brierley, 1976). Experimental studies have now shown that brain damage produced by either cyanide (Brierley, 1975) or azide (Mettler and Sax, 1972) cannot be attributed to histotoxic hypoxia alone but results from their secondary effects on respiration and circulation.

5 HYPOGLYCAEMIC BRAIN DAMAGE

Hypoglycaemia in man may lead to permanent brain damage. It may be due to an excess of insulin given either for the treatment of diabetes mellitus or psychosis and in rare instances of islet cell tumour of the pancreas and in examples of idiopathic hypoglycaemia in infants (Brierley, 1976).

In cases of short survival the brain may appear normal. There may be atrophy of the cortex and hippocampi and enlargement of the ventricular system in cases surviving for a number of weeks. Microscopy shows that the brain damage is very similar in type and distribution to that seen in ischaemic hypoxic brain damage, ie, nerve cell loss and a glio-mesodermal reaction in the striatum, the cortex and the hippocampus, except that there is often relative sparing of the Purkinje cells in the cerebellum.

Studies of hypoglycaemia in experimental animals have shown that ischaemic cell change is the principal neuropathological consequence of uncomplicated hypoglycaemia (Meldrum *et al*, 1971; Brierley *et al*, 1971a and b) and in longer surviving animals there is nerve cell loss and a variable glio-mesodermal reaction in the striatum, the cerebral cortex and the hippocampus (Kahn and Myers, 1971). These experiments show that the blood glucose level must fall to about 1 mmol/l (20 mg/100 ml) if uncomplicated hypoglycaemia is to produce brain damage, though a higher level of blood sugar may produce similar damage if complicated by some hypotension, hypoxaemia or epileptic activity. It is therefore quite possible that if a patient has been in hypoglycaemic coma for some time, both oligaemic and hypoxic factors may have contributed to the brain damage.

A different type of neuropathological change has been described in the human infant as a consequence of hypoglycaemia (Anderson *et al*, 1967). Neuronal changes were generalized and included chromatolysis with cytoplasmic vacuolation in some and fragmentation of nuclear chromatin in others. It has, however, been suggested that these appearances could be attributed to autolysis (Brierley, 1976).

6 FEBRILE CONVULSIONS AND STATUS EPILEPTICUS

Status epilepticus may be defined broadly as a convulsive episode lasting over an hour without an intervening period of consciousness (Corsellis and Meldrum, 1976). It has long been recognized as a serious danger to life at any age but it offers a special threat in childhood. The basic neuropathology is that of severe and diffuse ischaemic damage of stagnant hypoxic type in which there is widespread necrosis of the cortex, Ammon's horn, basal ganglia, thalamus, cerebellum and parts of the brain stem (fig 14). Thus status epilepticus, particularly in children, constitutes a medical emergency. Fortunately many patients make an uneventful recovery but some have a permanent intellectual or neurological deficit caused by hypoxic brain damage.

Fig 14 *Status epilepticus. Celloidin section of right temporal lobe from a child who died in coma five days after a series of convulsions. Note widespread neuronal necrosis in cortex and Ammon's horn. There is also some nerve cell loss in the thalamus. Cresyl violet. x 1·8.*

Experimental studies in subhuman primate (Meldrum and Horton, 1973; Meldrum and Brierley, 1973; Meldrum *et al*, 1973) have emphasized that several factors may contribute to the brain damage, eg, arterial hypotension and hyperpyrexia. Evidence of an impaired neuronal energy metabolism was also found due to a combination of excessive neuronal activity and accumulative effects of secondary changes such as hypoxia, hypoglycaemia, hypotension, etc.

Conclusions

Hypoxic brain damage may occur in diverse clinical situations where there is an inadequate supply of oxygen or glucose to nerve cells. Many patients who experience an episode of severe hypoxia die within a few hours when the pathologist will not be able to

identify any macroscopic abnormalities in the brain. If the patient survives for more than a few hours, however, varying degrees of damage are easily identified, particularly if the brain has been properly dissected after adequate fixation.

The identification of early hypoxic brain damage is made difficult in the human brain because of histological artefact. The earliest clearly identifiable structural damage is selective neuronal necrosis as shown by ischaemic nerve cell change with incrustation formation. If the hypoxic insult is more severe then frank infarction may occur. In each instance the necrotic tissue is replaced by a glio-mesodermal reaction.

The distribution of hypoxic damage is most easily assessed in large representative sections of the brain. It is not usually feasible for the general pathologist to undertake a comprehensive neuropathological analysis in every case of suspected hypoxic brain damage. Fortunately, however, it is possible to establish that a patient has experienced an episode of hypoxia sufficiently severe to produce widespread hypoxic damage by the histological examination of bilateral small blocks from the 'selectively vulnerable areas', namely, the arterial boundary zones, the Ammon's horns, the thalamus and the cerebellum.

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Respiratory Acidosis

Respiratory acidosis is primary increase in PCO_2 with or without compensatory increase in HCO_3^-; pH is usually low but may be near normal. Cause is a decrease in respiratory rate, volume (hypoventilation), or both due to CNS, pulmonary, or iatrogenic conditions. Respiratory acidosis can be acute or chronic; the chronic form is asymptomatic, but the acute, or worsening, form causes headache, confusion, and drowsiness. Signs include tremor, myoclonic

Treatment

- Adequate ventilation
- $NaHCO_3$ almost always contraindicated

Treatment is provision of adequate ventilation by either endotracheal intubation or noninvasive positive pressure ventilation (for specific indications and procedures, see Respiratory Failure and Mechanical Ventilation). Adequate ventilation is all that is needed to correct respiratory acidosis, although chronic hypercapnia generally must be corrected slowly (eg, over several hours or more), because too-rapid PCO_2 lowering can cause a posthypercapnic "overshoot" alkalosis when the underlying compensatory hyperbicarbonatemia becomes unmasked; the abrupt rise in CNS pH that results can lead to seizures and death. Any K^+ and Cl^- deficits are corrected.

$NaHCO_3$ is almost always contraindicated, because HCO_3^- can be converted to PCO_2 in serum but crosses the blood-brain barrier slowly, thus increasing serum pH without affecting CNS pH. One exception may be in cases of severe bronchospasm, in which HCO_3^- may improve responsiveness of bronchial smooth muscle to β-agonists.

Key Points

- Respiratory acidosis involves a decrease in respiratory rate and/or volume (hypoventilation).
- Common causes include impaired respiratory drive (eg, due to toxins, CNS disease), and airflow obstruction (eg, due to asthma, COPD, sleep apnea, airway edema).
- Recognize chronic hypoventilation by the presence of metabolic compensation (elevated HCO_3^-) and clinical signs of tolerance (less somnolence and confusion than expected for the degree of hypercarbia).
- Treat the cause and provide adequate ventilation, using tracheal intubation or noninvasive positive pressure ventilation as needed.

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Suicide By Asphyxiation Due to Helium Inhalation

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Abstract: Suicide by asphyxiation using helium is the most widely promoted method of "self-deliverance" by right-to-die advocates. However, little is known about persons committing such suicides or the circumstances and manner in which they are completed. Prior reports of suicides by asphyxiation involving helium were reviewed and deaths determined by the North Carolina Office of the Chief Medical Examiner to be helium-associated asphyxial suicides occurring between January 1, 2000 and December 31, 2008 were included in a new case series examined in this article. The 10 asphyxial suicides involving helium identified in North Carolina tended to occur almost exclusively in non-Hispanic, white men who were relatively young (M age = 41.1 ± 11.6). In 6 of 10 cases, decedents suffered from significant psychiatric dysfunction; in 3 of these 6 cases, psychiatric disorders were present comorbidly with substance abuse. In none these cases were decedents suffering from terminal illness. Most persons committing suicide with helium were free of terminal illness but suffered from psychiatric and/or substance use disorders.

Key Words: asphyxia, helium, suicide, right-to-life

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Publication, in 1991, of the right-to-die manifesto and suicide "how-to" guide, Final Exit: The Practicalities of Self-Deliverance and Assisted Suicide for the Dying,[1] roused a maelstrom of controversy regarding the appropriateness of suicide as a response to terminal or "hopeless" physical illness and exposed divisions within the right-to-die movement itself. In the 1990s, many right-to-die advocates were engaged in public education as to the purported virtues of advanced directives, living wills, and legalized physician-assisted suicide.[2] At the same time, other elements of this movement, including the Self-Deliverance New Technology (NuTech) Group, were developing technologies to "empower people to die on their own terms by controlling the timing and manner of their own death."[2(p. 87)] NuTech members, including Derek Humphry, author of Final Exit, sought to identify multiple suicide methods that were swift, painless, failure-proof, inexpensive, and nondisfiguring. The group also considered it vital that the method be simple, leave little or no indication that the death was unnatural in nature, and not require a physician's assistance or prescription.[2]

With its detailed descriptions of diverse suicide methods and specific endorsement of the plastic bag asphyxiation method, publication of Final Exit brought an easily understood and generally effective suicide method to the masses. The book was a commercial success, appearing on the New York Times bestseller list and selling more than 1.5 million copies in the decade following its publication. In 2007, Final Exit was named one of the 25 most influential books of the past quarter-century by book critics and editors of USA Today.[3]

Concerns that suicides in nonterminally ill depressed persons might follow exposure to methods elucidated in Final Exit were soon raised,[4] and dramatic increases in plastic bag asphyxial suicides were observed in New York City[5] and the United States[6] in the year following publication of Final Exit. Investigators concluded that "most persons exposed to Final Exit were not terminally ill and had used it as a suicide manual ... (and that) it is likely that a psychiatric disorder would have been diagnosed in most of these people."[5(p. 1500)]

Efforts by NuTech and others to develop a more effective suicide method and widely disseminate it to the public have continued to the present. In 2000, a supplement to Final Exit was published that presented the first description of helium-assisted plastic bag asphyxiation.[7] Advocates emphasized the enhanced lethality of this approach, reduction in time required for death to occur to less than 5 minutes, and elimination of the need for a sedative prescription. Proponents of the method also noted that materials needed to complete such suicides are readily accessible and that asphyxiation due to helium inhalation is often undetected by autopsy (where findings are typically nonspecific) or toxicological analysis (because special sampling and assay methods are required). Thus, such suicides are likely to remain undetected in cases where the helium delivery apparatus and plastic bag are removed before the death scene is examined and no other information is available implicating death by helium-assisted asphyxiation. Modifications of the helium method were published in 2002[8] and 2009,[9] a DVD including a step-by-step demonstration of the method is available for purchase,[10] and instructional videos depicting the method are accessible on the internet. A schematic of the helium delivery apparatus is presented in Figure 1.[9]

Given the recent development, broad dissemination, and notable lethality of helium-assisted suicide, we endeavored to better understand characteristics of suicides by this method. First, we reviewed findings of extant studies examining suicides by asphyxiation due to helium inhalation. Second, we report new findings from the largest series of these suicides heretofore examined. Results of this investigation may lead to improved identification of helium-assisted suicides by medical examiners, enhanced screening and prevention efforts on the part of physicians and other professionals treating individuals at risk for suicide, and shed new light on unintended deleterious consequences of widespread dissemination of detailed suicide methods to the general public.

MATERIALS AND METHODS

The current report presents findings from 2 related studies. The first is a review of published investigations of suicides by asphyxiation due to helium inhalation. The second is a case series of suicides by asphyxiation due to helium inhalation occurring in North Carolina between 2000 (the year in which the method was first described) and December 31, 2008.

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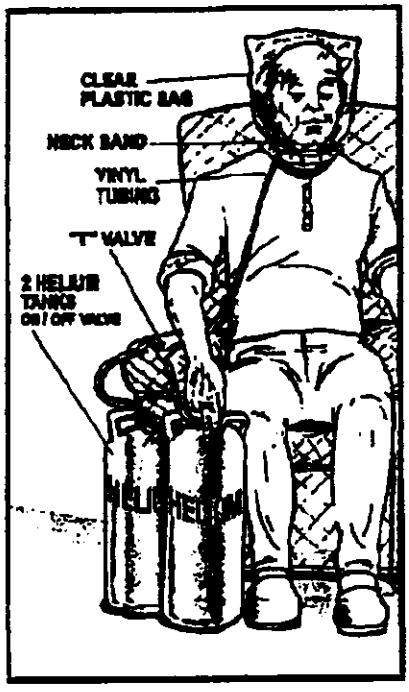

FIGURE 1. Schematic of plastic bag asphyxiation suicide using helium gas in final exit. Reprinted with permission from *Final Exit: The Practicalities of Self-deliverance and Assisted Suicide for the Dying.*[9 (p.4)]

Identification of Published Reports

A broad search of the general medical literature was undertaken for any relevant reports addressing suicide by asphyxiation due to helium inhalation. This process entailed searching the PubMed database for the period January 1, 1957 to November 1, 2009 using the search phrase "suicide and helium." Seven pertinent records were identified as follows: 6 English-language case studies[11–16] and a Danish-language case study.[17] A search of EMBASE using the identical approach for the period January 1, 1988 to November 1, 2009 identified the same 7 reports. The 6 English-language reports relevant to this review were published between 2002 and 2007 and present a total of 14 cases.[11–16] The Danish study included a synoptic abstract in English indicating that the decedent was a 35-year-old man who had committed suicide with a plastic bag and helium using a "new and highly lethal technique."[17] The case reports included in this review constitute the entirety of published research on helium-assisted suicide and are presented in Table 1.

Identification of Suicides by Asphyxiation Due to Helium Inhalation in North Carolina

All deaths determined by the North Carolina Office of the Chief Medical Examiner (NCOCME) to be asphyxial suicides due to helium inhalation that occurred between January 1, 2000 and December 31, 2008, were included in this study. These suicides were identified through a search of the manner and cause of death fields of the electronic records maintained by the NCOCME. The presence of helium was confirmed by toxicological testing in 9 of 10 identified cases. Only the first reported case (ie, 2001) was not subjected to toxicological testing for helium. Specimens from suspected helium asphyxiation cases autopsied at the NCOCME are collected in 20 mL headspace vials. In some cases, given that one central laboratory conducts testing for all medical examiner cases in the state, blood samples are delivered to the NCOCME in standard collection vials. Immediately upon arrival, 5 mL of blood from the standard autopsy vial is transferred to a headspace vial for later analysis. Medical records associated with these deaths were manually reviewed and abstracted including the OCME Report of Investigation, State of North Carolina Death Certificate, Report of Autopsy, Toxicology Report, Case Encounter Form, Pathologist's Notes, and Supplemental Report of Cause of Death. On January 5, 2010, the University of North Carolina Institutional Review Board determined that the reported research does not require Institutional Review Board approval under pertinent federal regulations. Characteristics of the 10 cases identified are presented in Table 2.

RESULTS

Review of Published Cases

The first death attributed to suicide by asphyxiation due to helium inhalation reported in the medical literature occurred in September 2000,[11] shortly after the description of the method was published. Several investigators asserted that suicides by the helium method had not been seen in their localities prior to publication of the 2000 Supplement to Final Exit.[11,12,15,16]

The 14 decedents whose cases were presented in the 6 published reports ranged in age from 19 to 81 (M age = 50.0, SD = 21.8, median = 48.5). Between these extremes, decedents were approximately evenly divided between those in their 20s, 30s, 40s, 60s, and 70s. Medical and psychiatric histories were scant or entirely unreported for some cases, but revealed a history of depression, prior suicide attempt(s), paranoid schizophrenia, or some combination thereof in 4 (25.6%) cases. In 4 (25.6%) additional cases, psychiatric dysfunction may have contributed to the suicide, given that 3 of these decedents were determined to be in good health (ages 49, 49, and 76) and one mentioned the recent death of his wife as a reason for his suicide in a note left at the death scene. In 5 other cases (including 4 decedents in their 20s or 30s), no medical or psychiatric histories were reported. A terminal disease process was present in only 2 of 14 (14.3%) cases. In 2 (14.3%) additional cases involving men ages 71 and 78, "failing health" and "unspecified health problems" were possible contributing factors. Medical disorders were not implicated in 10 of 14 (71.4%) suicides.

In all reported cases, routine toxicological testing did not reveal the presence of helium and manner and cause of death determinations relied heavily on death scene investigations. Autopsy findings tended to be absent or nonspecific in the 12 cases that involved an autopsy.

In 8 cases (57.1%), a suicide note was found, and in 4 cases (28.6%) right-to-die literature was found at the death scene.

A number of helium delivery devices were employed. Five cases involved use of a mask; 4 of these cases were reported in 2002 or 2003, before plastic bag asphyxiation (without use of a mask) became preferred by advocates of the helium method.[9] Characteristics of the plastic tubing used, use of rubber bands and Velcro straps to secure plastic bags to the neck, types of helium canisters employed, and use of multiple plastic bags in 1 case were consistent with published descriptions of helium-assisted suicide.[9]

Characteristics of Suicides by Asphyxiation due to Helium Inhalation in North Carolina

Asphyxial suicides in North Carolina involving helium inhalation tended to occur almost exclusively in non-Hispanic, white

TABLE 1. Published Case Reports of Suicides by Asphyxia Due to Helium Inhalation

Authors/Date/ Location	Characteristics of Decedent	Medical/Psychiatric History	Helium-Delivery Apparatus	Death Scene	Autopsy Findings	Toxicology Findings
Ogden and Wecht (2002), South Carolina[14]	Woman, 60, white, suffering from adenoid cystic carcinoma with reduced eye involvement and diplopia. Death occurred 9/2000	History of depression and a prior suicide attempt. Unclear whether depression/suicide attempt antedated carcinoma diagnosis.	Found with surgical mask over face and clear plastic bag over head. Next to body was refillable industrial tank of helium. Clear plastic tube led from plastic bag to helium tank valve.	Decedent discovered on living room floor of home with suicide note and copy of her will. The book Final Exit, Final Exit videotape, and Spring 2000 Hemlock society newsletter were found on a nearby coffee table.	Does not appear an autopsy was conducted. It was noted at death scene that decedent's skin color was unremarkable and no external signs of poisoning were observed.	Blood/urine tests for medications and psychoactive substances were negative.
Chiasson et al. (2002) Tucson, Arizona[15]	Cases 1 and 2: man, 49 and woman, 48, who were common-law married.	No specific information presented; decedents were reportedly in good health. Motivation for suicide unclear.	Each decedent had 3 plastic bags over their heads, which were secured by elastic straps around their necks.	Couple found lying supine by police on floor of master bedroom in their residence. Couples' attorney had called police after receiving a mailed suicide note. No right-to-die materials found.	Remarkable only for early decompositional changes.	Unremarkable for both decedents.
	Cases 3 and 4: husband, 78; wife, 76	Husband reportedly in "Failing health" and "depressed"; wife in "good health" other than a recent minor elective surgery.	Both decedents were wearing filter cartridge-style masks attached to helium tanks with plastic tubing.	Couple found dead in bed by neighbor. Suicide notes were found close to bodies. Notes referring to the Hemlock society were found in apartment. No other right-to-die materials found.	External exams unremarkable. Internal exams not performed per family's wishes.	Negative for ethanol, medications, and illicit drugs for both decedents.
Chiasson et al. (2002) Tucson, Arizona (continued)	Case 5: man, 81	Advanced squamous cell carcinoma of throat, cachectic.	Plastic bag over head with plastic tube running from inside plastic bag to helium tank.	Found by daughter in bed. Family unable to provide information as to whether "right-to-die" literature or suicide note were found at death scene.	Not clear that an autopsy was conducted.	Blood and urine tests were negative, but it was not clear what substances were assayed.
	Case 6: man, 71	Decedent mentioned unspecified health problems and the recent death of his wife as principal reasons for his suicide.	Plastic bag over head secured with elastic band and Velcro strap at neck. Plastic tube from helium tank connected to the mask inside plastic bag.	Found expired in chair in living room of home by police. A suicide note found, but no right-to-die literature.	External exam unremarkable except for decomposition.	Toxicology tests not performed due to decomposition.
	Case 7: man, 25	Medical history unknown; motivation for suicide unclear.	Plastic bag over head with plastic tube running from helium tank to bag with tube passing through a sink where water was running.	Found dead in empty bedroom of his apartment by landlord. Right-to-die literature and suicide note were not found.	Unremarkable except for decompositional changes.	Remarkable only for ethanol (2.34 mg/dL) in decomposition fluid.
Gallagher et al (2003), Indiana[16]	Woman, 19, well-nourished	History of prior suicide attempts (number and nature not described). No description of medical history. Had searched methods of suicide on the Internet.	Decedent wore air filter gas mask coated with a substance similar to corrosion fluid. A helium tank obtained from a local supply company was attached via clear plastic tubing to the mask. Duct tape sealed mask to skin of face covering nose and mouth.	Decedent found supine in backseat of car with helium tank on floor and valve between knees. Many signed suicide notes and a page from the "Church of Euthanasia" website entitled "How to kill yourself" were left in an envelope on the driver's seat. A hand-written map to a local general store was also found in the envelope with a list including tubing, mask and duct tape. A letter was found in decedent's residence describing where her body was located.	Conjunctival petechial hemorrhages bilaterally. Hands and oral cavity contained frothy white edema fluid. R lung = 670 g; L lung = 630 g. Lungs congested with severe pulmonary edema. No evidence of trauma, injury, or explanation for death other than helium inhalation.	Routine toxicology unremarkable. Presents a method by which specimens can be collected and analyzed for the presence of helium.
Auwaerter et al (2007) Freiburg, Germany[17]	Man, 21	No information presented.	A helium gas canister was connected to a plastic bag with polypropylene tubing. The bag was over the decedent's head and affixed to neck with a rubber band.	Decedent was found dead in "lying" position in undisclosed location. A nearly empty bottle of ropinirole, blister pack of travel sickness medication, and pack of ibuprofen tablets were found.	Nonspecific findings included "an edematous swelling of the brain and of the lungs and an acute hyperemia of the kidneys." No evidence of severe illness or injury.	Routine tests revealed a BAC of 0.9 mg/g; diphenhydramine in brain serum (0.86 μg/mL) and urine (2.2 μg/mL). Ibuprofen found in urine and gastric contents. A positive test for helium by novel assay method was reported.

(Continued)

TABLE 1. (Continued)

Author/Date/Location	Characteristics of Decedent	Medical/Psychiatric History	Helium-Delivery Apparatus	Death Scene	Autopsy Findings	Toxicology Findings
Gaszberger & Kronsbopf (2007) Vienna, Austria[13]	Case 1: man, 28	History of paranoid schizophrenia; otherwise, no medical history reported.	Found with plastic bag over head sealed at neck with duct tape. A 10 L tank of party balloon helium was connected to the bag via plastic tubing.	Decedent found expired in his apartment reclining in a chair. Mouth contained frothy white edema fluid. A suicide note was left which named his mental illness as the primary reason for his suicide. No right-to-die literature found in domicile.	External exam unremarkable. Engorgement of right atrium and ventricle, pulmonary edema, and a few subpleural petechiae.	Blood/urine tests for 6 classes of illicit drugs were negative. Not clear whether ethanol was assayed.
	Case 2: man, 30	Not reported	Plastic tubing led from industrial helium tank into plastic mask.	Found expired in an empty bathtub wearing a plastic mask over face. Right-to-die literature and suicide note were found.	Autopsy remarkable, only for early decompositional changes.	Tests of decomposition fluid identified a BAC of 1 mg/L.
	Case 3: man, 39	Not reported.	Plastic bag over head connected via plastic tubing to a 10 L helium tank affixed to neck with rubber band.	Found supine on floor of his apartment with plastic bag over head. A suicide note was found.	External/internal exams unremarkable except for advanced decompositional changes.	Negative except for traces of benzodiazepines in urine.
Schon & Ketterer (2007) Bern, Switzerland[14]	Man, 64, white	Not reported	A gas canister labeled "balloon" was found on a table at side of room opposite from where body was found. The balloon canister was not connected to the 17 L blue plastic garbage bag that was found over the decedent's head. In addition to the plastic ribbon used to tie the bag, the decedent had inserted a rubber band into the bag's collar. The bag was secured tightly around decedent's neck.	Decedent found expired in hotel room lying supine on bed with garbage bag over head. No alcohol bottles, medications or drug paraphernalia were found. A rental receipt for the balloon canister was found, but no suicide note or self-help materials. An inquiry at the decedent's home town revealed that another person in the area had committed suicide using the same method within the same week.	No external injuries/petechial hemorrhages found, except for a ligature mark impression attributed to a rubber band around neck. Nose, mouth, and airways filled with frothy reddish fluid. Lungs/brain edematous. Internal organs acutely congested. Pulmonary emphysema and hypertrophy/dilation of right atrium/ventricle noted. No other potential causes of death were identified.	No obvious evidence of alcohol/drug abuse, but no toxicology assays performed.

TABLE 2. Characteristic of Suicides by Asphyxiation due to Helium Inhalation in North Carolina: 2000–2008

Year of Death	Characteristics of Decedent	Medical/Psychiatric History	Helium-Delivery Apparatus	Death Scene Description	Autopsy Findings	Toxicology Blood Findings
2001	Man, 47, never-married, white (non-Hispanic) graduate school alumnus	Long history of depression treated by his physician. Depression listed as a contributing cause of suicide. Little information available about medical or psychiatric history or event precipitants of suicide.	Plastic bag over head, secured with velcro tie around neck. Plastic tubing was taped to top of head, extended down left arm under shirt sleeve and exited at left cuff. The tubing was connected to a T-valve and attached to 2 helium tanks.	Found in living room of his home by a co-worker and police. Two bottles of imipramine and a will and suicide note found at scene.	Early decompositional changes noted at death scene; no autopsy conducted.	Trace levels of 7-aminoclonazepam, and temazepam (0.016 mg/L) were identified in a 1 mL sample of vitreous humor.
2003	Man, 31, married, white (non-Hispanic), 13 yr of education	Suicide note mentioned "chronic pain" as a reason for suicide. However, medical and psychiatric history are not known.	Clear bike, thin plastic bag over head secured with 2 large yellow rubber bands around neck. Clear plastic tube taped to inside of plastic bag extending out of bag, looping around left arm and connected to helium tank.	Decedent found in his apartment. Had left a suicide note describing how he planned the suicide. No medications found in apartment.	Pathological diagnosis: bilateral pulmonary congestion. No significant external/internal injuries. Lungs: R lung: 750 g; L lung: 640 g. Petechiae of both lungs show extensive congestion with diffuse consolidation or fluid lesions. Brain: 1500 g. Leptomeninges dilated and congested. Cerebral hemispheres unremarkable with generalized edema with evidence of herniation. Microscopic exam of lungs, kidneys, and brain show vascular congestion. No evidence of injury.	Two 8.0 mL aortic blood samples were positive for helium as was one lung sample. No ethanol detected in an 18.0 mL aortic blood sample.
2005	Man, 37, married, white (non-Hispanic), 16 yr of education	Medical and psychiatric history and acute precipitants of suicide are unclear.	Found with white plastic trash bag secured head with tape looped to helium tank valve at one end and the other end within the plastic bag. Tubing was connected to the helium tank with electrical tape. The bag was secured to neck with bag tie, which was knotted in a bow knot on right anterior neck. A clear vinyl plastic tube extended from the rear of the bag apparently held in place by black electrical tape.	Death occurred in motel. Decedent found supine in bed. Medications found at scene were an OTC sleep aid, ibuprofen, and hydrocodone. Receipts from a local hardware store were found for helium tank, tubing, and tape. No suicide note or right-to-die materials were found.	Pathological diagnosis: pulmonary vascular congestion and edema, slight diffuse cerebral swelling, moderate coronary atherosclerosis. R lung: 920 g; L lung: 700 g. Lungs on section demonstrate marked vascular congestion. Bronchial branches contain clear fluid and brain-alveolar edema. Brain: 1,890g with mild diffuse swelling and narrowing of gyri. No evidence of acute trauma.	10 mL aortic blood sample revealed trace levels of cyclobenzaprine and propoxyphene and was positive (0.01 mg/L) for diphenhydramine and helium. Diphenhydramine was believed to have contributed to the death. No ethanol or organic ions were identified.
2005	Man, 21, never married, white (non-Hispanic) 12 yr of education	History of symptoms, treatment, and hospitalization for paranoia/suicidal ideation. Not clear whether patient suffered from psychotic illness.	Plastic bag over head with elastic strap securing bag around neck. An empty helium canister found on floor beside decedent. A cylinder of helium and plastic tubing were found in decedent's bedroom closet.	Found in bedroom at parent's home sitting in chair. The following medications were found in home: Trazodone (100mg), Clonidine (100mg), Risperdal (2mg), Trilafon (200mg), and Zoloft (50mg).	Pathological diagnosis: pulmonary vascular congestion and edema, cerebral edema, and early decompositional changes. R lung: 640 g; L lung: 590 g. Brain: 1,400 g. Microscopic lung sections show variable degrees of pulmonary vascular congestion and intra-alveolar hemorrhage.	Post-mortem exam revealed an ethanol level of .40 mg/dL and the presence of helium in 15.0 mL and 5.0 mL aortic blood samples, respectively.
2005	Man, 39, never married, white (non-Hispanic), 12 yr of education	No history of suicide attempts per family. Little information available about medical or psychiatric history and acute precipitants of suicide.	Found with plastic bag over head secured with a metal clip to hold bag tight around neck. Plastic tubing ran from a nearby helium tank to the back of the plastic bag. Duct tape secured front of bag and had 0.5 cm circular hole in it. Tube was connected to helium tank, which was found on bed near decedent's head.	Found lying supine in bed at home by mother. No suicide note left, but insurance policy and will were found on coffee table.	Final anatomic diagnosis: congestion of lungs with early pulmonary edema. Brain: 1,335 g. Vessels over right hemisphere congested. R lung: 610 g; L lung: 560 g. Lungs boggy with congestion. Microscopic sections show that alveolar spaces were partially filled with clear edema fluid.	Positive for helium in 4.0 mL subclavian vessel blood sample, but negative for ethanol in 17.0 mL subclavian blood sample.

(Continued)

TABLE 2. *(Continued)*

Year of Death	Characteristics of Decedent	Medical/Psychiatric History	Helium-Delivery Apparatus	Death Scene Description	Autopsy Findings	Toxicology Exam Findings
2005	Man, 34, unmarried, white (non-Hispanic); 9 yr of education	History of alcohol dependence and bipolar disorder. Prior psychiatric treatment for both disorders. Was living in car and taking Zoloft.	Had clear plastic bag over head with tubing connecting it to a helium tank. A velcro closure secured the bag around neck	Found dead in driver's seat of a car parked in the yard of a relative's house. A picture of his girlfriend was found on dashboard.	Pathological diagnoses: pulmonary edema and vascular congestion; atherosclerotic coronary artery disease, focal, mild to moderate. R lung: 960 g; L lung 820 g. Lungs heavy and congested. Lung sections revealed areas of atelectasis, pulmonary edema, and collections of pigment-laden intra-alveolar macrophages.	20.0 mL and 6.0 mL aortic blood samples were positive for ethanol (70 mg/dL) and helium, respectively. Ethanol was listed as a contributing cause of suicide.
2006	Woman, 60, never married white (non-Hispanic), 12 yr of education	Obese (5'9", 303 lbs). No medical or psychiatric history information available except that EKG leads were found on right lower leg, left lower leg and left arm. No acute precipitants of suicide were identified	Decedent had clear plastic bag over head with 1/2 inch plastic tubing attached to helium tank in back car seat and inside of plastic bag. A tan elastic band was used to secure bag to neck. The plastic tubing was taped to lower margin of plastic bag.	Decedent found in front passenger seat of car in motel parking lot where she had stayed. Letters to different people and "a very organized" suicide note were found in car. Note referred to pgs. 132–137 in Final Exit 3rd edition which describe helium-assisted suicide. Decedent had set e-mail to respond to messages with "Return to Sender due to Suicide."	Pathological diagnoses: Plastic bag over head with evidence of helium inhalation; pulmonary vascular congestion (R lung: 430 g; L lung: 400 g); decomposition. Sectioned lungs showed vascular congestion with patchy intra-alveolar edema. No evidence of acute trauma.	A 20-mL blood sample from pleural cavity was positive for helium and ethanol (40 mg/dl). Elevated BAC may have been partially or totally due to decomposition.
2007	Man, 41, married (but recently separated from wife), white (non-Hispanic), 14 yr of education	Previously disabled in motor vehicle accident with neck and back injuries. Was reportedly depressed due to recent separation from wife and pending sale of home. Wife reported that decedent was taking prescribed antidepressants, Neurontin, Oxycontin, and Vicodin.	Clear blue plastic bag covered head and was wrapped with duct tape. Black tubing was connected at one end to the inside of bag and at the other end to a 65lb helium tank used to fill balloons for parties.	Found expired at home sitting in chair in basement. No suicide note left.	No autopsy.	A 13.0 mL subclavian blood sample was negative for ethanol, but positive for helium.
2007	Man, 45, never married, white (non-Hispanic)	History of alcohol and drug abuse and diabetes. Decedent has been very depressed per family's report. Family noted a history of social, medical and emotional problems. Was taking Coumadin, Clonidine, Aspirin, Verapamil, Atenolol, and Lovastatin.	Clear plastic bag was found over head. Two black tubes led from helium tank into the plastic bag. Had purchased these materials at local hardware store. The helium tank was from a party store balloon-filling kit.	Found sitting in chair in parent's home. Patient was pulseless and not breathing. The book Final Exit was lying open and face down on the bed. A suicide note was left describing how severely depressed the decedent had felt and apologizing for the suicide.	No autopsy, but blue nail beds and burst capillaries in lower legs bilaterally were observed at death scene.	19.8 mL subclavian blood sample was negative for ethanol and positive for helium.
2008	Man, 56, married, white (non-Hispanic), 12 yr of education	History of depression and substance abuse	Decedent had a bag over his head with a tube attached to it and to a helium tank positioned on car passenger seat	Found in car in garage of home by wife with car running and exhaust piped into the vehicle. A suicide note was found.	No autopsy	18.0 mL subclavian blood sample was positive for helium and negative for ethanol. Carbon monoxide detected at <5.0% saturation.

OTC indicates over-the-counter; BAC, blood alcohol concentration; EKG, electrocardiogram.

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men who were relatively young (M age, 41.1; SD, 11.6; range, 21–60; median, 40.0). In 6 of 10 cases, decedents suffered from significant psychiatric dysfunction; in 3 of these 6 cases, psychiatric problems were present comorbidly with substance abuse. Medical histories identified chronic pain, disability, and chronic pain associated with injuries suffered in a motor vehicle accident, and diabetes (with probable coronary artery disease in 3 decedents). One decedent was found with electrocardiogram leads attached to her body, but autopsy and toxicological findings were negative for potential explanations for the death other than helium-assisted suicide. In none of the 10 cases were decedents suffering from terminal illness.

Helium delivery devices were consistent with those recommended in Final Exit (eg, use of T-valves, 2 helium tanks, Velcro and other neck fasteners), and all were associated with use of a plastic bag rather than mask.[6] In 5 cases, a suicide note was found; in 2 cases, a will was left; in 1 case, insurance papers were left; and in 2 cases, right-to-die materials were found.

Autopsies were performed in a majority of cases and typically revealed evidence of pulmonary vascular congestion and mild cerebral edema. Ethanol and diphenhydramine were considered contributing causes of death in 1 case each.

DISCUSSION

Despite reports identifying a plethora of prosuicide internet sites providing detailed instructions in methods of suicide including helium-assisted asphyxiation,[10] media accounts of helium-assisted suicides,[19–21] and the recent arrests of Final Exit Network members for allegedly assisting in asphyxial suicides involving helium,[22] scientific investigations of such suicides are largely absent from the medical literature. This dearth of information is unfortunate given the tragic consequences of such acts and because it is possible that suicides by the helium method are underestimated and increasingly common for reasons described later in the text.

The methods by which helium-assisted suicides are carried out have been carefully detailed and widely publicized and the approach is promoted as simple, painless, and quick.[6] Materials needed for helium-assisted suicides are easily obtained and inexpensive. One well-known internet vendor currently sells disposable helium tanks for less than $50, and reports that customers who bought helium tanks also often bought the book Final Exit.[23] Unless there is a high index of suspicion for helium involvement in a death, the death may be erroneously attributed to natural causes or underlying illness because standard toxicological assays are unlikely to detect helium and autopsy findings are generally nonspecific.[14,16] Standard toxicological assays using GC/MS employ helium as the carrier gas and therefore cannot detect helium unless another gas (eg, nitrogen) is substituted for the helium. Auwaeter et al[24] and Gallagher et al[13] developed useful methods of collecting, preserving, and analyzing gas samples taken from decedents' for qualitative detection of helium. In all North Carolina cases, helium-delivery devices were found at the death scene, and toxicological testing was conducted in 9 of 10 cases. However, it is possible that an unknown number of such suicides went undetected, if and when helium-delivery devices and plastic bags were removed from the death scene prior to investigation. The author of Final Exit states that a person may choose to leave right-to-die materials to be found to make an ethical statement that they are committing "rational suicide" or, conversely, make plans to have the helium delivery apparatus and plastic bag removed following their death if they prefer to keep the suicidal nature of the death concealed.[6] Toxicological testing for helium has been conducted at the NCOCME in suspected cases since 2003 by a novel testing procedure using a dual cell thermal conductivity detector.[24]

Of particular concern, are recent national reports of notable increases in the prevalence of suicide due to suffocation (a category that includes deaths by plastic bag asphyxiation with or without helium assistance as well as hanging and strangulation) since the 1990s and especially since 2000.[25–27] Such increases have been observed in respondents of widely varying ages, including adolescents, and both genders. Observers have noted that the reasons for these increases are poorly understood, that declining rates of suicide observed in the 1990s have been largely reversed, and that recent increases in suicides due to suffocation account for most of the recent overall increases in rates of suicide.[28] It is possible that greater awareness of the plastic bag asphyxiation method and the enhanced lethality of the method when used with helium may account for the significant increases in suicides due to suffocation reported since 2000.

Given the national growth in adolescent, young adult, and adult suffocation suicides since 2000,[25,26] and relatively young age, psychiatric dysfunction, and absence of terminal illness characteristic of many identified cases, it is possible that many persons committing suicide by the helium method are neither hopelessly nor terminally ill, but rather psychiatrically disordered. Although the author of Final Exit cautions readers to be certain they are hopelessly ill, and not just depressed and to talk to their doctor,[6] depressive illness and substance dependency often impair the very capacities required to make these assessments and undertake these actions.

Prospective studies are needed to better understand the prevalence, incidence, predictors, and characteristics of asphyxial suicides due to helium inhalation. It is important to learn more about decedents' medical and psychiatric histories and the circumstances in which depressed and/or suicidal persons encounter descriptions of the helium method (eg, internet demonstrations of the process). At present, professionals working with persons at risk for suicide should routinely assess whether patients have read or viewed instructional materials describing specific methods of suicide such as helium-assisted plastic bag asphyxiation. Inquiries of this nature do not increase subsequent risk for suicide and can provide critically important information to guide appropriate preventative actions where indicated.[29,30] Medical examiners should also increase their index of suspicion for suicides by asphyxiation associated with helium inhalation. Medical ethicists and the general public may also want to carefully weigh the unintended adverse consequences of widely disseminated suicide methods likely to appeal to some depressed persons (irrespective of their physical health status or age) against the putative benefits associated with making these methods more widely known and available.

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EXHIBIT 7

Report on Study of Methods of Execution & Recommendations for Procedures

Submitted by: Louisiana Department of Public Safety & Corrections

February 18, 2015

House Resolution 142 of the 2014 Regular Legislative Session was enrolled and signed by the Speaker of the House on June 5, 2014 to study and make recommendations relative to the different forms of execution and the methods of execution to determine the best practices for administering the death penalty in the most humane manner.

The Secretary of the Louisiana Department of Public Safety and Corrections, James Le Blanc, chaired this work and held an organizational meeting on July 22, 2014 to organize a study committee to conduct this work. At that time, he assigned the following individuals to serve on the committee:

Burl Cain, Warden, Louisiana State Penitentiary
William Kline, Executive Counsel, DPS&C Legal Department
Seth Smith, Chief of Operations, DPS&C Office of Adult Services
Stephanie LaMartinere, Assistant Warden, Louisiana State Penitentiary
Bruce Dodd, Deputy Warden, Louisiana State Penitentiary
James Hilburn, Attorney, Shows Cali & Walsh, LLP
Jeff Cody, Attorney, Shows Cali & Walsh, LLP
Angela Whittaker, Executive Mgmt Officer, DPS&C Secretary's Office

The committee met on the following dates:

August 11, 2014: Planning meeting to develop resource and research needs of the group.

September 2, 2014: Report and discussion on research findings.

October 31, 2014: Report and discussion regarding identifying experts and discussion on additional research compiled.

December 4, 2014: Report and discussion regarding research and protocol options and drafting the required written report.

January 8, 2015: Review of research and draft report and consensus on recommendations for protocol options.

January 22, 2015: Review and approval final report.

Background:

Capital punishment, or the death penalty, is a sentence used in the justice process whereby an offender is put to death as punishment for a crime he/she committed. The death penalty in the United States is a legal sentence and states determine whether the death penalty will be used as a form of punishment for crimes committed within their borders.

In Louisiana, the death penalty may be applied in cases involving first degree murder, a violation of La. R.S. 14:30, in circumstances such as:

(1) The murder was committed during the commission of or attempt of, a specified felony such as aggravated kidnapping, second degree kidnapping, aggravated escape, aggravated arson, aggravated rape, forcible rape, aggravated burglary, armed robbery, assault by drive-by shooting, first degree robbery, second degree robbery, simple robbery, terrorism, cruelty to juveniles, or second degree cruelty to juveniles.

(2) The murder was committed while the defendant was engaged in "ritualistic acts."

(3) The murder was committed for pecuniary gain or pursuant to an agreement that the defendant would receive something of value.

(4) The defendant caused or directed another to commit murder, or the defendant procured the commission of the offense by payment, promise of payment, or anything of pecuniary value.

(5) The defendant has been convicted of, or committed, a prior murder, a felony involving violence, or other serious felony.

(6) The capital offense was committed by a person who is incarcerated, has escaped, is on probation, is in jail, or is under a sentence of imprisonment.

(7) The defendant was a drug dealer or has prior convictions involving the distribution of a controlled substance.

(8) The victim was under the age of 12 years.

(9) The victim was 65 years or older.

(10) The victim was a fireman, peace officer, or correctional officer engaged in his lawful duties.

(11) The victim was a witness in a prosecution against the defendant, gave material assistance to the state in any investigation or prosecution of the defendant, or was an eyewitness to a crime alleged to have been committed by the defendant or possessed other material evidence against the defendant.

(12) The murder was especially heinous, atrocious, cruel or depraved (or involved torture).

Before a jury may impose the death penalty it must consider whether there were any mitigating circumstances against imposing the death penalty. Louisiana Code of Criminal Procedure Art. 905.5 provides for the following mitigating circumstances:

(a) The offender has no significant prior history of criminal activity;

(b) The offense was committed while the offender was under the influence of extreme mental or emotional disturbance;

(c) The offense was committed while the offender was under the influence or under the domination of another person;

(d) The offense was committed under circumstances which the offender reasonably believed to provide a moral justification or extenuation for his conduct;

(e) At the time of the offense the capacity of the offender to appreciate the criminality of his conduct or to conform his conduct to the requirements of law was impaired as a result of mental disease or defect or intoxication;

(f) The youth of the offender at the time of the offense;

(g) The offender was a principal whose participation was relatively minor;

(h) Any other relevant mitigating circumstance.

Pursuant to La. R.S. 15:569 and 570, every sentence of death executed on or after September 15, 1991, shall be by lethal injection, that is, by the intravenous injection of a substance or substances in a lethal quantity into the body of the offender until such person is dead.

Including Louisiana, there are currently 34 states that authorize the death penalty. Most all of these states have adopted lethal injection as the primary means of implementing the death penalty. While 18 of those states have solely authorized lethal injection as the execution method, the rest of the states that impose the death penalty have also set forth alternative methods of execution such as electrocution, lethal gas, hanging, and the use of firing squads. The methods of execution for each such state are set forth in the chart below.

Research from Other Capital Punishment States:

State	Lethal Injection	Electrocution	Gas Chamber	Hanging	Firing Squad	Methods and Alternatives	Lethal Injection Drugs
Alabama	x	x				Lethal injection, unless inmate affirmatively selects electrocution	500 mg - midazolam hydrochloride; 600 mg - rocuronium bromide; 240 milliequivalents - potassium chloride
Arizona	x		x			Lethal injection; inmate sentenced on or before 11/15/92 may choose lethal injection or lethal gas	midazlam/ hydromorphone
Arkansas	x	x				Lethal injection, but electrocution if lethal injection declared unconstitutional	Statute specifies a barbituate preceded by a benzodiazepine
California	x		x			Lethal gas or lethal injection may be chosen by inmate; if inmate fails to choose either method, then lethal injection	
Colorado	x					Lethal injection	Statute specifies sodium thiopental or equivalent
Connecticut	x					Lethal injection	
Delaware	x					Lethal injection	
Florida	x	x				Lethal injection, unless inmate affirmatively selects electrocution; if both deemed unconstitutional, then any constitutional method	
Georgia	x					Lethal injection	
Idaho	x					Lethal injection	
Indiana	x					Lethal injection	
Kansas	x					Lethal injection	
Kentucky	x	x				Lethal injection; inmates sentenced on or before 3/31/98 may choose lethal injection or electrocution	

State	Lethal Injection	Electrocution	Gas Chamber	Hanging	Firing Squad	Methods and Alternatives	Lethal Injection Drugs
Louisiana	x					Lethal injection	midazlam/hydromorphone
Mississippi	x					Lethal injection	Statute specifies an ultra short-acting barbituate in combination with a paralytic agent
Missouri	x		x			Lethal gas or lethal injection	
Montana	x					Lethal injection	Statute specifies an ultra-fast-acting barbituate in combination with a chemical paralytic agent
Nebraska	x					Lethal injection	
Nevada	x					Lethal injection	
New Hampshire	x			x		Lethal injection; but may be by hanging if lethal injection deemed "impractical"	Statute specifies an ultrashort-acting barbituate in combination with a chemical paralytic agent
New Mexico	x					Lethal injection, but only for crimes committed prior to July 1, 2009; otherwise, capital punishment repealed	
North Carolina	x					Lethal injection	
Ohio	x					Lethal injection	midazlam/ hydromorphone
Oklahoma	x	x			x	Lethal injection; but electrocution if lethal injection held unconstitutional; if both lethal injection and electrocution held unconstitutional, then firing squad	midazlam/ hydromorphone

State	Lethal Injection	Electrocution	Gas Chamber	Hanging	Firing Squad	Methods and Alternatives	Lethal Injection Drugs
Oregon	x					Lethal injection	Statute specifies an ultra-short-acting barbituate in combination with a chemical paralytic agent and potassium chloride
Pennsylvania	x					Lethal injection	Statute specifies an ultrashort-acting barbituate in combination with chemical paralytic agents
South Carolina	x	x				Electrocution, but inmate may choose lethal injection; if fails to choose either, then lethal injection; but if convicted prior to date of statute, then electrocution unless chooses lethal injection; if lethal injection held unconstitutional, then electrocution	
South Dakota	x					Lethal injection	
Tennessee	x	x				Lethal injection; but offender, whose capital offense occurred prior to 1/1/99, may choose electrocution; if those methods deemed unconstitutional, then use any constitutional method	
Texas	x					Lethal injection	
Utah	x				x	Lethal injection; but firing squad if court determines inmate has a right to this alternative; if lethal injection is held unconstitutional, then firing squad	Statute specifies that one of the intravenous injections shall be sodium thipoental or equivalent

State	Lethal Injection	Electrocution	Gas Chamber	Hanging	Firing Squad	Methods and Alternatives	Lethal Injection Drugs
Virginia	x	x				Inmate may choose lethal injection or electrocution; if refuses to choose, then lethal injection	
Washington	x			x		Lethal injection, unless inmate chooses hanging	
Wyoming	x		x		*	Lethal injection; if lethal injection is held unconstitutional, then lethal gas. *Wyoming Senate recently approved legislation that allows for the use of a firing squad. Concurrence is pending by the House.	Statute specifies an ultra-short-acting barbituate, alone or in combination with a chemical paralytic agent and potassium chloride

It may be noted that the basis for utilizing a particular method of execution is not necessarily uniform among the states that offer more than one execution method. In some states, lethal injection is the primary execution method unless it should be declared unconstitutional, in which case the statute next provides for an alternate method, or a series of alternate methods in the event a successive method should be deemed unconstitutional. In other states, the condemned inmate is actually given a choice between lethal injection and another alternate method of execution.

In Louisiana, between 1919 and May 21, 1957, executions were conducted by the local parish law authorities. Prior to August 6, 1941, the penalty in Louisiana was carried out by hanging. The last hanging in Louisiana was on March 7, 1941. Between August 6, 1941 and June 9, 1961, executions were performed by electrocution in the electric chair. Between 1941 and 1957, a portable electric chair was transported from parish to parish in order that the death penalty could be administered in the parish where the crime was committed. After 1957, the State became responsible for administering the death penalty. Prior the reinstatement of capital punishment, the last death in the electric chair was on June 9, 1961.

In 1967, there was a rising tide of litigation against the death penalty. Federal courts suspended all executions pending a final decision by the U.S. Supreme Court. In 1972, the U.S. Supreme Court struck down all capital punishment laws as unconstitutional. All individuals under death sentenced at that time were re-sentenced to life in prison.

Effective October 1, 1976, the new Louisiana death penalty statute was adopted. The state's death penalty law was again revised in 1978, specifying that the sentencing judge must sign the death warrant rather than the governor. Capital punishment was reinstated in Louisiana on June 29, 1979.

In 1990, the legislature approved the use of lethal injection for those sentenced after January 1, 1991. In 1991, the legislature provided that every death sentence executed after September 15, 1991 would be by lethal injection. Since the reinstatement of the death penalty in 1979, there have been 28 executions performed, 20 by electrocution and 8 by lethal injection. The last one was on January 7, 2010.

The death penalty has risen to the forefront of national headlines recently due to the shortage of drugs historically used in the lethal injection process. States continuing to carry out executions have been forced to obtain drugs from other sources or substitute drugs normally used in the process. The alternatives have provided inmates with new grounds for appeal as they request transparency regarding execution methods.

To date, Louisiana has 85 offenders in custody who have been sentenced to death.

Study:

This study was conducted by reviewing available scientific, technical and safety literature related to various methods of execution. It is not intended to express an opinion about Louisiana's law for administration of capital punishment.

Lethal Injection Protocols:

Through February 2011, Louisiana had in place a three drug protocol which included 3 gm sodium thiopental, 50 mg pancuronium bromide and 240 meq potassium chloride.

In February 2011, after lawsuits, international trade restrictions and raw materials shortages complicated the market for drugs used in executions and the lack of availability of sodium thiopental, a decision was made to modify the three 3 drug protocol to use pentobarbital in lieu of sodium thiopental. This decision was based on experiences in Oklahoma using pentobarbital and the use of it being upheld in the United State District Court in the Western District of Oklahoma. Base on the change, the protocol then called for 1 gm of Pentobarbitol, 50 mg pancuronium bromide and 240 meq potassium chloride.

In January 2014, the protocol was again updated to provide two options for lethal injection. They are:

A) 5 gm of Pentobarbital or
B) 10 mg of Midazolam and 40 mg of Hydromorphone

Recommended Protocols:

A. Lethal Injection

We are recommending for consideration a lethal injection protocol that calls for the use of a one drug protocol utilizing 5 gm of Pentobarbital injected intravenously (IVP). This protocol has been used in numerous states, including Texas, as a one drug method. The availability of this drug to Departments of Corrections is however severely hampered and there could be issues obtaining a supply of Pentobarbitol or any other drug to be used for lethal injection. Drug suppliers have refused to sell drugs to the prison systems for use in executions and other entities have refused to sell to Louisiana DOC. It is this committees understanding that suppliers have threatened providers with no longer supplying the drugs to their businesses if they in turn sell to correctional agencies for the purpose of lethal injection. As a result, suppliers fear the backlash of bad publicity to their businesses if involved in providing the drugs to correctional agencies.

This committee also recommends reconsideration of a bill that combines the language from the original and amended versions of House Bill 328 of the 2014 Legislative Session authored by Representative Lopinto. The attached draft legislation (Appendix A) amending LA R.S. 15:569 outlines what is needed to allow for the recommendations within this report and will provide for the confidentiality of information related to the execution of a death sentence. The amended version of the prior bill stated that "The name, address, qualifications, and other identifying information of any person or entity that manufactures, compounds, prescribed, dispenses, supplies or administers the drugs or supplies utilized in an execution shall be confidential, shall not be subject to disclosure, and shall not be admissible as evidence or discoverable in any action of an kind in any court or before any tribunal, board, agency, or person. The same confidentiality and protection shall also apply to any person who participates in an execution or performs any ancillary function related to an execution and shall include information contained in any department records, including electronic records, that would identify any such person." Such legislation would provide some security to those tasked to and involved in carrying out the state's order to execute an individual as punishment for a qualifying crime.

It should also be noted that the U.S. Supreme Court will consider in April whether a multi-drug protocol used in recent lethal injections in other states violates the Constitution with regard to cruel and unusual punishment.

B. Induced Hypoxia via Nitrogen

It is the recommendation of this study group that hypoxia induced by the inhalation of nitrogen be considered for adoption as an alternative method of administering capital punishment in the State of Louisiana.

It is important to note that the recommendation would induce hypoxia, which is a deficiency of oxygen reaching the tissues of the body. In nitrogen induced hypoxia, there is no buildup of carbon dioxide in the bloodstream so the subject passes out when the blood oxygen falls too low. The research reviewed suggests that this method would be the most humane method and would not result in discomfort or cruel and unusual punishment to the subject.

Though the exact protocol and nitrogen delivery device have not been finalized, it has been determined that a Gas Chamber would not be used. Options for the nitrogen delivery device include a mask or a device similar to an oxygen tent house (small clear oxygen tent covering only the head and neck area). Research as to the best method of delivery is ongoing.

Oklahoma has recently filed similar legislation to allow for induced hypoxia (refer to Appendix B). Also, you will find attached the Executive Summary (Appendix C) of the research conducted in Oklahoma that supports this method as a humane method which does not require the assistance of licensed medical professionals. We have also attached the documents (Appendix D) which make up the research used in Oklahoma by this committee in developing this recommendation. This method is believed to be simple to administer and nitrogen is readily available.

Conclusion:

This committee submits this study response to House Resolution 142 of the 2014 Regular Legislative Session to make recommendations to consider relative to the different forms of execution and the methods of execution upon agreement that the above considerations represent the best practices for administering the death penalty in the most humane manner. There are two sides to the debate on the death penalty. Proponents believe that the death penalty reduces crime and provides safe communities, while also honoring the victim and those left behind who grieve a loss. Opponents believe that the cost of capital punishment doesn't justify the outcome, that it does not deter crime, and that there are social injustices that are not addressed that make justice system inequitable. As a whole, this committee takes no stand on either side of this debate, but submits this response based on the request for this study and the research and materials available to the group.

We close reminding readers that many are directly impacted by the process of capital punishment: the victim, the victim's friends and family; law enforcement; the judiciary, the prosecutor, the defense attorney, the jurors, the public, the offender, the offender's family, and the staff tasked to carry out the protocol, to name just a few. We understand that the decision to act on these recommendations for consideration is an enormous task before you that cannot be taken lightly. We trust that we have provided the information you needed to consider Louisiana's options.

Amendment to LSA-R.S. 15:569

**Delete current Sections A and B; rewrite statute to read as follows:

Section 1. R.S. 15:569 is hereby amended to read as follows:

§569. Place for execution of death sentence; manner of execution; confidentiality

Every sentence of death executed in this state on or after August 1, 2015, shall be conducted by either of the following methods:

(1) Lethal injection, which is the intravenous injection of a substance or substances in a lethal quantity into the body of a person convicted until such person is dead. Execution by lethal injection shall be permitted in accordance with procedures developed by the department.

(2) Induced hypoxia via nitrogen or an inert gas, which is the administration of gas in a lethal quantity upon the body of a person convicted until such person is dead. Execution by nitrogen or inert gas shall be permitted in accordance with procedures developed by the department.

A. The method of execution shall be chosen by the secretary of the department based upon the availability of the department to administer the lethal injection or induced hypoxia.

B. Every sentence of death imposed in this state shall be executed at the Louisiana State Penitentiary at Angola. Every execution shall be made in a room entirely cut off from view of all except those permitted by law to be in that room.

C. No licensed health care professional shall be compelled to administer the lethal injection or induced hypoxia.

D. The name, address, qualifications, and other indentifying information of any person or entity that manufactures, compounds, prescribes, dispenses, supplies, or administers the drugs or supplies utilized in an execution shall be confidential, shall not be subject to disclosure, and shall not be admissible as evidence or discoverable in any action of any kind in any court or before any tribunal, board, agency, or person. The same confidentiality and protection shall also apply to any person who participates in an execution or performs any ancillary function related to an execution and shall include information contained in any department records, including electronic records, that would identify any such person.

E. The provisions of the Administrative Procedure Act, R.S. 49:950, et seq., shall not apply to the procedures and policies concerning the process for implementing a sentence of death.

STATE OF OKLAHOI

1st Session of the 55th Legislature (2015)

HOUSE BILL 1879 By: Christian

AS INTRODUCED

An Act relating to criminal procedure; amending 22 O.S. 2011, Section 1014, which relates to the manner of inflicting punishment of death; providing alternative method for inflicting punishment of death; and providing an effective date.

BE IT ENACTED BY THE PEOPLE OF THE STATE OF OKLAHOMA:

SECTION 1. AMENDATORY 22 O.S. 2011, Section 1014, is amended to read as follows:

Section 1014. A. The punishment of death shall be carried out by the administration of a lethal quantity of a drug or drugs until death is pronounced by a licensed physician according to accepted standards of medical practice.

B. If the execution of the sentence of death as provided in subsection A of this section is held unconstitutional by an appellate court of competent jurisdiction or is otherwise unavailable, then the sentence of death shall be carried out by nitrogen hypoxia.

C. If the execution of the sentence of death as provided in ~~subsection~~ subsections A and B of this section is held unconstitutional by an appellate court of competent jurisdiction or is otherwise unavailable, then the sentence of death shall be carried out by electrocution.

~~C.~~ D. If the execution of the sentence of death as provided in subsections A ~~and~~, B and C of this section is held unconstitutional by an appellate court of competent jurisdiction or is otherwise unavailable, then the sentence of death shall be carried out by firing squad.

SECTION 2. This act shall become effective November 1, 2015.

55-1-6354 GRS 01/20/15