

## **EXECUTIVE SUMMARY**

The danger of importing prescription drugs is real and the reason we don't see all the dead bodies is because we don't much look for that anymore. The incentive to import prescription drugs is, essentially, greed and these people need to follow the same rules which apply to all pharmacies in the United States including state licensure where called for. Inspections of pharmacy locations can be accomplished through a private organization and there's a definite role for the Federal Customs Service in policing these imports.

Credit card companies and delivery service operations should be held responsible for aiding and abetting illegal activity. State standards need to be followed by importers as a classic function of the police power of the state. Many prescription drugs are available illegally in Mexican tiendas including drugs which are not approved for human use in the United States. Any regulatory scheme should include all prescription drugs not just controlled substances.

There could be a role for the United Nations including the World Health Organization in a multilateral agreement involving the importing or exporting of pharmaceuticals including the use of the Internet.

## The Danger is Real

In this day of anxiety over terrorism we see the vivid red-orange flash on television of an explosion making the death and destruction real. The same kind of damage can happen with pharmaceuticals but it doesn't make the evening news.

We all have seen the aftermath of the bus bombings in Madrid but people don't realize that many more deaths occurred in the 1990's worldwide due to just one pharmaceutical ingredient, tainted glycerin. [See Appendix 1 "China Exported Sweet Poison"] About 200 people died in Madrid recently but poisonous glycerin killed over 300 in the final decade of the last century. My interest is above average in this area as I was privileged to be an invited observer at the WHO Conference on Starting Materials for Pharmaceutical Products in Geneva in May of 1998 that produced recommendations to prevent these tragedies.

Other calamities occur such as the incident in Brazil where 650,000 monthly packages of birth control tablets were sold which contained no active ingredient. Counting the women and their partners this certainly affected the private lives of over 1 million people, not counting the surprise babies.

The World Health Organization estimates that the circulation of counterfeit medicines is at least 10% of the world market. And this includes drugs that are not just placebos but have actively harmful ingredients.

### Where are the Dead Bodies?

This is a question that legislators and bureaucrats always ask when the safety issue is raised. The sad fact is that we seldom do autopsies, due either to liability concerns or arrogance. The National Center for Health Statistics has stopped collecting autopsy statistics altogether. [See Appendix 2, “Final Cut” *The New Yorker*, March 19, 2001.] Take my case for example. I take Warfarin daily due to an artificial heart valve installed about two years ago. If I were to get a bogus batch of Warfarin with no active ingredient I would be dead in two weeks and it wouldn’t make any sense to do an INR level on a dead body. Corpses are notoriously poor responders during an investigation.

So the people that are in good faith asking for evidence in the form of dead bodies are actually requesting proof that doesn’t exist anymore.

### Incentive is Greed

A recent segment on National Public Radio's "Morning Edition" highlighted the problem with counterfeit drugs in international commerce.

Pharmaceuticals are extremely expensive. A one month supply of Procrit, a drug for anemia caused by cancer chemotherapy, costs \$1,800 for just four vials. There's an increased awareness by criminals that they can make much better money with less risk to them by dealing with fake pharmaceuticals rather than drugs like Heroin and Crack.

### State Licenses or Permits Necessary

As Executive Director of the state board of pharmacy I am particularly concerned about the accountability and responsibility for prescription products sent to our state's citizens. We have a state statute which requires registration in the form of a permit for out-of-state (mail order) pharmacies. We view the Internet and Canadian pharmacies as just another entry point for mail-order pharmacies. Over forty states have a requirement for registration of out-of-state pharmacies that do business in this way. The subject here is the protection of the public health, safety and welfare; a

classic example of the state exercise of the police power. The short story is that if these operators are not required to get an out-of-state license then they have nothing to lose.

### Inspect Locations

The National Association of Boards of Pharmacy has a program which verifies Internet Pharmacy Practice Sites (VIPPS). This is a service operated by the Association which provides an on-site inspection by a trained and experienced pharmacy board inspector to evaluate each location where Internet pharmacies operate.

If the location passes the rigorous inspection they are awarded a “seal of approval” in the form of the service mark VIPPS owned by the National Association of Boards of Pharmacy. This is a valuable assurance to the public that this business operates in conformance with the applicable statute and rules. Any decision about verifying quality should include this kind of inspection which already exists. It would not need to be duplicated at the federal level.

### Role for Customs

The North Carolina Board believes that the U. S. Customs and Border Protection Division of the United States Department of Homeland Security is in a unique position to review all packages declared as prescription drug products entering this country intended for United States consumers.

Customs could perform a valuable function by reviewing the source of these products with a list of state licensees in the more than forty states which require registration for mail order pharmacies. Shipments from locations which are not licensed in designated states should be returned to the shipper.

When a shipper such as FedEx or UPS delivers prescription drugs in violation of state law they should be held responsible for aiding and abetting such violations. When credit card companies such as Visa, Mastercard and American Express enable payments for these transactions contrary to state law they are also aiding and abetting this illegal conduct.

### Ability to Discipline

We have had numerous reports of irregularities involving prescription orders sent from Canada to North Carolina citizens. Just as this statement was being prepared we had an incident of a consumer complaint regarding a

prescription originally written by a North Carolina physician for Toprol XL which was filled with Lopressor. When the patient called to complain about an apparent dispensing error the response was that a Canadian physician had changed the order from one drug to another. This also involved a change from a time-release dosage form to immediate release in violation of FDA standards published in the Orange Book.

#### Prescription Order Definition

Under North Carolina rule a physician cannot issue a valid prescription without examining the patient or having a prior physician/patient relationship. This patient had never met the Canadian physician who changed the order to a different product in violation of state law and FDA standards.

The matter of individual state definitions for prescription order validity is one critical topic which needs to be addressed by the Task Force. We believe that one group of practitioners should not be put at a significant advantage or disadvantage under these circumstances.

### Meet U.S. Standards

The standard form used by most Canadian pharmacies requires the consumer to accept non-child resistant packaging, contrary to U.S. standards which have saved the lives of hundreds of children. Consumers also surrender all rights to claim against the pharmacy or their employees and any dispute must be resolved by arbitration in Canada using Canadian criteria.

Other Canadian businesses operate in our state and conform to federal and state standards. RBC Centura Bank is a Canadian company and is a good corporate citizen. At least four Canadian insurance companies are licensed with the North Carolina Department of Insurance to do business here.

Canadian pharmacies seeking to do business here should follow the same laws applied to all other pharmacies including mail-order activities. The refusal of Canadian pharmacies to even attempt to comply with U.S. laws reveals an attitude of contempt which foreshadows future trouble.

### Mexican Connection

A North Carolina citizen was traveling through Mexico and purchased what was represented to be Levsin .125 mg., a product available without a prescription in that country. When she returned to the United States she



noticed that the color, though similar, looked somewhat different. A close examination at her family pharmacy revealed that she had received Lanoxin .125 mg. Had she continued the same three times a day dosage with Lanoxin there is no doubt she would have expired soon.

There is a significant amount of prescription drug traffic through Mexican grocery stores in the United States. Hispanics in their native lands often have no physician available so they self-diagnose their conditions and obtain pharmaceuticals at food stores known as Tiendas. Along with tacos and piñatas they brought this self-treatment custom with them from their homeland.

Physicians in North Carolina complain that Spanish-speaking patients arrive at emergency rooms with unprescribed antibiotics, steroids and even controlled substances. Every hospital is obliged to treat patients who arrive under emergency conditions. Charges not covered by health plans are absorbed and contribute to increased costs in health care. This Latino population is a new and growing burden on hospitals with much of it caused by their unorthodox and unsupervised use of pharmaceuticals.

One fundamental fact of drug use is that there is an immense difference between oral and injectable products. A patient who is in distress from an adverse reaction to an oral product can have their intestinal tract evacuated on both ends if necessary. This is uncomfortable but effective in removing the offending product from the body. Drugs administered by injection, however, are virtually impossible to remove once inside the skin. Treatment is much more difficult and sometimes it is not possible to save the patient from an adverse reaction from an injected drug.

Part of the transplant of Hispanic culture is self-diagnosis followed by use of injectable drugs. This results in very powerful antibiotics such as Lincocin and Gentamicin, obtained in Tiendas, being used indiscriminately without a competent diagnosis.

Serious allergic reactions or run-away infections and deaths have resulted from using wrong antibiotics to treat an infection. Even the injectable steroid Phenylbutizone, which can only be used in horses in this country, has been found in Tiendas in North Carolina.

The Food and Drug Protection Division at the North Carolina Department of Agriculture has state jurisdiction over this conduct and has investigated complaints on this activity. When their investigators were stalked by an obvious criminal element they wisely retreated to re-evaluate their procedures. These dedicated civil servants are not trained to deal with or expect to confront this kind of intimidating behavior.

Complaints have been filed for selling this contraband at at least seven different locations in our state. The Burke County Sheriff raided a store twice and seized over 75 products including controlled substances. There are now nearly 400,000 Hispanics in this state, a population about the size of Greensboro and Winston-Salem combined.

This is an interstate and international matter which needs to be addressed by the Food and Drug Administration without delay.

#### Internet Access

It is now possible for consumers to get access to prescription drugs including controlled substances with only two requirements: access to the Internet and a credit card number. A news story from California related the death of a

young man from an overdose of Diazepam/Propoxephene/Codeine obtained from an Internet source. Many of these websites are located in foreign countries and control in the United States will depend on the diligence of the United States Customs Service.

Internet pharmacies seem to be ubiquitous. Just as I am on the final draft of this submission, two solicitations for controlled substances available without prescriptions appeared on my computer screen, at least one of which comes from Germany. [See Appendixes 3 & 4]

Perhaps this practice needs to be regulated by an international agreement negotiated at the United Nations.

#### Include All Prescription Drugs

It's important that any procedure to assure quality of imports includes all prescription drugs and not just controlled substances. We have data from more than ten years of reports from our no fault reporting system. This has revealed that over 80% of deaths due to drugs dispensed through pharmacies in North Carolina are attributable to regular prescription drugs that are not

controlled substances. There is no reason to believe that national statistics would be any different from our results. [ See Appendix 5]

### Conclusion

The danger of importing prescription drugs is real and the reason we don't see all the dead bodies is because we don't much look for that anymore. The incentive to import prescription drugs is, essentially, greed and these people need to follow the same rules which apply to all pharmacies in the United States including state licensure where called for. Inspections of pharmacy locations can be accomplished through a private organization and there's a definite role for the Federal Customs Service in policing these imports. Credit card companies and delivery service operations should be held responsible for aiding and abetting illegal activity. State standards need to be followed by importers as a classic function of the police power of the state. Many prescription drugs are available illegally in Mexican tiendas including drugs which are not approved for human use in the United States. Any regulatory scheme should include all prescription drugs not just controlled substances.

There could be a role for the United Nations including the World Health Organization in a multilateral agreement involving the importing or exporting of pharmaceuticals including the use of the Internet.

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## China exported a sweet poison

By DAVID R. WORK

CARRBORO

Once again China has ducked the spotlight of public scrutiny on its responsibility for human rights abuses.

In a recent maneuver in Geneva at a meeting of the U.N. Human Rights Commission, Chinese diplomats succeeded in preventing a vote on a resolution condemning China's activities. Gloating over the victory, a spokesman said China prefers cooperation over confrontation.

But that's not the attitude experienced by health officials who investigated a tragedy in Haiti recently.

### POINT OF VIEW

The problem arose from the use of glycerin, a sweet and thick liquid used in many commercial products, including soap. In this case, the glycerin was used in making Afebril, a brand name of an acetaminophen product used to treat fever and pain in children.

At least 89 children died from this product in Haiti.

A reconstruction of events shows that a shipment left China for the Netherlands on Dec. 14, 1994. It was labeled as 98.36 percent glycerin.

Several transactions occurred, some only on paper, before a Haitian pharmaceutical manufacturer purchased some of the glycerin. It left the Netherlands on Feb. 25, 1995, for Port Au Prince.

Apparently neither the Chinese manufacturer, the Dutch/German shipper or the Haitian pharmaceutical firm had test-

ed the glycerin. All relied on the labeling from China.

A batch from the same shipment was later analyzed, in part, at 55 percent glycerin and 22 percent diethylene glycol.

All participants agreed that the children's deaths in Haiti were caused by the diethylene glycol. This impurity, used commercially to make antifreeze for automobiles, is well known in the pharmaceutical trade. In fact, it caused hundreds of deaths in the United States in 1937, when substandard glycerin was used to make a drug product.

The public uproar over that tragedy produced the U.S. Food, Drug and Cosmetic Act of 1938, which is the foundation for today's law.

The World Health Organization investigated the Haitian matter with the cooperation of Dutch, German and Haitian officials. China stubbornly declined to answer inquiries.

It is morally inexcusable for this to occur today, 60 years after the problem was identified and addressed. China's callous refusal to cooperate with the investigation is a shining example of the conduct which human rights advocates find objectionable.

Defenders of China in this matter, if any could be found, might claim that China's glycerin manufacturing is an internal matter and not subject to scrutiny by outsiders. This is clearly a bogus argument when the glycerin and diethylene glycol mixture is exported and exposed to world standards. No nation can claim to be insulated from the rest of the world today, especially the world's most populous country, with an immense international trade.

Given the casual and disorganized nature of gathering and reporting such information in developing countries, we

could expect that many more such incidents occur than are reported. Even under these conditions, we know that almost 350 children have died in recent years in Haiti, Nigeria and Bangladesh from this poisonous glycerin, with minimal public concern. Compare these numbers, for example, to the 230 people who died on TWA Flight 800 and the media attention to that event.

Recent years have also seen many shipments of defective clothing from China,

either directly or through Hong Kong, clothing that burns faster than newspaper. Combusting sweat-shirts are the latest example in a long line of lethal prod-

*...And Haitian children paid the ultimate price.*

ucts from China. Promoters of property rights see nothing wrong in the processing and sale of such articles because, after all, *caveat emptor*.

It has been alleged that China uses prison labor to make products or add value to existing materials. Prison labor is nothing more than another term for transient slavery when the efforts are aimed at profit. Surely we haven't developed a blind spot to this despicable conduct.

An opportunity for progress in human rights will occur in the near future when the trained engineers slated to succeed the old revolutionaries in the Deng Xiaoping regime move into power. They are familiar with product standards — and their recognition of similar principles in human relations would be a giant step forward.

The most recent president of the United States educated as an engineer was Jimmy Carter; both countries could benefit if China's new leaders could speak with him on human rights matters.

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## APPENDIX 2

Medical Dispatch

The New Yorker, March 19, 2001

### FINAL CUT

#### Medical arrogance and the decline of the autopsy

BY ATUL GAWANDE

Your patient is dead; the family is gathered. And there is one last thing that you must ask about: the autopsy. How should you go about it? You could do it off handedly, as if it were the most ordinary thing in the world: "Shall we do an autopsy, then?" Or you could be firm, use your Sergeant Joe Friday voice: "Unless you have strong objections, we will need to do an autopsy, ma'am." Or you could take yourself out of it: "I am sorry, but they require me to ask, Do you want an autopsy done?"

What you can't be these days is mealy-mouthed about it. I once took care of a woman in her eighties who had given up her driver's license only to get hit by a car driven by someone even older-- while she was walking to a bus stop. She sustained a depressed skull fracture and cerebral bleeding, and, despite surgery, she died a few days later. So, on the spring afternoon after the patient took her last breath, I stood beside her and bowed my head with the tearful family. Then, as delicately as I could--not even using the awful word--I said, "If it's all right, we'd like to do an examination to confirm the cause of death."

"An autopsy?" a nephew said, horrified. He looked at me as if I were a buzzard circling his aunt's body. "Hasn't she been through enough?"

The autopsy is in a precarious state. A generation ago, it was routine; now it has become a rarity. Human beings have never quite become comfortable with the idea of having their bodies cut open after they die. Even for a surgeon, the sense of violation is inescapable.

Not long ago, I went to observe the dissection of a thirty-eight-year-old woman I had taken care of who had died after a long struggle with heart disease. The dissecting room was in the subbasement, past the laundry and a loading dock, behind an unmarked metal door. It had high ceilings, peeling paint, and a brown tiled floor that sloped down to a central drain. There was a Bunsen burner on a countertop, and an old-style grocer's hanging scale, with a big clock face red-arrow gauge and a pan underneath, for weighing organs. On shelves all around the room there were gray portions of brain, bowel, and other organs soaking in formalin in Tupperware-like containers. The facility seemed run-



down, chintzy, low-tech. On a rickety gurney in the corner was my patient, sprawled out, completely naked. The autopsy team was just beginning its work..

Surgical procedures can be grisly, but dissections are somehow worse. In even the most gruesome operations--skin- grafting, amputations--surgeons maintain an attitude of tenderness and aestheticism toward their work. We know that the bodies we cut still pulse with life, and that these are people who will wake again. But in the dissecting room, where the person is gone and only the carcass remains, you find little of this delicacy, and the difference is visible in the smallest details. There is, for example, the simple matter of how a body is moved from gurney to table. In the operating room, we follow a careful, elaborate procedure for the unconscious patient, involving a canvas-sleeved rolling board and several gentle movements. We don't want so much as a bruise. Down here, by contrast, someone grabbed my patient's arm, another person a leg, and they just yanked. When her skin stuck to the stainless steel dissecting table, they had to wet her and the table down with a hose before they could jerk her the rest of the way.

The young pathologist for the case stood on the sidelines and let a pathology assistant take the knife. Like many of her colleagues, the pathologist had not been drawn to her field by autopsies but by the high-tech detective work that she got to do on tissue from living patients. She was happy to leave the dissection to the P.A., who had more experience at it anyway.

The P.A. was a tall, slender woman of around thirty with straight sandy-brown hair. She was wearing the full protective garb of mask, face shield, gloves, and blue plastic gown. Once the body was on the table, she placed a six-inch metal block under the back between the shoulder blades, so that the head fell back and the chest arched up. Then she took a scalpel in her hand, a big No. 6 blade, and made a huge Y-shaped incision that came down diagonally from each shoulder, curving slightly around each breast before reaching the midline, and then continued down the abdomen to the pubis.

Surgeons get used to the opening of bodies. It is easy to detach yourself from the person on the table and become absorbed by the details of method and anatomy. Nevertheless, I couldn't help wincing as she did her work: she was holding the scalpel like a pen, which forced her to cut slowly and jaggedly with the tip of the blade. Surgeons are taught to stand straight and parallel to their incision, hold the knife between the thumb and four fingers, like a violin bow, and draw the belly of the blade through the skin in a single, smooth slice to the exact depth desired. The P.A. was practically sawing her way through my patient.

From there, the evisceration was swift. The P.A. flayed back the skin flaps. With an electric saw, she cut through the exposed ribs along both sides. Then she lifted the rib cage as if it were the hood of a car, opened the abdomen, and removed all the major organs--including the heart, the lungs, the liver, the bowels, and the kidneys. Then the skull was sawed open, and the brain, too, was removed. Meanwhile, the pathologist was at a back table, weighing and examining everything and preparing samples for microscopy and thorough testing.

Despite all this, the patient came out looking surprisingly undisturbed. The PA had followed the usual procedure and kept the skull incision behind the woman's ears, where it was completely hidden by her hair. She had also taken care to close the chest and abdomen neatly, sewing the incision tightly with weaved seven-cord thread. My patient actually looked much the same as before, except now a little collapsed in the middle. (The standard consent allows the hospital to keep the organs for testing and research. This common and long established practice is now causing huge controversy in Britain--the media have branded it "organ stripping"--but in America it remains generally accepted.) Families can still have an open-casket funeral' and most do. Morticians employ fillers to restore a corpse's shape and when they're done you cannot tell that an autopsy has been performed.

Still, when it is time to ask for a family's permission to do such a thing the images weigh on everyone's mind--not least the doctor's. You strive to achieve a cool, dispassionate attitude toward these matters. But doubts nevertheless creep in.

One of the first patients for whom I was expected to request an autopsy was a seventy-five-year-old retired New England doctor who died one winter night while I was with him. Herodotus Sykes (not his real name, but not unlike it, either) had been rushed to the hospital with an infected, rupturing abdominal aortic aneurysm and taken to emergency surgery. He survived it and recovered steadily until eighteen days later, his blood pressure dropped alarmingly and blood began to pour from a drainage tube in his abdomen. "The aortic stump must have blown out," his surgeon said. Residual infection must have weakened the suture line. We could have operated again, but the patient's chances were poor, and his surgeon didn't think he would be willing to take any more.

He was right. No more surgery, Sykes told me. He's been through enough. We called Mrs. Sykes, who was staying with a friend, about two hours away, and she set out for the hospital.

It was about midnight. I sat with him as he lay silent and bleeding, his arms slack at his sides, his eyes without fear. I imagined his wife out on the Mass Pike, frantic, helpless, with six lanes, virtually empty at that hour, stretching far ahead.

Sykes held on, and at 2:15 A.M. his wife arrived. She turned ashen at the sight of him, but she steadied herself. She gently took his hand in hers. She squeezed, and he squeezed back. I left them to themselves.

At two-forty-five, the nurse called me in. I listened with my stethoscope, then turned to Mrs. Sykes and told her that he was gone. She had her husband's Yankee reserve, but she broke into quiet tears, weeping into her hands, and seemed suddenly frail and small. A friend who had come with her soon appeared, took her by the arm, and led her out of the room.

We are instructed to request an autopsy on everyone as a means of confirming the cause of death and catching our mistakes. And this was the moment I was supposed to ask--

with the wife despondent and reeling with shock. But surely, I began to think, here was a case in which an autopsy would be pointless. We knew what had happened --a persistent infection, a rupture. We were sure of it. What would cutting the man apart accomplish?

And so I let Mrs. Sykes go. I could have caught her as she walked through the ICU's double doors. Or even called her on the phone later. But I never did.

Such reasoning, it appears, has become commonplace in medicine. Doctors are seeking so few autopsies that in recent years The Journal of the American Medical Association has twice felt the need to declare "war on the nonautopsy."

According to the most recent statistics available, autopsies have been done in less than ten per cent of deaths; many hospitals do none. This is a dramatic turnabout. Through much of the twentieth century, doctors diligently obtained autopsies in the majority of all deaths --and it had taken centuries to reach this point. As Kenneth Iserson recounts in his fascinating almanac, "Death to Dust," physicians have performed autopsies for more than two thousand years. But for most of history they were rarely performed, and only for legal purposes (if religions permitted them at all--Islam, Shinto, and the Greek Orthodox Church still frown on them). The Roman physician Antistius performed one of the earliest forensic examinations on record, in 44 BC, on Julius Caesar, documenting twenty-three wounds, including a final, fatal stab to the chest. In 1410, the Catholic Church itself ordered an autopsy on Pope Alexander V, to determine whether his successor had poisoned him. No evidence of this was found.

Even in the nineteenth century, long after church strictures had loosened, people in the West rarely allowed doctors to autopsy their family members for medical purposes. As a result, the practice was largely clandestine. Some doctors went ahead and autopsied hospital patients immediately after death, before relatives could turn up to object. Others waited until burial and then robbed the graves, either personally or through accomplices, an activity that continued into the twentieth century. To deter such autopsies, some families would post nighttime guards at the grave site--hence the term : "graveyard shift." Others placed heavy stones on the coffins. In 1878, one company in Columbus, Ohio, even sold "torpedo coffins," equipped with pipe bombs rigged to blow up if they were tampered with. Yet doctors remained undeterred. Ambrose Bierce's "The Devil's Dictionary," published in 1906, defined "grave" as "a place in which the dead are laid to await the coming of the medical student."

By the turn of the century, however, prominent physicians such as Rudolf Virchow, in Berlin, Karl Rokitansky, in Vienna, and William Osler, in Baltimore, began to win popular support for the practice. They defended it as a tool of discovery, one that was used to identify the cause of tuberculosis, reveal how to treat appendicitis, and establish the existence of Alzheimer's disease. They showed that autopsies prevented errors--that without them doctors could not know when their diagnoses were incorrect. Most deaths were a mystery then, and perhaps what clinched the argument was the notion that autopsies could provide families with answers--give the story of a loved one's life a

comprehensible ending. Once doctors had insured a dignified and respectful dissection at the hospital, public opinion turned. With time, doctors who did not obtain autopsies were viewed with suspicion. By the end of the Second World War, the autopsy was firmly established as a routine part of death in Europe and North America.

So what accounts for its decline? It's not because families refuse--to judge from recent studies, they still grant that permission up to eighty per cent of the time. Doctors, once so eager to perform autopsies that they stole bodies, have simply stopped asking. Some people ascribe this to shady motives. It has been said that hospitals are trying to save money by avoiding autopsies, since insurers don't pay for them, or that doctors avoid them in order to cover up evidence of malpractice. And yet autopsies lost money and uncovered malpractice when they were popular, too.

Instead, I suspect, what discourages autopsies is medicine's twenty-first-century, tall-in-the-saddle confidence. When I failed to ask Mrs. Sykes whether we could autopsy her husband, it was not because of the expense, or because I feared that the autopsy would uncover an error. It was the opposite: I didn't see much likelihood that an error would be found. Today, we have MRI. scans, ultrasound, nuclear medicine, molecular testing, and much more. When somebody dies, we already know why. We don't need an autopsy to find out.

Or so I thought. Then I had a patient 'who changed my mind.

He was in his sixties, whiskered and cheerful, a former engineer who had found success in retirement as an artist. I will call him Mr. Jolly, because that's what he was. He was also what we call vasculopath--he did not seem to have an undiseased artery in him. Whether because of his diet or his genes or the fact that he used to smoke, he had had, in the previous decade, one heart attack, two abdominal aortic-aneurysm repairs, four bypass operations to keep blood flowing past blockages in his leg arteries, and several balloon procedures to keep hardened arteries open. Still, I never knew him to take a dark view of his lot. "Well, you can't get miserable about it," he'd say. He had wonderful children. He had beautiful grandchildren. "But, aargh, the wife," he'd go on. She would be sitting right there at the bedside, and would roll her eyes, and he'd break into a grin.

Mr. Jolly had come into the hospital for treatment of a wound infection in his legs. But he soon developed congestive heart failure, causing fluid to back up into his lungs. Breathing became steadily harder for him, until we had to put him in the ICU, intubate him, and place him on a ventilator. A two-day admission turned into two weeks. With a regimen of diuretics and a change in heart medications, however, his heart failure reversed, and his lungs recovered. And one bright Sunday morning he was reclining in bed, breathing on his own, watching the morning shows on the TV set that hung from the ceiling. "You're doing marvellously," I said. I told him we would transfer him out of intensive care by the afternoon. He would probably be home in a couple of days.

Two hours later, a code-blue call went out on the overhead speakers. When I got to the ICU and saw the nurse hunched over Mr. Jolly, doing chest compressions, I blurted out

an angry curse. He'd been fine, the nurse explained, just watching TV, when suddenly he sat upright with a look of shock and then fell back unresponsive. At first, he was asystolic--no heart rhythm on the monitor--and then the rhythm came back, but he had no pulse. A crowd of staffers set to work. I had him intubated, gave him fluids and epinephrine, had someone call the attending surgeon at home, someone else check the morning lab-test results. An X-ray technician shot a portable chest film.

I mentally ran through possible causes. There were not many. A collapsed lung, but I heard good breath sounds with my stethoscope, and when his X-ray came back the lungs looked fine. A massive blood loss, but his abdomen wasn't swelling, and his decline happened so quickly that bleeding just didn't make sense. Extreme acidity of the blood could do it, but his lab tests were fine. Then there was cardiac tamponade--bleeding into the sac that contains the heart. I took a six-inch spinal needle on a syringe, pushed it through the skin below the breastbone, and advanced it to the heart sac. I found no bleeding. That left only one possibility: a pulmonary embolism-- a blood clot that flips into the lung and instantly wedges off all blood flow. And nothing could be done about that.

I went out and spoke to the attending surgeon by phone and then to the chief resident, who had just arrived. An embolism was the only logical explanation, they agreed. I went back into the room and stopped the code. "Time of death: 10:23 A.M.," I announced. I phoned his wife at home, told her that things had taken a turn for the worse, and asked her to come in.

This shouldn't have happened; I was sure of it. I scanned the records for clues. Then I found one. In a lab test done the day before, the patient's clotting had seemed slow, which wasn't serious, but an ICU physician had decided to correct it with vitamin K. A frequent complication with vitamin K is blood clots. I was furious. Giving the vitamin was completely unnecessary--just fixing a number on a lab test. Both the chief resident and I lit into the physician. We all but accused him of killing the patient.

When Mrs. Jolly arrived, we took her to a family room where it was quiet and calm, with table lamps instead of fluorescent lights and soft, plump chairs. I could see from her face that she'd already surmised the worst. His heart had stopped suddenly, we told her, because of a pulmonary embolism. We said the medicines we gave him may have contributed to it. I took her to see him and left her with him. After awhile, she came out, her hands trembling and her face stained with tears. Then, remarkably, she thanked us. We had kept him for her all these years, she said. Maybe so, but neither of us felt any pride about what had just happened.

I asked her the required question. I told her that we wanted to perform an autopsy and needed her permission. We thought we already knew what had happened, but an autopsy would confirm it, I said. She considered my request for a moment. If an autopsy would help us, she finally said, then we could do it. I said, as I was supposed to, that it would. I wasn't sure I believed it.

I wasn't assigned to the operating room the following morning, so I went down to observe the autopsy. When I arrived, Mr. Jolly was already laid out on the dissecting table, his arms splayed, skin flayed back, chest exposed, abdomen open. I put on a gown, gloves, and mask, and went up close. The PA began buzzing through the ribs on the left side with the electric saw, and immediately blood started seeping out, as dark and viscous as crank case oil. Puzzled, I helped him lift open the rib cage. The left side of the chest was full of blood. I felt along the pulmonary arteries for a hardened, embolized clot, but there was none. He hadn't had an embolism after all. We suctioned out three litres of blood, lifted the left lung, and the answer appeared before our eyes. The thoracic aorta was almost three times larger than it should have been, and there was a half-inch hole in it. The man had ruptured an aortic aneurysm and had bled to death almost instantly.

In the days afterward, I apologized to the physician I'd reamed out over the vitamin, and pondered how we had managed to miss the diagnosis. I looked back through the patient's old X-rays and now saw a shadowy outline of what must have been his aneurysm. But none of us, not even the radiologists, had caught it. Even if we had caught it, we wouldn't have dared to do anything about it until weeks after treating his infection and heart failure, and that would have been too late. It disturbed me, however, to have felt so confident about what had happened that day and to have been so wrong.

The most perplexing thing was his final chest X-ray, the one we had taken during the code blue. With all that blood filling the chest, I should have seen at least a haze over the left side. But when I pulled the film out to look again there was nothing.

How often do autopsies turn up a major misdiagnosis in the cause " of death? I would have guessed this happened rarely, in one or two per cent of cases at most. According to three studies done in 1998 and 1999, however, the figure is about forty per cent. A large review of autopsy studies concluded that in about a third of the misdiagnoses the patients would have been expected to live if proper treatment had been administered. George Lundberg, a pathologist and former editor of *The Journal of the American Medical Association* who has done more than anyone to call attention to these figures, points out the most surprising fact of all: the rates at which misdiagnosis is detected have not improved in autopsy studies since at least 1938.

With all the recent advances in imaging and diagnostics, it's hard to accept that we not only get the diagnosis wrong in two out of five of our patients who die but that we have also failed to improve over time. To see if this could really be true, doctors at Harvard put together a simple study. They went back into their hospital records to see how often autopsies picked up missed diagnoses in 1960 and 1970, before the advent of CT, ultrasound, nuclear scanning, and other 'technologies, and then in 1980, after they became widely used. The researchers found no improvement. Regardless of the decade, physicians missed a quarter of fatal infections, a third of heart attacks, and almost two-thirds of pulmonary , emboli in their patients who died.

In most cases, it wasn't technology that failed. Rather, the physicians did not consider the correct diagnosis in the first place. The perfect test or scan may have been available, but the physicians never ordered it.

In a 1976 essay, the philosophers Samuel Gorovitz and Alasdair MacIntyre explored the nature of fallibility. Why would a meteorologist, say, fail to correctly predict where a hurricane was going to make landfall? They saw three possible reasons. One was ignorance: perhaps science affords only a limited understanding of how hurricanes behave. A second reason was ineptitude: the knowledge is available, but the weatherman fails to apply it correctly. Both of these are surmountable sources of error. We believe that science will overcome ignorance, and, that training and technology will overcome ineptitude. The third possible cause of error the philosophers posited, however, was an insurmountable kind, one they termed "necessary fallibility."

There may be some kinds of knowledge that science and technology will never deliver, Gorovitz and MacIntyre argued. When we ask science to move beyond explaining how things (say, hurricanes) generally behave to predicting exactly how a particular thing (say, Thursday's storm off the South Carolina coast) will behave, we may be asking it to do more than it can. No hurricane is quite like any other hurricane. Although all hurricanes follow predictable laws of behavior, each one is continuously shaped by myriad uncontrollable, accidental factors in the environment. To say precisely how one specific hurricane will behave would require a complete understanding of the world in all its particulars--in other words, omniscience.

It's not that it's impossible to predict anything; plenty of things are completely predictable. Gorovitz and MacIntyre give the example of a random ice cube in a fire. Ice cubes are so simple and so alike that you can predict with complete assurance that an ice cube will melt. But when it comes to inferring exactly what is going on in a particular person, are people more like ice cubes or like hurricanes?

Right now, at about midnight, I am seeing a patient in the emergency room, and I want to say that she is an ice cube. That is, I believe I can understand what's going on with her, that I can discern all her relevant properties. I believe I can help her.

Charlotte Duveen, as we will call her, is forty-nine years old, and for two days she has had abdominal pain. I began observing her from the moment I walked through the curtains into her room. She was sitting cross-legged in the chair next to her stretcher and greeted me with a cheerful, tobacco-beaten voice. She did not look sick. No clutching the belly. No gasping for words. Her color was good--neither, flushed nor pale. Her shoulder-length brown hair had been brushed, her red lipstick neatly applied.

She told me the pain had started out crampy, like a gas pain. But then, during the course of the day, it had become sharp and focussed, and as she said this she pointed to a spot on the lower right side of her abdomen. She had developed diarrhea. She constantly felt as if she had to urinate. She didn't have a fever. She was not nauseated. Actually, she was hungry. She told me that she had eaten a hot dog at Fenway Park two days ago, and she

asked if that might have anything to do with this. She had also seen the birds at the zoo a few days earlier. She has two grown children. Her last period was three months ago. She smokes half a pack a day. She used to use heroin but said she's clean now. She once had hepatitis. She has never had surgery.

I felt her abdomen. It could be anything, I thought: food poisoning, a virus, appendicitis, a urinary-tract infection, an ovarian cyst, a pregnancy. Her abdomen was soft, without distension, and there was an area of particular tenderness in the lower right quadrant. When I pressed there, I felt her muscles harden reflexively beneath my fingers. On the pelvic exam, her ovaries felt normal. I ordered some lab tests. Her white-blood-cell count came back elevated. Her urinalysis was normal. A pregnancy test was negative. I ordered an abdominal CT scan.

I am sure I can figure out what's wrong with her, but, if you think about it, that's a curious faith. I have never seen this woman before in my life, and yet I presume that she is like the others I've examined. Is it true? None of my other patients, admittedly, were forty-nine-year-old women who had had hepatitis and a drug habit, had recently been to the zoo and eaten a Fenway frank, and had come in with two days of mild lower-right-quadrant pain. Yet I still believe. Every day, we take people to surgery and open their abdomens, and, broadly speaking, we know what we will find: not eels or tiny chattering machines or a pool of blue liquid but coils of bowel, a liver to one side, a stomach to the other, a bladder down below. There are, of course, differences--an adhesion in one patient, an infection in another--but we have catalogued and sorted them by the thousands, making a statistical profile of mankind.

I am leaning toward appendicitis. The pain is in the right place. The timing of her symptoms, her exam, and her white-blood-cell count all fit with what I've seen before. She's hungry, however; she's walking around, not looking sick, and this seems unusual. I go to the radiology reading room and stand in the dark, looking over the radiologist's shoulder at the images of Duveen's abdomen flashing up on the monitor. He points to the appendix, wormlike, thick, surrounded by gray, streaky fat. It's appendicitis, he says confidently. I call the attending surgeon on duty and tell him what we've found. "Book the OR," he says. We're going to do an appendectomy.

This one is as sure as we get. Yet I've worked on similar cases with identical results from the CT scan--in which we opened the patient up and found a normal appendix. Surgery itself is a kind of autopsy. "Autopsy" literally means "to see for oneself," and, despite our knowledge and technology, when we look we're often unprepared for what we find. I want to think that my patient's condition is as predictable as the sun's rising, as the melting of an ice cube, and maybe I have to. But I've been around long enough to know that in human beings the simplest certainties can be dashed.

Whether with giving patients or cadavers, we do not know until we look. Even in Mr. Sykes's case, I now wonder whether we put our stitches in correctly, or whether the bleeding had come from somewhere else entirely. Doctors are no longer asking these questions. And our arrogance only deepens. In 1995, the National Center for Health



Statistics stopped collecting autopsy statistics altogether. We can no longer even say how rare autopsies have become

## APPENDIX 3

**From:** Moffiex@aol.com  
**Sent:** Tuesday, April 27, 2004 8:52 AM  
**To:** David R. Work  
**Subject:** Fwd: Re Hydrocodone

Dr. Work,

I'm a registered pharmacist here in North Carolina but only work in long term care. I received this email on my AOL account. Is this legal? Don't we have enough diversion problems without someone advertising controlled substances without a prescription on the Internet? What can we do to stop this?

Margaret Sgritta, Pharm.D., CGP, FASCP  
Holladay Healthcare  
Winston-Salem, NC

**From:** Saul Helton [s\_heltonki@modellbahn-an-und-verkauf.de]  
**Sent:** Monday, April 26, 2004 5:34 PM  
**To:** moffiex@aol.com; moffin@aol.com  
**Subject:** Re Hydrocodone  
Buy top painkillers without prescription

Today's special: Free overnight Fedex delivery

Vicodin.....\$2.56/dose  
Hydrocodone.....\$2.12/dose  
Norco.....\$2.97/dose

Stock is limited and selling fast, so hurry  
[Buy them here](#)

## APPENDIX 4

**From:** Robin B. Huffman [rhuffman@ncpsychiatry.org]  
**Sent:** Tuesday, April 27, 2004 10:57 AM  
**To:** David R. Work  
**Subject:** FW: bu.y .prescriptio,n meds online w/out ;pre:script:ion;  
Mr. Work--

Before I deleted this spam message, I was terribly curious about who is getting away with doing this and what can be done? Is this within the purview of the Pharmacy Board???? Thanks so much.

Robin Huffman  
Executive Director NC Psychiatric Association  
4917 Waters Edge Drive, Suite 250  
Raleigh, NC 27606  
919-859-3370  
fax: 919-851-0044  
email: rhuffman@ncpsychiatry.org  
web: www.ncpsychiatry.org

-----Original Message-----

**From:** Elvin Hutchison [mailto:ehutchisonwt@tvtv.de]  
**Sent:** Tuesday, April 27, 2004 3:39 PM  
**To:** rhuffman@ncpsychiatry.org  
**Subject:** bu.y .prescriptio,n meds online w/out ;pre:script:ion;

Buy top painkillers without prescription

Today's special: Hydrocodone (10mg/500mg) bulk offer available

Hydrocodone.....\$2.27/dose  
Vicodin.....\$3.24/dose  
Valium.....\$2.86/dose

Overnight FedEx delivery on all purchases

[Buy them here](#)

[No, thanks](#)

THE CHARLOTTE OBSERVER

THURSDAY, JUNE 15, 2000 ...

## It's the legal drugs that are killing

Study by N.C. Board of Pharmacy finds 90 percent of drug deaths in this state are result from use of legal prescription drugs, not misuse of controlled substances.

By DAVID WORK

Special To The Observer

**L**ate last year the Institute of Medicine released a report that jolted the American public. Headlines noted nearly 100,000 deaths per year due to medical errors and other equally sensational statements. Our president also made the network news when he announced plans for health workers to report their own mistakes to a federal agency.

Consumers were alarmed, while physicians, nurses and pharmacists believed they were victims of a federal smear. And critics openly questioned what could be learned from collecting reports on these events.

It's not news that malfeasance by members of the health care team can produce disastrous results. Such an event occurred at a large hospital in Charlotte in 1988. Fluids used in surgery were mislabeled resulting in two patient deaths. About one year later at another large hospital in Durham a death occurred due to a mistake with a cancer drug and these events caused the North Carolina Pharmacy Board to pioneer a rule on reporting deaths due to drugs dispensed through pharmacies. At the time board members were seeking bad pharmacists to protect the public. A few were found, but other unexpected information was produced.

When the rule was adopted in 1992, observers expected narcotics or other controlled substances to cause most of the reports. But that has not been the case. A recent summary revealed that the largest single category of drugs causing deaths are anticoagulants such as warfarin and heparin. Another surprising fact is that controlled substances are responsible for less than 20 percent of reports, and that was down to about 10 percent for the last two years.

Certainly the most startling fact is that 80 to 90 percent of deaths are from regular prescription drugs, and not from abusable and addicting narcotic controlled substances.

Some readers may find these

statistics difficult to accept. I live in a community where research studies are more abundant than pine pollen in the spring, and massaging data from these projects has been known to distort results to support a predetermined position. That didn't occur in this case. There is a clear delineation of drugs that are controlled or non-controlled, and reports came from random sources that were not controlled by board staff.

Public policy now dictates that we spend resources on activities such as separate controlled substance registration for doctors, pharmacists, hospitals and pharmacies at both the federal and state level. Substantial resources are also devoted to inventories, audits, shift counts in hospitals and even duplicate or triplicate prescription blanks in some states.



BARRE MAGUIRE

However, tracking non-controlled drugs, which cause at least 80 percent of deaths, is such a minor matter that it is not separately listed in the federal budget, while over a billion dollars is spent each year on controlled substances that cause less than 20 percent of deaths. The FDA is under tremendous pressure to approve new drugs, and I know they want to follow such products closer after marketing, but public policy makers in Congress have yet to recognize this problem.

Certainly controlled substances cause problems with abuse and addiction that deserve government attention, but both of these conditions are treatable. The ultimate drug reaction — one that causes a patient to die — is not

treatable and cries out for close examination. To paraphrase a recently fashionable political slogan, "It's the other drugs, not the controlled substances, stupid!"

Fault is presumed in the Institute's report when an event is labeled as an error even if the facts may not clearly point to culpability. As a person with eight years experience examining reports of deaths due to drugs dispensed through pharmacies, I can state that few cases are clear-cut. One example is a patient taking the blood thinner warfarin who is bruised from a fall and expires from loss of blood due to the bruise. How can fault be assigned in this situation? We should not forget that nearly all of these reports involve patients who are extremely ill often with multiple medical problems.

Any incident reporting system will succeed only if the reporting physicians, nurses and pharmacists trust the agency and know that their reports won't be considered as confessions. The national government does not cultivate such trust, so another organization should collect such reports.

The most viable alternative is the existing MedMARx program operated by the United States Pharmacopeial Convention (USP), a private non-profit group located in Rockville, Md. The USP is an online anonymous collection system with tremendous potential. It is a respected standard-setting organization consisting primarily of doctors and pharmacists with broad representation from other health professions. It was organized in 1820 and is one of the oldest medical organizations in this country (predating the American Medical Association, which was founded in 1847).

The North Carolina experience demonstrates that much can be learned from a reporting system that works to protect the public without automatic vengeance against doctors and nurses. Licensing boards and peer review organizations are best suited to weed out incompetent performance and keep the national government out of the equation.

David R. Work is the executive director of the North Carolina Board of Pharmacy and adjunct professor at the UNC School of Pharmacy in Chapel Hill.