

Welcome to the forensic toxicology podcasts. This is Dr. Sanela Martić, a faculty member in the Department of forensic science at Trent University. Opioids are drugs that have been used for millennia. They've been used for the treatment of pain, they've been used for spiritual purposes and for recreational purposes because opioids can provide effective pain relief, they can also produce a euphoria.

Opioids are drugs that come from opium. And it was about 200 years ago that a German chemist figured out how to isolate one of the more potent molecules in opium, the sap from the opium poppy. What this chemist figured out how to do was to isolate morphine. And it didn't take very long for morphine to begin to make its way into many different medical products. Products that were either prescribed or in some cases sold over-the-counter. It was in the mid 1800s that the United States began to experience its first opioid crisis. This was an epidemic of opioid addiction that was developing because the population in the US was becoming overexposed to opioids. You had Civil War soldiers who were becoming addicted to morphine that was prescribed to them. But you also had many middle-class, middle aged housewives who were becoming addicted to morphine. You had many doctors who had as the business model, their medical practice prescribing lots of morphine. These were doctors who might have patients visiting their office multiple times a day to receive a morphine injection. By the late 1800s, the opioid addiction epidemic had grown severe.

Overdose deaths involving morphine had risen to very high levels, and there was an awareness among health officials across the United States about the risks and dangers of products containing morphine. It was in the midst of that morphine epidemic that the Bayer Corporation introduced a new opioid called heroin. And when the Bayer Corporation introduced heroin, it actually promoted heroin as a safer alternative to morphine. There was lots of concern about overdose risk with morphine, and so heroin was promoted as having a lower risk of overdose death, and the Bayer Corporation pointed to studies that they had done in mice to try and show that there was less risk of overdose death from decreased breathing. We'll probably never know whether or not those studies were done incorrectly or whether it was all made up as part of a marketing strategy, but we do know that heroin is not safer than morphine. Shortly after heroin was released onto the market, we began seeing a new type of opioid addiction problem. We began seeing young Americans, particularly in urban areas, begin using heroin non-medically. These were young white street toughs in New York City. They were the children of immigrants, they were Italian, Irish, Jewish. They were purchasing pharmaceutical grade heroin tablets, crushing them and snorting them. And so we began to see this overlapping epidemic of opioid addiction in non-medical users of prescription opioids. By 1914, the problem had grown so severe that the federal government stepped in and began passing laws to better regulate the sale and prescribing of narcotics. You just heard a short audio from History of Opioid use in America by Dr.

Andrew Kolodny, who discussed how opiates and opioids entered North America and their uses. *R. v. Worrall* 2004 Canlii 66306 ON SC. About mid afternoon on January 2, 2000, a pedestrian walking by a construction site noticed a fully clothed body of a young man lying on the ground, the pedestrian flagged a police cruiser and told the officer what he had seen. The person on the ground was Brendan Carlin, the chef at a restaurant nearby. There was no signs of violence apparent on the body and no indication that Brendan Carlin had been robbed. Shortly before four o'clock that same afternoon on January 2nd, the attending coroner pronounced Brendan Carlin dead. Brendan Carlin lived in a two-bedroom basement apartment at 50 Gerrard Street East with his step brother, Joseph Worrall, who also worked at the same restaurant. Almost a month later, on February 4, 2000, police officers arrested Joseph on a charge of manslaughter in connection with the death of Brendan Carlin. Now let's consider a current case *R. v. Worrall* 2004, where heroin and its metabolite play an important role. Specifically, the post-mortem analysis of biological fluids was used in this case to determine the presence of heroin and metabolites, and ultimately factors that contributed to death. We will hear about evidence provided by two forensic toxicologists. The first evidence will come from Dr. Robert Langille, who is a forensic toxicologist at the CFS. And a second evidence will come from Dr.

Bruce Goldberger, who is a forensic toxicologist at the University of Florida. Let's hear the evidence by toxicologists and reflect on their findings. Dr.

Robert Langille is a forensic toxicologist from the CFS. He directs and performs analyses on samples for the presence of drugs, poisons, and alcohol. His specific expertise include the absorption, distribution, and elimination of alcohol, and the metabolism, and pharmacokinetics of drugs, their effects on the body and behavior. He gave evidence as an expert in the field of toxicology, pharmacology, and the behavioral effects of alcohol and drugs. Dr. Langille reported that a

concentration of 117 nanogram per mil of morphine was found in Brendan Carlin's blood. Morphine is a drug itself, and an active metabolite of heroin. It was the evidence of Dr. Langille that traces of codeine were detected in the deceased's heart blood.

In large amounts, codeine may be metabolized to morphine. In cross-examination, Dr. Langille acknowledged that there was no testing done on the skin of the deceased's left forearm around what appeared to be an injection site. And similarly for 6-MAM, 6-monoacetylmorphine. The witness explained that such testing was not done by toxicologists and in all events was unlikely to reveal traces of heroin since the drug breaks down so quickly and is very hard to extract from a large piece of skin, rather than the blood as used here in this case. Dr. Langille acknowledged that a single-site could be misleading or produce misleading results. For example, he analyzed only heart blood, not femoral blood, although femoral blood was available for morphine and other drug testing. He pointed out, however, that there was no redistribution of morphine in blood. So he rejected analysis of the liver to determine concentrations because he did not consider the analysis valuable. It was the evidence of Dr. Langille that as soon as heroin is injected into the blood, a large amount of it is converted to 6-MAM. The presence of 6-MAM in biological tissues or bodily fluids establishes the presence of heroin, of which 6-MAM is an active metabolite. In this case, 6-MAM was detected but not quantified in the deceased's urine. Dr. Langille reported that a wide range of post-mortem morphine blood concentrations had been found in persons who have died from a heroin overdose. In some cases, the level is so low that it is undetected. In others, the concentrations may be as high as 1400 nanograms per milliliter, more than ten times what was found in the case of Brendan Carlin. The median level, according to the literature, is about 60 nanograms per mL, about half the level in Brendan Carlin when he died. In non-tolerant persons, the level found could cause death. Tolerance is a factor in more experienced users. Dr. Langille gave evidence that persons may die immediately or within hours of heroin injection, a rapid onset or acute death, or several hours later after falling asleep or passing into unconsciousness, then a coma, and finally, death. Studies support the view that if a person urinates after taking heroin, the drug generally disappears after about two hours. Dr. Langille testified that heroin breaks down in the consumer's body. It has a half-life of five minutes and rapidly breaks down into 6-MAM, which has a half-life of 30 minutes, then further into morphine. During each half-life, one half of the concentration leaves the blood. Morphine is detectable in the blood for as few as 10 to 12 hours and as many as 20 to 24 hours, but certainly not more than a day. It is a general rule of thumb that most drugs are essentially eliminated after five half-lives. In cross-examination, Dr.

Langille acknowledged that the best way to determine whether a person was a chronic or naive heroin user was to look for withdrawal symptoms over a period of one or two days without the drug. Hair analysis is also beneficial in determining the use frequency, but it lacks specificity. The CFS does not test hair and did not test the deceased's hair to determine the frequency in this case. Dr. Langille testified that the morphine noted in this case was free, not total morphine for which the CFS does not test. There was no analysis of the deceased's urine for morphine concentration because blood, where morphine was detected, provides a much more accurate picture. The use of heart blood is not misleading because there is no postmortem redistribution of morphine, at least in Dr. Langille's view. Those who differ about postmortem distribution, differ about whether it increases or decreases the concentration. Dr.

Langille conceded that persons survive with a greater morphine concentration than that found in Brendan Carlin. He pointed out however, that many, many more guys with lower concentrations than occurred here. In this case, there was a low-level of 6-MAM in the deceased's urine, indicative of either recent consumption or previously high consumption of heroin, reduced by urination, leaving only a small concentration in the blood to be filtered into the urine. The level of 6-MAM permits no real inference about timing or earlier concentrations, unfortunately, Dr.

Langille expressed the view that the concentration of heroin/morphine he detected in Brendan Carlin's blood was potentially fatal, especially in a naive user. He considered heroin a more significant contribution to Brendan Carlin's death than any other drugs that were tested for. In cross-examination, Dr.

Langille agreed that although he assigned more weight to heroin, meaning morphine, than other drugs on board with the deceased, the others could not be ruled out. He, however, made it clear that he does not determine or express an opinion about cause of death. He's able to say by comparing the concentrations of drugs found and reviewing the literature whether a concentration was potentially fatal. The cause of death is up to the pathologist or coroner. Dr. Langille agreed that the morphine concentration found in Brendan Carlin had been fatal in some cases, but was not absolutely consistent with that from heroin intoxication. He pointed out, however, that determining cause of death was the role of the

pathologist, not a toxicologist, because other factors beyond the concentration itself required consideration. Dr. Langille agreed that he had not measured the concentration of free morphine and its metabolites in the deceased's blood. This measurement may have helped to determine whether Carlin's death was immediate, let's say under 15 minutes, or more prolonged. He suggests that, that the concentration of 6-MAM in the deceased's urine, should be assigned weight because it would not necessarily indicate immediate death from heroin, only the recently use. Let's reflect on the evidence presented by Dr.

Robert Langille in the case where biological fluids from deceased Brendan Carlin were tested. So Dr. Robert Langille is quite qualified to testify and to present evidence as he's a forensic toxicologist at the Centre of Forensic Science. What can we conclude about his findings? We can conclude that morphine was found in the blood. We also conclude that heroin was not found, whatsoever, in any biological fluid. We can also conclude that 6-monoacetylmorphine was found as well, specifically in the urine. So the presence of morphine and 6-MAM clearly indicates consumption of heroin, as 6-MAM is a metabolite of heroin and an indicator of heroin use. Now this case also discusses a couple of other chemicals or drugs that we didn't go into detail. But Dr.

Langille interprets his finding as heroin being the major contributor to the death itself. However, no heroin was actually detected in any biological fluids tested.

Why is that? Well, as Dr. Langille nicely puts it, the heroin breaks out in the body quickly within minutes. So that means if you want to analyze biological fluids many hours or days later, you're not likely to find that heroin there. You are likely to find, for example, metabolites. So as in this case, heroin falls apart to 6-MAM and 6-MAM has a half-life of about a half an hour, so almost ten times longer than heroin itself. And then morphine actually has an even longer half-life than 6-MAM itself, so that would mean that morphine concentrations would still be measurable, but not heroin, for example, concentrations after a day or so. The second point in this case is really interesting, is the biological fluids tested. Specifically the biological fluids tested were blood and urine. Now what is important is that hair, for example, was raised in this case as an alternative, but it was not tested at the time, and that hair would actually perfectly provide you a biological tissue or a matrix that could be used to chronologically along the hair length, analyze for heroin metabolites. And that would give you information about the types and frequency of use, and you can differentiate if that person was a chronic or naive heroin user. This however was not done in this case. The other bit that is really interesting in the case is the analysis of biological fluids came postmortem, and Dr.

Langille, only analyzed in blood from a single site, specifically used the heart blood. Now there's a second site potentially available, which is the femoral blood, and both of those should be analyzed. What we find often is that the concentration of a drug X could be very different in these two sites, and that would indicate very significant postmortem redistribution. Now of course, Dr. Langille did not test femoral blood. He only tested a single site, meaning the heart blood, and his argument was that he's testing for morphine and morphine undergoes negligible, no distribution whatsoever. So his assumption is that morphine will be equal in concentrations and heart blood and femoral blood. That is of course, an assumption based on knowing how likely is morphine to redistribute. For completeness, likely both types of blood should have been tested for. The second part that is really interesting is that Dr.

Langille did not test for free morphine and its metabolites in the blood. So that's something of interest. And you'll find out in the second part of this case that the second toxicologist, Dr.

Bruce Goldberger picks at and finds challenges and limitations of some of the data collection, analysis and interpretation provided by Dr.

Langille. And one of those certainly will be testing for free morphine. The evidence of Dr.

Bruce Goldberger. Dr.

Bruce Goldberger is a forensic toxicologist and he's a professor and Director of Toxicology at the University of Florida. Dr.

Goldberger reviewed the several toxicology and post-mortem reports completed by the witnesses who testified for the

prosecution. He also prepared his own reports which critique the work of others and stated his own conclusions with reasonable scientific or toxicological certainty about the cause of Brandon Carlin's death. At the outset of his testimony, Dr.

Goldberger criticized Dr. Langille's term "indicated" as a method of describing a finding of a drug by one form of analysis, but without quantification. This description is not used in the scientific community. There are other ways to notify a medical examiner about the presumptive finding that has not been confirmed. Similarly, Dr.

Goldberger denied the use of preliminary as a description of a report, although he confessed that he had used the term himself and recognized its utility on occasion. He no longer issues preliminary reports, although he once did. It was the evidence of Dr. Goldberger that the procedures used to analyze the samples were state of the art, and involved the same instruments that he would have used if he had been asked to do the testing himself. Dr.

Goldberger would have gone further in three specific aspects. He would have 1. quantitated the levels of free and total morphine to establish the ratio between them, which can be very helpful in determining the cause and manner of death. This was not done by Dr.

Langille. Number two, tested for 6-MAM in the blood to determine whether the death was acute or otherwise. Numbers three, quantitated the other drug, according specifically MDMA, according to a readily available standard. Dr.

Goldberger, considered it reckless not to determine the free and total morphine ratio because of its value in determining the timing of death. In cross-examination, Dr.

Goldberger agreed that in determining whether a death was rapid or attributable to a particular cause, it is essential to look at the entire picture, and not simply the numbers or the free total morphine ratio. It was the evidence of Dr. Goldberger that the moderately elevated morphine concentration in the deceased's heart blood within a range typically observed in heroin related deaths, was more than insufficient evidence to assign heroin intoxication as the cause of the deceased's death. Femoral blood was available and would have provided a better sample. But heart blood was a relatively decent sample for morphine. Despite the concentration, it would have been preferable to have a measure of 6-MAM in the blood and the free and total morphine in the blood and other fluids. And some indication of the disease tolerance as a chronic or naive user would assist since a chronic or regular user may tolerate the level found quite well. The low-level of 6-MAM in the deceased's blood confirmed pre-death use of heroin, but could not distinguish between recent use and rapid death or the use the preceding day. In cross-examination, Dr.

Goldberger explained that finding 6-MAM in the deceased's urine is an indication of recent heroin use, or a rapid death from heroin because 6-MAM has a short secretion half-life of about six to eight hours. If a similar dose had been taken, a smaller amount of morphine would be left even from 24 hours earlier. Voiding and the volume of fluids consumed are influential factors. Dr.

Goldberger would not expect morphine to remain in the system from a non-lethal dose administered 24 hours earlier. Finally, Dr. Goldberger defined a chronic heroin user as a person who took the drug daily or even every day and suffered withdrawal symptoms if she or he did not take it. A chronic user would be unlikely to work 70 hours a week, and return to work during his or her spare time. He considered a non user as naive and a frequent user as the next step up. An infrequent user would not suffer the same withdrawal problems as a chronic user and would not likely display track mark scar tissues along the arm. In cross-examination, Dr.

Goldberger acknowledged that considering in isolation either heroin alone or the other drug found MDMA alone could have caused death since both were found in concentrations in which fatalities have occurred. Dr.

Goldberger did not dispute the role of heroin along with other drugs, but said that he could not be more specific about its role because some data like free or total morphine, were lacking. He could not agree with the suggestion that heroin delivered the knockout punch. Let's reflect on the evidence and cross-examination of Dr.

Bruce Goldberger. Certainly Dr.

Goldberger was brought in and is criticizing Dr.

Langille's report. There are several key things that Dr. Goldberger points at that Langille's case report did not provide. Number one, is testing of 6-MAM in blood. As you know, Dr. Langille has tested only urine but not blood sample. And it is Dr. Goldberger's suggestion that testing for 6-MAM in the blood would have been beneficial in order to determine whether the death was acute or otherwise. Number two, the point that Dr. Goldberger brings up is this lack of measurement of various morphines. For example, the quantitation of free and total morphine was not done. But however, that ratio between free and total morphine would have been very helpful because it could indicate what caused the death in general. The third point that's really important, that Dr. Goldberger brings up is this blood analysis where the heart blood was tested for morphine and used and is a quite decent sample type for morphine as Dr. Goldberger mentioned. However, Dr.

Goldberger also suggests that that femoral blood testing was available and should have been used. You could have provided an even better sample type. And of course, that ties to detection of six mm in blood, which was not performed based on Dr.

Goldberger's description, it would be preferable to measure 6-MAM in the blood and compare that to the ratio of free and total morphine in the blood. That would have given indication of the deceased's tolerance to the drug, chronic versus naive user, and ultimately the cause of death or what has contributed to the cause of death. And at the end, we find that Dr. Goldberger certainly acknowledges that heroin or morphine concentrations were high enough where fatalities could have occurred from heroin. He also suggests that MDMA alone at the concentrations tested could also have contributed to fatalities. Ultimately, Dr. Goldberger could not agree with Dr. Langille's suggestion that heroin was the cause of death here.

This takes us to the end of the podcast on opiates, specifically heroin and its metabolite and it's testing in biological fluids as illustrated in this Canlii case. This podcast was supported by the department of forensic science at Trent University, Trent University online, and VLS Ontario funding.