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Guests:
Ms. Nathalie A. Desrosiers is a doctoral candidate at the University of Maryland. Dr. Marilyn A. Huestis is Chief of the Chemistry and Drug Metabolism Branch at the National Institute on Drug Abuse.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

Law enforcement throughout the world use small handheld devices to assess driver impairment due to alcohol, but driver impairment can be the result of drugs other than ethanol. In the October 2012 issue of *Clinical Chemistry,* Dr. Marilyn Huestis, Chief of the Chemistry and Drug Metabolism Branch of the National Institute on Drug Abuse and her team at NIH evaluated an on-site test for cannabinoids in oral fluid. Dr. Huestis is our guest in this podcast, along with her co-author, Nathalie Desrosiers.

And we'll start with you, Nathalie. What can you tell us about the role of cannabis in drugged driving?

Nathalie Desrosiers: Well, cannabis is actually the most commonly abused illegal drug in the world. So if you look at, in 2009, there was one study that surveyed people worldwide and they thought that there was 125 to 203 million people worldwide who reported smoking cannabis in the past year. If you look closer to home, in 2010, 17.4 million Americans reported smoking cannabis in the previous month alone.

And this is also seen, if you look at drugged driving, so in 2007, NHTSA or the National Highway Traffic Safety Administration conducted the US roadside survey and in the study, they saw that cannabis was actually the most prevalent drug and it was present in 8.6% of nighttime drivers.

Cannabis is also the most prevalent illicit drug detected in injured drivers in Victoria, Australia, and it was detected in this case, in 9.8% of the injured drivers. So it is actually quite prevalent both in the population worldwide and in drugged driving.

Bob Barrett: Dr. Huestis, what are the current practices regarding cannabis testing and roadside oral fluid testing and driving under the influence of drugs in general?

Dr. Marilyn Huestis: This has been an area where there's been tremendous research and efforts over the last 10 years and to be truthful, the United States has been well behind the European Union and also Australia in our efforts.

So the European Union conducted a number of tests and financed, at a very high degree, research in this area and they wanted first to determine what would be the best biological matrix to do testing for the roadside, because as you are aware, there is a breathalyzer test and if someone is seen weaving or having any other driving impairment, they may be stopped and the first thing that will happen is that they will do a breathalyzer test and determine whether there is a presence of alcohol. That can be done right at the roadside by a police officer. We don't have any such approach for drugs until very recently.

So the first aspect of this testing was to determine whether or not sweat or saliva or urine would be the best matrix to test at the roadside, and after a great deal of effort, it was determined that oral fluid testing, oral fluid is the proper term for saliva, that that would be the matrix that should be developed.

However, at that time, the technology for detecting cannabis or cannabinoids in oral fluid was very preliminary and was not very accurate or sensitive. So a lot of effort has gone underway to try to develop these tests.

Now in Victoria, Australia, they already started random drug stops at the side of the roads using oral fluid on-site tests as early as 2004. And despite the fact that the tests don't work very well, it has been seen to be a very positive outcome as a deterrent to drugged driving, and that has been reduced significantly.

What's interesting is that they actually used two on-site tests. The first test produced many, many false positive results, but the second test had a very poor detection rate. And so, that screening then, they would take a second oral fluid sample to the laboratory and confirm definitively with mass spectrometry.

Another difference between the Australian situation and the United States is that first of all, we wanted to wait to enact laws until we had good on-site devices, despite the public health positive findings that's occurred in Australia, and by the way, that policy has spread from Victoria, Australia, all across the continent of Australia. But in the United States, we require that we have a positive screening test and then a positive confirmation test before we report a result as positive.

But in Australia, if a sample screened positive for methamphetamine or also MDMA or Ecstasy, they also in their law said that they could test for cannabis, and truthfully, the positive tests they're getting for cannabis are primarily those that are positive also for methamphetamine or MDMA. But they have very good data to show how well the system works.

Now in Europe, after improving oral fluid testing, they've had roadside screening for a number of years now in multiple countries across Europe, after their major research, and what they have done is go ahead and instituted, and on-site testing has worked very well for basic drugs like methamphetamine, MDMA, cocaine, heroin, and it has not worked very well for cannabinoids.

And that's why this paper is so important, because for many years, many manufacturers have been trying hard to improve the on-site oral fluid tests to be much more sensitive for cannabinoids. And this is the first testing of this new device that has improved sensitivity to the point where now, it's a very good sensitive assay for evaluating drugged driving under the effect of cannabis.

Bob Barrett: Nathalie, are there any advantages with oral fluid testing compared to other specimens like blood and urine?

Nathalie Desrosiers: Actually, there are a lot of advantages to oral fluid testing, the main one being the ease of collection. So if you take something like blood, you will require somebody who is trained to draw blood, and it's actually quite uncomfortable to get your blood drawn. So, oral fluid is a lot less invasive and it doesn't require that you get poked and prodded. And then if you look at something like urine, it's very invasive as well, because it requires, oftentimes, that you actually collect the urine in front of an observer to make sure that the specimen is not adulterated or changed.

So with oral fluid, you can actually collect the specimen with somebody of opposite sex without having any problem. It's also more difficult to adulterate, so you can't actually add things as easily as you would with urine. And so it's thought to be a lot a better representation of what is actually in the

actual sample. For most drugs, it's actually also a closer relationship to the impairment window, if you compare it to urine.

Bob Barrett: Well, what about the disadvantages? There must be a few?

Nathalie Desrosiers: So one of the disadvantages is that with oral fluids, especially after smoking, sometimes you can have dry mouth. So it can be difficult to collect enough specimens, but usually when it is right after smoking, the concentrations will be so high that you will actually be able to detect THC in the oral fluid, even if you don't collect a full milliliter of oral fluid.

Bob Barrett: Nathalie, what is so particularly novel about the on-site device that you studied in this paper?

Nathalie Desrosiers: Well, as Dr Huestis mentioned earlier, there have been other on-site oral fluid tests that have been developed, but there was a lot of problems, specifically for cannabinoids or cannabis. And this particular device actually has a lower cutoff, so the concentration that indicates that something is positive is actually lower than some of the other devices, and this lower cutoff is set at 5 µg of THC per milliliter of oral fluid, so it's a lot lower than the 25 µg/L that was seen in some of the other on-site tests.

Another thing that's quite interesting about this particular device is that it actually has an objective reading for the positive/negative screening of the oral fluid. So the device is set up to actually read the immunoassay and give you either positive or negative readout result, and so you don't have to use subjective decision-making in order to decide if color line is present to decide if something is positive or negative. And because of this lower cutoff and this positive and negative, it's actually one of the first on-site tests to actually achieve good efficiency for cannabis. And so that is quite interesting that we finally have something that we can use for cannabis testing.

Bob Barrett: Dr. Huestis, what are the implications of such devices for drug treatment in workplace and pain management, as well as driving under the influence of drugs testing?

Dr. Marilyn Huestis: Well, as you know, the many members of AACC come from many different walks of life, so we have individuals involved in drug treatment programs, many involved in workplace or clinical environments, pain management specialists, and also individuals involved in driving under the influence of drugs. And what is so important about this on-site drug test and testing for cannabinoids in oral fluid in general is the fact that it can be adapted to the needs of the different monitoring programs.

So we've talked a lot already today about the importance for roadside drug testing, to have a device that can test right at the roadside, to see whether someone has been using cannabis and may be impaired at the time of the police stop, and why sensitivity is so important there. But in roadside drug testing, you'd like to have the window of detection be as close to the window impairment as possible. You don't really want to identify individuals who are not impaired, but still having residual drug in their system.

In workplace drug testing program, they want to have the widest window of detection as possible. They want to know whether hiring this individual in a safety sensitive position creates a risk or not. So there they would like to have a wide window of detection.

And that's the same for pain management. So pain management only have individuals come in once a month or less maybe, and in those cases, they want to ensure that if someone is using or abusing drugs that could interact or could derail treatments, they want to understand whether or not that individual has been using drugs over the widest period of time as possible.

And if you look at drug treatment programs, they have intermediate needs. They want to be very sensitive and identify if an individual has relapsed to drug use, because that creates an entire discussion between the counselor and the individual on what has caused the relapse and what tools would be helpful to them to avoid drug relapse.

But if the person comes in on a Monday and is positive for cannabis relapse, they want to know that, but they come back on Wednesday, and in general, in drug treatment programs, they are taking biological specimens between once to three times a week. If they come back again, and the test is positive, they don't want it to be from the original relapse. They don't want a wide window of detection, because they won't be able to understand whether or not there was new drug use in the interim between the two tests. So in those cases, an interim window of detection would best serve that program's drug monitoring needs.

So by selecting the analytes that you confirm for, so you will screen for THC, but then by selecting which analytes you confirm for, and also by selecting your cut-off concentration, you can tailor the program to best meet the drug testing program's needs. So that's a very interesting way to take a single test and then adapt it to get the most information. And of course that all relates to the way in which you interpret the drug test results.

Bob Barrett: In the paper, you state that THC was detected for at least 22 hours after smoking cannabis. What are the implications of this detection window?

Dr. Marilyn Huestis: Well, the first group of individuals tested in this study turned out to be heavier cannabis users, and so we are repeating the study again, in fact, the last subject runs tomorrow, where we are comparing the detection of different devices over different periods of time in both chronic and heavy cannabis users with occasional cannabis users.

And this is important, because in general, many people believe that the period of impairment is in the neighborhood of 8 hours, 6 to 8 hours, and so the fact that it was still positive for THC greater than 22 hours, means that you could still detect the drug beyond that period of impairment, which was quite surprising because we know how rapidly THC decreases in the blood.

But now we know, comparing the light users to the heavier users, that there is a difference in that detection time, just as we found the very long detection in blood of chronic daily cannabis smokers. So that's why the 22 hours is important.

It also emphasizes another really important point. The Substance-Abuse Mental Health Services Administration is in the process now of deciding on the regulations and the cut-off concentrations and many other aspects about having positive oral fluid tests. And so these tests are going to go out, these regulations are going to go out to the public for public comment. And one of the things that is important is which analyte ought to be measured.

Should we be measuring for the THC alone? Should we be measuring for carboxy-THC? Should we be measuring for other markers of recent use? And when we've studied this under our Control Drug Administration Studies, we have looked for all the different cannabinoid markers and we have found that cannabidiol and cannabinol are very good markers for recent cannabis use.

So one of the things that we think is important is it's fine to screen for THC in the on-site device like the one described in this study, but that when you confirm, it'd be important to confirm for THC, for carboxy-THC and for CBD and CBN, then you have more information available to you to interpret the result. So that's why this is such an important issue.

Bob Barrett: Dr. Marilyn Huestis is the Chief of the Chemistry and Drug Metabolism Branch at the National Institute on Drug Abuse. Nathalie Desrosiers is a doctoral candidate at the University of Maryland. They have been our guests in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening!