Cannabis, the most common illicit drug identified in motor vehicle crashes, had a higher prevalence than alcohol in drivers’ blood or oral fluid specimens in the US in the 2013–2014 National Roadside Study (1). In fact, the percentage of weekend nighttime drivers with measurable Δ⁹-tetrahydrocannabinol (THC)² in blood or oral fluid increased to 12.6%, a 48% increase since 2007 (2). Cannabis use is increasing since the legalization of cannabis in 4 US states and the approval of medical cannabis in 23 US states and many countries. The incidence of THC-impaired driving increased in Washington state in 23 US states and many countries. The incidence of THC-impaired driving increased in Washington state from 19.1% before to 24.9% after cannabis legalization (3). These statistics highlight an important public health and safety concern: cannabis-impaired driving.

In this issue of Clinical Chemistry, for the first time, Andrews et al. compare cannabinoid blood concentrations in fatal road traffic collision (RTC) victims with non-RTC victims in London and southeast England from 2011 to 2013 (4). Drivers’ postmortem cannabinoid concentrations were reported previously from driver culpability studies (5), comparing the prevalence of cannabinoid-positive biological samples in culpable drivers to those not judged culpable for the crash. However, blood cannabinoid concentrations in postmortem non-RTC victims from the same population base are rarely available.

Controlled human cannabinoid administration data, on-the-road driving data after cannabinoid administration, and epidemiological data provide evidence of cannabis’s effects on driving. Two recent metaanalyses (6, 7) showed an approximate 2-fold risk of a motor vehicle collision after cannabis intake, and my group recently reported significant cannabis impairment of lateral driving control with and without low-dose alcohol (8).

Authentic postmortem drug concentrations are needed for evaluating drug crash risk, but there are many difficulties in obtaining these data. Recent regulations prohibit testing that is not directly related to determining cause of death, as was the case in the present investigation conducted under the auspices of the 2004 UK Human Tissue Act. In addition, cannabinoids are frequently found in combination with other illicit drugs, alcohol, and prescription drugs, complicating interpretation of the effects due to cannabinoids alone in any polydrug case. Drummer et al. collected data from almost 3400 fatal Australian road traffic crashes, obtaining sufficient THC-only cases to describe a significant increase in the odds ratios: 2.7 for a fatal crash with any measurable blood THC, and 6.6 for THC blood concentrations ≥5 μg/L (5).

Blood cannabinoid analyses are challenging, and many medical examiner, coroner, and crime laboratories do not test for them or do not yet offer quantitative concentrations, despite recommendations by the National Safety Council’s consensus conference on minimum drug tests and cutoff concentrations to be included in drugged driving testing (9). Unfortunately, in the US, many traffic laws do not differentiate between alcohol- and drug-impaired driving, with no additional penalties for drug presence if alcohol is greater than the US limit of 0.08%. Furthermore, quantifying drugs in blood is expensive and time-consuming compared with breath or blood alcohol testing, and state and local government forensic laboratories tend to be poorly funded. The National Highway Traffic Safety Administration’s Fatal Analysis Reporting System does not allow calculation of unbiased, reliable, and valid estimates of the risk of crash involvement that results from drug use (10). Combined, these deficiencies result in a lack of reliable data on the prevalence of drug-impaired driving, including cannabis intake by drivers.

Another major impediment to improving the interpretation of cannabis blood results is the lack of good control data. Cannabis use is common in the general population, but we do not have accurate cannabinoid blood concentrations to compare with cannabinoid concentrations in potential drugged driving cases. Case control studies that collect random blood samples from drivers at the same location, at the same time of day, and under similar weather conditions as a motor vehicle crash are the ideal control samples, but these studies are costly and difficult to conduct. The National Highway Traffic Safety Administration recently released a report on its latest case-control drugged-driving study, which failed to
find a significant effect of cannabis on motor vehicle crashes (11).

Another major consideration and challenge with postmortem cannabinoid concentrations is the potential for postmortem redistribution of THC tissue stores in the blood after death. Ideally, antemortem and postmortem blood obtained close to the time of death would be available to define the potential for postmortem redistribution, but few such data are available. The few studies that compared postmortem central and peripheral blood cannabinoid concentrations close to the time of death showed a <2-fold increase in central blood cannabinoids (12). This was unexpected, because highly lipophilic compounds demonstrate postmortem redistribution. THC is highly lipophilic and stored in fat and other body tissues, creating a large body burden of THC with chronic frequent cannabis use that is slowly released over time. My group found measurable THC in the blood of some chronic frequent cannabis smokers 30 days after initiation of sustained cannabis abstinence (13), and in the same individuals documented significant impairment in psychomotor performance validated to predict poor driving 22 days after last cannabis administration, further complicating the interpretation of blood cannabinoid concentrations (14).

With the increasing legalization of cannabis and approval of medical cannabis, determining an appropriate THC concentration for a legal per se limit or zero tolerance concentration, based on a laboratory’s methodological limit of quantification, is an urgent international priority. Others prefer a single blood THC concentration that is always associated with impairment in both occasional and frequent cannabis users after cannabis smoking, inhalation, or oral consumption. Unfortunately, there is no one THC blood concentration that will achieve this goal—not now, nor after much more additional research. The same is true for alcohol. In the US, the legal per se limit for alcohol is 0.08%, in much of Europe 0.05%, and in Sweden 0.02%. Clear impairing effects of alcohol are present at ≤0.04% on some driving skills in some individuals, but not all skills and all people. Each country’s citizens, after much debate, selected the per se alcohol limit they believed best balanced the health and safety of the non–drug-using public with the rights of alcohol consumers to drive. Clearly there is a need to drive for employment and social and family responsibility purposes, more so in the US than many European populations with better public transportation systems. But is there a right to drive under the influence of a drug that can impair driving performance and risk injury or death to others?

The variability in alcohol per se limits illustrates the differences between countries in balancing the rights of the public for road safety and the rights of individuals to use drugs. Multiple THC blood concentrations associated with driving impairment have been proposed, including 3.5–5 µg/L (15) and 5 µg/L by Washington state legislation for legal recreational cannabis use. The Driving Under the Influence of Drugs, Alcohol, and Medicines (DRUID) European Union initiative requiring analysis of blood samples, with a limit of quantification of 1 µg/L, recently found drivers with measurable blood THC to be at significantly increased risk for being responsible for a fatal accident, but there was no statistically increased risk of injury at that concentration (16).

The data provided by Andrews et al. (4) in this issue of Clinical Chemistry informs the debate with valuable blood cannabinoid data from 100 consecutive fatal motor vehicle crashes compared with 114 non-RTC deaths, all with drug testing performed to determine the manner of death. The data are highly valuable, because concentrations were provided for 11-hydroxy-THC, 11-nor-9-carboxy-THC, cannabidiol, and cannabinol, in addition to THC, further improving result interpretation. Although blood cannabinoid prevalence, defined as any case in which ≥1 cannabinoid markers were present above the limit of detection, was similar for RTC and other death types, THC concentrations in cannabinoid-positive fatal RTC victims had a greater range and were significantly higher than those in non-RTC subjects positive for cannabinoids. The authors evaluated relevant blood THC concentration ranges based on evidence in the literature regarding concentrations associated with crash risk and driver culpability and impairment (3, 15). Ideally, the RTC cases would have all been drivers, but 7 cases included passengers, bicyclists, and pedestrians. The significant difference noted in blood THC concentrations between postmortem RTC victims and non-RTC victims was no longer significant when only drivers’ blood THC concentrations were analyzed, most likely because of a lack of statistical power.

Considering the complexity of relating blood THC concentrations to impairment or increased odds ratios of motor vehicle crashes and deaths, a 2-tiered system of drugged driving enforcement currently used in some European countries and Australia offers deterrence of cannabis-impaired driving. A low blood THC per se concentration of 1–5 µg/L is enforced with limited penalties, fines, and driver’s license points, whereas a proof of impairment standard incurs much more serious penalties, including loss of driver’s license, fines, and sometimes imprisonment. Readers are encouraged to read the article by Andrews et al. and consider appropriate means to address this critical public safety issue in the context of medical and legal cannabis.

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