



## Pathology Biology Section – 2011

### G113 Was This Drug Overdose Due to Intravenous Injection or Oral Ingestion of Heroin — Can You Tell?

Johan A. Dufflou, MM\*, Department of Forensic Medicine, PO Box 90, Glebe, Sydney, 2037, AUSTRALIA; Shane Darke, PhD, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, 2052, AUSTRALIA; and Jennifer Easson, BSc, Division of Analytical Laboratories, Sydney West Area Health Service, Joseph Street, Lidcombe, 2141, AUSTRALIA

After attending this presentation, attendees will be alerted to and understand potential pitfalls associated with interpreting opioid levels in various body fluids and other matrices. This will be illustrated by presentation of a recent case where a question requiring an answer was whether heroin had been taken intravenously or orally. Research data will be presented followed by an explanation of the various mechanisms thought to cause these apparently anomalous findings.

This presentation will impact the forensic science community by informing attendees of the pharmacokinetics of opioids in the gastrointestinal system, and alerting them to the dangers of not fully understanding the behavior of these drugs in the body.

Death due to heroin overdose is almost always the result of intravenous injection of the drug in Australia. A case is described where a heroin overdose was initially thought to be the result of oral ingestion of the drug, primarily as a result of higher concentrations of morphine in stomach contents than in blood. During the subsequent criminal trial and investigation, however, the issue of the entero-hepatic circulation of morphine was raised as a possible reason for the presence of morphine in the stomach contents.

For many drugs and poisons, a simple way of making the distinction between oral and parenteral administration is to analyze the stomach contents and compare the levels of the drug in the stomach with those in blood; a higher stomach contents concentration of the drug would generally be strong supportive evidence for the assertion that the drug or poison was administered orally. Morphine; however, in common with a range of other drugs, undergoes entero-hepatic circulation as part of the metabolism and elimination of the drug. The entero-hepatic circulation is a complex mechanism whereby chemicals that have undergone conjugation reactions in the liver, such as morphine, once in the gastrointestinal tract, may be subject to passive re-uptake, entering the circulation via the hepatic portal vein, returning to the liver where the chemical can be biotransformed again and then re-eliminated. Morphine may undergo several cycles of entero-hepatic circulation resulting in a significant increase in the retention time and its consequent duration of action. Further, both during life and in the perimortem and postmortem period, the pyloric sphincter offers at best a partial barrier to reflux of morphine-containing gastrointestinal contents from the duodenum to the stomach.

These mechanisms would explain the presence of significant concentrations of morphine in the stomach contents of intravenous heroin users and we hypothesised that such physiological mechanisms can result in higher concentrations of morphine in stomach contents than in blood, despite the drug having been administered intravenously.

This study reports on the distribution of opioids in blood, stomach contents, urine, liver and bile in 29 deaths due to intravenous heroin overdose. The mean total and free blood morphine concentrations were 1.60 mg/L and 0.32 mg/L, respectively, and the mean stomach contents total morphine concentration was 1.16 mg/kg. All cases had detectable morphine in the stomach contents, and 24 of 29 cases had higher concentrations of total morphine in stomach contents than in blood. The mean total morphine concentration in bile was approximately 100 times that in blood, and the liver total morphine concentration averaged twice that of blood levels.

Morphine was detected in the stomach contents in all cases in this study, and in 83% of cases the stomach morphine level was higher than that in blood. This would indicate that the entero-hepatic circulation materially affects morphine levels in the body, and that reflux of morphine from the duodenum into the stomach appears to be the norm, at least after death. Furthermore, even if the gall bladder had been removed surgically at some prior time, stomach morphine concentrations can still be higher than the blood total morphine levels, as illustrated in one case.

It's concluded that the current study demonstrated that stomach morphine levels cannot be relied upon to determine whether heroin had been orally or intravenously administered. Given the large number of drugs and poisons which undergo entero-hepatic circulation, it would appear prudent to not make comment on route of administration of such drugs unless definite evidence of oral ingestion of the drug can be obtained, for example through visualization of appropriate pill fragments.

**Heroin Overdose, Illicit Drug Use, Pharmacokinetics**