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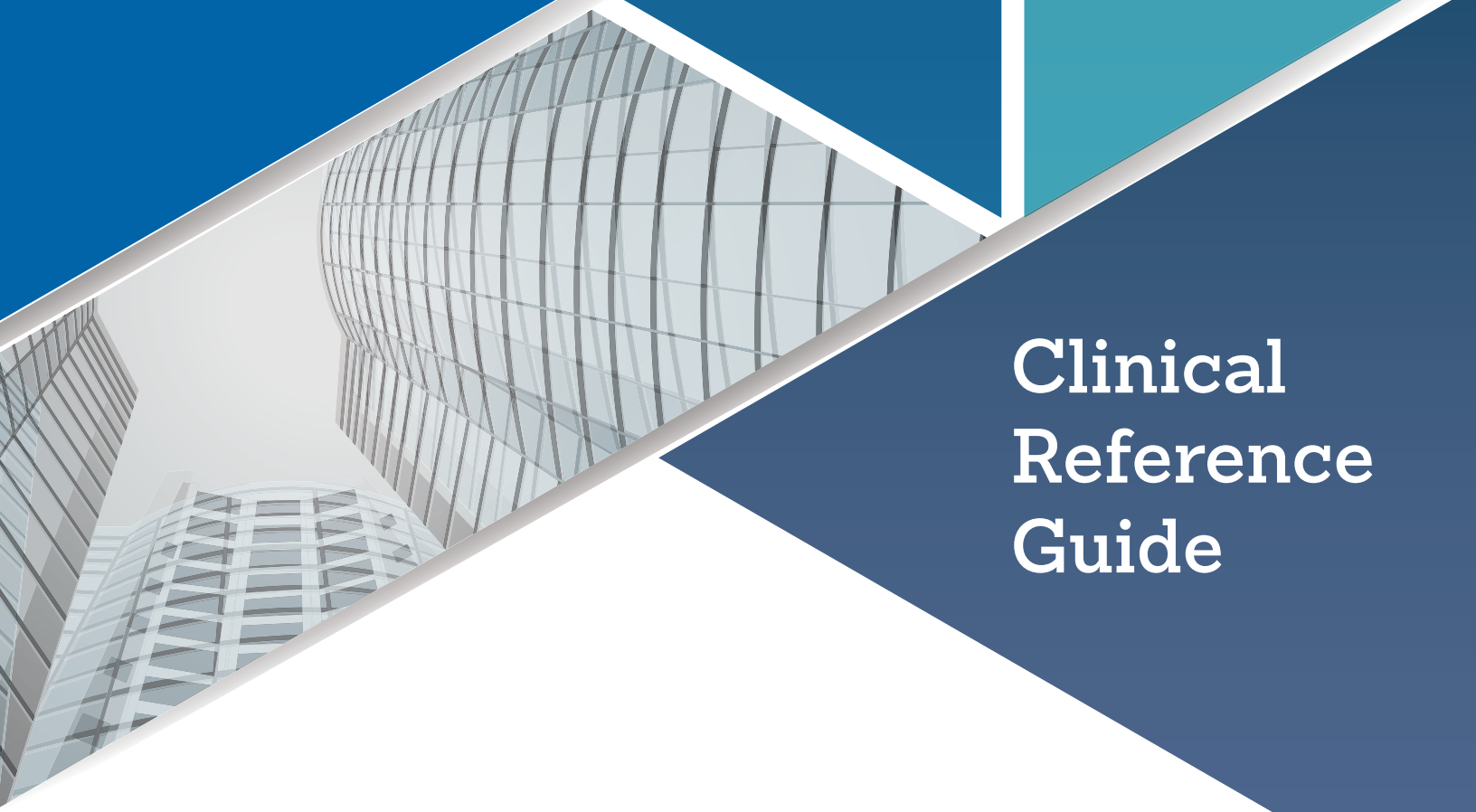

Clinical Reference Guide

Oral Fluid Testing

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Oral Fluid Testing

Oral fluid testing has provided an excellent alternative to urine with its accuracy, ease of collection, and resistance to tampering.

A. Accuracy

Oral fluid is an acceptable alternative to urine in pain management, especially in cases of shy bladder or severe renal impairment (e.g., the patient cannot provide a urine sample) or suspected urine tampering/substitution. Use of this specimen type is increasing due to the ease of collection, limited invasiveness, and the opportunity for direct observation. The medications of interest in pain management, both licit and illicit, are detectable in oral fluid.[1,2]

Multiple studies in pain management and addiction treatment settings have compared oral fluid results with simultaneously collected urine results and found substantial agreement between results, despite expected differences due to varying periods of detection. Overall agreement between results ranged from 85-98%.[3-6] For some drugs, the oral fluid positivity rate has been noted to exceed that of urine, most notably for heroin and cocaine.[3,4,7,8] Oral fluid could potentially be the preferable specimen type for detection of these illicit drugs in some circumstances.

B. Collection Procedures

While adulteration of oral fluid under direct observation during collection is difficult, altering saliva pH can change the disposition of drugs excreted into oral fluid.[1] Consequently, the patient should rinse out his/her mouth with water 10 minutes prior to collection and refrain from consuming food or beverages until collected. Stimulating saliva production with sour candy or gum will increase salivary flow and alter pH, therefore reducing some drug levels in oral fluid. This practice is not recommended as it may cause false negative results.[8]

The proper collection of oral fluid is absolutely crucial to ensure an accurate test. Aegis uses the Quantisal™ device which has an indicator that turns blue once an adequate sample (1 mL oral fluid) has been collected. If an inadequate amount of oral fluid is collected, there is an increased risk of false negatives due to the ratio of oral fluid to buffer solution being disproportionate.

Patients with xerostomia (dry mouth), especially drug-induced, may experience difficulty providing an adequate specimen. In such cases, waiting for ten minutes may still not result in an adequate collection, even if water is provided beforehand. If a patient cannot provide an adequate oral fluid sample, an alternative specimen type should be collected.

C. Adulteration

Commercial oral fluid adulterants generally work in the same manner as mouthwashes, rather than destroying drugs or altering saliva pH. There is a sterilizing tablet containing sodium dichloroisocyanurate which may destroy drugs present in oral fluid if it is sucked immediately prior to collection. However, these should not affect the integrity of results if proper collection procedures are followed and the patient's mouth is clear for ten minutes prior to specimen collection.

Some patients may attempt to appear adherent when not taking the drug prescribed by contaminating their oral cavity with a chewed drug immediately prior to specimen collection. Such an attempt may result in a very high drug concentration in oral fluid. Rinsing and spitting ten minutes prior to collection may help alleviate this concern.[8]

Additionally, precautions should be taken to avoid accidental contamination of the collection device. Drug residue may be present on object surfaces; therefore, Aegis recommends having patients wash their hands before inserting the device into his/her mouth. After the indicator turns blue, the device can be removed by office staff with a gloved hand.

D. Interpretation

One principal difference between oral fluid and urine testing is the amount of time a substance can be

detected in each. The presence of drug in oral fluid more accurately reflects current use, because drugs are secreted into oral fluid from the blood. Consequently, the period of detection is shorter than urine. In general, drugs which are chronically administered in pain management may be detectable for up to 48 hours in oral fluid. Studies have observed extended oral fluid detection of 6-monoacetylmorphine (heroin metabolite), methadone, amphetamine, and methamphetamine for up to 8 days in patients on an observed detoxification unit; however, these extended periods of detection are atypical in the context of other oral fluid studies.[9,10] Conversely, ethanol may only be detected for up to 8 hours in oral fluid.[11,12]

Use of medications on an as-needed (PRN) basis may shorten the detection period. For example, a single-dose of hydromorphone may only be detectable in oral fluid for six hours.[13] If a PRN medication is negative in oral fluid, the patient's pattern of use should be assessed with a follow-up urine test to extend the detection period if warranted. Many drugs may be detectable in oral fluid as early as fifteen minutes following ingestion, as opposed to a longer time for drugs or their metabolites to show up in urine (2-6 hours for most medications).[8,14-19]

One other key difference between oral fluid and urine is that the disposition of parent drug and metabolites is reversed. While metabolite concentrations typically exceed parent drug in urine, parent drugs are generally more readily detectable than metabolites in oral fluid. This may be relevant for patients who exhibit impaired or absent metabolism due to pharmacogenetics or drug-drug interactions, especially for drugs that are extensively metabolized. The increased detection of parent drugs in oral fluid may be useful to assess adherence in these circumstances.[8]

Some exposures are less likely to cause positive findings in oral fluid compared to urine. The literature indicates that morphine, and to a lesser extent codeine, may be detected in oral fluid for a few hours after typical poppy seed consumption. In the context of this discussion, "typical" poppy seed ingestion refers to ingestion of normal amounts of baked goods, salad dressing, etc. rather than deliberate ingestion of unusual amounts of raw poppy seeds or ingestion of poppy seed tea. Unusual poppy seed ingestion may result in higher concentrations of both morphine and codeine with extended periods of detection. Samano et al. conducted a two part study in which volunteers first consumed a baked poppy seed roll, followed by ingestion of 15 grams of raw poppy seeds at least two days later. Morphine levels were detected above the 7.5 ng/mL cutoff at 1.5 hours and 3 hours for parts one and two, respectively, with peak concentrations occurring 15 minutes post-ingestion. In addition, codeine levels were detectable at 1.5 hours and 2 hours, again with peak concentrations occurring at 15 minutes. Codeine may be seen at lower concentrations than morphine, with peak concentrations of 35 ng/mL for morphine and 18 ng/mL for codeine.[20] In contrast, Concheiro et al. detected morphine in oral fluid (>1 ng/mL) for up to 24 hours and codeine up to 18 hours following consumption of 45 grams of raw poppy seeds.[21] However, this is likely considered an exaggerated scenario for opiate exposure and does not represent what would typically be expected in a person's day-to-day consumption of food products. Poppy seed ingestion could be a concern if a food product, or an excess of raw poppy seeds, is consumed within a short time period prior to specimen collection.

Ingestion of dronabinol (Marinol®) is unlikely to cause a positive test for THC or its metabolite in oral fluid at a 2 ng/mL threshold, which is used at Aegis.[22] Using oral fluid as a specimen type may therefore be beneficial when assessing patients who claim to ingest Marinol® to explain marijuana positives. Passive inhalation of marijuana is also unlikely to cause a positive test in oral fluid at typical laboratory thresholds, except in circumstances of extreme exposure within hours of the collection.[23,24]

There are some medications that may pose a challenge when performing adherence testing in oral fluid. Medications administered intrathecally (in the spinal subarachnoid space) are usually not detectable in oral fluid. Additionally, the buprenorphine transdermal patch (Butrans®) is unlikely to be detected in oral fluid due to its low plasma concentrations and saliva:plasma ratio.[17,25,26]

Other drugs deserve unique consideration for oral fluid interpretation. Buccal contamination has been known to occur following sublingual administration of

buprenorphine (Suboxone®) and may sometimes result in unusually high drug concentrations in oral fluid.[27] Positives for THC in oral fluid are generally due to a depot effect after smoking, which limits interpretation to recent use.[8] This is in direct contrast to urine testing, where marijuana positives may persist in urine for longer periods of time following discontinuation.

While drug concentrations in oral fluid are 10- to 100-fold lower than in urine, there is no direct relationship between oral fluid and urine concentrations.[1-3] Oral fluid concentrations should not be used to interpret adherence to dosage or serve as an estimate for blood concentrations because many factors influence drug concentrations in oral fluid (e.g. pH).

E. Laboratory Challenges

The combination of small specimen volume and low drug concentrations in oral fluid presents a unique challenge to toxicology testing. Specialized liquid chromatography/tandem mass spectrometry (LC/MS/MS) instrumentation may be used to achieve greater sensitivity for oral fluid. Oral fluid thresholds for medication adherence testing must be lower than thresholds used for urine testing and for workplace testing.[1-3] Testing recommendations by the Substance Abuse and Mental Health Services Administration (SAMHSA) for workplace settings are typically aimed at detecting abuse, not necessarily adherence to a prescribed medication. Aegis employs thresholds in oral fluid that are optimal for detection of prescribed medications and illicit substances without being excessively subject to incidental exposures or detection after prolonged time intervals.

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