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STEADY STATE FOR SERUM TOXICOLOGY DRUG SCREENING

Following administration of a dose of drug, its effects usually show a characteristic temporal pattern. The onset of the effect is preceded by a lag, after which the magnitude of the effect increases to a maximum and then declines; if a further dose is not administered, the effect eventually disappears. This time-course reflects changes in the drug's concentration, as determined by the pharmacokinetics of its absorption, distribution, and elimination accordingly. The intensity of a drug's effect is related to its concentration above a minimum effective concentration, whereas the duration of this effect is a reflection of the length of time the drug level is above this value. These considerations, in general, apply to both desired and undesired (adverse) drug effects, and as a result, **a therapeutic window exists** reflecting a concentration range that provides efficacy without unacceptable toxicity. Similar considerations apply after multiple dosing associated with long-term therapy; therefore, they determine the amount and frequency of drug administration to achieve an **optimal therapeutic effect.** For many drugs, toxicity and lack of efficacy are both potential dangers and the therapeutic index may be narrow. In these circumstances, doses must be titrated carefully and drug dosage is limited by toxicity, rather than efficacy. **Thus, the therapeutic goal is to maintain steady state drug levels within the therapeutic window. For most drugs, the actual concentrations associated with this desired range are not and need not be known. It is sufficient to understand that efficacy and toxicity are generally concentration-dependent.** Metabolism can be subject to a number of factors such as genetics, disease state and co-administration of other compounds. Other compounds may inhibit or induce metabolic activity. Therefore, a patient's blood concentration relative to the predicted steady state range should be assessed on a patient-by-patient basis. Expected steady state ranges are calculated using pharmacokinetic parameters associated with specific medications and patient-specific information.

In most clinical situations, drugs are administered in a series of repetitive doses to maintain a steady state concentration of drug associated with the therapeutic window. **Thus, calculation of the appropriate maintenance dosage is a primary goal.** Certain practical details and pitfalls associated with therapeutic drug monitoring should be kept in mind for intermittent dosing; a concentration of drug measured in a sample taken **virtually any time during the dosing interval will provide information that may aid in the assessment of drug toxicity.** When concentrations of drugs are used for purposes of adjusting dosage regimens, the sample should be taken well after the previous dose, as a rule of thumb, just before the next planned dose, when the concentration is at its minimum. In general, this is how we sample in this office, in that patients drive here and are cautioned not to take medication when they are driving, unless they have a driver.

Another important aspect of the timing of sampling is its relationship to the beginning of the maintenance dosage regimen. **When constant dosage is given, steady state is reached only**

after four half lives have passed. In almost all of the situations in this clinical practice, the sampling occurs well beyond the first four half lives. **Ultimately, therapeutic success is dependent on the patients actually taking the drug according to the prescribed dosage regimens. Non-compliance with the dosing schedule is a major and often unappreciated reason for therapeutic failure, especially in the long term management of diseases, such as chronic pain. Many times, reduction in the number of required dosing occasions will improve adherence to a prescribed dosing regimen. In this practice, we attempt to reduce the number of required dosing. Equally important, is the need to involve patients in the responsibility for their own health, using a variety of strategies based on improving communication regarding the nature of their chronic pain and the overall therapeutic plan. This is reinforced continually in every office visit. (Goodman and Gilman 12th edition)**

Achieving steady state in this particular patient is directly reflective of appropriate prescribing and appropriate utilization of the medication as prescribed, based on the previous discussion.

Patients will fall into three risk categories: Low, moderate and high. High risk patients are those who take schedule II opioids. Patients on schedule III opioids are considered moderate risk by the DEA guidelines. Patients on schedule IV opioids are considered low risk. Anyone taking schedule I drugs (illicit) is also considered high risk. High risk patients will be tested **at least** four times per year. Moderate risk patients will be tested two to four times per year. Low risk patients will be tested up to two times per year.

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Rev: 8/2015