**WHAT IS DRUG LEVEL TESTING?**
It can be helpful to test a patient’s blood to check the levels of a medication they are taking. Drug levels that are too high sometimes cause serious side effects. Levels that are too low might allow HIV to multiply and develop resistance. Testing drug levels is also called therapeutic drug monitoring, or TDM.

TDM is not generally used or available yet in the United States. Doctors do not agree on its benefits.

**HOW CAN TDM HELP?**
Even when people take the same dose of a drug, blood levels can be very different. If the viral load isn’t going down far enough, it might be because drug levels are too low. A doctor might be able to increase the dose and bring HIV under control.

If a patient is having serious side effects, it might be because drug levels are too high. If they are, a smaller dose might still control HIV but relieve some side effects.

Several factors can affect drug levels:
- **Food effects:** More or less drug can be absorbed depending on the amount and kind of food in the stomach
- **Body weight:** Very low weight can increase drug levels. Very high body weight may reduce drug levels.
- **Metabolism:** Different people break drugs down faster or slower. This is partly due to genetic factors.
- **Age:** Children and adolescents process drugs differently than adults.
- **Drug interactions:** Some drugs affect the metabolism of other drugs, and can raise or lower their levels.
- **Smoking and drinking habits**
- **Herbal and other supplements.** For example, St. John’s Wort reduces blood levels of protease inhibitors.
- **Kidney or liver problems,** including hepatitis, can cause higher drug levels
- **Pregnancy:** As body size changes, drugs levels can also change
- **Women** nearing menopause go through changes in body chemistry that can affect drug levels

**DOES TDM WORK FOR ALL HIV DRUGS?**
TDM might work well for protease inhibitors and for non-nucleoside reverse transcriptase inhibitors (non-nukes). Research shows that blood levels of these types of drugs affect their ability to control HIV and to cause side effects.

The nucleoside analog reverse transcriptase inhibitors (nukes) are a different case. They must be processed inside individual cells before they’re active against HIV. The blood level of these drugs is less important than the amount inside cells. Researchers are working on ways to measure the level of drug inside cells. Then they will have to show that these drug levels affect how well the nukes work, or the side effects they cause. TDM is not yet being used with the nukes.

**DIFFICULTIES WITH TDM**
1. **TDM is not ready for use with the “nuke” drugs.**
   As noted above, blood levels of the nukes aren’t as important as the levels inside HIV-infected cells. The technology for measuring these levels is not very good yet.

2. **There isn’t just one target blood level for each drug.**
   The “best” amount of drug for a patient depends on how resistant their virus is to that drug. The more resistant the virus, the higher the blood level of drug needed to control it.

3. **It’s difficult to measure drug levels accurately.**
   With the current technology, repeated tests can give very different results.

4. **Adherence is very important.**
   Missing doses of a drug can make more of a difference than any other factor in how well HIV is controlled, and can throw off the results of TDM.

5. **TDM might not make any difference.**
   Many doctors use a dose of ritonavir to boost blood levels. It might not be possible to increase the blood levels any further, even with an increased dose.

6. **Lowering blood levels won’t decrease all side effects.**
   Some side effects aren’t linked to the amount of drug in the body. Higher doses probably cause more stomach problems with the protease inhibitors, or kidney stones with indinavir. However, the hypersensitivity reaction to abacavir is unrelated to the dose of the drug. TDM won’t reduce this side effect.

7. **TDM is expensive.**
   Because it’s still experimental, it’s difficult to get reimbursement for TDM.

**WHEN CAN TDM HELP?**
TDM could provide useful information in several situations:
- For patients with high levels of side effects
- When treatments fail to control HIV even though patients are taking all their doses
- For patients with very high or very low body weight
- For children and teen-aged patients
- To assess interactions between HIV medications
- To assess interactions with non-HIV medications such as birth control pills, methadone, or TB medications
- For patients with kidney or liver problems, including hepatitis
- For pregnant patients
- For women nearing menopause

**FUTURE DIRECTIONS**
Research will continue on several key questions related to TDM:
1. For each drug, what is the relationship between drug levels and viral control? How sensitive is it?
2. For each drug side effect, how do drug levels affect the amount or severity of side effects?
3. How can drug levels of the nukes, inside the cells, be measured more accurately?

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