What Big Enzymes You Have

Heart attack? Drug reaction? Relax. Stephen Gendin's Popeye-size CPK just means he's been hitting the gym by Howard Grossman, MD, as told to Lark Lands

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This month, Howard Grossman, MD, a cutting-edge physician with a large AIDS practice in New York City, interprets the meaning of the elevated CPK in his patient, *POZ* Contributing Editor Stephen Gendin.

Because a standard blood chemistry had shown that Stephen had a massively elevated creatine phosphokinase (CPK) of 1,157 (shown here as CK, TOTAL)—the REFERENCE (normal) RANGE is 40 to 285—we redid the test. CPK is an enzyme normally present in low levels in the blood. It's found mainly in both heart and skeletal muscle (such as in the arms and legs), the liver and the brain. When those tissues are stressed, inflamed or injured, higher amounts leak out of muscle cells into the blood.

If CPK levels have been normal and there's suddenly an isolated elevation, the first culprit you should consider is exercise. Strenuous workouts can stress muscles enough to elevate the enzyme—which in this case is not only harmless, but actually indicates the start of the healthy process of muscle repair and growth. It turns out that Stephen was working out heavily during this period. He'd started on his latest HAART regimen a month before this blood test, and was trying to regain 35 lost pounds by hitting the gym five times a week. (The increased incidence of elevated CPK levels seen since the introduction of antiretrovirals leads many doctors to suspect—with no proof—that these drugs boost exercise's ability to harmlessly break down muscle.)

Another possible explanation for an elevated CPK—but only in those with relevant risk factors—is a heart attack in progress. If there's reason to suspect this, you must interpret the CPK in light of symptoms (chest pressure or pain, shortness of breath, nausea and sweating), medical history, physical exam findings and electrocardiogram (EKG) reading. In Stephen's case, there were no cardiac symptoms, making his frequent workouts a probable cause of the enzyme elevation.

In general, I don't worry if the CPK is in the hundreds. However, if, like Stephen's, it breaks 1,000, I ask patients to not work out for two or three days, then repeat the test. (Stephen—afraid to interrupt his weight-gain efforts—ignored this advice and waited a month to follow the protocol. Fortunately, his CPK returned to a low normal reading of 98.) If the repeat is elevated and there is no muscle pain or tenderness, I tell patients to redo the break/retest routine after one month. In

patients with no muscle problems but readings that reach the several thousands, I'd also run a test that separates the CPK into subunits, showing whether the source of the elevation is the heart or skeletal muscle.

If someone with a high CPK also has muscle pain or tenderness, I might send them to a rheumatologist or neurologist for diagnostic tests. I'd also run a urine test for myoglobin, a blood protein whose presence can indicate rhabdomyolysis, the rapid breakdown of muscle tissue, occasionally caused by a long list of drugs (see "Meds & Muscles"). If the reading is suspicious, a muscle biopsy is needed to confirm this problem; meanwhile, I would take the patient off the possibly offending drugs.
In sum, the elevated CPK levels we see commonly in HIVers on drug treatment—particularly those who work out—are usually nothing to worry about. But if I saw them in a sedentary person, I might follow up more closely and perhaps even stop potentially problematic drugs sooner. You have to look carefully at each individual—their history, exercise habits, cardiac status and lab results—and then use your gut. It's not cookbook medicine. If it was, we wouldn't need doctors.

MEDS & MUSCLES

An HIVer's medicine chest may hold many drugs that (in rare cases) can cause muscle breakdown and a high CPK. Among the most commonly used:

Antivirals: ddI (Videx); 3TC (Epivir or, combined with AZT, Combivir); indinavir (Crixivan); alpha-interferon (Intron); ganciclovir (Cytovene)

Antibiotics: TMP/SMX (Bactrim); itraconazole (Sporanox); clarithromycin (Biaxin); erythromycin (Erythrocyn,
E-mycin, Ilosone); penicillin G (Bicillin)

Lipid-lowering agents: (when taken with Lopid) Lipitor, Mevachor, Pravachol

Stimulants: Dexedrine; methamphetamine (crystal)

Aspirins: Enteric-coated (Ecotrin)

Antidepressants: Wellbutrin, Zyban, Serzone

Neuropathy drugs: Lamictal