

## Evaluation of aminotransferase elevations in a bodybuilder using anabolic steroids: hepatitis or rhabdomyolysis?

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**The use of anabolic steroids among competitive athletes, particularly bodybuilders, is widespread. Numerous reports have noted "hepatic" dysfunction secondary to anabolic steroid use based on elevated serum aminotransferase levels. The authors' objective was to assess whether primary care physicians accurately distinguish between anabolic steroid-induced hepatotoxicity and serum aminotransferase elevations that are secondary to acute rhabdomyolysis resulting from intense resistance training.**

Surveys were sent to physicians listed as practicing family medicine or sports medicine in the yellow pages of seven metropolitan areas. Physicians were asked to provide a differential diagnosis for a 28-year-old, anabolic steroid-using male bodybuilder with an abnormal serum chemistry profile. The blood chemistries showed elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatine kinase (CK) levels, and normal gamma-glutamyltransferase (GGT) levels. In the physician survey (n = 84 responses), 56% failed to mention muscle damage or muscle disease as a potential diagnosis, despite the markedly elevated CK level of the patient. Sixty-three percent indicated liver disease as their primary diagnosis despite normal GGT levels.

Prior reports of anabolic steroid-induced hepatotoxicity that were based on aminotransferase elevations may have overstated the role of anabolic steroids. Correspondingly, the medical community may have been led to emphasize anabolic steroid-induced hepatotoxicity and disregard muscle damage when interpreting elevated aminotransferase levels. Therefore, when evaluating enzyme elevations in patients who use anabolic steroids, physicians should consider the CK and GGT levels as essential elements in distinguishing muscle damage from liver damage.

(Key words: androgens, exercise, muscle, creatine kinase, hepatitis, aminotransferases, gamma-glutamyltransferase, rhabdomyolysis, steroids)

During the past decade there has been an increase in the nontherapeutic use of anabolic steroids by athletes. The literature clearly suggests that unsupervised use of these drugs can lead to a

variety of pathologic conditions, though the mechanisms by which the anabolic steroids cause such deleterious effects remain unclear.<sup>1-4</sup> In particular, the literature indicates that anabolic steroids

may induce hepatocellular carcinoma, cholestatic jaundice, peliosis hepatitis, and general liver dysfunction.<sup>3,5-11</sup> Currently, numerous reports suggest that physicians should diagnostically evaluate anabolic steroid-related hepatic damage by monitoring alanine aminotransferase (ALT) and aspartate aminotransferase (AST).<sup>12-17</sup>

Most anabolic steroid-related hepatitis cases are thought to arise from the oral use of C-17 alkylated androgens.<sup>18</sup> Today, the use of C-17 alkylated androgens is minimal because of two primary factors: the widely reported side effects of such androgens and reduced production of these androgens by pharmaceutical companies. Despite the decrease of C-17 alkylated steroid use, however, many physicians continue to report hepatic dysfunction in athletes abusing other anabolic steroids—using elevations in ALT and AST as their primary criteria for such diagnoses.<sup>12-17</sup> This is problematic because physicians are apparently neglecting to consider the skeletal muscle damage that results from resistance training in which steroid-abusing athletes engage. This concomitant resistance training releases various types of aminotransferases into the circulation. Based on the literature, physicians also presumably fail to use gamma-glutamyltransferase (GGT) testing, which is a more sensitive diagnostic tool for hepatic dysfunction than ALT and AST testing. Physicians also do not seem to be paying enough attention to creatine kinase (CK) levels, which serve as a more sensitive and specific marker for muscle damage than either ALT or AST levels.

In a recent report,<sup>19</sup> we concluded that reports of anabolic steroid-induced hepatitis based solely on ALT and AST levels may be unfounded. In this study, we conducted a mail survey of primary care physicians to assess prevailing views on anabolic steroid use and liver damage when faced with the blood chemistry profile and altered serum enzyme levels of an anabolic steroid-using bodybuilder.

### Materials and methods

To assess the response of physicians to a routine blood chemistry profile, we mailed a form letter with the blood chem-

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**Table 1**  
**Blood Chemistry Profile of Hypothetical Bodybuilder**  
**Using Anabolic Steroids**

Test	Result	Normal range
Glucose	75 mg/dL	65 to 110
Urea nitrogen	15 mg/dL	7 to 21
Creatinine	1.4 mg/dL	7 to 1.5
Sodium	144 mmol/L	137 to 145
Potassium	4.0 mmol/L	3.6 to 5.0
Chloride	101 mmol/L	98 to 107
Enzymatic CO <sub>2</sub>	28 mmol/L	22 to 31
Anion gap	16 mmol/L	
Amylase	49 U/L	28 to 110
Calcium	9.8 mg/dL	8.4 to 10.2
Phosphorous	3.9 mg/dL	2.4 to 4.4
Cholesterol	119 mg/dL	108 to 200
Triglycerides	45 mg/dL	35 to 160
Uric acid	5.2 mg/dL	2.5 to 8.5
Total protein	7.5 g/dL	6.3 to 8.2
Albumin	4.7 g/dL	3.9 to 5.0
A/G Ratio	1.7	
AST/SGOT	HI	5 to 40
ALT/SGPT	HI	7 to 56
LDH	HI	313 to 618
CK	HI	30 to 170
ALKP	61 U/L	38 to 126
GGT	17 U/L	8 to 78
Total BILI	0.5	0.2 to 1.3

istry profile (*Table 1*) of a hypothetical 28-year-old competitive bodybuilder who admits during a routine examination that he has been using anabolic steroids for 4 years. This survey, mailed with a stamped return envelope, asked recipients to provide as many as three differential diagnoses, in order of most to least likely; additional tests that should be ordered, if any; and proposed treatment, if any. Surveys were sent to osteopathic and allopathic physicians who practiced family medicine or sports medicine.

In the blood chemistry profile provided, almost all of the levels were within the normal range, including the GGT (*Table 1*). The exceptions were the CK level, the AST and ALT levels (listed as AST/SGOT and ALT/SGPT, respectively, in *Table 1*), and the lactic dehydrogenase (LDH) level.

Physicians' names and addresses were selected from the listings of family physicians and sports medicine specialists (n = 644) in the yellow pages of telephone books from Fort Worth, Tex; Dallas,

Tex; Nashville, Tenn; New York City (Manhattan), NY; Atlanta, Ga; Los Angeles, Calif; and San Francisco, Calif. However, the Manhattan yellow pages we used listed only 25 physicians under family practice and sports medicine. Physicians in the Atlanta, Dallas, Fort Worth, and Manhattan phone books whose surnames began with the letter K were added to the list of survey recipients (n = 422). Of the 1066 forms sent, 114 were returned as undeliverable. From the remaining 952 surveys, we received 84 responses (8.8% response rate).

## Results

As shown in the results of our survey (*Table 2*), 63% of the physicians who responded indicated liver disease as their primary diagnosis, even though the CK level was grossly elevated and the GGT level was in the normal range (*Table 1*). In addition, 56% of the physicians who responded failed to even mention muscle damage or muscle disease in the differential diagnosis.

## Comments

Even though the number of responses to our mailing was small (84 of 952 mailings), the results indicate that in the general collective consciousness of the medical community, use of anabolic steroids is closely associated with liver disease.

Previous reports on athletes who use anabolic steroids have suggested that anabolic steroids may cause serious hepatic dysfunction, but these reports were based on serum elevations of ALT and AST rather than the more sensitive liver marker, GGT.<sup>12-17</sup> In our recent study,<sup>19</sup> we concluded that reports of anabolic steroid-induced hepatitis, when based solely on ALT and AST, may be unfounded.

In the case of our hypothetical patient, the presence of elevated CK in addition to ALT and AST levels should have suggested muscle damage as a likely diagnosis. Such a diagnosis is supported by reports of elevated CK levels in association with anabolic steroid treatment in nonexercising patients with hereditary angioedema,<sup>20,21</sup> as well as reported findings of significantly higher, postexercise

**Table 2**  
**Differential Diagnostic Responses of Physicians (n = 84) to Serum Blood Profile of**  
**a Hypothetical Bodybuilder Using Anabolic Steroids**

	Diagnosis			Total n (%)
	Primary n (%)	Secondary n (%)	Tertiary n (%)	
<b>Liver</b>	53 (63.1)	40 (61.5)	25 (55.6)	118 (60.8)
<b>Muscle*</b>	17 (20.2)	14 (21.5)	12 (26.7)	43 (22.2)
<b>Cancer</b>	4 (4.8)	6 (9.2)	4 (8.9)	14 (7.2)
<b>Other</b>	10 (11.9)	5 (7.7)	4 (8.9)	19 (9.8)
<b>Total</b>	84 (100)	65 (100)	45 (100)	194 (100)

\*Diagnosis of hepatic dysfunction only: 47 (56%) of 84 failed to indicate muscle disease or injury as a possibility in the differential diagnosis.

CK levels in androgen-using athletes versus drug-free strength training athletes.<sup>22</sup> These reports concluded that elevations of CK were due to the ability of anabolic steroids to increase muscle cell membrane permeability. Other reports have demonstrated elevations in ALT and AST following exercise.<sup>23,24</sup> Many bodybuilders and other competitive resistance training athletes who use anabolic steroids may have acute rhabdomyolysis that remains undiagnosed because it is often being misdiagnosed as steroid-induced hepatotoxicity. Because the breakdown of striated muscle in acute rhabdomyolysis is more severe with eccentric exercise, bodybuilding tends to cause more striated muscle damage than other forms of exercise.<sup>25,26</sup>

In our earlier report on the overdiagnosis of anabolic steroid-induced hepatotoxicity, all of the exercising groups had elevations in CK and AST with normal GGT levels, whether they were bodybuilders or medical students.<sup>19</sup> The anabolic steroid-using subjects did have the highest enzyme levels, but the steroid-free subjects and exercising male medical students had significantly elevated levels of CK and AST. The elevations in these enzymes were proportional to body mass, exercise type, and exercise intensity.<sup>19</sup>

Previous reports of anabolic steroid hepatotoxicity all failed to examine the

relationship between CK, AST, and GGT in users of anabolic steroids. This may have been due to the lack of routine analysis of both CK and GGT on serum auto-analyzers, a phenomenon we noted among the medical students in our earlier study.<sup>19</sup> Definitive diagnoses could be made by obtaining biopsies; however, liver and muscle biopsies are expensive and represent an invasive procedure. We recommend that clinicians who examine or treat anabolic steroid-using patients request both CK and GGT, if such results are not routinely included in serum chemistry panels.

This investigation does not dispute the ability of anabolic steroids to induce liver disease, but contends that this connection has been overreported. This overreporting has, in turn, biased physicians against considering muscle damage as a possible cause for aminotransferase elevations. Furthermore, inflated concerns over hepatotoxicity may have thwarted investigation of potential therapeutic uses for anabolic steroids.

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### References

1. Griggs RC, Kingston W, Jozefowicz RF, Herr BE, Forbes G, Halliday D. Effect of testosterone on muscle mass and muscle protein synthesis. *J Appl Physiol* 1989;66:498-503.
2. Dickerman RD, McConathy WJ, Schaller F, Prather I. Sudden cardiac death in a 20-year-old bodybuilder using anabolic steroids. *Cardiology* 1995;86: 172-173.
3. Westaby D, Williams R. Androgen and anabolic steroid related liver tumours. In: Davis M, Tedger JM, Williams R, eds. *Drug Reactions and the Liver*. London, UK: Pitman Medical; 1981.
4. Dickerman RD, McConathy WJ, Schaller F, Zachariah NY. Cardiovascular complications and anabolic steroids [letter]. *Eur Hrt J* 1996;17:1912.
5. Appell HJ. Morphological alterations in myocardium after application of anabolic steroids. *Int J Sports Med* 1983;4:62.
6. Murphy P. Steroids: not just for athletes any more. *Phys Sports Med* 1986;14:48.
7. Bagheri SA, Boyer JL. Peliosis hepatitis associated with androgenic anabolic steroid therapy. *Ann Intern Med* 1974; 81:610.
8. Bird DR, Vowles KDJ. Liver damage from long-term methyltestosterone. *Lancet* 1977;2:400-401.
9. Johnson FL. The association of oral androgenic-anabolic steroids in life threatening disease. *Med Sci Sports* 1975;7: 284-286.
10. Wilson JD, Griffin JE. The use and misuse of androgens. *Metabolism* 1980; 29:1278-1295.

11. Erlinger S. Drug-induced cholestasis. *J Hepatol* 1997;26(Suppl 1):1-4.

12. Lamb DR. Anabolic steroids in athletics: how well did they work and how dangerous are they? *Am J Sports Med* 1984;12:31-38.

13. O'Connor JS, Baldini FD, Skinner JS, Einstein M. Blood chemistry of current and previous anabolic steroid users. *Milit Med* 1990;155:72-75.

14. Kiraly CL. Androgenic-anabolic steroid effects on serum and skin surface lipids, on red cells, and on liver enzymes. *Int J Sports Med* 1988;9:249-252.

15. Lenders JM, Demacker PM, Vos J, et al. Deleterious effects of anabolic steroids on serum lipoproteins, blood pressure, and liver function in amateur bodybuilders. *Int J Sports Med* 1988;9:19-23.

16. Alen M. Androgenic steroid effects on liver and red cells. *Br J Sports Med* 1985; 19:15-20.

17. Manore MM, Thompson J, Russo M. Diet and exercise strategies of a world-class bodybuilder. *Int J Sport Nutr* 1993;3:76-86.

18. Sweeney EC, Evans DJ. Hepatic lesions in patients treated with synthetic anabolic steroids. *J Clin Pathol* 1976; 29:626-633.

19. Dickerman RD, Pertusi RM, Zachariah NY, Dufour DR, McConathy WJ. Anabolic steroid-induced hepatotoxicity: is it overstated? *Clin J Sport Med* 1999;9:34-39.

20. Spaulding WB. Myalgia and elevated creatine phosphokinase with danazol in hereditary angioedema. *Ann Intern Med* 1979;90:854.

21. Sheffer AL, Fearon DT, Austen KF. Clinical and biochemical effects of stanozolol therapy for hereditary angioedema. *J Allergy Clin Immunol* 1981;68:181-187.

22. Hakkinen K, Alen M. Training volume, androgen use and serum creatine kinase activity. *Br J Sports Med* 1989;23: 188-189.

23. Koutedakis Y, Raafat A. Serum enzyme activities in individuals with different levels of physical fitness. *J Sports Med Phys Fitness* 1993;33:252-257.

24. Mena P, Maynar M, Campillo JE. Changes in plasma enzyme activities in professional racing cyclists. *Br J Sports Med* 1996;30:122-124.

25. Hamer R. When exercise goes awry: exertional rhabdomyolysis. *Southern Med J* 1997;90:548-551.

26. Bolgiano EB. Acute rhabdomyolysis due to body building exercise. Report of a case. *J Sports Phys Fitness* 1994;34:76-78.

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