

Severe Hepatotoxicity Associated with the Dietary Supplement LipoKinetix

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Background: LipoKinetix (Syntrax, Cape Girardeau, Missouri) is a dietary supplement marketed for weight loss.

Objective: To describe a possible causal association between LipoKinetix and hepatotoxicity.

Design: Case series.

Setting: Outpatient clinic, tertiary care hospital, and U.S. Food and Drug Administration databases.

Intervention: Routine medical and supportive care.

Measurements: Clinical and laboratory evaluation.

Results: All patients developed acute hepatotoxicity within 3 months of starting LipoKinetix. At presentation, symptoms and

results of laboratory tests were characteristic of acute hepatitis. All patients recovered spontaneously after LipoKinetix use was discontinued. Three of the seven patients, including one who developed fulminant hepatic failure complicated by cerebral edema, were taking LipoKinetix alone at the time of presentation. Of the four patients who were taking multiple supplements, two resumed taking supplements other than LipoKinetix without incident.

Conclusions: The use of LipoKinetix may be associated with hepatotoxicity. Despite extensive evaluations, no other cause for hepatotoxicity could be identified in the seven patients studied.

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Unlike licensed drugs, dietary supplements are not subject to review by the U.S. Food and Drug Administration (FDA) before marketing. Issues pertaining to the use of certain herbal products range from contamination with heavy metals (including lead, arsenic, and mercury) (1–3) to substitution of a product ingredient or misidentification of raw herbs that can result in toxicity (4). Hepatotoxicity has been associated with various herbal products (5, 6).

LipoKinetix (Syntrax, Cape Girardeau, Missouri) capsules are sold as a dietary supplement for weight loss. In the United States, \$33 billion is spent yearly on weight-loss products and services (7), despite the absence of scientific evidence in humans to support such use (8). According to the manufacturer, the purported mechanism of action of LipoKinetix is “modifying a process in the body called oxidative phosphorylation” that thereby “mimics exercise.” LipoKinetix contains the following ingredients: norephedrine hydrochloride (25 mg), sodium usniate (100 mg), 3,5-diiodothyronine (100 μ g), yohimbine hydrochloride (3 mg), and caffeine (100 mg). We describe seven patients who between July and December 2000 developed acute hepatitis, including one patient who developed fulminant hepatic failure complicated by cerebral edema, after ingesting LipoKinetix.

CASE SERIES

Five patients (four women and one man) were treated at Cedars-Sinai Medical Center, Los Angeles, California, and two patients (both men) were identified through the FDA MedWatch program. All seven patients had taken LipoKinetix according to the manufacturer’s recommendations, and none were taking prescription or over-the-counter medications (including acetaminophen). No patient had a medical history, and none were obese. Results of serologic testing for hepatitis A, B, and C were negative in all patients. Results of autoimmune serologic testing (for antinuclear antibodies and anti-smooth-muscle antibodies) and results of testing for cytomegalovirus and Epstein-Barr virus were also negative in five patients who were tested. The five patients from Cedars-Sinai Medical Center were Japanese nationals residing in the Los Angeles area. They had purchased different lot numbers of the product at the same health food store. Symptoms appeared within 4 weeks after initial ingestion of LipoKinetix.

The other two patients, identified from the MedWatch program, were white bodybuilders who were acquaintances and had purchased the product through the Internet. They sought medical attention at 9 and 12 weeks, respectively, after first taking LipoKinetix. It is

Context

Dietary supplements, unlike drugs, are not tightly controlled by the U.S. Food and Drug Administration (FDA) before marketing.

Contribution

LipoKinetix, a dietary supplement sold as an aid to promote weight loss, was associated with severe hepatotoxicity in seven previously healthy patients. None had evidence of viral infection or autoimmune disease or had ingested other hepatotoxic drugs. All patients recovered spontaneously after discontinuing use of LipoKinetix.

Implications

Although the FDA has issued warning letters to the manufacturer, physicians, and the public regarding LipoKinetix, federal oversight of dietary supplements remains problematic. Physicians should inquire about the use of dietary supplements when patients present with evidence of hepatotoxicity.

—The Editors

unclear whether the lot numbers of the product used by these two patients differed. The clinical summary is presented in **Table 1**. Three of the seven patients, including the patient who developed fulminant hepatic failure, were taking only LipoKinetix at the time symptoms occurred (**Table 2**). Two of the four patients taking multiple supplements subsequently resumed taking supplements other than LipoKinetix without incident.

CASE REPORT

A previously healthy, 20-year-old female Japanese exchange student began taking LipoKinetix for weight loss 2 weeks before presenting with a low-grade fever, malaise, and worsening epigastric pain. She had jaundice, was alert and oriented, and did not have hepatosplenomegaly. Laboratory studies revealed an aspartate aminotransferase level of 49.64 μ kat/L (2978 U/L), alanine aminotransferase level of 47 850 nkat/L (2871 U/L), total bilirubin level of 222 μ mol/L (13.0 mg/dL), and international normalized ratio of 2.8. Aminotransferase levels continued to increase and peaked 5 days after the patient discontinued taking LipoKinetix. The patient became increasingly coagulopathic and developed stage 2 hepatic encephalopathy. She was evaluated for liver transplantation. With the subsequent develop-

ment of stage 3 encephalopathy, the patient was intubated. Intracranial pressure was 35 mm Hg, and mannitol was administered. The intracranial pressure decreased with supportive care, and liver function test results improved over the next 6 days. On discharge, she had no neurologic sequelae and the international normalized ratio was normal. Aminotransferase levels returned to normal within 12 weeks.

ANALYSIS

Three different lot numbers of LipoKinetix capsules were obtained from three patients treated at Cedars-Sinai Medical Center. The FDA analyzed these samples at Pacific Regional Laboratory SW (Los Angeles, California) using liquid chromatography–electrospray mass spectrometry and Fourier transform infrared spectroscopy. Analyses confirmed that the product samples contained norephedrine, yohimbine, 3,5-diiodothyronine, sodium usniate (analyzed as usnic acid), and caffeine, as listed on the product label. No contaminants (including heavy metals) were detected.

DISCUSSION

Unlike with licensed drugs, the safety of herbal products has relied on their traditional use and formulations for appropriate dosage, administration, and avoidance of harmful interactions. The dietary supplement market is a multibillion-dollar industry; use of herbal products has increased an estimated 380% from 1990 to 1997 (9). Competition has driven dietary supplement manufacturers to seek obscure ingredients and to use them in nontraditional ways and combinations.

We report on seven healthy people who were not taking any prescription drugs and developed severe hepatotoxicity while taking LipoKinetix. All patients had used the manufacturer's recommended dosages. Five patients had taken the supplement for 1 month or less, and two patients had used the product for 2 to 3 months. All presented with symptoms characteristic of acute hepatitis, including fatigue and abdominal pain. In addition, results of biochemical testing were consistent with acute hepatitis. The peak aminotransferase levels and pattern of liver test results were compatible with drug-induced acute hepatocellular necrosis. There was no evidence of allergy, such as rash or eosinophilia. Three patients developed significant jaundice, and one developed fulmi-

Table 1. Patient Characteristics*

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age, y	20	32	31	28	23	26	31
Sex	Female	Female	Male	Female	Female	Male	Male
Duration of LipoKinetix use, d	14	10	30	30	21	84	63
Jaundice	Yes	Yes	Yes	No	No	Yes	Yes
Abdominal pain	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nausea or vomiting	No	Yes	No	Yes	Yes	No	No
Peak AST level, $\mu\text{kat/L}$ (U/L)	49.64 (2978)	156.03 (9360)	23.27 (1396)	34.47 (2068)	63.78 (3826)	125.86 (7550)	9.40 (564)
Peak ALT level, nkat/L (U/L)	47 850 (2871)	117 335 (7040)	7300 (438)	34 784 (2087)	63 767 (3826)	235 838 (14 150)	18 317 (1099)
Peak bilirubin level, $\mu\text{mol/L}$ (mg/dL)	250 (14.6)	197 (11.5)	79 (4.6)	67 (3.9)	38 (2.2)	104 (6.1)	41 (2.4)
Ethnicity	Japanese	Japanese	Japanese	Japanese	Japanese	White	White
Medical history	None	None	None	None	None	None	None
Required hospitalization	Yes	Yes	Yes	No	No	No	No
Other product use (see Table 2)	No	Yes	Yes	Yes	No	Yes	No
Time between starting LipoKinetix and onset of symptoms, d	14	10	30	30	21	84	63
Time between discontinuing LipoKinetix and normalization of aminotransferase levels, d	84	84	28	70	Improving after 7 days; declined further follow-up	90	Symptoms resolved after 60 days; declined further follow-up
Resumed using supplements other than LipoKinetix without incident	NA	No	Yes	No	NA	Yes	NA

*ALT = alanine aminotransferase; AST = aspartate aminotransferase, NA = not available.

nant hepatic failure. All recovered spontaneously after discontinuing use of LipoKinetix, and results of liver tests as well as symptoms normalized within 4 months in five patients (two patients declined to have further testing). No other hepatotoxic agent or other cause for hepatotoxicity could be identified. Of the four patients taking multiple supplements, only one had taken multiple Chinese herbal formulations; however, none of the ingredients were associated with hepatotoxicity according to the Chinese *Materia Medica*, the standard reference for Chinese herbs (10).

LipoKinetix-induced hepatotoxicity appears to be idiosyncratic (5, 11, 12). No published reports have described hepatotoxicity associated with any of the other

individual substances contained in LipoKinetix. *Ephedra* alkaloids have been associated with multiple adverse cardiovascular and central nervous system events (13). Only a single reported case of acute hepatitis has been associated with *Ephedra*; however, that patient had taken numerous other products (14). The FDA notes relatively few cases of hepatitis or elevated aminotransferase levels associated with dietary supplements containing ephedrine alkaloids (approximately 25 of 1400 cases). These adverse event reports are often complex, with patients concurrently using many other products (dietary supplements and drugs), some of which have known hepatotoxic effects. Although a direct hepatotoxic effect has not been reported for ephedrine or norephedrine

Table 2. Supplements: Use and Duration*

Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
LipoKinetix, 2 wk	LipoKinetix, 10 d Flaxseed oil, 10 d	LipoKinetix, 4 wk Ripped Fuel (contains <i>Ephedra</i>), 1 y	LipoKinetix, 4 wk QualiHerb: Ginseng and Zizyphus Formula, 4 wk	LipoKinetix, 3 wk	LipoKinetix, 12 wk Myoplex, Myoplex Deluxe, and HMB, 6 mo Creatine, 6 mo Animal Pak, 6 mo	LipoKinetix, 9 wk
	Pyruvate, 10 d Chitosan, 10 d	Therbuterol, 1 y Yellow Jacket (contains <i>Ephedra</i>), 1 y	Yao San #21124 TB, 4 wk Lotus Herb: Gui Pi Tang-Ginseng and Longan Combination, 4 wk			

* Ingredients contained in each supplement are described in the Appendix.

(also a metabolite of ephedrine), phenylpropanolamine (racemic norephedrine) has been reported to potentiate the hepatotoxicity of carbon tetrachloride and acetaminophen in mice (6, 15).

Sodium usniate, the salt form of usnic acid, is a secondary metabolite found in several genera of lichens, including *Usnea*, *Letharia*, and *Parmelia*. Toxic reactions, including ataxia leading to paralysis and death, have been reported in animals ingesting lichens containing usnic acid; data in humans, however, are limited. Usnic acid uncouples oxidative phosphorylation in murine liver mitochondria, resulting in inhibition of adenosine triphosphate synthesis and enhancement of Mg^{2+} -adenosine triphosphate activity, which may contribute to hepatic toxicity (16). None of the seven patients, however, exhibited lactic acidosis, a typical feature of drug-induced liver injury due to mitochondrial dysfunction.

Yohimbine is an indole alkaloid from the bark of the African *Pausinystalia yohimbe* tree and is also found in *Rauwolfia* root (17). The FDA has not evaluated yohimbine for safety or efficacy for any indication. It is widely touted as a remedy for male impotence, but the mode of action is by selective blockade of the presynaptic α_2 -receptor (17). Yohimbine penetrates the central nervous system and can stimulate mood and motor activity (17). Nausea, vomiting, abdominal pain, dizziness, and headache have been reported when yohimbine is used at therapeutic doses (17).

Unintentional thyrotoxicosis factitia, a condition related to ingestion of exogenous thyroid hormone from adulterated products (for the purpose of weight loss) is well described (18). None of the seven patients exhibited clinical signs of hyperthyroidism, and abnormal liver tests results in these seven patients were not typical of the pattern of hepatic dysfunction seen in hyperthyroidism (19).

Although a hepatotoxin was not identified in LipoKinetix, many mechanisms could be responsible for the observed hepatotoxicity. These include toxic effects related to interactions of the ingredients in the product, such as the potentiation (noted earlier) between phenylpropanolamine (norephedrine) and acetaminophen or carbon tetrachloride. Various factors may explain these interactions, including the induction of certain enzymes or formation of secondary toxic metabolites due to alterations in pharmacokinetic and pharmacodynamic

properties of certain ingredients. Alternatively, pharmacogenetic predisposition may contribute to LipoKinetix-induced hepatotoxicity.

Dietary supplement products are not subject to review by the FDA before marketing. The current system for monitoring herbal products relies on the voluntary reporting of any serious adverse events by physicians. This case series highlights the need for public and medical community awareness that some supplements may contain ingredients in combinations and at doses not previously used. Patients often do not disclose information on supplement use; this underscores the need for a responsible dialogue between physicians and patients about all health-related products (including botanicals and supplements) being used by the patient (7) and the timely reporting of all adverse events to public health agencies. We refer readers to the MedWatch Web site www.fda.gov/medwatch/report/hcp.htm and telephone number (800-FDA-1088).

APPENDIX: INGREDIENTS IN DIETARY SUPPLEMENTS

Flaxseed Oil (multiple manufacturers): Linolenic, linoleic, and oleic acids.

Chitosan (multiple manufacturers): Shellfish fiber.

Twinlab Ripped Fuel (Twin Laboratories, Ronkonkoma, New York): Chromium picolinate, 200 μ g; Mahuang extract (standardized for 20-mg ephedra alkaloids), 334 mg; guarana seed extract (standardized for 22% caffeine), 910 mg; L-carnitine, 100 mg; gelatin; cellulose; purified water; MCT; silica; and magnesium stearate.

Therbuterol (Alternative Pharmaceuticals, Roselle, New Jersey): *Sida cordifolia*; synephrine; guarana (contains caffeine); guggulsterone; L-carnitine; and white willow bark, 650 mg.

Yellow Jacket (NVE Pharmaceuticals, Newton, New Jersey): Ephedra extract, *Sida cordifolia*, *Citrus aurantium* (standardized for 4% synephrine), kola nut, ginseng, ginger root, and *Capsicum*.

QualiHerb: Ginseng and Zizyphus Formula (Sheng Chang Pharmaceuticals, Bentley Place Cerritos, California): Rehmanniae, ginseng, Polygalae, *Acori graminei*, Scrophulariae, Biotae, Blatycodi, Asparagi, *Salviae miltiorrhizae*, *Zizyphus spinosae*, Ophiopogonis, Coptidis, Pararadicis Poriae, *Angelicae sinensis*, and Schisandrae.

Yao San #21124 TB: Chai Hu, Bupleuri, Dang Gui, *Angelicae sinensis*, Bai Zhu, *Atractylodis alba*, Shong Jiang, Zingiberis, Bo He, Menthae, Bai Shao, *Paeoniae alba*, Fu Ling, Poriae Cocos, Gan Cao, and Glycyrrhizae.

Lotus Herb: Gui Pi Tang—Ginseng and Longan Combina-

tion: Ren Shen, Gwsong, Bai Zhu, *Atractylodis*, Fu Ling, Poriae, Suan Zao Ron, Zizyphus seeds, Long Yan Rou, Longan, Huang Q, *Astragali*, Dang Gui, Tangkuei, Yuan Zhi, Polygalae, Mu Xiang, Saussurea, Gan Cao, licorice, Shong Jiang, ginger, Da Zao, and red jujube.

Myoplex (Experimental and Applied Sciences, Inc., Golden, Colorado): MyoPro (unique blend of whey-protein concentrate from specially filtered and ion-exchanged whey protein, calcium caseinate, milk-protein isolate, taurine, L-glutamine, sodium caseinate, egg albumin, and calcium α -ketoglutarate), maltodextrin, corn syrup solids, vitamin and mineral blend (potassium chloride, disodium phosphate, magnesium oxide, calcium phosphate, potassium citrate, potassium phosphate, choline bitartrate, β -carotene, ascorbic acid, DL- α -tocopheryl acetate, ferrous fumarate, molybdenum amino acid chelate, boron proteinate, manganese gluconate, selenium amino acid chelate, niacinamide, zinc oxide, D-calcium pantothenate, chromium citrate, copper sulfate, vitamin A palmitate, pyridoxine hydrochloride, riboflavin, thiamin hydrochloride, vitamin D₃, folic acid, biotin, potassium iodide, and cyanocobalamin), aspartame, CitriMax (garcinia cambogia), Dutch processed cocoa, natural and artificial flavor, partially hydrogenated canola oil, salt, medium-chain triglycerides, xanthan gum, soy lecithin, monoglycerides and diglycerides, cellulose gum, and borage oil.

Myoplex Deluxe (Experimental and Applied Sciences, Inc., Golden, Colorado): MyoPro (proprietary protein blend containing whey-protein isolate from ion exchanged whey, milk-protein isolate, calcium caseinate, sodium caseinate, and egg albumin), maltodextrin, GKG (proprietary blend containing L-glutamine, calcium α -ketoglutarate, taurine, potassium chloride, potassium phosphate, magnesium phosphate, magnesium oxide, sodium RNA, and manganese glycinate), natural and artificial flavors, Dutch processed cocoa, CLA (calcium conjugated linoleic acid from sunflower oil), partially hydrogenated canola oil, xanthan gum, V2G (proprietary blend containing taurine, vanadyl sulfate, and sodium selenate), vitamin and mineral blend (choline bitartrate, β -carotene, ascorbic acid, DL- α -tocopheryl acetate, ferrous fumarate, molybdenum amino acid chelate, boron proteinate, niacinamide, zinc oxide, calcium pantothenate, chromium citrate, copper sulfate, vitamin A palmitate, pyridoxine hydrochloride, riboflavin, thiamin hydrochloride, vitamin D₃, folic acid, biotin, potassium iodide, and cyanocobalamin), corn syrup solids, salt, soy lecithin, aspartame, cellulose gum, carrageenan, CitriMax (*Garcinia cambogia*), medium-chain triglycerides, monoglycerides and diglycerides, and borage oil.

HMB (multiple manufacturers): Calcium β -hydroxy β -methylbutyrate monohydrate.

Animal Pak (Universal Nutrition, Inc., New Brunswick, New Jersey): Vitamin A acetate, β -carotene, ascorbic acid, ergocalciferol, thiamin HCl, riboflavin, niacin, pyridoxin HCl, folic

acid, calcium pantothenate, biotin, citrate, carbonate, calcium phosphate, kelp, magnesium oxide, zinc oxide, selenium, copper sulfate, manganese sulfate, chromium picolinate, potassium sulfate, lactalbumin, Siberian ginseng (from root), Oriental ginseng (from root), *Smilax officinalis* (from root), protogen A, inosine, pyridoxine α -ketolutarate, L-carnitine, coenzyme A, coenzyme B-12, phosphatidylcholine, para-aminobenzoic acid, bovine colostrum, bovine Argentine liver, shark cartilage, choline complex, bioflavonoids, linoleic acid, oleic acid, betaine HCl, pepsin, papain, ox bile, pancreatin, mycozyme, maltodextrin, calcium sulfate, magnesium stearate, choline citrate, stearic acid, parsley, goldenseal, don quai, burdock, alfalfa, water cress, rice bran, cellulose, and rose hips.

From Cedars-Sinai Medical Center, Burns and Allen Research Institute, University of California, Los Angeles, School of Medicine, Los Angeles, California; and Center for Food Safety and Applied Nutrition, Food and Drug Administration, Washington, D.C.

On 19 November 2001, the U.S. Food and Drug Administration released a letter to health care professionals (www.cfsan.fda.gov/~dms/ds-ltr25.html) that contained the following sentence: "We urge you to review your cases of hepatitis in order to determine if any may be related to the use of dietary supplements in these patients."

—The Editors

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References

- Perharic L, Shaw D, Murray V. Toxic effects of herbal medicines and food supplements [Letter]. *Lancet*. 1993;342:180-1. [PMID: 8101281]
- Dunbabin DW, Tallis GA, Popplewell PY, Lee RA. Lead poisoning from Indian herbal medicine (Ayurveda). *Med J Aust*. 1992;157:835-6. [PMID: 1454025]
- Kew J, Morris C, Aihie A, Fysh R, Jones S, Brooks D. Arsenic and mercury intoxication due to Indian ethnic remedies. *BMJ*. 1993;306:506-7. [PMID: 8383555]
- Slifman NR, Obermeyer WR, Aloï BK, Musser SM, Correll WA Jr, Cichowicz SM, et al. Contamination of botanical dietary supplements by *Digitalis lanata*. *N Engl J Med*. 1998;339:806-11. [PMID 9738088]
- Vessey D. Metabolism of xenobiotics. In: Zakin B, ed. *Hepatology: A Textbook of Liver Disease*. 3rd ed. Philadelphia:WB Saunders; 1996:257-98.
- James RC, Harbison RD, Roberts SM. Phenylpropanolamine potentiation of acetaminophen-induced hepatotoxicity: evidence for a glutathione-dependent mechanism. *Toxicol Appl Pharmacol*. 1993;118:159-68. [PMID: 8382844]

7. Mokdad AH, Serdula MK, Dietz WH, Bowman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991-1998. *JAMA*. 1999;282:1519-22. [PMID: 10546690]
8. Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB. Annual deaths attributable to obesity in the United States. *JAMA*. 1999;282:1530-8. [PMID: 10546692]
9. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA*. 1998;280:1569-75. [PMID: 9820257]
10. Bensky D, Gamble A, Kaptchuk TJ. *Chinese Herbal Medicine: Materia Medica*. Seattle, WA: Eastland Pr; 1993.
11. Kaplowitz N. Mechanisms of liver cell injury. *J Hepatol*. 2000;32:39-47. [PMID: 10728793]
12. Dahm L, Jones D. Mechanisms of chemically induced liver disease. In: Zakin B, ed. *Hepatology: A Textbook of Liver Disease*. 3rd ed. Philadelphia:WB Saunders; 1996:875-87.
13. Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Engl J Med*. 2000;343:1833-8. [PMID: 11117974]
14. Nadir A, Agrawal S, King PD, Marshall JB. Acute hepatitis associated with the use of a Chinese herbal product, ma-huang. *Am J Gastroenterol*. 1996;91:1436-8. [PMID: 8678010]
15. Roberts SM, Harbison RD, Seng JE, James RC. Potentiation of carbon tetrachloride hepatotoxicity by phenylpropanolamine. *Toxicol Appl Pharmacol*. 1991;111:175-88. [PMID: 19573-8]
16. Abo-Khatwa AN, al-Robai AA, al-Jawhari DA. Lichen acids as uncouplers of oxidative phosphorylation of mouse-liver mitochondria. *Nat Toxins*. 1996;4:96-102. [PMID: 8726330]
17. Hoffman BB, Lefkowitz RJ. Adrenergic receptor antagonists: Yohimbine. In: Goodman LS, Gilman A, Gilman AG, Rall TW, Nies AS, Taylor P, eds. *Goodman and Gilman's Pharmacological Basis of Therapeutics*. 8th ed. New York: Pergamon Pr; 1990:229.
18. Braunstein GD, Koblin R, Sugawara M, Pekary AE, Hershman JM. Unintentional thyrotoxicosis factitia due to a diet pill. *West J Med*. 1986;145:388-91. [PMID: 3765621]
19. Fong TL, McHutchison JG, Reynolds TB. Hyperthyroidism and hepatic dysfunction. A case series analysis. *J Clin Gastroenterol*. 1992;14:240-4. [PMID: 1564300]

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