Appendix IV: Liver-Toxic Medications and Herbs

The following information is based on an appendix found in The Hepatitis C Help Book and is reprinted with the permission of the publisher, St. Martin's Griffin.

There is a great deal of research still to be done to identify those prescription medications, over-the-counter drugs, herbs and chemicals that are liver toxic. Some substances affect everyone negatively, some are dangerous for people who have liver disease. Others are hazardous when taken in too large a quantity, in combination with other substances or by people who have unusual immune responses.

The following list of suspected or confirmed liver-toxic medications and herbs should help guide anyone with hepatitis. It is not comprehensive, however, and any time a person with liver disease contemplates taking a drug or herb, even when prescribed by a health care practitioner, he or she should be on the lookout for negative reactions. Combining herbs with interferon and/or ribavirin demands particular care. Anyone with HCV should discuss potential reactions and drug interactions with both western and Chinese medicine practitioners before taking any medication or herbal remedy. Although liver-toxic substances are identifiable in the laboratory, liver hypersensitivity problems are not predictable. In some cases, hypersensitivity may result in organ failure. Although hypersensitivity is hard to anticipate, some indicators offer clues as to who may be vulnerable. Indicators of possible negative reactions to medical substances include:

- having multiple allergies and having had previous adverse reactions to drugs or herbs
- a history of chronic skin rashes
- current liver disease

Important! You should discontinue taking any drug or herb if you experience a skin rash, substantial nausea, bloating, fatigue and/or aching in the area of the liver, yellowing of the skin, or pale feces.

Dr. Gish has contributed information on liver-toxic drugs.

David L. Diehl, MD, FACP, an associate clinical professor of medicine at UCLA School of Medicine, focuses on herbal toxicity. He, Ken Flora, MD, formerly of the University of Oregon Health Sciences Center, and Misha Cohen are currently undertaking an extensive survey of the literature concerning the liver toxicity of herbal medicines.

Prescription and Over-The-Counter Drugs

Patients who take the following medications regularly should undergo monthly laboratory testing for the first three months and then every three to six months to check on changes in liver function. Sample brand names are listed after the pharmaceutical name. Other products in addition to those mentioned may contain these drugs. Talk with your doctor and read all package inserts carefully.

- acetaminophen or APAP (Tylenol®), particularly hazardous when taken with alcohol or anti-seizure medications
- alpha-methyldopa (Aldomet®)
- amiodarone (Cordarone®)
- azathioprine (Imuran®, 6-mecaptopurine [6MP])
- carbamazapine (Tegretol®, Epitol®, Mazepine®, Atretol®, Carbatrol®)
- chlorzoxazone (Parfon Forte DSC®, Paraflex®, Chlorzone Forte®, Algisin®)
- dantrolene (Dantrium®)
- diclofenac (Voltaren®, Cataflam®)
- fluconazole or ketoconazole (Diflucan®, Nizoral®)

- flutamide (Drogenil®, Euflex®, Eulexin®)
- hydralazine (Apresolin®, Novo-Hylazin®)
- ibuprofen (Advil®, Motrin®, Nuprin®)
- isoniazid (INH) (Laniazid®, Nydrazid®)
- long-acting nicotinic acid
- leukotriene synthase inhibitors (Zafirlukast®, Accolate® and Zileuton®, Zyflo®)
- methotrexate (Maxtrex®)
- nitrofurantoin (Macrodantin®)
- perihexilene maleate
- phenylbutazone (Mapap®, Marnal®, Lanatuss®)
- phenytoin (Ethotoin®, Mephenytoin®, Dilantin®)
- pravastatin, fluvastatin, simavastatin, lovastatin
- quinidine (Cardoquin®, Cin-Quin®, Duraquin®)
- rifampin (Rifampicin®, Rifadin®, Rimactane®)
- sulfa medications (especially Septra® or Bactrim®)
- tacrine (Cognex®)
- ticlopidine (Ticlid®)
- tolcapone (Tasmar®)
- troglitzone (Rezulin®)
- vitamin A (in doses greater than 5,000 units a day; beta-carotene is safe at all doses)

According to an article published in the April 1996 New England Journal of Medicine, the most common cause of acute liver failure in the United States is the negative interaction between acetaminophen (Tylenol) and alcohol. In addition, there are interactions that are less common but equally as serious. Research suggests individual genetic variations in liver enzymes may be the cause.

Chinese Herbal Perparations

Herbal patent medicines, tonics, elixirs and prepackaged solutions are particularly risky for anyone, whether they have liver disease or not. Ingredient labels may be incomplete or mistranslated. Herbs may be mistakenly used in the concoctions that are dangerous or inappropriate in combination with other herbs. Toxic herbs may be substituted for beneficial ones. The best bet is to avoid self-prescribed premixed preparations. Rely on the best-trained and most experienced herbalist available to individualize your herbal therapy and monitor your reactions.

Some reportedly hazardous herbs and herb formulas:

- **Shosaikoto –** a Japanese preparation used for improving hepatic dysfunction in chronic hepatitis. Its Chinese name is Xiao Chai Hu Tang. It may trigger interstitial pneumonia in people with chronic HCV who also are taking interferon, according to Precautions from the Pharmaceutical Affairs Bureau.
- **Jin Bu Huan –** for insomnia and pain. This formula caused some liver problems but the exact trigger was never identified.

- **Aristolochia** – used to treat fluid retention and rheumatic symptoms; has been banned in England after it was confused with an herb from the clematis plant that has the same name in Chinese as aristolochia: Mu Tong. The Mu Tong used was in fact the toxic species aristolochia rather than the other harmless herb. Aristolochia was part of a formula implicated in seventy cases of kidney failure in Belgium in 1993.

In addition, some Chinese patent medicines may contain heavy metals, poisons, and other potentially liver-toxic substances. In other cases, patent medicines contain western pharmaceutical agents that are not listed on the label.

Common Toxic Ingredients Found in Asian Patent Medicines

Be on guard for these ingredients:

- aconite or aconitum: causes paralysis and death if not highly processed before use
- acorus: causes convulsions and death
- borax: triggers severe kidney damage
- borneol: triggers internal bleeding and death
- cinnabar or calomel: a mercury compound
- litharge and minium: contain lead oxide
- myiabris: can trigger convulsions, vomiting and death
- orpiment or realgar: contains arsenic
- scorpion or buthus: causes paralysis of the heart and death
- strychnos nux vomica or semen strychni: strychnine-containing seeds cause respiratory failure and death
- toad secretion or bufonis: can paralyze heart muscle and lungs

Toxic Individual Herbs

Dr. Diehl writes: "Herbal medicine is generally safe – safer than western pharmaceuticals. There are certain plants that are highly toxic. The most common examples are those that contain pyrolizidine alkaloids." Those that contain alkaloids or that reportedly have triggered toxic reactions include the following.

- Chaparral (creosote bush, greasewood)
- Comfrey (if taken internally)
- Crotalaria (Ye Bai He)
- Eupatorium
- Germander (This toxic herb is often substituted for skullcap, and skullcap is not toxic in well-formulated herbal remedies. However, always insist that any ingredient identified as skullcap be the genuine article and not germander.)
- Groundsel (senecio longilobus)
- Heliotropium
- Mentha pulegium
- Mistletoe
- Pennyroyal (squawmint) oil or Hedeoma pulegoides
- Sassafras
- Senicio species

Special Cases

Licorice: a mainstay of Chinese formulas, licorice is used in very small quantities to balance herbal action and often appears as glycyrrhizin (licorice root). However, licorice produces well-documented side effects such as hyperaldosteronism (an increase in levels of the adrenal hormone aldosterone, triggering imbalance of electrolytes) when taken in doses of more than 50 grams a day or for six weeks or longer. However, no side effects have been seen in smaller doses over thirty days or in higher doses for a very short period of time.

Skullcap: also called scutelleria or scute, this herbv is used in many formulas to good effect. However, it appears that the toxic substance germander often is substituted for skullcap in formulas without being properly identified. As a result skullcap looks like the offending substance. Dr. Diehl found several mentions of skullcap toxicity in the literature, but those mentions may in fact refer to unidentified substitutions of germander. Further research is needed to clarify this. Until then, whenever skullcap appears in a formula, make sure that it, not germander, is in fact being used. If you cannot be sure, do not take the formula or herb.

Dr. Diehl has found one mention of toxicity in the literature for the following herbs. Further documentation of toxicity is needed.

- Calliepsis laureola
- Atractylis gunnifera
- margosa oil
- valerian (Valerian officinalis)

For more detailed information on substances toxic to the liver, please see:
***The HIV Wellness Sourcebook*, Henry Holt & Misha Cohen, 1998 and *The Hepatitis C Help Book, Revised Edition*, Misha Cohen & Robert Gish, St. Martin's Griffin, 2007.**