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LIPOWATCH[®]

NEWS

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The LipoWatch program from Visionary Health Concepts is designed to support providers and patients with education that integrates a "real world" focus with scientific data. This month's topic is the statin drugs used for lowering blood lipids after lifestyle changes fail or in the case of immediate patient need.

The statins are a family of lipid-lowering drugs also called HMG-CoA reductase inhibitors. That stands for 3-Hydroxy-3-methylglutaryl coenzyme A, which is needed to synthesize cholesterol. The family includes atorvastatin (Lipitor), fluvastatin (Lescol), lovastatin (Mevacor), pravastatin (Pravachol), and simvastatin (Zocor). Rosuvastatin (Crestor) is another statin still in development. Cerivastatin (Baycol) was withdrawn from the US market in August of 2001 because of sometimes fatal cases of rhabdomyolysis (see below).

Statin are the drugs of choice when treating high LDL cholesterol as the primary lipid abnormality. For the general population, if statins alone are not sufficient to achieve cholesterol targets, they may be combined with bile-sequestering

agents (resins) or niacin. To treat combined high LDL, low HDL and high triglycerides, the statins are recommended in combination with fibrates or niacin.

The statins seem to cause fewer side effects than other lipid-lowering agents. However, they can cause liver toxicity, myositis (muscle inflammation), and rhabdomyolysis (muscle destruction). Rhabdomyolysis is a condition characterized by dark urine and muscle weakness or stiffness, where myoglobin is released from muscles and "clogs" the kidneys. Thirty-one cases of rhabdomyolysis, mostly in elderly patients also taking gemfibrozil (a fibrate discussed in next month's fax), led to the withdrawal of cerivastatin.

Despite their generally good reputation as lipid-lowering agents, the statins can be difficult to use with patients who are HIV+ due to their interactions through the CYP3A4 enzyme pathway with several HIV antiviral medications.¹ Inhibition of CYP3A4 by protease inhibitors can increase blood levels of the statins and increase the risk of rhabdomyolysis. Liver function tests

and levels of creatinine phosphokinase (CPK or CK) should be monitored.

Lovastatin and simvastatin are contraindicated with any protease inhibitor² due to the risk of significantly higher blood levels that result in an increased risk of side effects; however, amprenavir's manufacturer has not contraindicated its use with either of these drugs.³ On the other hand, fluvastatin appears unlikely to have any significant interactions with protease inhibitors and pravastatin levels are likely decreased, while atorvastatin levels may increase by only 3- to 5-fold. Most HIV physicians use a reduced dose of atorvastatin and increase it as needed to achieve desired results, or pravastatin, which may also be titrated up.

To complicate matters further, a recent paper found a link between statin use and neuropathy⁴ and notes that statins also inhibit synthesis of ubiquinone, a key mitochondrial respiratory enzyme. On the plus side, despite several contradictory findings in the past two years, statins may be linked to improvements in bone mineral density.

Next month's LipoWatch fax will discuss the fibrates and other lipid-lowering agents.

¹ Dubé et. al., Preliminary Guidelines for the Evaluation and Management of Dyslipidemia in Adults Infected with Human Immunodeficiency Virus and Receiving Antiviral Therapy, *Clinical Infectious Diseases* 2000;31:1216-24

² See Table 17 in the *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* February 4, 2002, available at http://www.hivatis.org/guidelines/adult/May23_02/AAMay23.pdf

³ See for example the University of Liverpool's web site at <http://www.hiv-druginteractions.org/>

⁴ Gaist, D et. al., Statins and Risk of Polyneuropathy: A Case-Control Study. *Neurology* 2002;58:1321-1322, 1333-1337

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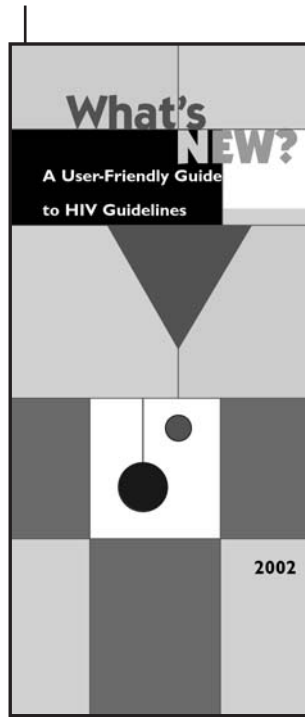
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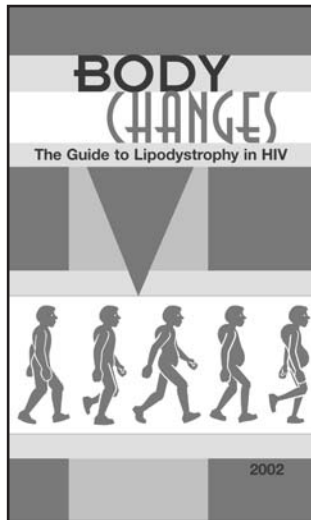
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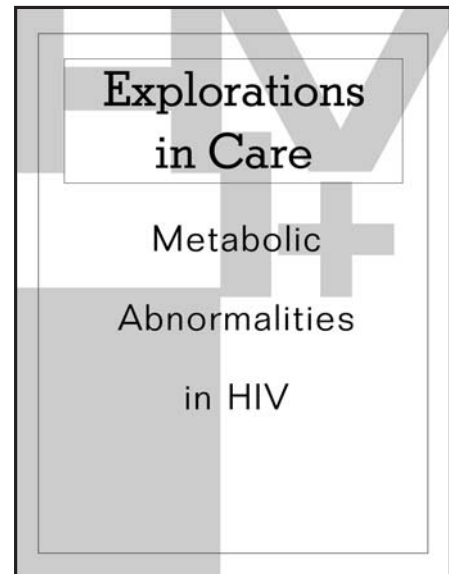
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