An Unusual “Side Effect” of an Acne Drug

What is the problem and what is known about it so far?
Isotretinoin (Accutane) is a vitamin A–like drug used to treat severe acne. It is a pill that is taken by mouth and is usually given to people who do not respond to treatment applied directly to the skin (topical). Isotretinoin may cause side effects, including birth defects, liver problems, hair loss, and increases in fatty substances in the blood (triglycerides). Researchers do not know why or how isotretinoin increases triglyceride levels. They think that persons who have a family or genetic tendency to develop very high levels of triglycerides and cholesterol are the ones who develop this side effect. Thus, if persons develop high triglyceride levels while taking isotretinoin, it could indicate that they have an inherited problem with fatty substances in the blood (familial combined hyperlipidemia). This inherited disorder is usually diagnosed in early adulthood. People with the disorder have high levels of triglycerides and cholesterol (fatty substances) and can develop diabetes, high blood pressure, and obesity. They have increased risks for having a heart attack at a young age.

Why did the researchers do this particular study?
To see whether the development of elevated triglyceride levels in persons taking isotretinoin actually indicates an inherited problem with fatty substances in the blood.

Who was studied?
102 persons (average age, 28 years) who had increased levels of triglycerides while taking isotretinoin for severe acne and 100 persons (average age, 27 years) who took isotretinoin but did not have increased triglyceride levels.

How was the study done?
The researchers reviewed the records of patients who took isotretinoin between 1988 and 1998. Most took isotretinoin for about 6 months and had had their blood checked monthly for triglyceride levels. The researchers divided the patients into those with (group 1) and without (group 2) elevated triglyceride levels while taking isotretinoin. The researchers then contacted the patients about 4 years after they had stopped taking isotretinoin, and they also contacted some of the patients’ parents. The researchers examined the patients and their parents and did several blood tests for fatty substances, glucose, insulin, and genetic material.

What did the researchers find?
At follow-up, group 1 patients more often had high levels of fatty substances (triglycerides and cholesterol) than group 2 patients. They weighed more and had greater waist obesity, higher blood pressure, and higher insulin levels. They also more often had patterns of genetic material known to be associated with familial lipid problems (particular apoE gene patterns). Finally, parents of group 1 patients more often had high levels of fatty substances in their blood than did parents of group 2 patients.

What were the limitations of the study?
Only patients with no or definite changes in triglyceride levels while taking isotretinoin were studied. Many patients (n = 321) who had very small increases in triglyceride levels were not studied. We do not know their genetic patterns or whether they developed problems with obesity and abnormal lipids.

What are the implications of the study?
Young people who develop increased levels of triglycerides while taking isotretinoin may have an inherited familial lipid problem.