

Animi-3™

Each Capsule contains:

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|------------------------------|---------|
| Folic Acid | 1 mg |
| Vitamin B6 | 12.5 mg |
| Vitamin B12 | 500 mcg |
| Omega-3 Acids | 500 mg |
| -Docosahexaenoic Acid (DHA) | 350 mg |
| -Eicosapentaenoic Acid (EPA) | 35 mg |

Patent Pending

Rx Only

Description

Animi-3™ Capsules are intended for oral administration.

Each Capsule Contains: 1 mg Folic Acid USP, 12.5 mg Vitamin B-6 (Pyridoxine Hydrochloride, USP), 500 mcg Vitamin B-12 (Cyanocobalamin, USP) and Pharmaceutical Grade Omega-3 Fish Oil providing 500 mg Omega-3 Acids; including 350 mg Docosahexaenoic Acid (DHA) and 35 mg Eicosapentaenoic Acid (EPA).

Also Contains: Yellow Beeswax NF, Sunflower Oil FCC, Bleached Lecithin NF, Ascorbic Acid USP, Mixed Tocopherols NF, Ascorbyl Palmitate NF and a soft shell capsule (which contains; Gelatin USP, Glycerin NF, Titanium Dioxide USP, FD&C Red 40 and USP Purified Water).

Indication

Animi-3™ Capsules are indicated for nutritional support and folic acid supplementation.

Contraindications

This product is contraindicated in patients with a known hypersensitivity to any of the ingredients.

Precautions

Folic Acid in doses above 0.1 mg daily may obscure pernicious anemia in that hematological remission can occur while neurological manifestations remain progressive.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Adverse Reactions

Allergic sensitization has been reported following both oral, enteral and parenteral administration of folic acid.

Dosage and Administration

Adults – One capsule daily or one capsule twice daily, or as directed by a physician.

How Supplied

Animi-3™ supplied as red opaque oblong Capsules. Each Capsule is imprinted with "PBM 540" in black opacode.

Animi-3™ Capsules are available in bottles of 60 capsules (NDC 66213-540-60).

Keep out of reach of children.

Dispense in a well-closed, tight light-resistant container as defined in the USP using a child-resistant closure.

Storage Conditions: Store at 20-25°C (68-77°F). See USP Controlled Room Temperature. Protect from light and moisture.

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Pregnancy Can Alter Liver Function

BY JEFF EVANS

Senior Writer

CAMBRIDGE, MD. — The liver is a dynamic organ during pregnancy, and standard physiologic changes may mimic pregnancy-induced hepatic disease.

The clinical challenge of distinguishing the normal from abnormal liver during pregnancy was addressed by Ayman Koteish, M.D., of Johns Hopkins University, Baltimore.

For example, a clinician may detect spider angiomas and palmar erythema, which are associated with liver diseases, during a physical examination of a pregnant woman, but these signs are to be expected in pregnancy and do not indicate liver disease. These two signs are thought to result from a high-estrogen state, he said.

On the other hand, a palpable liver in pregnancy, especially in late pregnancy, is not to be ignored, he said at a hepatobiliary update sponsored by the university.

Laboratory results during pregnancy commonly show decreases in albumin of 1 g/dL. Alkaline phosphatase may rise

to levels two to four times normal, and increases in total bile acids to 11 $\mu\text{mol/L}$ or less are common. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels may rise a little, but stay within the normal range.

Hyperemesis gravidarum

The nausea and vomiting that characterize this condition in 2% of pregnant women may lead to dehydration and malnutrition. Some women develop a transient hyperthyroidism that eventually gets better as hyperemesis gravidarum resolves.

Liver histology is not warranted to diagnose the condition, but AST and ALT levels may be increased to less than three times the normal values and bilirubin can be mildly elevated. Physicians normally give supportive treatment, including antiemetics such as phenothiazines or 5-HT₃ antagonists such as ondansetron; dexamethasone can be used for severe cases.

Preeclampsia and eclampsia

About 25% of patients with preeclampsia and 90% of those with eclampsia will have AST and ALT values anywhere from 5 to 100 times normal and a bilirubin level less than 5 $\mu\text{mol/L}$. Jaundice, if present, is usually mild; it won't be clinically evident if the bilirubin level is less than 3 $\mu\text{mol/L}$, Dr. Koteish pointed out.

HELLP syndrome

This is the most severe form of preeclampsia, consisting of hemolysis, elevated liver enzymes, and low platelets. Most women (80%) who experience HELLP develop it during the third trimester, but 15% have the condition before week 27. Proteinuria and hypertension develop in up to 85% of patients. A liver biopsy is

not needed to make the diagnosis.

The deterioration of patients with HELLP is unpredictable and can include subcapsular hematoma, infarction, renal failure, maternal death in 1%-3% of patients, prematurity or intrauterine growth restriction in about one-third of fetuses, and perinatal mortality rates of 7%-60%.

Patients with the HELLP syndrome need an "expeditious delivery," Dr. Koteish said. Delivery eliminates any fetal liver dysfunction or thrombocytopenia, as well as maternal chronic liver dysfunction. Most patients recover within 72 hours after delivery, but 4%-27% can have a recurrence of the syndrome in future pregnancies.

Intrahepatic cholestasis of pregnancy

ICP occurs in the second half of pregnancy, with intractable pruritus that is worse at night on the palms and soles without specific skin findings except scratch marks.

The rate of ICP is only 0.5%-1.5% in the United States and Europe, but is as high as 15% in Chile. Between 45% and 70% of women with ICP have a recurrence in future pregnancies. They carry a predisposition to develop cholesterol stones. Women who have had a cholecystectomy or multiple pregnancies are at higher risk for ICP.

The diagnosis of ICP is usually made with a serum bile acid level greater than 11 $\mu\text{mol/L}$ and a high bilirubin level in about 20% of patients. The ratio of cholic acid to chenodeoxycholic acid has been reported to be significantly higher in ICP pregnancies than in normal pregnancies (4 to 1 vs. 1.5 to 1). Liver biopsies are not warranted to obtain the diagnosis because no sequelae follow in the liver, and the condition generally lasts until delivery and is reversible.

"If pruritus lasts beyond 2 weeks after delivery, an alternative diagnosis such as primary sclerosing cholangitis or primary biliary cirrhosis should be entertained," Dr. Koteish advised.

For treating ICP, ursodeoxycholic acid to 10-15 mg/kg per day has been shown to be safe and effective; 20-25 mg/kg per day may be more effective, he noted.

Acute fatty liver of pregnancy

This type of liver dysfunction develops in only 1 out of every 7,000 to 16,000 pregnant women, but carries a 70% maternal mortality and a 90% fetal mortality because of acute liver failure and coagulopathy. It usually strikes between 30 and 38 weeks, about half the time along with preeclampsia. In general, hypertension is absent, and there is a prolonged prothrombin time and low fibrinogen.

Some of the complications of acute fatty liver of pregnancy include diabetes insipidus, disseminated intravascular coagulopathy, spontaneous labor, and postpartum hemorrhage.

The disease has been associated with a deficiency of long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD). The fetus

is usually homozygous for the mutation while the mother is heterozygous. Long-chain fatty acids accumulate on the fetal side and then transfer to the mother's circulation, Dr. Koteish said.

He advised performing genetic tests on the mother, father, and infant for the various mutations that can occur to the LCHAD gene, because the infant is at risk of sudden death, cardiomyopathy, and neuromyopathy.

Diseases coincidental with pregnancy

Patients with hepatitis B or C virus infections that occur coincidentally with pregnancy do not need therapy, Dr. Koteish advised. HBV infection is transmitted to the fetus 90% of the time when the mother is positive for hepatitis B e antigen. However, hepatitis B vaccine given at birth provides protection against transmission.

HCV transmission to the fetus occurs 6%-10% or more of the time, depending on the mother's viremic load.

Once the disease activity of women with autoimmune hepatitis or Wilson's disease becomes stable, fertility returns. These patients may conceive but should continue therapy.

Herpes simplex virus hepatitis represents a threat to the fetus. Visceral dissemination of HSV, though normally rare, occurs more commonly in pregnancy, typically in the second or third trimester. The symptoms and signs of HSV hepatitis include a flulike prodrome, vesicles in about half of patients, and high ALT and AST levels. A biopsy and serology or culture are enough to make the diagnosis. Once the infection is under control with acyclovir, delivery can occur with less risk of transmission to the infant.

Hepatitis E virus infection is possible on trips to endemic areas, such as tropical and subtropical countries including India and Mexico. The virus normally has a fecal-oral route of transmission, but vertical transmission has been reported. A self-limited illness develops in about 80% of women, but up to 20% progress to liver failure; the disease can lead to high fetal complication rates as well as an increasing risk of fatality as term approaches.

Fertility is reduced in cirrhosis, making pregnancy rare, but pregnancy is more common in women with noncirrhotic portal hypertension. Little data exist on the risks involved in pregnancy with noncirrhotic portal hypertension, but reports have documented rates of fetal wastage in 8%-20%, spontaneous abortion in 15%-20%, and perinatal mortality in 11%-18%. Maternal complications develop in 30%-50% of women, but these tend to be less common and less severe if the woman is diagnosed and undergoes decompression before conception.

If a woman has received a liver transplant, pregnancy does not seem to affect the functioning of the graft. However, conception needs to be delayed for at least 6 months after the transplant surgery because of the risk of cytomegalovirus infection. Immunosuppressive drugs should be continued throughout the pregnancy. ■