

Hepatitis C May Be Next 'Big Virus,' Expert Says

BY BETSY BATES

LAS VEGAS — Amid the alphabet soup of hepatitis virus types, the one that should most concern physicians these days is hepatitis C.

"This is going to be the big virus in the next 20 years in the U.S.," Dr. Marsha H. Kay predicted at a meeting sponsored by the American Academy of Pediatrics.

Hepatitis C virus already infects 1.6% of the general U.S. population—4 million people—but "the vast majority of people who are infected do not know it," said Dr. Kay, a pediatric gastroenterologist and director of pediatric endoscopy at the Cleveland Clinic Children's Hospital.

Known to be at risk are infants born to mothers with hepatitis C; young adult survivors of leukemia, childhood malignancies, and childhood cardiac surgery; hemophiliacs; dialysis patients; intravenous drug users; sexual partners of a person with hepatitis C; recipients of blood transfusions prior to 1989; first responders; and health care workers.

However, 32% of the current cases involve no known risk factor.

"We don't know exactly how this virus is transmitted," said Dr. Kay.

There is no way to prevent hepatitis C (except for universal body fluid precau-

tions) and there is no vaccine.

Among those infected, 80%-85% will develop chronic hepatitis, and of those, half will develop cirrhosis, putting them at highly elevated risk for hepatocellular carcinoma. Hepatitis C is already the leading cause of liver transplantation in the nation.

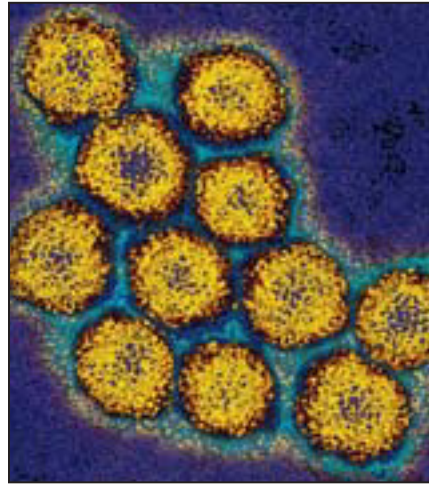
All things considered, the perfect storm of hepatitis C constitutes "a really terrible outcome compared to hepatitis B infection," she said, adding, "I lose a lot of sleep about this."

Among children, the leading cause of hepatitis C transmission is perinatal exposure, with transmission risk correlated to the mother's viral load at delivery.

Unfortunately, drugs used to treat acute hepatitis C are teratogenic and cannot be used during pregnancy. Some experts recommend avoiding fetal scalp monitoring and prolonging labor beyond 6 hours after the rupture of membranes to reduce the risk of transmission.

Breastfeeding, Dr. Kay said, is controversial. Hepatitis C acquired via perinatal transmission has an increased likelihood of becoming chronic.

Anti-HCV testing is ideally performed between 15 and 18 months of age. Although HCV RNA testing may be positive at 2 months and 6 months,



Of those infected with hepatitis C virus, 80%-85% develop chronic hepatitis.

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manufacturer during 1993 and 1994 may also be at risk.

Health care providers, especially those who work in emergency departments, surgery, or procedurally related specialties, have an estimated 1% prevalence rate that is rising, she said.

"I have to say, the majority of the kids I see in my practice with hepatitis C are the children, typically, of a nurse—a health care provider who likely got it occupationally," she noted.

New data suggest that prompt treatment with interferon and ribavirin may produce a sustained virologic response in up to 80% of patients with acute hepatitis C. "If you're sure of [acute infection], you want to treat them early," she said.

Antibody testing has been available for nearly 20 years, but the antibody just signals exposure to the virus, not immunity. By 1994, Japanese researchers had characterized the virus particle, a single-stranded RNA molecule. At least 9 genotypes and 90 subtypes have been identified to date, with genotype 1, unfortunately, most prevalent in the U.S. population. Patients with this genotype are less responsive to treatment, she said. ■

Disclosures: None was reported.

Recent Advances Pave Way For Novel Acne Therapies

BY BRUCE JANCIN

BERLIN — It is quite possible, 5-10 years from now, that adolescents will be able to get an antiacne vaccine, according to an acne expert.

That was one of the potential therapeutic developments Dr. Harald P. Gollnick discussed at the annual congress of the European Academy of Dermatology and Venereology.

For a quarter century, acne therapy has revolved around antimicrobials and retinoids, alone or together, but recent advances in the understanding of acne pathogenesis have opened the door to novel therapeutic possibilities, according to Dr. Gollnick, professor of dermatology and venereology at Otto von Guericke University in Magdeburg, Germany, and chairman of the Global Alliance to Improve Outcomes in Acne, an international panel of experts.

An impetus for the development of these novel strategies is their nonreliance upon antimicrobials, which means they won't contribute to the growing problem of antimicrobial resistance. That is an important consideration, given the vast amount of antibiotics prescribed for a condition that affects more than 50 million patients in the United States alone.

He discussed several potential new acne therapeutic possibilities:

► **Vaccination.** Dermatologists at the University of California, San Diego, have

developed *Propionibacterium acnes* vaccines with demonstrated efficacy in mouse models (Infect. Disord. Drug Targets 2008;8:160-5). Both inactivated whole *P. acnes*-based vaccines and vaccines built around cell wall-anchored sialidase of *P. acnes* are being studied.

► **Dietary manipulations.** The hormones present in commercial dairy-produced cow's milk as a potential aggravating factor in acne have drawn increasing attention, particularly in Europe. A low-glycemic-index diet proved effective in treating acne in an Australian randomized controlled study (Am. J. Clin. Nutr. 2007;86:107-15). A recent Harvard University study found skim milk consumption to be positively associated with acne in teenage boys (J. Am. Acad. Dermatol. 2008;58:787-93).

► **Ectopeptidase inhibition.** This may fight acne by inhibiting sebaceous hyperplasia, follicular hyperkeratosis, and inflammation.

► **Insulin sensitizing agents.** Metformin and the thiazolidinediones have demonstrated a beneficial anti-acne effect in the setting of polycystic ovarian disease (Expert Opin. Ther. Targets 2009;13:1205-26), and follow-up studies are underway. ■

Disclosures: Dr. Gollnick is an adviser for Immune Technologies and Medicine, manufacturer of IP10.C8, an ectopeptidase inhibitor.

Pataday™ (olopatadine hydrochloride ophthalmic solution) 0.2%

INDICATIONS AND USAGE

PATADAY™ solution is indicated for the treatment of ocular itching associated with allergic conjunctivitis.

CONTRAINDICATIONS

Hypersensitivity to any components of this product.

WARNINGS

For topical ocular use only. Not for injection or oral use.

PRECAUTIONS

Information for Patients

As with any eye drop, to prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. Patients should be advised not to wear a contact lens if their eye is red.

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% should not be used to treat contact lens related irritation. The preservative in PATADAY™ solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red, should be instructed to wait at least ten minutes after instilling PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% before they insert their contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size and a 50 kg person, these doses were approximately 150,000 and 50,000 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of approximately 100,000 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of approximately 15,000 times the MROHD level.

Pregnancy:

Teratogenic effects: Pregnancy Category C

Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 150,000 times the MROHD and rabbits treated at 400 mg/kg/day, or approximately 100,000 times the MROHD, during organogenesis showed a decrease in live fetuses. In addition, rats treated with 600 mg/kg/day of olopatadine during organogenesis showed a decrease in fetal weight. Further, rats treated with 600 mg/kg/day of olopatadine during late gestation through the lactation period showed a decrease in neonatal survival and body weight. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Nursing Mothers:

Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is administered to a nursing mother.

Pediatric Use:

Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

Geriatric Use:

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

The following adverse experiences have been reported in 5% or less of patients:

Ocular: blurred vision, burning or stinging, conjunctivitis, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, pain and ocular pruritus.

Non-ocular: asthenia, back pain, flu syndrome, headache, increased cough, infection, nausea, rhinitis, sinusitis and taste perversion. Some of these events were similar to the underlying disease being studied.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye once a day.

HOW SUPPLIED

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is supplied in a white, oval, low density polyethylene DROP-TAINER® dispenser with a natural low density polyethylene dispensing plug and a white polypropylene cap. Tamper evidence is provided with a shrink band around the closure and neck area of the package.

NDC 0065-0272-25

2.5 mL fill in 4 mL oval bottle

Storage:

Store at 2°C to 25°C (36°F to 77°F)
U.S. Patents Nos. 4,871,865; 4,923,892; 5,116,863; 5,641,805;
6,995,186

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