

# Hepatic Encephalopathy Diagnostic Test Effective

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VIENNA — The same brief, Web-based neuropsychologic test that is used by all National Football League teams to assess players for the effects of concussion appears to be advantageous for the diagnosis of minimal hepatic encephalopathy.

The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT v4.0) is a well-validated, computer-based neuropsychologic test that takes about 10 minutes. It's billable as a neu-

ropsychologic test, user friendly, available in 13 languages, can be administered by anybody in the office, and produces immediate results without need of a clinical neuropsychologist to interpret the scores, Dr. Michel H. Mendler explained at the congress, which is sponsored by the European Association for the Study of the Liver.

"ImPACT could become a new standard for minimal hepatic encephalopathy

testing, both in routine clinical practice and to evaluate treatments," said Dr. Mendler, a gastroenterologist at Loma Linda (Calif.) University.

Minimal hepatic encephalopathy (MHE) is a greatly underdiagnosed neurocognitive disorder present in 60%-80% of patients with cirrhosis. It results in impaired quality of life, increased work disability, and impaired driving made more hazardous by lack of insight. If

unchecked, MHE can progress to overt hepatic encephalopathy, a more serious neuropsychiatric syndrome characterized by cognitive and motor deficits that often require hospitalization.

MHE includes deficits in mental processing speed, fine motor skills, memory, complex attention, constructive abilities, and visual-spatial orientation. These deficits, unlike those in overt hepatic encephalopathy, are subtle and re-

## Screening Tests

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cirrhosis who were screened for HCC with an initial ultrasound liver scan and alpha-fetoprotein (AFP) test, and then had a follow-up CT or MRI within 6 months.

There were 35 cases of HCC in the group. Ultrasound alone detected HCC in 26, for a sensitivity of 77% and a specificity of 99%. There were eight false negatives and one false positive. In the eight false-negative cases, a subsequent CT scan identified HCC. The mean AFP level in this group of patients was 32,325 ng/mL; only two patients had a level lower than 20 ng/mL.

In the 75 patients with a true negative ultrasound, the mean AFP level was 17 ng/mL. In all, 9% of the patients in this group had an AFP greater than 20 ng/mL, and one patient had a level of more than 400 ng/mL.

"In this series alone, 74 CT or MRI studies could have been avoided with the combined use of ultrasound and AFP for screening," said Dr. Soloway, the Marie B. Gale Centennial Professor of Medicine at the University of Texas Medical Branch, Galveston. "Ultrasound can eliminate more expensive imaging studies until confirmation is necessary, thus reducing the overall cost of medical monitoring for patients in HCC screening populations."

Dr. Jason B. Welch, also of the University of Texas Medical Branch at Galveston, was a coinvestigator. ■

**VITALS** **Major Finding:** A combination of ultrasound and alpha-fetoprotein testing has a specificity of 100% and a sensitivity of 87% for detecting hepatocellular carcinoma in patients with cirrhosis.

**Data Source:** A retrospective review of 140 patients with cirrhosis who had the combination screening method followed within 6 months by CT or MRI.

**Disclosures:** Dr. Soloway reported having no relevant financial disclosures.

People who have had chicken pox are at risk for shingles and postherpetic neuralgia (PHN) pain<sup>1,2</sup>  
This year, ~1 million Americans will develop shingles<sup>1,2</sup>.  
1 in 5 of them will go on to develop PHN pain<sup>1</sup>



### Indication

LIDODERM (lidocaine patch 5%) is indicated for relief of pain associated with post-herpetic neuralgia. Apply only to **intact skin**.

### Important Safety Information

LIDODERM is contraindicated in patients with a history of sensitivity to local anesthetics (amide type) or any product component.

Even a *used* LIDODERM patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used LIDODERM patch, although the risk with this formulation has not been evaluated. It is important to **store and dispose of LIDODERM out of the reach of children, pets, and others**.

Excessive dosing, such as applying LIDODERM to larger areas or for longer than the recommended wearing time, could result in increased absorption of lidocaine and high blood concentrations leading to serious adverse effects.

Avoid contact of LIDODERM with the eye. If contact occurs, immediately wash the eye with water or saline and protect it until sensation returns.

Avoid the use of external heat sources as this has not been evaluated and may increase plasma lidocaine levels.

Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of lidocaine, because of their inability to metabolize lidocaine normally. LIDODERM should be used with caution in patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic. LIDODERM should also be used with caution in pregnant (including labor and delivery) or nursing mothers.

Allergic reactions, although rare, can occur.

During or immediately after LIDODERM treatment, the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritus, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours. Other reactions may include dizziness, headache, and nausea.

When LIDODERM is used concomitantly with local anesthetic products, the amount absorbed from all formulations must be considered.

quire neuropsychologic testing for diagnosis, Dr. Mendler said.

Conventional neuropsychologic testing is cumbersome, he said. It's complex, lengthy, and the results require interpretation by a specialist. A widely used alternative is paper-and-pencil testing using several psychometric tests, such as Digit Symbol and Number Connection tests A and B. But the results of these tests are confounded by the substantial practice effect with repeated testing.

In contrast, ImpACT, which was developed by neuroscientists at the University of Pittsburgh, generates an un-

limited number of alternate forms, avoiding the practice effect, Dr. Mendler continued.

He compared ImpACT with paper-and-pencil testing in 90 cirrhotic patients with no history of overt hepatic encephalopathy and 131 matched healthy controls. ImpACT scores identified 25 of 90 cirrhotic patients as having abnormal results consistent with MHE; paper-and-pencil testing identified 16, only 10 of whom were also ImpACT-positive.

In addition, ImpACT identified 12 of 74 paper-and-pencil test-negative patients as having MHE. Seven of 131

healthy controls were ImpACT-positive, a significantly lower false-positive rate than with paper-and-pencil testing, which was positive in 19 controls.

ImpACT-positive cirrhotic patients had a mean total Sickness Impact Profile score of 17.6, compared with 13.5 in ImpACT-negative patients and 2.6 for controls. The Sickness Impact Profile reflects physical and psychosocial functioning.

The ImpACT test ([www.impacttest.com](http://www.impacttest.com)) yields four composite scores in the domains of visual memory, verbal memory, reaction time, and visual motor speed.

At present, there are no treatments approved for MHE. Studies are ongoing. It is thought likely, but is as yet unproven, that MHE will respond to the same therapies that are effective in overt hepatic encephalopathy, including lactulose, rifaximin (Xifaxan), and dietary manipulations. ■

**Disclosures:** Dr. Mendler's study was funded by a research grant from Salix Pharmaceuticals Ltd. He has no other financial relationship with the company, nor any financial interest in the ImpACT test.

# For the many places patients may experience PHN pain LIDODERM® fits

Proven efficacy in 2 randomized, placebo-controlled clinical trials<sup>3-6</sup>

- In a 12-hour study, patients experienced pain relief at 30 minutes after the first dose vs observation cohort ( $P=0.0001$ ;  $N=35$ )<sup>4,a</sup>
  - Significant reduction in pain intensity vs placebo at hours 4-12 ( $P<0.001$  to  $P=0.038$ )
- In a 2-week study, 84% of patients had moderate to complete pain relief at 2 weeks vs placebo ( $P<0.001$ ;  $N=32$ )<sup>5,b,c</sup>

## Favorable safety profile<sup>3</sup>

- Nonnarcotic, nonsedating, nonscheduled
- May be used in patients who have comorbidities or are taking concomitant medications

Immediately discard used patches or remaining unused portions of cut patches in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

Before prescribing LIDODERM, please refer to the accompanying brief summary of full Prescribing Information.

<sup>a</sup> A randomized, double-blind, placebo-controlled, 4-way crossover trial ( $N=35$ ) assessed safety and efficacy of LIDODERM. Patients were allodynic with a mean age of 75 years and mean PHN duration of 48 months. Pain intensity measured with horizontal 100-mm Visual Analogue Scale: 0=no pain and 100=worst pain imaginable. Measurements were recorded before patch application, at 30 minutes, and hours 1, 2, 4, 6, 9, and 12. Least-squares means were used as the best unbiased estimate of patients' mean values.

<sup>b</sup> Demonstrated over 14 days in a post hoc analysis of a randomized, enriched-enrollment, double-blind, placebo-controlled, crossover trial. Patients enrolled in the study had been using LIDODERM for  $\geq 1$  month (ie, enriched enrollment); mean age of 77.4 years and mean PHN duration of 7.3 years. Pain relief measured using 6-item verbal scale: 0 (worse), 1 (no relief), 2 (slight relief), 3 (moderate relief), 4 (a lot of relief), and 5 (complete relief). Patients exited the study if their verbal pain relief rating decreased more than 2 categories for any 2 consecutive days from baseline.

<sup>c</sup> Results of enriched-enrollment studies can't be generalized to the entire population; subjects in such studies may be able to distinguish the active drug from placebo based on nontherapeutic features of the treatments.

**References:** 1. Cluff RS, Rowbotham MC. *Neural Clin.* 1998;16(4):813-832. 2. Weaver BA. *J Am Osteopath Assoc.* 2007;107(3 suppl 1):S2-S7. 3. Lidoderm Prescribing Information. Chadds Ford, PA: Endo Pharmaceuticals Inc; 2010. 4. Rowbotham MC et al. *Pain.* 1996;65(1):39-44. 5. Data on file, DOF-LD-02, Endo Pharmaceuticals Inc. 6. Galer BS et al. *Pain.* 1999;80(3):533-538.

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