

# Third Dose of Mumps Vaccine May Halt Outbreaks

BY HEIDI SPLETE  
Senior Writer

WASHINGTON — Despite recent mumps outbreaks in vaccinated populations, a two-dose vaccination strategy appears effective, according to findings from an analysis of the 2006 mumps outbreak in the United States.

That said, a third dose may be warranted during an outbreak, Dr. Jane Seward suggested during a presentation at the

joint annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy and the Infectious Diseases Society of America.

"A resurgence of mumps in countries using mumps vaccine programs should be kept in the perspective of the tremendous gains from the entire program," said Dr. Seward, deputy director of the division of viral diseases at the National Center for Infectious Diseases, a division of the Centers for Disease Control and Prevention.

Findings from previous studies demonstrate that the effectiveness of one dose of mumps vaccine is approximately 80%, and the effectiveness of two doses is about 90%. Outbreaks have been reported in several countries in populations that have received a single dose of vaccine.

After vaccination was introduced in the United States in 1977, the number of mumps cases underwent a "sharp and sustained decline," Dr. Seward said.

Nevertheless, two recent outbreaks in

populations that were highly vaccinated with two doses of mumps vaccine raise concerns that the vaccine's effectiveness might be waning, she said.

The 2006 mumps outbreak in the United States involved 6,584 people. The outbreak was heavily centered on college campuses in the Midwest. Most cases occurred in individuals aged 18-24 years, and the vaccine coverage rate among the cases was more than 95%.

Most people in the United States who

## ADVERTISEMENT

Brought to you by **sanofi aventis**

THE-PRINCE (Thromboembolism Prevention in Cardiac or Respiratory Disease With Enoxaparin) was a multicenter, controlled, randomized, open-label trial that assessed the efficacy and safety of unfractionated heparin (UFH) and LOVENOX® (enoxaparin sodium injection) in patients with CHF or severe respiratory disease.<sup>14</sup> LOVENOX® was shown to be at least as effective as UFH in the prevention of thromboembolic events in patients with heart failure or severe respiratory disease. The overall VTE rate for LOVENOX® was 8.4% vs 10.4% for UFH.

### LOVENOX® Was Effective in Reducing the Incidence of DVT/PE in Patients Undergoing Abdominal or Pelvic Surgery for Cancer

In ENOXACAN (Enoxaparin and Cancer), patients undergoing abdominal or pelvic surgery for cancer were randomized to either LOVENOX® 40 mg subcutaneously (SC) once daily or UFH 5000 IU 3 times daily given 2 hours before surgery and continued for 10 ± 2 days.<sup>15</sup> There was no significant difference in thromboembolic events comparing LOVENOX® 40 mg SC once daily with UFH 5000 IU SC 3 times daily (14.7% vs 18.2%, respectively).<sup>15</sup>

Overall, there was no difference in the incidence of major hemorrhagic events between LOVENOX® 40 mg SC once daily and UFH 5000 IU SC 3 times daily (4.1% vs 2.9%, respectively).<sup>15</sup>

LOVENOX® was demonstrated to be as safe and effective as UFH given 3 times daily for prophylaxis of DVT/PE in patients undergoing abdominal or pelvic surgery for cancer.<sup>15</sup>

#### Incidence of DVT/PE in patients undergoing cancer surgery<sup>15</sup>

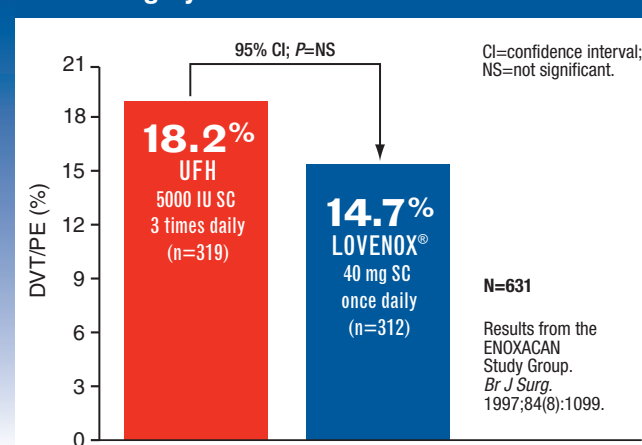


Figure 3. Incidence of DVT/PE in patients undergoing cancer surgery.

### In Patients Undergoing Hip- or Knee-Replacement Surgery, LOVENOX® Reduced the Incidence of DVT/PE Compared to Warfarin

In a large, randomized, multicenter, open-label, parallel-group clinical trial with over 3000 patients undergoing total hip arthroplasty, LOVENOX® significantly reduced DVT risk versus warfarin during hospitalization (0.3% vs 1.1%, respectively).<sup>16</sup>

The incidence of major bleeding episodes was comparable between LOVENOX® and warfarin-treated patients (0.6% vs 0.3%, respectively).<sup>16</sup>

#### Incidence of DVT in patients undergoing hip-replacement surgery<sup>16</sup>

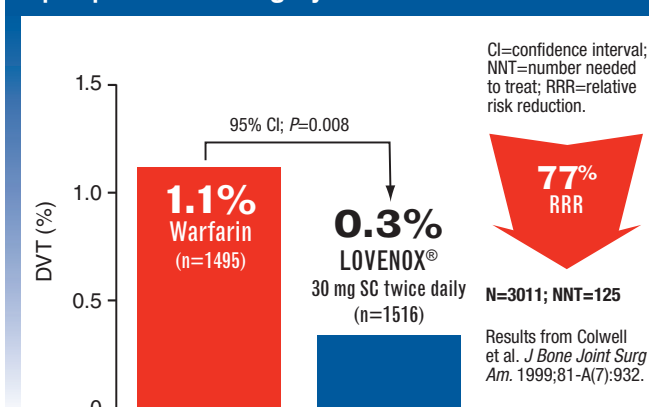


Figure 4. Incidence of DVT in patients undergoing hip-replacement surgery.

In patients undergoing total knee arthroplasty, a randomized, multicenter, open-label, parallel-group study demonstrated that LOVENOX® was able to significantly reduce the incidence of DVT/PE compared to warfarin (25.4% vs 45.5%, respectively).<sup>17</sup>

There was no significant difference in the number of major bleeding episodes between both treatment groups.<sup>17</sup>

#### Incidence of DVT/PE in patients undergoing knee-replacement surgery<sup>17</sup>

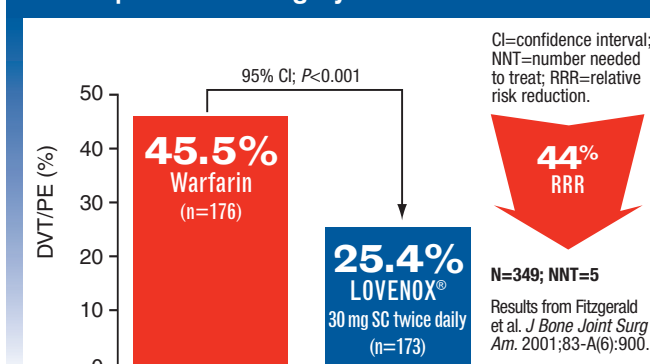


Figure 5. Incidence of DVT/PE in patients undergoing knee-replacement surgery.

Please see a brief summary of prescribing information, including boxed WARNING, at the end of the article.

had received two doses of vaccine didn't get mumps, Dr. Seward emphasized. Before the 2006 outbreak, fewer than 300 cases had been reported annually for several years.

In addition to waning vaccine effectiveness, possible factors associated with the 2006 outbreak also include a lack of exposure to the wild mumps virus, the high-transmission environment of university settings, and transmission of the mumps virus from subclinical infections, Dr. Seward said.

Data from studies conducted during the outbreak showed that infection was most common among college freshman and that infection was more likely among in-

dividuals who had received their second dose of vaccine more than 10 years before the outbreak.

An analysis of blood samples from students at an unaffected campus indicated that mumps antibody levels were significantly higher in those who had received their second dose of vaccine less than 5 years earlier, compared with those who had received it more than 15 years earlier.

During a similar outbreak in the Czech Republic, 6,000 cases of mumps were reported over an 18-month period in 2006-2007. The median age of the patients during this outbreak was 16 years. The incidence was 230/100,000 in 15- to 19-

year-olds, compared with the national incidence of 39/100,000. About 70% of those infected had received two doses, and the median age of the two-dose recipients was 15 years, Dr. Seward said.

"We are starting a project to understand the immune response to a third dose, and we will follow those patients," Dr. Seward said at a press conference. The cause of mumps outbreaks in vaccinated populations remains unknown, and more research is needed to determine whether a third dose of vaccine given routinely or in cases of outbreaks would be beneficial, she noted.

"If we see outbreaks [as] we saw in

2006, especially on college campuses where there is a lot of transmission, we would consider offering a third dose during an outbreak."

Adolescents and adults without evidence of immunity should receive two doses of the mumps vaccine. Mumps vaccination has had a dramatic impact on morbidity and mortality in the United States, and has reduced the rates of serious complications including meningitis and deafness. "There were probably 2 million cases of mumps per year before the vaccine came into use," Dr. Seward said.

Dr. Seward stated that she had no financial conflicts to disclose. ■

Despite evidence-based clinical practice guidelines for the prophylaxis of DVT and PE, recommendations are underutilized and many patients are not receiving proper anticoagulation. This is not only detrimental to patient care but also increases the burden on the health care system.

*Authored by Frank Michota, MD; Cleveland Clinic; sanofi-aventis consultant.*

## Important Safety Information

### WARNING: SPINAL/EPIDURAL HEMATOMAS

**When neuraxial anesthesia (epidural/spinal anesthesia) or spinal puncture is employed, patients anticoagulated or scheduled to be anticoagulated with low-molecular-weight heparins or heparinoids for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma, which can result in long-term or permanent paralysis.**

**The risk of these events is increased by the use of indwelling epidural catheters for administration of analgesia or by the concomitant use of drugs affecting hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture.**

**Monitor patients for signs and symptoms of neurological impairment. If neurologic compromise is noted, urgent treatment is necessary.**

**Consider the potential benefit versus risk before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis (see *Warnings and Precautions* [5.1] and *Drug Interactions* [7]).**

- LOVENOX® (enoxaparin sodium injection) cannot be used interchangeably with other low-molecular-weight heparins or unfractionated heparin (UFH), as they differ in their manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage
- As with other anticoagulants, use with extreme caution in patients with conditions that increase the risk of hemorrhage. Dosage adjustment is recommended in patients with severe renal

impairment. Unless otherwise indicated, agents that may affect hemostasis should be discontinued prior to LOVENOX® therapy. Bleeding can occur at any site during LOVENOX® therapy. An unexplained fall in hematocrit (HCT) or blood pressure should lead to a search for a bleeding site. (See WARNINGS and PRECAUTIONS)

- In the ST-segment elevation myocardial infarction (STEMI) pivotal trial, the rates of major hemorrhages (defined as requiring 5 or more units of blood for transfusion, or 15% drop in HCT or clinically overt bleeding, including intracranial hemorrhage [ICH]) at 30 days were 2.1% in the LOVENOX® group and 1.4% in the UFH group. The rates of ICH at 30 days were 0.8% in the LOVENOX® group and 0.7% in the UFH group. The 30-day rate of the composite endpoint of death, myocardial infarction (MI), or ICH (a measure of net clinical benefit) was significantly lower in the LOVENOX® group (10.1%) as compared to the UFH group (12.2%)
- Thrombocytopenia can occur with LOVENOX®. In patients with a history of heparin-induced thrombocytopenia (HIT), LOVENOX® should be used with extreme caution. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm<sup>3</sup>, LOVENOX® should be discontinued. Cases of HIT have been observed in clinical practice. (See WARNINGS and PRECAUTIONS)
- The use of LOVENOX® has not been adequately studied for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves. (See WARNINGS and PRECAUTIONS)
- LOVENOX® is contraindicated in patients with hypersensitivity to enoxaparin sodium, heparin, or pork products, and in patients with active major bleeding

**References:** 1. U.S. Department of Health and Human Services. *The Surgeon General's Call to Action to prevent deep vein thrombosis and pulmonary embolism: 2008*. US Department of Health and Human Services, Office of the Surgeon General, 2008. 2. Hooper WC, Evatt BL. The role of activated protein C resistance in the pathogenesis of venous thrombosis. *Am J Med Sci*. 1998;316(2):120-128. 3. Gerotziakas GT, Samama MM. Prophylaxis of venous thromboembolism in medical patients. *Curr Opin Pulm Med*. 2004;10(5):356-365. 4. Moll S, Mackman N. Venous thromboembolism: a need for more public awareness and research into mechanisms. *Arterioscler Thromb Vasc Biol*. 2008;28(3):367-369. 5. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest*. 2008;133(6 suppl):381S-453S. 6. Wheeler AP. Identifying at-risk patients for venous thromboembolism prophylaxis. In: Merli GJ, ed. *Thrombosis: Prophylaxis of Venous Thromboembolism*. Bridgewater, NJ: Elsevier; 2005:9-21. 7. American Public Health Association. Deep-vein thrombosis: advancing awareness to protect patient lives: white paper. Paper presented at: Public Health Leadership Conference on Deep-Vein Thrombosis; February 26, 2003; Washington, DC. 8. Mismetti P, Laporte-Simitsidis S, Tardy B, et al. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: a meta-analysis of randomised clinical trials. *Thromb Haemost*. 2000;83(1):14-19. 9. Amin A, Stemkowski S, Lin J, Yang G. Thromboprophylaxis rates in US medical centers: success or failure? *J Thromb Haemost*. 2007;5(8):1610-1616. 10. Goldhaber SZ, Tapson VF; DVT FREE Steering Committee. A prospective registry of 5,451 patients with ultrasound-confirmed deep vein thrombosis. *Am J Cardiol*. 2004;93(2):259-262. 11. Guyatt GH, Cook DJ, Jaeschke R, Pauker SG, Schünemann HJ. Grades of recommendation for antithrombotic agents: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest*. 2008;133(6 suppl):123S-131S. 12. Samama MM, Cohen AT, Darmon J-Y, et al; Prophylaxis in Medical Patients with Enoxaparin Study Group. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. *N Engl J Med*. 1999;341(11):793-800. 13. LOVENOX® (enoxaparin sodium injection) Prescribing Information. sanofi-aventis, Bridgewater, NJ. 14. Kleber F-X, Witt C, Vogel G, Koppenhagen K, Schomaker U, Flosbach CW; THE-PRINCE Study Group. Randomized comparison of enoxaparin with unfractionated heparin for the prevention of venous thromboembolism in medical patients with heart failure or severe respiratory disease. *Am Heart J*. 2003;145(4):614-621. 15. ENOXACAN Study Group. Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deep vein thrombosis in elective cancer surgery: a double-blind randomized multicentre trial with venographic assessment. *Br J Surg*. 1997;84(8):1099-1103. 16. Colwell CW Jr, Collis DK, Paulson R, et al. Comparison of enoxaparin and warfarin for the prevention of venous thromboembolic disease after total hip arthroplasty: evaluation during hospitalization and three months after discharge. *J Bone Joint Surg Am*. 1999;81-A(7):932-940. 17. Fitzgerald RH Jr, Spiro TE, Trowbridge AA, et al; Enoxaparin Clinical Trial Group. Prevention of venous thromboembolic disease following primary total knee arthroplasty: a randomized, multicenter, open-label, parallel-group comparison of enoxaparin and warfarin. *J Bone Joint Surg Am*. 2001;83-A(6):900-906.

**Please see a brief summary of prescribing information, including boxed WARNING, at the end of the article.**