**Infectious Diseases** 

#### CLINICAL CAPSULES

#### Rapid Flu Test Trims Further Tests, Tx

Rapid viral testing for influenza as part of the routine care plan for febrile infants reduced antibiotic use, emergency department visits, and the use of additional tests, based on data from a prospective study of 206 infants during the course of two flu

Nonspecific fevers without obvious signs of infection send many infants to the pediatric emergency department, and rapid flu testing in these settings can help triage patients more effectively and reduce unnecessary tests and treatment, wrote Dr. Javier Benito-Fernandez of the pediatric emergency department in Hospital de Cruces, Barakaldo, Spain, and colleagues.

Overall, 84 of 206 (41%) infants aged 0-36 months tested positive based on commercially available rapid flu tests. The influenza-positive infants were significantly less likely than influenza-negative infants to undergo blood tests (33% vs. 100%), urinalysis (81% vs. 100%), chest radiographs (14% vs. 32%), and lumbar punctures for cerebrospinal fluid analysis (2% vs. 21%). In addition, none of the influenza-positive infants received antibiotics at the time of diagnosis, compared with 39% of the influenza-negative infants (Pediatr. Infect. Dis. J. 2006;25:1153-7).

Only two influenza-positive infants (2%) required hospital stays for observation, compared with 20 influenza-negative infants (16%) admitted for diagnoses including pneumonia, meningitis, urinary tract infection, and bacteremia. All influenza-positive patients had a favorable clinical course, the investigators said.

## **New Coronavirus Subtypes on Rise**

Two recently discovered coronavirus subtypes, NL63 and HKU1, accounted for a majority of the 66 coronaviruses identified in a review of 1,043 samples from children with acute respiratory illness.

Overall, coronavirus subtypes HKU1, OC43, NL63, and 229E were identified in 28, 19, 11, and 8 specimens, respectively, reported Jane Kuypers, Ph.D., of the University of Washington, Seattle, and her colleagues (Pediatrics 2007;119:e70-6 [doi:10.1542/peds.2006-1406]).

The researchers collected specimens from patients aged 0-19 years who presented to a children's hospital with upper respiratory illness from October 2003 through September 2004. The acute clinical features experienced by the children were not significantly different based on the virus type.

A coronavirus was the only respiratory viral pathogen identified in 32 (57%) of the 56 children for whom complete clinical data were available, including 14 patients with HKU1, 11 with OC43, 5 with NL63, and 2 with 229E. Of these, children infected only with a coronavirus were significantly more likely to have underlying medical conditions, compared with children who were infected with more than one respiratory virus.

Three children (one each infected with HKU1, OC43, and 229E) were treated in the intensive care unit, and two of them needed ventilators. In addition, six immunocompromised children had coronavirus as the sole pathogen, including five children with acute lymphocytic leukemia and one renal transplant patient. Three of the children with leukemia and the transplant patient required hospital stays ranging from 2 to 12 days.

The findings diverge from previous coronavirus research by showing that the viruses were present year-round; specimens from at least one virus were collected during each month, although the monthly specimen total peaked at 218 in December 2003.

### Levofloxacin Succeeds vs. AOM

Treatment with oral levofloxacin is safe and effective against bacteria in the middle-ear fluid of children with recurrent or persistent acute otitis media, based on data from children aged 6 months to 5 years.

The open-label study, sponsored by Johnson and Johnson Pharmaceutical Research and Development, included 204 children with confirmed acute otitis media who received at least one 10-mg/kg dose of the study medication (Pediatr. Infect. Dis. J. 2006;25:1102-9). The full course of therapy was 10 mg/kg of levofloxacin twice daily for 10 days.

A total of 105 pathogens were recovered from the middle-ear fluid of 89 bacteriologically evaluable children using tympanocentesis. Haemophilus influenzae, the most common pathogen, was identified in 54 children, either alone or along with Streptococcus pneumoniae or Moraxella ca-

All of the *H. influenzae* and *S. pneumoniae* isolates were susceptible to levofloxacin, and the eradication rates for these pathogens were 100% and 84%, respectively. The eradication rate for M. catarrhalis was 100%, wrote Dr. Adriano Arguedas of the Universidad de Ciencias Médicas, in San José, Costa Rica, and colleagues. No cartilage damage was reported in any patients.

# Tetanus Toxoid, Reduced **Diphtheria Toxoid and Acellular** Pertussis Vaccine Adsorbed ADACEL™

R only

ry: Please see package insert for full prescribing information

Brief Summary: Please see package insert for full prescribing information

NDICATIONS AND USAGE ADACEL vaccine is indicated for active booster immunization for the prevention of tetanus, diphtheria and pertussis as a single dose in persons 11 through 64 years of age. The use of ADACEL vaccine as a primary series, or to complete the primary series, has not been studied. As with any vaccine, ADACEL vaccine may not protect 100% of vaccinated individuals. CONTRAINDICATIONS Known systemic hypersensitivity to any component of ADACEL vaccine or a life-threatening reaction after previous administration of the vaccine or a vaccine containing the same substances are contraindications to vaccination with ADACEL vaccine. Because of uncertainfuly as to which component of the vaccine may be responsible, additional vaccinations with the diphtheria, tetanus or pertussis components should not be administrated. Alternatively, such individuals may be referred to an allergist for evaluation if further immunizations are to be considered. The following events are contraindications to administration of any networks containing vaccine: (1)

anergist for evaluation in further immunizations are to be considered. The following events are contraindications to administration of any perfussis containing vaccine; (1)

• Encephalopathy within 7 days of a previous dose of perfussis containing vaccine not attributable to another identifiable cause.

• Progressive neurological disorder, uncontrolled epilepsy, or progressive encephalopathy, Perfussis vaccine should not be administered to individuals with these conditions until a treatment regimen has been established, the condition has stabilized, and the benefit dearly outweighs the risk.

ADACEL vaccine is not contraindicated for use in individuals with HIV infection. (1)

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WARNINGS Because intramuscular injection can cause injection site hematoma, ADACEL vaccine should not be given to persons with any bleeding disorder, such as hemophilia or thrombocytopenia, or to persons on anticoagulant therapy unless the potential benefits clearly outweigh the risk of administration. If the decision is made to administer ADACEL vaccine in such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection. (1) If any of the following events occurred in temporal relation to previous receipt of a vaccine containing a whole-cell pertuss's (eg. DTP) or an acellular pertuss's component, the decision to give ADACEL vaccine should be based on careful consideration of the potential benefits and possible risks: (2) (3)

\*\*Temperature of \*Ad5°C (105°P) within 48 hours or not due to another identifiable cause;

\*\*Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours;

\*\*Persistent, incorsolable crying tasting a3 hours, occurring within 48 hours;

\*\*Seizures with or without fever occurring within 3 days.

When a decision is made to withhold pertussis vaccine, Td vaccine should be given. Persons who experienced Arthus-type hypersensitivity reactions (eg. severe local reactions associated with systemic symptoms) (4) following a prior dose of tetanus toxoid usually have high serum tetanus antitoxin levels and should not be given emergency doses of tetanus toxoid-containing vaccines more frequently than every 10 years, even if the wound is entitler dean nor minor. (4) (5) if Guildian-Barré Syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give ADACEL vaccine or any vaccine containing tetanus toxoid should be

than every 10 years, even if the wound is neither dean nor minor. (4) (5) if cullian-Barre Syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxioid, the decision to give ADACEL vaccine or any vaccine containing tetanus toxioid should be based on careful consideration of the potential benefits and possible risks. (1) The decision to administer a pertussis-containing vaccine to individuals with stable central nervous system (CNS) disorders must be made by the health-care provider on an individual basis, with consideration of all relevant factors and assessment of potential risks and benefits for that individual. The ACIP has issued guidelines for immunizing such individuals. (2) A family history of seizures or other CNS disorders is not a contraindication to pertussis vaccine. (2) The ACIP has published guidelines for vaccination of persons with recent or acute illness. (1)

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PRECAUTIONS General Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel. ADACEL vaccine should not be administered into the buttods nor by the intradermal route, since these methods of administration have not been studied, a weaker immune response has been observed when these routes of administration have been used with other vaccines. (1) The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Epinephine Hydrochloride Solution (1:1,000) and other appropriate agents and equipment should be available for immediate use in case an anaphyadactic or acute hypersensitivity reaction occurs. Prior administration of ADACEL vaccine, the vaccine region trad/or the parent or guardian must be asked about personal health history, including immunization history, current health status and any adverse event after previous immunizations. In persons who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, administration of ADACEL vaccine must be carefully considered. The ACIP has published guidelines for the immunization of immunocompromised presons (whether from disease or treatment) has not been studied. A separate, sterile syringe and needle, or a sterile disposable unit, must be used for each person to prevent transmission of blood bome infectious agents. Needle of the transmission of sterile disposable unit, must be used for each person to prevent transmission of blood bome infectious agents. Needle inform the vaccine recipient and/or parent or guardian of the benefits and risks. The health-care provider should inform the vaccine recipient and/or parent or guardian of the benefits and risks. The health-care provider s

Drug Interactions Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. (See PRECAUTIONS, General.) For information regarding simultaneous administration with other vaccines refer to the ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections.

ADMINISTRATION sections.

Carcinogenesis, Mutagenesis, Impairment of Fertility No studies have been performed with ADACEL vaccine to evaluate carcinogenicity, mutagenic potential, or impairment of fertility.

Pregnancy Category C Animal reproduction studies have not been conducted with ADACEL vaccine. It is also not known whether ADACEL vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. ADACEL vaccine should be given to a pregnant woman only if clearly needed. Animal fertility studies have not been conducted with ADACEL vaccine. The effect of ADACEL vaccine on embryo-fetal and pre-weaning development was evaluated in two developmental toxicity studies using pregnant rabbits. Animals were administered ADACEL vaccine twice prior to gestation, during the period of organogenesis (gestation day 6) and later during pregnancy on gestation day 29, 0.5 ml/rabbit/occasion (a 17-fold increase compared to the human dose of ADACEL vaccine on a body weight basis), by intramuscular injection. No adverse effects on pregnancy, parturition, lactation, embryo-fetal or pre-weaning development were observed. There were no vaccine related fetal malformations or other evidence of teratogenesis noted in this study. (8)

Pregnancy Registry Health-care providers are encouraged to register pregnant women who receive ADACEL vaccine in Sanofi Pasteur

Pregnancy Registry Health-care providers are encouraged to register pregnant women who receive ADACEL vaccine in Sanofi Pasteur Inc.'s vaccination pregnancy registry by calling 1-800-822-2463 (1-800-VACCINE).

Nursing Mothers It is not known whether ADACEL vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ADACEL vaccine is given to a nursing woman.

Pediatric Use ADACEL vaccine is not indicated for individuals less than 11 years of age. (See INDICATIONS AND USAGE.) For immunization of persons 6 weeks through 6 years of age against diphtheria, tetanus and pertussis refer to manufacturers' package inserts for DTaP vaccines.

for DTaP vaccines.

Geriatric Use ADACEL vaccine is not indicated for individuals 65 years of age and older. No data are available regarding the safety and effectiveness of ADACEL vaccine in individuals 65 years of age and older as clinical studies of ADACEL vaccine did not include subjects in the geriatric population.

ADVERSE REACTIONS The safety of ADACEL vaccine was evaluated in 4 clinical studies. A total of 5,841 individuals 11-64 years of age inclusive 3,293 adolescents 11-17 years of age and 2,448 adults 18-64 years) received a single booster dose of ADACEL vaccine. The principal safety study was a randomized, observer blind, active controlled trial that enrolled participants 11-17 years of age (ADACEL vaccine N = 1,184; Td vaccine N = 792) and 18-64 years of age (ADACEL vaccine N = 1,752; Td vaccine N = 573). Study participants had not received teamus or diphtheria containing vaccines within the previous 5 years. Observer blind design, is, study personnel collecting the safety data differed from personnel administering the vaccines, was used due to different vaccine packaging (ADA-

CEL vaccine supplied in single dose vials; Td vaccine supplied in multi-dose vials). Solicited local and systemic reactions and unsolicited events were monitored daily for 14 days post-vaccination using a diapy card. From days 14-28 post-vaccination, information on adverse events necessitating a medical contact, such as a telephone call, visit to an emergency room, physician's office or hospitalization, was obtained via telephone interview or at an interim clinic visit. From days 28 to 6 months post-vaccination, participants were monitored for unexpected visits to a physician's office or to an emergency room, onset of serious illness and hospitalizations. Information regarding adverse events that occurred in the 6 month post-vaccination time period was obtained via a scripted telephone interview. Approximately 96% of participants completed the 6-month follow-up evaluation. In the concomitant vaccination study with ADACEL and Hepatitis B vaccines, local and systemic adverse events were monitored daily for 14 days post-vaccination using a diary card. Local adverse events were only monitored at site/arm of ADACEL vaccine administration. Unsolicited reactions (including immediate reactions, serious adverse events and events that elicited seeking medical attention) were collected at a dinic visit or via telephone interview for the duration of the trial, is, up to six months post-vaccination. In the concomitant vaccination study with ADACEL vaccine and trivalent inactivated influenza vaccines local and systemic adverse events were monitored for 14 days post-vaccination using a diary card. All unsolicited reactions occurring through day 14 were collected. From day 14 to the end of the trial, is, up to 84 days, only events that elicited seeking medical attention were collected. In all studies, subjects were monitored for serious adverse throughout the duration of the study. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot b

in the other trials and there were no additional neuropathic events reported.

Solicited Adverse Events in the Principal Safety Muly The frequency of selected solicited adverse events (enythema, swelling, pain and fever) occurring during Days 0-14 following one dose of ADACEL vaccine or Td vaccine were reported at a similar frequency in both groups. Few participants (<1%) sought medical attention for these reactions. Pain at the injection site was the most common adverse reaction occurring in 62-78% of all vaccineses. In addition, overall rates of pain were higher in adolescent recipients of ADACEL vaccine compared to Td vaccine recipients. Rates of moderate and severe pain in adolescents did not significantly differ between the wor groups. Rates of pain did not significantly differ for adults. Ever of 38°C and higher was uncommon, although in the adolescent age group, it occurred significantly more frequently in ADACEL vaccine recipients than Td vaccine recipients. (8) The rates of other local and systems: solicited reactions occurred at similar rates in ADACEL vaccine and Td vaccine recipients in the 3 day post-vaccination period. Most local reactions occurred within the first 3 days after vaccination (with a mean duration of less than 3 days). Headache was the most frequent systemic reaction and was usually of mild to moderate intensity.

Adverse Events in the Concomitant Vaccine Studies

Adverse Events in the Concomitant Vaccine Studies

Local and Systemic Reactions when Given with Hepatitis B Vaccine The rates reported for fever and injection site pain (at the ADA-CEL vaccine administration site) were similar when ADACEL and Hep B vaccines were given concurrently or separately. However, the rates of injection site erythema (23.4% for concomitant vaccination and 21.4% for separate administration) and swelling (23.9% for concomitant vaccination and 17.9% for separate administration) and when the ADACEL vaccine administration and set were increased when co-administered. Swollen and/or sore joints were reported by 22.5% for concomitant vaccination and 17.9% for separate administration. The rates of generalized body aches in the individuals who reported swollen and/or sore joints were 86.7% for concomitant vaccination and 72.2% for separate administration. Nots joint complaints were mild in intensity with a mean duration of 1.8 days. The incidence of other solicitied and unsolicited adverse events were not different between the 2 study groups. (8)

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Local and Systemic Reactions when Given with Trivalent Inactivated Influenza Vaccine The rates of fever and injection site erythema and swelling were similar for recipients of concurrent and separate administration of ADACEL vaccine and TIV. However, pain at the ADACEL vaccine injection site occurred at statistically higher rates following concurrent administration (66.6%) versus separate administration (60.8%). The rates of sore and/or swellen joints were 13% for concurrent administration and 66.6% for separate administration. Most joint complaints were mild in intensity with a mean duration of 2.0 days. The incidence of other solicited and unsolicited adverse events were similar between the 2 study groups. (8)

Additional Studies An additional 1,806 adolescents received ADACEL vaccine as part of the lot consistency study used to support ADACEL vaccine in pressure. The kindly was a anadomized double-billed multi-center trial designed to assess lot consistency as meas-

Additional Studies An additional 1,806 adolescents received ADACEL vaccine as part of the lot consistency study used to support ADACEL vaccine licensure. This study was a randomized, double-blind, multi-center trial designed to assess lot consistency as measured by the safety and immunogenicity of 3 lots of ADACEL vaccine when given as a booster dose to adolescents 11-17 years of age inclusive. Local and systemic adverse events were monitored for 14 days post-vaccination using a diary card. Unsolicited adverse events were collected for 28 days post-vaccination. Pain was the most frequently reported local adverse event occurring in approximately 44% of all subjects. Sore and/or swollen joints were reported by approximately 14% of participants. Most joint complaints were mild in intensity with a mean duration of 20 days. (80 har additional 962 addescents and adults received ADACEL vaccine in three supportive Canadian studies used as the basis for licensure in other countries. Within these clinical trials, the rates of local and systemic reactions following ADACEL vaccine were similar to those reported in the four principal trials in the Vs with the exception of a higher rate (66%) of adults experiencing 'any local injection site pain. The rate of severe pain (0.8%), however, was comparable to the rates reported in the four principal trials. (8) There was one spontaneous report of whole-arm swelling of the injected limb among the 277 Td vaccine recipients, and two spontaneous reports among the 962 ADACEL vaccine rice; each ADACEL vaccine recipients.

ble to the rates reported in the four principal frials. (8) There was one spontaneous report of whole-arm swelling of the injected limb among the 277 fd vaccine recipients, and two spontaneous reports among the 962 ADACEL vaccine recipients.

Postmarketing Reports The following adverse events have been spontaneously reported during the post-marketing use of ADACEL vaccine in other countries. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or restablish a causal relationship to vaccine exposure. The following adverse events were included based on severily, frequency of reporting or the strength of causal association to ADACEL vaccine. General disorders were included based on severily, frequency of reporting or the strength of causal association to ADACEL vaccine. General disorders were included based on severily, frequency of reporting or several subcreases. Skin and subcutaneous tissue disorders: puritus, urticaria. There have been spont-neous reports of nervous system disorders such as myositis and muscle spasms temporally associated with ADACEL vaccine.

Reporting of Adverse Events. The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act of 1986, requires physicians and other health-care providers who administer vaccines to maintain permanent vaccination records of the manufacturer and lot number of the vaccine administered in the vaccine recipient's permanent medical record along with the date of administration of the vaccine and the name, address and title of the person administering the vaccine. The Act further requires the health-care professional to report to the US Department of Health and Human Services has established by the Vaccine Adverse the occurrence following immunization of any event set forth in the Vaccine Injury Table. These include anaphylaxis or anaphylactic shock within 7 days rehablal neurities within 28 days; an acute complication or sequelae (inc

STORAGE Store at 2° to 8°C (35° - 46°F). DO NOT FREEZE. Discard product if exposed to freezing. Do not use after

expiration date.

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Printed in Canada

Product information as of January 2006

Manufactured by: Sanofi Pasteur Limited Toronto Ontario Canada MKT10383-1R

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