



NSU College of Pharmacy
Drug Information & Resources Center
N e w s l e t t e r

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Question of the Day...

What is the Hawthorne effect and where did its name originate from?

In the News

New Drug Approvals

Abilify Approved; No QT Effects, Less Weight Gain

<http://www.reuters.com/newsArticle.jhtml;jsessionid=IN4OIGUMNCKBGCRAE0CFEY?type=topNews&storyID=1750921>

Bristol-Myers Squibb Co. and Otsuka Pharmaceutical Co. said on Friday they received U.S. approval to market a new schizophrenia drug, Abilify, which is expected to cut down on side effects seen with other treatments. Bristol-Myers, desperate for new drugs after a slew of patent expirations led to abysmal earnings this year, will co-market the drug with Otsuka in the United States. The companies said they expect Abilify to reach U.S. drugstores within two weeks. Abilify will join an increasingly crowded market of schizophrenia medicines, competing with Eli Lilly and Co.'s LLY.N Zyprexa, Johnson & Johnson's JNJ.N Risperdal and Pfizer Inc.'s PFE.N Geodon. Analysts have said Zyprexa is known as the most effective of the drugs, and it is the top-seller in the class, but it has been associated with weight gain. Weight gain increases the risk of diabetes and can worsen symptoms in patients who have both diabetes and schizophrenia. Abilify, which received conditional U.S. Food and Drug Administration approval in September, was associated with minimal weight change, Bristol-Myers and Otsuka said. The drug also showed no increased risk of a heart condition called "QT prolongation" that can lead to irregular heart beats and other serious heart complications. Geodon was associated with a slight prolongation of the QTc interval between heart beats. Such a clean safety profile has led analysts to forecast Abilify could become a \$2 billion-a-year product for Bristol-Myers. The Abilify approval is a rare piece of good news during a difficult year for Bristol-Myers. Bristol-Myers has been searching for new medicines, pumping its own pipeline of experimental drugs and signing up a

biotechnology partner, ImClone Systems Inc. IMCL.O , which has become involved in an insider trading scandal involving its former top official, Samuel Waksal. Despite its efforts to gain new drugs, Bristol-Myers has come up relatively dry in the past two years, during which time it lost U.S. patent protection over cancer medicine Taxol, anxiety treatment BuSpar and diabetes drug Glucophage. The company had been banking on experimental hypertension drug Vanlev to become a blockbuster. But clinical trial results released in March disappointed analysts. And Bristol-Myers is under investigation by federal regulators for loading up wholesaler inventories with its drugs to achieve its financial targets last year. The company intends to restate its earnings for 2000, 2001 and the first two quarters of 2002, and earlier Friday said the revisions would cause it to delay the filing of its third quarter report with the Securities and Exchange Commission until February. Since the disclosure of the inventory issue and a steep earnings warning in April, Chief Executive Peter Dolan has come under fire and several top executives have left.

Pegasys (Peginterferon alfa-2a) Approved for Treatment of adults with chronic hepatitis C who have compensated liver disease and who have not been previously treated with interferon alfa
<http://www.fda.gov/cber/products/pegihof101602.htm>

In the News

FDA, PHARMACIA UPDATE BEXTRA LABEL WITH NEW WARNINGS

<http://www.fda.gov/bbs/topics/ANSWERS/2002/ANS01170.html>

FDA and Pharmacia are advising health care professionals about new warnings and information in the product labeling of the drug Bextra (valdecoxib), a drug approved for treatment of osteoarthritis, rheumatoid arthritis and dysmenorrhea (menstrual pain). The labeling is being updated with new warnings following postmarketing reports of serious adverse effects including life-threatening risks related to skin reactions -- including Stevens Johnson Syndrome, and anaphylactoid reactions (serious allergic reactions). In addition, the labeling will state that the drug is contraindicated -- not to be used -- in patients allergic to sulfa containing products. On November 13, 2002, Pharmacia, the manufacturer of Bextra sent letters to health care professionals advising them of postmarketing reports and new warnings that will be included in the drug label. Since the firm began marketing the drug in March of 2002, cases of the serious skin and hypersensitivity reactions have been reported. These included cases of Stevens Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis and erythema multiforme. Although these adverse events are rare, some of these patients required hospitalization. Based on these reports, FDA has approved labeling changes for Bextra that include a

warning for serious skin reactions. As these reactions can be life threatening, people who start Bextra and experience a rash should discontinue the drug immediately. Health care professionals are encouraged to report any unexpected adverse or serious events associated with the use of Bextra directly to Pharmacia Corporation, Peapack, N.J. at 1-800-323-4204 or to the FDA MedWatch program at 1-800-FDA-1088. The Medwatch form is available online at <http://www.fda.gov/medwatch/safety/3500.pdf>

Most herbs fall short in treating menopause

http://www.boston.com/dailyglobe2/323/nation/Most_herbs_fall_short_in_treating_menopause+.shtml

Except for an herbal remedy developed by American Indians, most of the exotic berries, teas, herbs, and oils taken by women to ease menopause symptoms have been ineffective in clinical trials, according to a study. Alternative treatments for hot flashes, vaginal dryness, and other menopause symptoms have gotten additional attention since July, when researchers found evidence linking estrogen-progestin hormone supplements with breast cancer and heart disease. Researchers at Columbia University and George Washington University examined the results of 29 independent studies on alternative treatments for hot flashes and found that only the herb black cohosh appeared to work. Three of four trials found the herb had a benefit, according to the review in today's issue of the *Annals of Internal Medicine*. Black cohosh, a member of the buttercup family, is among the most popular of alternative treatments for menopause. Most clinical studies involved a concentrated brand called Remifemin, manufactured by GlaxoSmithKline. Other popular herbal treatments, including ginseng, red clover, dong quai, and oil of evening primrose, were found to have no discernible effect on such symptoms as hot flashes, vaginal dryness, sleeplessness, and other ills associated with menopause. Researchers said studies have also found few documented benefits from acupuncture, vitamin E, relaxation techniques, and progesterone creams. The study said a few alternative treatments showed promise. Women who ate soybean dietary supplements reported hot flashes that were less intense, though in many cases the benefits disappeared after a few weeks. Study authors Fredi Kronenberg and Adriane Fugh-Berman said, however, that most of the trials examining the benefits of alternative treatments were small and inconclusive. Few looked at the benefits or harm of using herbal remedies for many months or years.

American Heart Association Statement on High-Protein, Low-Carbohydrate Diet Study Presented at Scientific Sessions

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-19-2002/0001844661&EDATE=>

Media reports about a small study funded by the Robert C. Atkins Foundation may have created the erroneous impression that the American Heart

Association has revised its dietary guidelines. This is not the case. This study was released as one of over 3,600 abstracts presented at the American Heart Association's annual Scientific Sessions, a forum for the presentation of research pertaining to heart disease and stroke for scientists and physicians. These scientific abstracts do not represent official positions or statements of the American Heart Association.

Here are the American Heart Association's concerns with the study:

- The study is very small, with only 120 total participants and just 60 on the high-fat, low carbohydrate diet.
- This is a short-term study, following participants for just 6 months.

There is no evidence provided by this study that the weight loss produced could be maintained long term.

- There is no evidence provided by the study that the diet is effective

long term in improving health.

- A high intake of saturated fats over time raises great concern about increased cardiovascular risk -- the study did not follow participants

long enough to evaluate this.

- This study did not actually compare the Atkins diet with the current AHA dietary recommendations.

"The American Heart Association has dietary guidelines, rather than a rigid diet. These guidelines, revised in 2000, replaced the Step I and Step II diet, which emphasized fat restriction. The current guidelines, based on the best available evidence, emphasize a healthy dietary pattern rich in fruits, vegetables, whole grains, lean meats, fish and poultry, as well as low-fat dairy products," says Robert O. Bonow, M.D., the president of the American Heart Association. "It is important to note that there is no single

'American Heart Association Diet.' Rather there is a set of guidelines designed to be broad enough to accommodate many different food preferences, as

well as to provide specific guidance for individuals with specific conditions." By way of contrast with this small study, a 12-year Harvard study funded

by the National Heart, Lung and Blood Institute was also reported at this meeting. This study of 74,000 women showed that those who consumed more fruits and vegetables were 26 percent less likely to become obese than women who ate fewer fruits and vegetables over the same time period. "This is a much more compelling study regarding weight control, because it involved many

more individuals over a much longer period," says Bonow. "Bottom line, the American Heart Association says that people who want to lose weight and keep it off need to make lifestyle changes for the long term -- this means

regular exercise and a balanced diet," he says. "People should not change their eating patterns based on one very small, short-term study. Instead, we hope that the public will continue to rely on the guidance of organizations such as the American Heart Association which look at all the very best evidence before formulating recommendations."

Long-Term Dual Antiplatelet Therapy Reduces Risk of Death, Heart Attack and Stroke Following Stenting

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-18-2002/0001843571&EDATE=>

According to research published in the Nov. 20 Journal of the American Medical Association, long-term dual antiplatelet therapy of at least one year following percutaneous coronary intervention (PCI) significantly decreases the risk of death, heart attack and stroke. PCI techniques, such as balloon angioplasty and stenting, are used to relieve coronary narrowing in patients with cardiovascular disease. The current standard of care following PCI is a combination of an ADP (adenosine diphosphate) receptor for 2-4 weeks post-procedure to minimize the possibility of complications, and aspirin, which is continued for life. Results of the study were presented this week at the American Heart Association's Scientific Sessions 2002. A review of data from the multi-center CREDO trial revealed that at one year following PCI, patients on long-term antiplatelet therapy had a 26.9 percent reduction in the combined risk of death, heart attack and stroke compared with patients who stopped drug therapy after four weeks. In addition, patients who received an ADP receptor (clopidogrel) at least 6 hours before PCI experienced a relative risk reduction of 38.6 percent compared with patients who received the drug less than 6 hours prior to treatment. "The findings have a substantial impact on practice, for the first time showing how long-term continuation of double therapy (aspirin and clopidogrel) decreases major events after stenting," said Eric J. Topol, M.D., chairman of cardiovascular medicine at The Cleveland Clinic and chairman of the study's steering committee. CREDO is a randomized, double-blind, placebo-controlled trial conducted among approximately 2,100 patients in the United States and Canada. Researchers reviewed data from 99 participating centers of patients who were to undergo elective PCI or who were highly likely to undergo PCI between June 1999 and April 2001. An estimated 750,000 PCI procedures are performed yearly in the United States and more than 1.5 million worldwide. "Based on the results of the trial and the number of PCI procedures performed annually, nearly 50,000 patients per year would avoid death, heart attack or stroke by using clopidogrel treatment for at least one year following intervention," said Steven Steinhubl, M.D., principal investigator for the CREDO trial and associate director, cardiac cath lab at the University of North Carolina.

Lilly's Drug Evista Cuts Women's Stroke Risk -Study

http://abcnews.go.com/wire/Living/reuters20021117_275.html

The use of Evista, Eli Lilly and Co.'s drug to treat post-menopausal osteoporosis, cut the risk of stroke by nearly two-thirds in women at high risk for heart disease, researchers said on Sunday. The data, presented at the American Heart Association's annual Scientific Sessions conference in Chicago, showed that Evista was linked with a 62 percent reduction in the risk of all strokes -- fatal and non-fatal -- in post-menopausal women at high risk for heart disease.

The research comes in the wake of recent findings by a Women's Health Initiative study that showed Wyeth's hormone replacement therapy Prempro, which is often prescribed for post-menopausal osteoporosis, increased the risk of stroke by 41 percent. The WHI study's results, released in July, triggered a huge debate over how doctors treat post-menopausal women. Lilly's Evista findings were part of a four-year study of 7,705 patients, who were post-menopausal women with osteoporosis. It found that of the 1,035 women in the group who were at high risk of heart disease, Evista cut the risk of non-fatal strokes by 68 percent. "These data are particularly interesting in light of recent findings from the WHI trial examining hormone therapy," said Dr. Elizabeth Barrett-Connor, professor of family and preventative medicine at the University of California, San Diego, who presented the results. "While raloxifene and hormone therapy are both prescribed for osteoporosis, the WHI data showed that combined estrogen-progestin hormone therapy actually increased the risk of stroke." Dr. Cheryl Keech, clinical research physician at Lilly, said the Evista results suggest a place for "smart" estrogen therapy that can target specific receptors within a cell. "The one thing WHI has shown us is you have to do randomized controlled trials," Keech told Reuters. Known by the chemical name of raloxifene HCl, Evista is a selective estrogen receptor modulator used for both the prevention and treatment of osteoporosis. Along with the decreased risk of stroke in the subgroup of women at high risk for heart disease, Evista showed no increased risk of stroke among the total 7,705-patient population. Evista also did not increase blood pressure, a high-risk factor for stroke. Lilly said it is studying Evista to determine its ability to reduce the risks of serious heart-related events and breast cancer in post-menopausal women in a number of clinical trials. In an ongoing 10,000-patient study of Evista in preventing heart disease, Lilly aims to determine whether Evista can have positive benefits without the problems of hormone replacement therapy. "We don't see any harm and we see both benefits in stroke and coronary," she said, adding that the observations need to be proven in a prospective trial. The company plans to use the data from that trial as part of a submission to the U.S. Food and Drug Administration to use Evista as a treatment to prevent heart disease. Early results of that study will be available in 2005.

Feds Crack Down on 'Blue Stuff' Products

http://story.news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=16&u=/nm/20021119/hl_nm/bluestuff_feds_dc

Makers of the heavily advertised Blue Stuff products said Tuesday that they would pay \$3 million to settle federal charges that the company's promotional campaigns were rife with false and misleading health claims. An attorney for Oklahoma City-based Blue Stuff, Inc. also said that the firm was in the process of revising its advertising and promotional materials related to nearly a dozen products to comply with Food and Drug Administration (news - web sites) (FDA) warnings that they violate federal drug laws. The company agreed to pay \$3 million in consumer redress to settle charges brought by the Federal Trade Commission (FTC), said attorney Jeffrey D. Knowles of the Washington firm Venable, Baetjer, Howard, & Civiletti. The suit alleged that national infomercials and the company's Internet site repeatedly made unsubstantiated claims about the ability of two of its products--Blue Stuff and Super Blue Stuff creams--to relieve pain. It also accused the company of improperly claiming that emu oil in a product called Essential Stuff could reduce cholesterol levels. Blue Stuff and Super Blue Stuff both cost \$59.95 for an 8-ounce jar. The company took in an estimated \$83 million selling the products, according to a statement issued by FTC Commissioner Orson Swindle. David Horowitz, the director of drug compliance at the Food and Drug Administration, said in an interview that regulators considered the case "particularly egregious" because of the breadth of unsubstantiated claims made by the company. FDA officials Monday warned the company in a letter that 11 of its products violate federal rules because their active ingredients do not qualify as over-the-counter drugs or their product labeling is inaccurate or unsubstantiated. The letter threatened further actions, including possible product seizures or a halt to distribution. One product sold by the company under the name Pure Emu Oil offered customers relief for arthritis and sore muscles as well as "faster healing for burn victims," according to the FDA. "We are generally concerned about products like this being marketed aggressively, making claims that are not approved by the FDA, and we intend to take additional actions in this area," Horowitz said in an interview. "I'm not aware of any approved products that represent emu oil as an active ingredient," he said. Blue Stuff, Inc.'s President Jack McClung said in a statement his decision to pay the \$3 million settlement "was based on avoiding extraordinary costs and distractions of litigation. The company did not admit to any wrongdoing." "Who is John Galt?" The five-member FTC voted unanimously to file the action against Blue Stuff, though two commissioners issued statements criticizing the \$3 million settlement as too limited. The settlement does not recover money given by McClung and his wife to a Christian charity affiliated with the company known as the Loyd McClung Foundation. "Profits...obtained by deceiving consumers, were funneled to the Loyd McClung Foundation. I am extremely frustrated that the Commission did not press the defendants harder to obtain more of the illicitly obtained

funds for consumer redress," FTC Commissioner Sheila F. Anthony wrote in a statement. McClung did not respond to requests for an interview. Knowles, the Blue Stuff, Inc. attorney, said that the company has changed the labeling of several of its products and has revamped all of the company's advertising and promotional materials. Some of the products have also been reformulated, and will still be sold, he said. "The company believes that these changes will resolve the outstanding issues with FDA," said Knowles. The changes are still subject to review by FDA officials.

\$4.1M Awarded in Diet Supplement Suit

<http://apnews1.iwon.com/article/20021120/D7NE155G0.html>

A jury ordered Metabolife International to pay \$4.1 million to four users of its appetite suppressants who fell seriously ill. The jury said the company should have warned customers that the over-the-counter Metabolife 356 pills contained ephedra, an herb that increases blood pressure and has been blamed for heart attacks and strokes. The supplement is commonly used for weight loss and body building. The case was the first among numerous such lawsuits around the country to go to trial. Tuesday's verdict came the same day that Metabolife gave the federal government records of 1,400 customer complaints, including 14 that mentioned serious side effects. The San Diego-based company already had turned over 14,700 other complaints in a criminal investigation into whether the company lied about ephedra's safety. Annie McClain, Shirley Franks, Connie Thornburg and Wilmer Hudson sued Metabolife last year over their health problems. McClain, Franks and Thornburg suffered strokes; Hudson had a heart attack. The four, and in some cases their spouses, were awarded varying amounts of compensatory and punitive damages on Tuesday. The jury found that Hudson was entitled to \$7,500, while Franks was awarded \$2.35 million, including \$150,000 on her husband's behalf. Their attorneys said the verdict should send a message that the product should be off the market. "We are glad that the jurors found this product unreasonably dangerous, that it poses a risk of harm to clients and to the public," said lawyer Robert Roden. Ed Bowron, a Metabolife lawyer, said in a statement that every plaintiff acknowledged not reading warnings on the supplement's label, including the need to consult a doctor. He said the company will appeal. The verdict came five months after the Bush administration ordered a start-from-scratch safety review of ephedra, outraging consumer advocates and doctors who wanted the herb banned.

Some Over-The-Counter Drugs Can Ease Migraines

http://story.news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=1&u=/nm/20021118/hl_nm/otc_migraines_dc

Inexpensive over-the-counter pain relievers may effectively treat migraines if taken as soon as symptoms appear, according to a joint statement by two

national medical organizations. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen should be used as the first line of treatment against migraines--severe headaches marked by throbbing pain, nausea, sensitivity to light and noise and vomiting. The pain can last anywhere from a couple of hours to several days. The recommendations, published in the November 19th issue of the Annals of Internal Medicine, may help to guide the roughly 28 million Americans who suffer from the chronic headaches. Many patients, especially those with family members who also get migraines, believe that they simply have to suffer through the attacks, Dr. Vincenza Snow, one of the authors of the paper, told Reuters Health in an interview. SOURCE: Annals of Internal Medicine 2002;137:840-849.

Many Schools Bar Allergy, Asthma Meds, Group Says

http://story.news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=17&u=/nm/20021118/hl_nm/allergy_schools_dc

Overzealous "zero-tolerance" anti-drug rules are preventing many American schoolchildren with asthma or serious allergies from carrying medications that could save their lives, according to representatives of the nonprofit advocacy group Allergy & Asthma Network Mothers of Asthmatics (AANMA). For vulnerable children, medications such as asthma inhalers or auto-injectable epinephrine (used in the case of severe anaphylactic shock brought on by allergy) can mean the difference between life and death. AANMA President Nancy Sander says her group is pressuring Congress to pass legislation that would guarantee children across the US the right to carry these and other essential medications on their person, instead of leaving them at the school health clinic, as is now sometimes the case. "You would not tell a child who needs a wheelchair to leave his wheelchair in a clinic," Sander told Reuters Health. "You would not tell a child who needs glasses to leave his glasses in the clinic. But this is a life-threatening condition, where children do die every single school year." In fact, the state of Georgia recently passed the Kellen Edwin Bolden Act, named after an asthmatic child who was barred by local school policy from carrying his asthma inhaler with him while on campus. Bolden died after suffering a severe asthmatic attack while boarding a school bus. Passage of the act now means that children in Georgia cannot be barred by individual school boards from carrying prescribed, lifesaving medications. But children in many states lack these protections. In their nationwide survey, presented here Saturday at the annual meeting of the American College of Allergy, Asthma & Immunology, Sander and Magnetti report that just 17 states have enacted laws explicitly protecting the right of schoolchildren to keep prescribed lifesaving drugs on their person while at school. Other states protect the rights of children with life-threatening allergies to carry auto-injectable epinephrine, but do not extend those protections to asthmatic children, who rely on their inhalers. And while Tennessee and Wyoming have general policies allowing schoolchildren to carry necessary drugs, these policies do

not extend to epinephrine. In most cases where children are barred from carrying essential drugs on their person, schools mandate that these medications be kept at the school health clinic, instead. "But these clinics are in many cases not staffed by RNs," Sanders pointed out. "They may be staffed by the school secretary or a parent volunteer--who may or may not have as much experience in administering that medication as the child does himself." Policies like these usually spring from overzealous efforts on the part of parents and school administrators to reduce kids' use of illicit drugs, Sander explained. "It's 'zero-tolerance' for drugs," she said. "There's also a fear that's been expressed--and it's not a rational fear--of 'What would happen if a child dropped his inhaler on the playground and another child finds it and uses it--the child may get high.'" Those fears are unfounded, according to Sander. "It's not fun to use an inhaler in the first place. And it's not going to harm a child who finds it and may try it--even if they could figure out how to use it." Right now, school policies governing kids' access to their medications vary widely from district to district and from state to state. "We're hoping to create (federal) legislation that would protect the rights of all children with asthma and anaphylactic conditions to carry prescribed, lifesaving medications," Sander said. "Once we get that policy for the entire United States, then what we will launch is a campaign that would let families know that they have the right to ask for this." The issue is a serious one, she said. "Kids have died. They've died on the way to the clinic after being sent there by themselves. They've died back in the classroom, after going to the clinic and asking for help and being told 'you look good to me.' There are legal battles that have been fought and won on behalf of children who died, because the school did not respond to their asthma emergency in an appropriate manner and did not allow the child to carry their inhaler on their person."

Lotronex(R) Tablets Now Available for Women with Severe Diarrhea-Predominant Irritable Bowel Syndrome

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-20-2002/0001845179&EDATE=>

Lotronex(alosetron hydrochloride) Tablets will now be available under restricted conditions of use, which include a narrower indication for specific use in female patients with severe diarrhea-predominant irritable bowel syndrome (IBS), an extensive Risk Management Program requiring participation of physicians, patients and pharmacists, and several additional safety and efficacy studies. "We're entering a new era for pharmaceuticals in the U.S.," said Peter Traber, M.D. Senior Vice President and Chief Medical Officer at GlaxoSmithKline. "The industry, the Food and Drug Administration, the medical

profession and patients are all recognizing our joint responsibility to understand appropriate use of medicines and find ways to successfully manage potential risks in order to reap the intended benefits." Lotronex is to be used by women with severe diarrhea-predominant irritable bowel syndrome who have failed to respond to conventional therapy, whose IBS symptoms are chronic and who have had other gastrointestinal medical conditions that could explain their symptoms ruled out. Symptoms that make diarrhea-predominant IBS severe are frequent and serious abdominal pain, fecal incontinence or the uncontrolled urge to have a bowel movement, or curtailment of daily activities because of IBS. Serious gastrointestinal events, specifically ischemic colitis and complications of constipation, have been reported in association with the use of Lotronex. These events have resulted in hospitalization, blood transfusion and/or surgery and some fatalities. In clinical trials, about three women in 1,000 developed ischemic colitis over six months. Lotronex was voluntarily withdrawn by GSK in November 2000 when the company and the FDA were unable to agree on a Risk Management Plan that would guide appropriate use of Lotronex without presenting undue obstacles to patients. However, GSK and the FDA resumed discussions in January 2001, after thousands of patients who had successfully used Lotronex implored both the company and the Agency to work out a plan that would allow them access to Lotronex. These discussions culminated with the submission of the Supplemental New Drug Application by GSK, which was approved by the FDA on June 7, 2002. Now, Lotronex becomes available to patients today.

ASSENT-3+ Shows Promising Results for LOVENOX(R) in Acute Myocardial Infarction

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/11-20-2002/0001845639&EDATE=>

Aventis announced today that ASSENT-3+ (Assessment of the Safety and Efficacy of New Thrombolytic regimens) corroborates the reduction in ischemic events seen in the ASSENT-3 study for patients suffering from a heart attack (acute ST elevation myocardial infarction, STEMI). The trial results were presented today at the American Heart Association's Scientific Sessions 2002. The ASSENT-3+ study, a hypothesis-generating trial, involved 1,639 heart attack patients from Canada and Europe, treated in the ambulance pre-hospital setting with a combination of the thrombolytic (clot-buster) Metalyse(R) /TNKase(TM) (tenecteplase, TNK) with LOVENOX(R) (enoxaparin sodium) Injection

or unfractionated heparin (UFH). "Pre-hospital thrombolysis with LOVENOX(R) plus TNK or UFH plus TNK reduces treatment delay by 45 minutes," explains Lars Wallentin, MD, professor of medicine, Thoracic Centre, University Hospital of Uppsala in Sweden. Overall, the composite efficacy end-point(1) rates were 14.2% for LOVENOX(R) plus TNK vs. 17.4% for UFH plus TNK (p=0.08). The composite efficacy-safety endpoint(2) rates were 18.3% and 20.3% respectively (p=0.3). In this complex and challenging population, there was an increase in the ICH (intracranial bleeding) rate in the LOVENOX(R) plus TNK group as compared to UFH plus TNK. This increase was driven by the event rates in the population over the age of 75. In patients under the age of 75, ASSENT-3+ demonstrated that LOVENOX(R) plus TNK was superior to UFH plus TNK in reducing the primary composite efficacy endpoint rates (11.2 % vs. 15.2%, p = 0.03) with comparable safety. ASSENT 3+ was a satellite study of ASSENT-3, a 6,000 patient trial published in The Lancet in August 2001, which evaluated several combination regimens with TNK in the hospital setting. ASSENT-3 showed significant benefit in efficacy and efficacy-safety with LOVENOX(R) as compared to UFH. A combined analysis of ASSENT-3 and ASSENT-3+ shows that LOVENOX(R) plus TNK is superior to UFH plus TNK in the primary composite efficacy and efficacy-safety endpoints. "ASSENT-3+ shows that pre-hospital thrombolysis with UFH plus TNK is as safe and efficacious as when given in-hospital. Taking into account the reduction of ischemic events, the ease of administration and the absence of monitoring, the combination of LOVENOX(R) and TNK emerges as a very promising treatment. Further trials with a reduced dose regimen in patients over 75 are warranted," says Lars Wallentin. Based on the results of the ASSENT-3 program and other phase II trials, Aventis is sponsoring the ExTRACT-TIMI 25 trial. ExTRACT is a 21,000 patient, multi-national and indication-seeking trial, investigating the efficacy and safety of LOVENOX(R) compared to UFH in patients with heart attack (STEMI) receiving thrombolytic therapy with TNK, streptokinase, alteplase or reteplase. Patients over the age of 75 are receiving a reduced dose regimen of LOVENOX(R).

- (1) The composite efficacy end-point is defined as 30-day mortality or pre/in-hospital reinfarction or pre/in-hospital refractory ischemia
- (2) The composite efficacy and safety end-point is defined as 30-day mortality or pre/in-hospital reinfarction or pre/in-hospital refractory ischemia or incidence of in-hospital ICH or in-hospital major bleeds (other than ICH)

Lopinavir/Ritonavir Regimen Results in Cost Savings Over Nelfinavir in Treatment-Naïve Patients with HIV

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C77006E2B>
A7?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610&abd=yes

Use of the combination of lopinavir/ritonavir appears to be less costly to the healthcare system than nelfinavir in treatment-naïve HIV-positive

patients, researchers report. According to the main finding of a study presented here this week at the sixth International Congress on Drug Therapy in HIV infection, the lopinavir/ritonavir combination results in a better response rate than nelfinavir in treatment-naïve HIV-positive patients. The double-blind, randomised trial comparing Kaletra® (lopinavir 400 mg plus ritonavir 100 mg) to nelfinavir in a background of d4T/3TC among 653 antiretroviral naïve HIV-positive individuals demonstrated an improved response rate for patients taking Kaletra®, reported Michelle P. Luo, PhD, from Abbott Laboratories, in Abbott Park, Illinois, United States, makers of Kaletra. Dr. Luo's team used the data from this trial to create a clinical decision tree that predicted the relative costs of each therapy. Based on the decision tree, all patients initially took Kaletra or nelfinavir plus two nucleoside transcriptase inhibitors (NRTIs). Response rate was determined every four weeks for 60 weeks. Nonresponders, defined as having two successive viral loads four weeks apart that were over 400 copies/mL, were assumed to be switched to another therapy. The decision tree also took into account patients who dropped out of the study for reasons other than viral load. It included costs related to opportunistic illnesses, genotype/phenotype testing, drugs, routine follow-up care and extra patient monitoring. According to the cost analysis, the improved response rate seen with Kaletra compared with nelfinavir translated to an approximate cost savings of \$1,454 USD per patient during the first 60 weeks of therapy. "Basically, what we found is, because of the differences in response rates, what that translates into is a cost savings," said Mary A. Cifa Ildi, R.Ph, M.S.H.A., assistant director, Center for Pharmaceutical Appraisal & Outcomes Research, Abbott Laboratories, who was not an author of the study, but was closely involved in its implementation.

Table of Contents

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THE NEW ENGLAND JOURNAL OF MEDICINE

Volume 347, Issue 21: November 21, 2002

<<http://content.nejm.org/content/vol347/issue21/index.shtml?query=TOC>>

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THIS WEEK IN THE JOURNAL

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Article Summaries:

<http://content.nejm.org/this_week/347/21/index.shtml?query=TOC>

Perspective: Transient Ischemic Attacks

<<http://content.nejm.org/cgi/content/short/347/21/1642?query=TOC>>

=====
ORIGINAL ARTICLES
=====

A Controlled Trial of a Human Papillomavirus Type 16 Vaccine
<<http://content.nejm.org/cgi/content/short/347/21/1645?query=TOC>>

Glycoprotein-D-Adjuvant Vaccine to Prevent Genital Herpes
<<http://content.nejm.org/cgi/content/short/347/21/1652?query=TOC>>

Extended Transthoracic Resection Compared with Limited Transhiatal Resection for Adenocarcinoma of the Esophagus
<<http://content.nejm.org/cgi/content/short/347/21/1662?query=TOC>>

Normal Vision despite Narrowing of the Optic Canal in Fibrous Dysplasia
<<http://content.nejm.org/cgi/content/short/347/21/1670?query=TOC>>

=====
IMAGES IN CLINICAL MEDICINE
=====

Oral Manifestations of Secondary Syphilis
<<http://content.nejm.org/cgi/content/short/347/21/1677?query=TOC>>

=====
SPECIAL ARTICLE
=====

Specialty of Ambulatory Care Physicians and Mortality among Elderly Patients after Myocardial Infarction
<<http://content.nejm.org/cgi/content/short/347/21/1678?query=TOC>>

=====
CLINICAL PRACTICE
=====

Transient Ischemic Attack
<<http://content.nejm.org/cgi/content/short/347/21/1687?query=TOC>>

=====
CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

=====
Weekly Clinicopathological Exercises: Case 36-2002: A 32-Year-Old Man
with Hemoptysis of Nearly Three Decades' Duration
<<http://content.nejm.org/cgi/content/short/347/21/1693?query=TOC>>

=====
EDITORIALS
=====

Online Submission of Manuscripts
<<http://content.nejm.org/cgi/content/short/347/21/1703?query=TOC>>

The Beginning of the End for Cervical
Cancer?<<http://content.nejm.org/cgi/content/short/347/21/1703-a?query=TOC>>

Surgical Treatment of Esophageal Cancer -- The Advent of the Era of
Individualization
<<http://content.nejm.org/cgi/content/short/347/21/1705?query=TOC>>

Health Disparities and the Quality of Ambulatory Care
<<http://content.nejm.org/cgi/content/short/347/21/1709?query=TOC>>

=====
CLINICAL IMPLICATIONS OF BASIC RESEARCH
=====

New Players in the Genetics of Stroke
<<http://content.nejm.org/cgi/content/short/347/21/1711?query=TOC>>

=====
SOUNDING BOARD
=====

Transient Ischemic Attack -- Proposal for a New Definition
<<http://content.nejm.org/cgi/content/short/347/21/1713?query=TOC>>

=====
CORRESPONDENCE
=====

<<http://content.nejm.org/cgi/content/short/347/21/1717?query=TOC>>

Arthroscopic Surgery for Osteoarthritis of the Knee

Insect Repellents and Mosquito Bites

Hepatitis B e Antigen and the Risk of Hepatocellular Carcinoma

Troponin T Levels and Acute Coronary Syndromes

Poison Ivy

Chronic Urticaria and Angioedema

Can Ticks Be Vectors for Hepatitis C Virus?

An Unusual, Nonhealing Ulcer on the Forearm

JAMA

Table of Contents - November 20, 2002

Vol 288, No 19, pp 2359-2498

<http://jama.ama-assn.org/issues/v288n19/toc.html>

This Week in JAMA

Highlights of selected articles

<http://jama.ama-assn.org/issues/v288n19/ffull/jtw20039.html>

Original Contributions

JAMA-EXPRESS

Early and Sustained Dual Oral Antiplatelet Therapy Following Percutaneous Coronary Intervention: A Randomized Controlled Trial

<http://jama.ama-assn.org/issues/v288n19/abs/joc21875.html>

Effect of Blood Pressure Lowering and Antihypertensive Drug Class on Progression

of Hypertensive Kidney Disease: Results From the AASK Trial

<http://jama.ama-assn.org/issues/v288n19/abs/joc20772.html>

Effects of Hormone Replacement Therapy and Antioxidant Vitamin Supplements on

Coronary Atherosclerosis in Postmenopausal Women: A Randomized Controlled Trial

<http://jama.ama-assn.org/issues/v288n19/abs/joc21018.html>

Clinical Cardiology

Oral Anticoagulants vs Aspirin in Nonvalvular Atrial Fibrillation: An Individual

Patient Meta-analysis

<http://jama.ama-assn.org/issues/v288n19/abs/jcc20007.html>

Review

Comparison of Mortality Between Private For-Profit and Private Not-For-Profit

Hemodialysis Centers: A Systematic Review and Meta-analysis

<http://jama.ama-assn.org/issues/v288n19/abs/jrv20067.html>

Special Communication

Pedophilia

<http://jama.ama-assn.org/issues/v288n19/abs/jsc20333.html>

Editorial

Hypertension Control and Kidney Disease: Some Questions Answered, Many Remain

<http://jama.ama-assn.org/issues/v288n19/ffull/jed20064.html>

Letters

Sertraline for Treatment of Depression in Acute Coronary Syndromes

<http://jama.ama-assn.org/issues/v288n19/ffull/jlt1120-1.html>

Counting Deaths Due to Medical Errors

<http://jama.ama-assn.org/issues/v288n19/ffull/jlt1120-2.html>

Virologic Outcomes of Complex Drug Regimens for Human Immunodeficiency Virus

<http://jama.ama-assn.org/issues/v288n19/ffull/jlt1120-3.html>

Allocation Concealment in Clinical Trials

<http://jama.ama-assn.org/issues/v288n19/ffull/jlt1120-4.html>

News and Analysis

Medical News & Perspectives

Hong Kong Flu Still Poses Pandemic Threat

<http://jama.ama-assn.org/issues/v288n19/ffull/jmn1120-1.html>

Questions About Hormone Therapy Remain Puzzling

<http://jama.ama-assn.org/issues/v288n19/ffull/jmn1120-2.html>

Miscellanea Medica

<http://jama.ama-assn.org/issues/v288n19/ffull/jmn1120-3.html>

Health Agencies Update

PHS Provides Immunoglobulin

<http://jama.ama-assn.org/issues/v288n19/ffull/jha20011-1.html>

Pooling Federal Health Care

<http://jama.ama-assn.org/issues/v288n19/ffull/jha20011-2.html>

Proteomics for Prostates

<http://jama.ama-assn.org/issues/v288n19/ffull/jha20011-3.html>

>From the Centers for Disease Control and Prevention

Q Fever--California, Georgia, Pennsylvania, and Tennessee, 2000-2001

<http://jama.ama-assn.org/issues/v288n19/ffull/jwr1120-1.html>

Nonfatal Choking-Related Episodes Among Children--United States, 2001

<http://jama.ama-assn.org/issues/v288n19/ffull/jwr1120-2.html>

Expansion of Eligibility for Influenza Vaccine Through the Vaccines for
Children

Program

<http://jama.ama-assn.org/issues/v288n19/ffull/jwr1120-3.html>

The Cover

The Cliff, Etretat, Sunset

<http://jama.ama-assn.org/issues/v288n19/ffull/jcs1120-1.html>

Poetry and Medicine

Magnified

<http://jama.ama-assn.org/issues/v288n19/ffull/jpm20188-1.html>

A Piece of My Mind

The Long and the Short of It

<http://jama.ama-assn.org/issues/v288n19/ffull/jpo20171-1.html>

JAMA 100 Years Ago

Etiology and Prophylaxis of Colds

<http://jama.ama-assn.org/issues/v288n19/ffull/jjy20036-1.html>

Innovations in Primary Care

Patient Self-management of Chronic Disease in Primary Care

<http://jama.ama-assn.org/issues/v288n19/abs/jip21007.html>

Books, Journals, New Media

>From Certainty to Uncertainty: The Story of Science and Ideas in the Twentieth Century (Peat)

<http://jama.ama-assn.org/issues/v288n19/ffull/jbk1120-1.html>

Medical Readers' Theater: A Guide and Scripts (Savitt, ed)

<http://jama.ama-assn.org/issues/v288n19/ffull/jbk1120-2.html>

Departing From Deviance: A History of Homosexual Rights and Emancipatory Science

in America (Minton)

<http://jama.ama-assn.org/issues/v288n19/ffull/jbk1120-3.html>

Medicine and Medical Ethics in Nazi Germany: Origins, Practices, Legacies (Nicosia, Huener, eds)

<http://jama.ama-assn.org/issues/v288n19/ffull/jbk1120-4.html>

Books, Journals, New Media Received

<http://jama.ama-assn.org/issues/v288n19/ffull/jbk1120-5.html>

JAMA Patient Page

Hypertensive Kidney Disease

<http://jama.ama-assn.org/issues/v288n19/fpdf/jpg1120.pdf>

Website of the Day

Cafe Pharma

<http://www.cafepharma.com/>

"The website for Pharmaceutical Professionals", Cafe Pharma is a site geared towards pharmaceutical sales people. An interesting site for information on the industry and the roles and challenges of detailers. Some relevant information for your practice and miscellaneous links makes this site worth

a peek.

Answer of the Day

The Hawthorne effect refers to the influence of subject expectation on outcome. Hawthorne is a city in Illinois where a series of experiments occurred at a Western Electric Company Plant that manufactured for Bell South. In the Mid-1920s one study looked at the effect of lighting intensity on production. As lighting intensity increased, worker productivity increased. They continued this experiment multiple times and found similar results. As a need to validate this study, they then decreased lighting intensity and what happened...production increased. They continued to lower the intensity and what happened...production increased. It was then suggested that subjects in a study act a certain way and introduce bias simply because they know they are being studied. Today we know this phenomenon as the "Hawthorne Effect"
