



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

13-February-2003

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## Question of the Day...

What antibiotic was inadvertently discovered in 1962 by George Leshner and his co-workers in a distillate during synthesis of chloroquine?

hint... "top" of the morning to you George

## In the News

### Yasmin Birth Control Pill Linked To 2 Deaths

<http://www.latimes.com/features/health/la-he-yasmin10feb10,1,3296447.story?coll=la%252Dheadlines%252Dhealth>

Although birth control pills carry some increased risk of blood clots, doctors have been debating whether the newest-generation pills are any safer than their predecessors. One of those new pills, a contraceptive called Yasmin that's been available in the United States since 2001, is attracting particular attention because of reports that European users have suffered serious blood clots in the legs and lungs. Like other combination pills, Yasmin contains forms of two female reproductive hormones, estrogen and progesterone. What's novel about the pill is that it uses a new, synthetic version of progesterone that closely resembles the progesterone made by a woman's body. Because it is chemically related to a diuretic called spironolactone, it also acts like a water pill and reduces bloating. And, like spironolactone, it helps lessen acne and oily skin. Dutch authorities recently reported on five cases in which women taking Yasmin developed serious blood clots, one of which proved fatal. A 17-year-old collapsed and died after taking the pills for six months. An autopsy revealed she had suffered a pulmonary embolism, despite having no obvious risk factors, such as smoking, immobilization for a long period or plane travel. Although doctors never had a chance to test her blood, her parents tested negative for clotting problems. The five Dutch cases were described in the Feb. 1 issue of the British Medical Journal. A 28-year-old suffered a leg thrombosis four months after switching to Yasmin; a 45-year-old had a deep

vein thrombosis after two months on the pill; a 50-year-old had a similar thrombosis after three months on Yasmin, and a 35-year-old survived a pulmonary thrombosis after 17 days on the medication -- four months after she'd given birth. They were among 40 European Yasmin users who suffered major clots -- two fatal -- first reported in the British journal in April 2002. That report led to several European warnings about the pill, manufactured by Berlex Laboratories, a unit of Germany's Schering. The pill has been available in Europe since late 2000. Dr. David Plourd, an assistant professor of obstetrics and gynecology at the Naval Medical Center, San Diego, said he was concerned that several of the Dutch women suffered clots so soon after starting the medication. "If they'd been on it for 10 years and then threw a blood clot, it's less likely to be due to the Yasmin," Plourd said. "However, we don't know among how many women these 40 events occurred. So while I have a concern, there is no clear-cut evidence that this is a particularly less-than-safe or potentially harmful formulation." Dr. Philip Darney, chief of obstetrics and gynecology at San Francisco General Hospital, said he was unaware of any similar complications in this country. "We may not have had a broad enough experience with Yasmin in the U.S. to have seen any of this yet," he said. Because the risk of suffering a blood clot rises with higher doses of hormones, Darney said he hoped physicians and patients would be interested in several new contraceptive options, including the vaginal ring and an intrauterine device, which have "much lower doses than birth control pills."

### Co-Pays Drive Patients to Switch Heartburn Meds

[http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=5&u=/nm/20030212/hl\\_nm/copays\\_heartburn\\_dc](http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=5&u=/nm/20030212/hl_nm/copays_heartburn_dc)

One in four patients taking prescription heartburn medication each month asks their doctor or pharmacist about other options because they are concerned about high co-payments, according to Internet survey results announced Wednesday. That conversation typically occurs when co-pays reach \$35 or more, it found. About half of those who re-evaluate their options end up switching to a lower-cost medicine, saving them about \$22 per prescription, according to Market Measures/Cozint, the market research firm that conducted the study. The findings are based on a September 2002 Internet survey of 639 patients and 298 pharmacists. The results illustrate the power of high co-pays to influence patients' medication decisions, at least among prescription heartburn relievers known as proton pump inhibitors, or PPIs. Co-pay sensitivity is "obviously a hot issue now and it's not going away," said Chris Droukas, associate vice president of the East Hanover, New Jersey-based research outfit. For price-sensitive patients, co-pay levels may sway drug-prescribing decisions, given that many physicians view these products as interchangeable, she noted. In about 80% of cases, patients were the ones to begin the conversation to explore PPI options with their doctor or pharmacist. Many pharmacists indicated that

they are willing to explore alternatives with lower co-pays. When patients raise the co-pay issue, nearly 40% of pharmacists tout the benefits of lower-cost PPIs and encourage switching, it said. With a majority of US health plans offering three-tier co-pay plans--where consumers pay more out-of-pocket for higher-tier drugs--it's critical for pharmaceutical companies to understand how a drug's co-pay position and the cost to the patient drive the ultimate prescribing decision, the research firm noted. Consumers who fill multiple prescriptions each month were most sensitive to higher-co-pays. Those taking another medication with a first- or second-tier co-pay were most likely to question their healthcare providers when faced with a higher co-pay amount for a high-tier PPI. People taking AstraZeneca's Nexium and Prilosec and TAP Pharmaceuticals' Prevacid were more likely to switch. About one fifth, or 20%, of prescriptions for these products were changed to lower-cost branded alternatives each month. Users of Wyeth-Ayerst's Protonix and Eisai Co. Ltd.'s Aciphex were much less likely to jump to another PPI. Cost-driven switches occurred only 14% and 13% each month, respectively. Most heartburn medication users, however, rely on their health plans for co-pay guidance, rather than actively seeking out that information, the study found. Three of every four PPI users have not even considered raising the issue of co-pays, with many believing that physicians or pharmacists have no control over cost, it said. "Someone who's maybe more educated, more healthcare savvy...may be more inclined to ask the question," Droukas suspects. Susan Winckler, a spokeswoman for the American Pharmaceutical Association, which represents pharmacists in the US, said health plans could do a better job of communicating their co-payment policies to consumers. Identifying lower-cost alternatives often becomes "an administrative nightmare" for pharmacists because preferred products and co-pay levels vary from plan to plan, she explained. Market Measures/Cozint, a unit of United Business Media's NOP World Health, also is planning to study the impact of co-pays on drug switching in the anti-hypertensive, lipid-lowering, allergic rhinitis, diabetes, migraine and Cox-2 inhibitor categories.

### JNJ Liked Drug So Much They Bought The Company

[http://www.usatoday.com/money/industries/health/drugs/2003-02-10-scios-jnj\\_x.htm](http://www.usatoday.com/money/industries/health/drugs/2003-02-10-scios-jnj_x.htm)

Johnson & Johnson (JNJ) said Monday it agreed to buy Scios (SCIO) for about \$2.4 billion, giving J&J a new congestive heart failure drug and rights to an experimental arthritis medicine. Johnson & Johnson has made multiple acquisitions over the past four years as it seeks new products to offset slowing sales of some of its biggest drugs, including anemia treatment Procrit and arthritis drug Remicade. In Scios, Johnson & Johnson gains Natrecor, a two-year-old treatment for congestive heart failure that analysts expect could generate peak annual sales of \$500 million. Johnson & Johnson also gains access to an arthritis drug that is in mid-stage clinical

trials.

"The whisper is that this is probably one of the more promising drug candidates in its class," said Michael Sjoström, chief investment officer at Sectoral Asset Management, which owns 2 million Scios shares. "But people have been trying the approach for a long time and there is still a question mark over whether it can be successful." Scios shareholders will receive \$45 a share, a 30% premium over the closing price last Thursday. The company's shares rose 22% Friday after the news of the deal was leaked. They rose again Monday. Shares of Johnson & Johnson rose modestly. The company said the transaction will dilute its earnings by 5 cents a share in 2003 but it will make that up through increased growth in other parts of its business. It will also take a charge of about \$700 million, or 23 cents a share, for acquired research and development.

The \$2.4 billion price tag includes cash that Johnson & Johnson expects to receive from Scios in the transaction. Officials from Johnson & Johnson and Scios said on a conference call with investors that they expect the partnership to help boost sales of Natrecor beyond current expectations. Scios's most recent forecast is that Natrecor will generate sales of between \$160 million and \$170 million in 2003. The company will release its earnings on Thursday. The companies said they plan to explore additional patient populations that could benefit from Natrecor and are looking at using the treatment as a diagnostic tool. Scios dismissed an article in The Wall Street Journal that questioned the efficacy of Natrecor, saying it was "much ado about nothing."

### Roche in deal to buy Disetronic

<http://main.pslgroup.com/news/industrynews.nsf/IndustryNewsId/204608BCC9F7316385256CC9005981C1?opendocument&id=>

In a move that should make Roche a leader in integrated diabetes management, the company announced Monday it has agreed to buy medical-device maker Disetronic Holding for 1.6 billion Swiss francs (\$1.18 billion), news sources report. Already the global leader in diabetes monitoring systems since its 1997 acquisition of Boehringer Mannheim, adding Disetronic, the world's second-largest manufacturer of insulin-injection pumps could help Roche stay ahead of its rival Medtronic. In 2001, Roche garnered \$1.7 billion in sales for its diabetes tests. The market for diabetes-care products is estimated to double in seven years to \$24 billion. Franz Humer, Roche chief executive, reportedly said he sees gaining Disetronic as a way of catapulting the company to the number one spot both technologically and from a marketing standpoint.

Under the terms of the deal, Roche will pay Disetronic 670 Swiss francs in cash, as well as offer two Roche non-voting shares per share. The company will acquire Disetronics Infusion System division, which will become part of Roche Diagnostics Diabetes Care unit. Disetronic Injection Systems will not be part of the agreement, but will be sold back to Willy Michel, founder and

principal shareholder of Disetronic. Industry experts see this acquisition as a sign that Roche has the financial clout to make such deals and as a signal to cross-town rival Novartis that Roche has every intention to remain an independent player in an era when the world's pharmaceutical companies are increasingly consolidating.

### Eli Lilly, Bristol-Myers Squibb reach \$71 million settlement in drug dilution case

<http://main.pslgroup.com/news/industrynews.nsf/IndustryNewsId/92832AC565767FD985256CC90059D489?opendocument&id=>

Eli Lilly and Bristol-Myers Squibb have reportedly agreed to a \$71 million settlement over claims that a Kansas City pharmacist diluted drugs and pocketed the profits, news sources report. The case drew global attention when Robert Courtney admitted he watered down cancer drugs. He was sentenced in December to 30 years in prison. The two companies reached a confidential settlement in October as it was alleged that they "knew or should have known" about the pharmacist's actions. News sources, citing the Kansas City Star, report that in January arbitrators for the case assessed Lilly \$48.55 million and Bristol \$23.55 million. The companies have so far declined to comment on the case.

### New England Journal of Medicine Retracts Study

[http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=5&u=/nm/20030210/hl\\_nm/journal\\_retract\\_dc](http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=5&u=/nm/20030210/hl_nm/journal_retract_dc)

The New England Journal of Medicine retracted a study on Monday because one of the coauthors falsified signatures of the majority of the researchers named on the study as it was being reviewed. The study was published in October 2002, and concerned a technique in which alcohol is injected directly into the heart to treat hypertrophic cardiomyopathy, a leading cause of sudden cardiac death in children and adolescents. According to the journal, there was an "egregious disregard of the principles of authorship." "Of the eight persons named as authors of the article, some claimed that they had never reviewed the original data and most claimed that they had not seen or approved either the original version or one or more of the three revised versions of the manuscript," according to the notice of retraction that is to be published in the March 6th issue of the journal. "One author claimed that he had seen neither the original data nor any version of the manuscript." The study's authors, led by Dr. Waqar Shamim of the Imperial College School of Medicine in London, requested the retraction in a letter to the journal. They note that the technique described in the study may be a "useful procedure in selected atients." "We also want to make clear that the Cleveland Clinic Foundation was not involved in the study but was mentioned purely as an address for correspondence," they wrote. To prevent the problem from happening again, the journal plans "to

inform all authors of record by e-mail when their manuscript is accepted." The "unfortunate incident serves as a reminder to the medical community that with the privilege of authorship comes a mandate for personal and professional responsibility that must be taken very seriously," according to the journal's editors.

### FDA approves Biovail's Cardizem LA

<http://main.pslgroup.com/news/industrynews.nsf/IndustryNewsId/3FBC76EF6959B42F85256CC6005D58AD?opendocument&id=>

Biovail announced Friday the FDA had approved Cardizem LA, the long acting version of its drug, news sources report. The company said that a single daily dose ranging from 120-milligrams to 540-milligrams of Cardizem LA controls blood pressure for 24 hours. Biovail anticipates launching the drug in the US on April 2 and will market it to physicians directly. Currently, Biovail's entire line of Cardizem drugs is expected to garner sales of \$140 million to \$200 million this year. The company said the sales would increase Biovail's total revenue by more than 30 percent. Other drugs in Biovail's pipeline that are expected to see launches this year include Teveten, Wellbutrin and Zovirax. Shares of Biovail's stock rose as much as 9 percent on news of the approval. The company forecasted its profit for 2003 could be \$2.25 to \$2.35 per share on sales of \$950 million to \$1.05 billion.

### Biogen's Avonex gets FDA nod for early MS treatment

<http://main.pslgroup.com/news/industrynews.nsf/IndustryNewsId/DEBF17BD3A0D186A85256CC60050C2B5?opendocument&id=>

Biogen said Friday that Avonex received FDA approval for the early treatment of multiple sclerosis, news sources report. Avonex, a billion-dollar drug, won European approval last year for this indication. Its US approval was based on research conducted over three years, which showed that patients treated with Avonex had a 44 percent decrease in the rate of developing a second attack. "Physicians can now initiate therapy with Avonex at the first signs and symptoms of MS, rather than waiting until the disease has further progressed and patients have experienced a second attack," said Dr. R. Philip Kinkel one of the study's investigators. This is a new approach to multiple sclerosis, which has historically been treated with medication only after a patient had at least two clinically defined attacks. Avonex competes with Serono's Rebif and Schering AG's Betaseron. The extended indication for the drug could help Biogen reclaim some of the MS market share. Sales of Avonex fell by 1.2 percent in the fourth quarter to \$256.3 million before the approval.

### Zoloft(R) Receives FDA Approval for Treatment of Social Anxiety Disorder

[http://biz.yahoo.com/djus/030210/1557000941\\_1.html](http://biz.yahoo.com/djus/030210/1557000941_1.html)

Pfizer Inc. received Food and Drug Administration approval to market its antidepressant Zoloft for acute and long-term treatment of social anxiety disorder. In a press release Monday, Pfizer said the drug is the only selective serotonin reuptake inhibitor approved for long-term treatment of the disorder. Studies found that 53% of social anxiety patients responded to Zoloft, compared with 29% of placebo patients. Social anxiety disorder is the most common anxiety disorder in the U.S., Pfizer said, characterized by a persistent fear of social or performance situations. Zoloft, which had 2002 sales of \$2.74 billion, is also indicated for depression, posttraumatic stress disorder, panic disorder, obsessive-compulsive disorder and premenstrual dysphoric disorder. New York Stock Exchange-listed shares of Pfizer closed Monday at \$29.57, up 27 cents, or 0.9%, on composite volume of 15 million shares. Average daily volume is 17 million shares.

### **New SYSTANE(TM) Lubricant Eye Drops Delivers a First in Dry Eye Therapy - The Proven Reduction of Both Symptoms and Signs**

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/02-03-2003/0001884250&EDATE=>

Patients with dry eyes can now enjoy longer-lasting comfort and protection thanks to new Systane Lubricant Eye Drops. Systane, from Alcon (NYSE: ACL), is clinically proven to reduce both the clinical signs and the symptoms of dry eye -- a benefit that should be welcome news to the more than 60 million Americans who suffer from the daily annoyance of dry eye. In a clinical study, Systane improved clinical signs in just days, as is demonstrated by its impressive 51 percent reduction in corneal staining from baseline. When compared to the leading artificial tear, Systane delivered superior relief of morning dryness, evening dryness and foreign body sensation. Behind this superior relief is the product's polymerizing protection that creates an ocular shield, allowing for epithelial repair in a healthy environment. With Systane, dry eye signs and symptoms improve over time. The result to patients: comfortable relief that lasts. Systane is scheduled to ship to retailers by mid-February. Promotional/sales materials as well as samples will also be made available at that time to eye care professionals.

### **Antibiotic Overuse Varies with State, Specialty**

[http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=8&u=/nm/20030211/hl\\_nm/antibiotics\\_states\\_dc](http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=8&u=/nm/20030211/hl_nm/antibiotics_states_dc)

Doctors in the US are overusing "broad-spectrum" antibiotics for common infections, such as the common cold, according to a study by three California doctors released on Tuesday. "The overuse of broad-spectrum antibiotics (drugs that are used to combat a variety of organisms) causes

bacteria to become resistant to these powerful drugs," said lead author Dr. Michael Steinman in an interview with Reuters Health. "So, when we need these antibiotics to treat people with severe and complicated infections, the bacteria will already have become resistant--and there will be few treatment options left," added Steinman, who is with the San Francisco VA Medical Center. Broad-spectrum antibiotics are effective against certain types of bacteria that cannot be treated by other, narrow-spectrum antibiotics, explained Steinman. These types of bacteria most often cause problems in severe, complicated infections, and are much less likely to be a problem in garden-variety respiratory tract infections treated in the clinic setting, according to the investigator. In the current investigation, Steinman and colleagues evaluated drug-prescribing data for nearly 2,000 patient visits to doctors for the common cold or upper respiratory tract infections. "Antibiotics were prescribed to 63% of patients with an acute respiratory tract infection...(and) broad spectrum agents were chosen in 54% of patients prescribed an antibiotic," the authors report. Steinman's team also found that certain types of primary care physicians are more likely to prescribe broad-spectrum antibiotics, "particularly doctors trained in the specialty of internal medicine, and doctors practicing in the Northeast and Southern United States," Steinman told Reuters Health. "This suggests that medicine is not a purely scientific enterprise," noted Steinman. "Rather, doctors can be influenced by a number of non-scientific sources such as pharmaceutical industry marketing, patient demand, and the attitudes and "culture" of their medical colleagues." Addressing such non-scientific factors that influence prescribing can help to improve the quality of care for all patients, according to the report in the February 12th issue of the Journal of the American Medical Association. "Many previous studies have found that doctors are overusing antibiotics for respiratory tract infections (but) our study is new in looking at the type of antibiotics that are being prescribed for these conditions," said Steinman. Not only should physicians prescribe fewer antibiotics for people with respiratory tract infections, but when they decide that an antibiotic is needed, they should be particularly careful about prescribing a broad-spectrum drug, concluded Steinman. Journal of the American Medical Association 2003;289:719-725.

Outcomes in elderly hypertensives better with ACE inhibitors than diuretics  
<http://www.reutershealth.com/archive/2003/02/12/professional/links/20030212clin010.html>

In elderly patients with hypertension, ACE inhibitor therapy and diuretic therapy produce similar reductions in blood pressure, but the former is associated with better outcomes than the latter, according to a report by Australian investigators. Hypertensive patients treated with an ACE inhibitor were 11% less likely to experience a cardiovascular event or death than patients treated with a diuretic ( $p = 0.05$ ), according to the findings published in the February 13th issue of The New England Journal of Medicine.

The results are based on a study of 6083 elderly subjects with hypertension who were randomized to receive ACE inhibitor or diuretic therapy and followed for a median of 4.1 years. The ability of ACE inhibitors to reduce the risk of adverse events or death was largely confined to male patients, note study author Dr. Christopher Reid, from the Baker Heart Research Institute in Melbourne, and colleagues. Also, ACE inhibitor therapy appeared to decrease the risk of myocardial infarction, but not the risk of stroke. So, should elderly patients with hypertension be treated with an ACE inhibitor instead of a diuretic? The answer is not clear, due in large part to a conflicting report that was released in December. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), researchers found that ACE inhibitor therapy provided better blood-pressure control and was tied to better outcomes than diuretic therapy (see Reuters Health report December 17, 2002, "Thiazide diuretics provide best first-step therapy for hypertension"). In an accompanying editorial, Dr. Edward D. Frohlich, from the Ochsner Clinic Foundation in New Orleans, discusses how the results from ALLHAT can be reconciled with those from the current study, known as the Second Australian National Blood Pressure Study (ANBP2). "In writing the editorial, I was concerned that people were going to ask which trial are we to believe?" Dr. Frohlich told Reuters Health. Given the contradictory nature of the two trials, "I think there is the potential for the media to stir up a lot controversy and send patients running to their physicians questioning" their current antihypertensive agent, he added. In general, "I don't think one class of antihypertensives is necessarily any better than another class," Dr. Frohlich said. The decision to use an ACE inhibitor versus a diuretic needs to be tailored to the individual patient, he noted. As to why the results from ALLHAT and ANBP2 differed, Dr. Frohlich believes that it has a lot to do with patient demographics. In ALLHAT, "35% of the patients were black--an ethnic group that is known to respond better to diuretics than to other agents," he said. In contrast, in ANBP2, "95% of the subjects were white." N Engl J Med 2003;348:583-592.

## New York Will Sue 2 Big Drug Makers on Doctor Discount

<http://www.nytimes.com/2003/02/13/business/13DRUG.html>

New York plans to sue two major pharmaceutical companies today, accusing them essentially of paying doctors and pharmacists to choose the companies' drugs over competing medicines.

The state is joining six other states, including California and Texas, in a growing legal attack on a longstanding practice that the states say has cost state and federal governments and consumers hundreds of millions of dollars in recent years. The lawsuits contend that GlaxoSmithKline and Pharmacia, the two large drug companies, gave discounts to doctors and pharmacies that bought their drugs. Doctors often buy and dispense injectable drugs like

chemotherapy medicines. Pharmacies buy drugs in bulk to fill prescriptions, and sometimes recommend particular drugs to doctors.

The discounts work this way. The drug companies establish a price for the drug that the government and insurance companies use to determine how much to reimburse the doctors and pharmacies for the drugs they buy. The companies then allow the doctors and pharmacies to buy their drugs at much lower prices than the ones reported to the government. The doctors and pharmacies then pocket the difference.

The lawsuits argue that the drug companies, doctors and pharmacists all profit from this arrangement, at the expense of the taxpayer and the patient, who has a higher co-payment.

The lawsuits are expected to be filed this morning in state court in Albany by Attorney General Eliot Spitzer, who is holding a news conference to announce New York's action. A third drug maker, Aventis, has been notified that it may also be sued.

### Miami Woman Reacts to Smallpox Vaccine

<http://apnews1.iwon.com/article/20030212/D7P55OCG0.html>

More than 500 people were vaccinated for smallpox Tuesday on the first day of the state's inoculation program for health workers, officials said. One woman suffered a mild allergic reaction, believed to be the first adverse reaction since the voluntary program started nationwide last month. The woman, who was not identified, was treated and released. State health secretary Dr. John Agwunobi said officials "were very relieved to see that the individual is getting better. Right now we're all feeling a great sigh of relief." Florida's vaccination program is designed to create a team that could safely respond if the disease is used as part of a bioterrorist attack. Officials said up to 2,000 state public health employees were expected to be vaccinated through the week. The number of first-day inoculations in Florida dwarfs the released totals of any of the other 19 states that have reported data from their inoculation programs. Through Sunday, 1,024 health employees in those states had volunteered to receive the inoculation, according to the federal Centers for Disease Control and Prevention.

\*\*\*\*\*On the Clinical Side\*\*\*\*\*

### Acetylcysteine Protects Renal Insufficiency Patients During Cardiac Angiography

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CC4006BDED3?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610>

Acetylcysteine, an antioxidant, protects against renal dysfunction in patients with chronic renal insufficiency who are undergoing coronary angiography, research from Hong Kong indicates. The agent's reno-protective effects are similar in patient subgroups, and there are minimal adverse effects with it, say investigators led by Dr. Jay Kay of Grantham Hospital at the University of Hong Kong. Protective effects were seen in patients undergoing coronary diagnostic and/or interventional procedures. Similar changes seen in serum urea and creatinine concentrations suggest "the changes in glomerular filtration underlie the prophylactic effects of acetylcysteine," the researchers add. Two hundred patients were randomised in a prospective, double-blind trial at Grantham Hospital between May 2000 and December 2001. On the day before and on the day of angiography, 102 participants were assigned to receive 600 milligrams of oral acetylcysteine twice a day. The other 98 patients received placebo tablets. Mean patient age was 68 years. Participants had stable, moderate renal insufficiency, defined as creatinine clearance less than 60 millilitres per minute. All were undergoing elective coronary angiography with or without intervention, and all received low-osmolality contrast agent. Main outcome measures included more than a 25% increase in serum creatinine level within 48 hours of contrast administration, change in creatinine clearance and serum creatinine level. Results indicate 12 placebo patients (12%) and 4 acetylcysteine patients (4%) developed a more than 25% serum creatinine level increase within 48 hours. Serum creatinine was lower in acetylcysteine patients during the first 48 hours following angiographic procedures. Therapy with acetylcysteine significantly increased creatinine clearance two days after contrast administration. "The benefit of acetylcysteine was consistent among various patient subgroups and persistent for at least seven days," the investigators report. JAMA, 2003;289:553-558.

### Ezetimibe Plus Simvastatin Safely Improves Lipid Profile

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CA100035520?OpenDocument&id=48DDE4A73E09A969852568880078C249>

Combination of the novel agent ezetimibe with simvastatin for treatment of primary hypercholesterolaemia is well tolerated and comparable to statin treatment alone. Clinicians believe that combination therapy with lipid-lowering agents which act via two complementary pathways might allow more patients to achieve recommended cholesterol goals. Ezetimibe is the first in a new class of potential lipid-management drugs known as cholesterol absorption inhibitors. Researchers at the Chicago Center for Clinical Research, Chicago, Illinois, United States, assessed the efficacy and safety of ezetimibe when administered with simvastatin in patients with primary hypercholesterolaemia. After dietary stabilisation, a 2 to 12-week washout and a 4-week single-blind, placebo lead-in period, patients with baseline low-density lipoprotein cholesterol of 145 to 250 mg/dL (3.8-6.5 mmol/L) and triglycerides below 350 mg/dL (9.1 mmol/L) were randomised to 10

different daily regimens for 12 consecutive weeks: ezetimibe 10 mg, simvastatin 10, 20, 40 or 80 mg, ezetimibe 10 mg plus simvastatin 10, 20, 40 or 80 mg, or placebo. The primary efficacy variable was the percentage reduction from baseline to end point in direct low-density lipoprotein cholesterol for the pooled ezetimibe plus simvastatin groups versus pooled simvastatin groups. Ezetimibe plus simvastatin significantly improved low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides compared with simvastatin alone. Ezetimibe plus simvastatin (pooled doses) provided an incremental 13.8% low-density lipoprotein cholesterol reduction, a 2.4% high-density lipoprotein cholesterol increase and a 7.5% triglycerides reduction compared with pooled simvastatin alone. Ezetimibe and simvastatin given together reduced low-density lipoprotein cholesterol by 44 to 57%, reduced triglycerides by 20 to 28% and raised high-density lipoprotein cholesterol by 8 to 11%, depending on the simvastatin dose. Ezetimibe 10 mg plus simvastatin 10 mg and simvastatin 80 mg alone each reduced low-density lipoprotein cholesterol by 44%. The co-administration of ezetimibe with simvastatin was well tolerated. The safety profile of this combination was similar to both simvastatin and placebo. When given with simvastatin, ezetimibe provided significant incremental reductions in low-density lipoprotein cholesterol and triglycerides, as well as increases in high-density lipoprotein cholesterol. *Journal of the American College of Cardiology* 2002 18;40(12):2125-2134.

### Antibiotics, SSRI's Implicated In QT Prolongation

<http://www.healthscout.com/template.asp?page=newsdetail&ap=1&id=511644>

Millions of Americans, especially women, could be putting themselves at risk by taking combinations of common medications with potentially deadly side effects. Or, they might not be in much danger at all. Those are the conflicting messages of a new study that examines how many people get prescriptions for drugs that could work together to create havoc in the heart. "The next step that's really crucial is for us to better understand what the real risks are associated with these drugs," says study co-author Lesley Curtis, a research associate with Duke University's Clinical Research Institute. Many drugs have the potential to disrupt the heart's rhythm and cause a condition known as torsade de pointes. In some cases, especially among susceptible people, the condition could make the heart thrash uncontrollably and lead to death. Some common drugs that could cause the condition include the antibiotics clarithromycin, levofloxacin and erythromycin, and the antidepressants Prozac and Zoloft, says Dr. Joe Selby, director of research for the Kaiser Permanente Health Plan in Northern California. Medical reference books let doctors know that the drugs could potentially lengthen the "QT interval," the time between beats when the heart reboots itself electronically, Selby says. To determine how often patients were prescribed the drugs, Curtis and colleagues examined

statistics compiled by a pharmaceutical benefits company about prescriptions for nearly 5 million people. The study appears in the new issue of the American Journal of Medicine. The researchers found that 23 percent of the subjects received prescriptions for one or more of 50 drugs that could cause irregular heartbeats. About 10 percent of these subjects were prescribed at least two potentially risky drugs or one drug that could cause the condition and another that could relieve it. Half of all potentially risky prescriptions were for antidepressants, and 64 percent of all the subjects were women, who are more likely to suffer from depression. Both Curtis and Selby says it's not clear how much danger the subjects face by taking the drugs either by themselves or in combination with others. It's possible that many of the doctors who prescribe the drugs know about the possible side effects and consider the potential benefits to be worth the risk, Selby says. "We can't tell whether these [prescriptions] are mistakes or conscious decisions," he says. According to Curtis, patients who are currently taking the drugs with potential side effects should talk to their doctor if they are concerned. "The message should not be to stop taking your drugs," she says.

### Alefacept Improves Quality Of Life For Patients With Psoriasis

<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256CBF00119821?OpenDocument&c=&count=10&id=9F874D6C503400D485256AFD0071B610&abd=yes>

Alefacept, a selective immunomodulator, appears to improve quality of life for patients with moderate to severe chronic plaque psoriasis. The profound effects of psoriasis impacts on the quality of life for patients due to adverse psychosocial influences, impaired daily activities, anxiety and depression. Consequently, a health-related quality of life randomised, placebo- controlled, double-blind trial of alefacept was undertaken by dermatologists at the University of Michigan Medical School, Ann Arbor. Two hundred and twenty nine patients with moderate to severe psoriasis were randomly assigned either alefacept (0.025, 0.075, or 0.150mg/kg) or a placebo, through 30-second intravenous bolus once weekly for 12 weeks. They were then followed for another 12 weeks. Patients completed a general health survey; a dermatological life quality index, (DLQ1) and dermatology quality of life scales (DQOLS) at each visit. Significantly greater improvements were noted on dermatology-specific QOL scales among patients treated with alefacept in comparison with those receiving a placebo. Those who achieved a higher reduction than 50 or 75% in Psoriasis Area and Severity Index (PASI) also reported similar improvements in their quality of life, say researchers. This was considerably greater than that experienced by other patients, they added.

American Journal of Clinical Dermatology 2003;4:2:131-139.

### Risk from Beta Blockers Minimal, Study Says

<http://news.yahoo.com/news?tmpl=story2&cid=594&ncid=594&e=18&u=/nm/20030212/>

hl\_nm/heart\_risk\_dc

Heart failure patients given beta-blocker drugs do not face undue risks in the initial stages of treatment as previously feared, a drug company-funded study said on Tuesday. The study of 2,289 heart failure patients, financed by Roche Holding AG and GlaxoSmithKline Plc, has previously found taking beta blockers reduced patients' risk of death compared to those taking a placebo. Both groups took other drugs commonly prescribed for heart failure. Beta blockers such as Roche's brand Eucardic and GlaxoSmithKline's Coreg block receptors for selected stress hormones and are approved for use to treat high blood pressure and heart attacks of varying severity. Last month however, investigators for the US Food and Drug Administration questioned the benefit of prescribing beta blockers for some heart attack victims. An FDA advisory panel recommended Coreg for some heart attack survivors but rejected claims that the drug lowered the risk of suffering another heart attack. Manufacturers of beta blockers hope to increase their use among victims of heart failure, a growing malady where a weakened heart progressively loses its ability to pump oxygenated blood through the body. It is not clear exactly how beta blockers help ease the risks from heart failure. Writing in this week's issue of the Journal of the American Medical Association, Henry Krum of Monash University, Melbourne, Australia, said the group who took beta blockers "experienced no increase in cardiovascular risk but instead had fewer patients who died. Differences in favor of (beta blockers) became apparent as early as 14 to 21 days following initiation of treatment," Krum wrote. Heart failure worsened among 6% of beta blocker users, which was similar in frequency to the 5% risk among those taking a placebo. "Patients treated with (beta blockers) had no increase in the risk of worsening heart failure, pulmonary edema, cardiogenic shock, or other serious adverse cardiovascular events, including death," Krum wrote. "If concerns about efficacy and safety during the initiation of beta-blocker therapy have caused physicians to deny or delay the use of these drugs, our findings should provide the reassurance needed to encourage the high levels of use that are warranted by the results of clinical trials," the report said.

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and from what the heck is going on file...

Man with bubonic plague leaves hospital

<http://www.cnn.com/2003/HEALTH/conditions/02/10/plague.reut/index.html>

A New Mexico man who had one of the first cases of bubonic plague in New York in more than a century, was released from hospital Monday after three months of treatment officials said. Lawyer John Tull, 53, and his wife Lucinda Marker, 47, a financial planner, were admitted to Beth Israel Medical Center in Manhattan on November 5 after becoming ill with fevers and body aches on a visit to the city. They were diagnosed with bubonic plague,

a potentially deadly bacterial disease that city health department officials suspect was contracted from infected fleas on their property in Santa Fe, New Mexico. Marker recovered fully and was released from the hospital after a week, but Tull's condition was much worse. Doctors amputated his feet because of severe tissue damage and he will be fitted with prostheses, a hospital spokesman said. "Other than that, Mr. Tull is in good health," hospital spokesman Mike Quane said. "He left this morning and will continue his rehabilitation in Albuquerque, New Mexico, immediately." The cases were believed to be the first instance of bubonic plague in New York in 100 years, city health officials said. About a dozen cases of the disease are diagnosed in the United States each year, mostly in Southwestern states including New Mexico. If detected early, plague can be treated with antibiotics. Bubonic plague, a disease of rodents transmitted to humans through the bites of infected fleas, is usually not communicable among people, health officials said. Pneumonic plague, a more serious form of the disease, occurs when plague bacteria are inhaled after direct contact with infected rodents and other animals.

### Cancer sufferer sues McDonald's over pepper on burrito

[http://www.ananova.com/business/story/sm\\_740238.html?menu=](http://www.ananova.com/business/story/sm_740238.html?menu=)

A Texas man is suing McDonald's claiming too much black pepper on a breakfast burrito caused him two months of daily nosebleeds. Marcus Long also says the burrito he ate on November 18 caused an infection in his mouth and possible damage to his vocal chords. The Houston Press says Mr Long's lawyer claims his client's health has been declining since eating the offending burrito on November 18. Last year the 61-year-old was diagnosed with cancer of the brain, colon, lung and spine after a routine procedure on his bladder. Radiation and chemotherapy treatments made his mouth sensitive and sore, so he stopped wearing his dentures. Almost every morning for the past year his wife Elaine bought him two pints of milk and three McDonald's sausage, egg and cheese breakfast burritos because he could eat the soft, processed dairy product with his gums. Mr Long said of the burritos she bought him on November 18: "I looked inside the burritos and they were just black. You couldn't hardly see the egg." She returned to the McDonald's outlet where the manager said they had stopped serving the burritos because of problems. A McDonald's representative is rejecting the claims from Mr Long: "After a thorough investigation, I have no reason to believe this claim has anything to do with my restaurant or my employees." He said Marcus Long was the only customer who complained. "I believe this claim is without merit. "Who is John Galt?" Food safety and the safe operations of my restaurant are among my highest priorities," added the representative.

### Online pharmacists turn up heat on Glaxo

<http://www.nationalpost.com/financialpost/story.html?id=%7BC20DB559-662E-4F3>

7-87DF-461101FE229E%7D

Canada's online pharmacists -- cut off by GlaxoSmithKline Inc. for selling prescription drugs to U.S. consumers at discount prices -- yesterday stepped up their campaign against the international drug giant in a bid to stave off extinction. In a dramatic full-page ad in the New York Times, Canadian Internet pharmacists and U.S. patient groups urged Americans to "fight back" and "stop Glaxo" from continuing a sales ban it announced last month. The ad, which features a large photo of an angry elderly woman, asks patients to consider selling their Glaxo shares, stop buying Glaxo's over-the-counter medication and writing to Congress. The Canadian International Pharmacists Association said the advertisement is part of a lobbying and legal strategy to thwart Glaxo, which says it took the action because of patient safety concerns. The online pharmacists warn if Glaxo is successful in its efforts, it could be the beginning of the end for the fledgling industry. Canadian pharmacists who sell through the mail or over the Internet say about 1 million U.S. residents -- mostly senior citizens -- obtain drugs they otherwise could not afford through Canadian online mail-order pharmacies. Glaxo products, in most Canadian pharmaceutical operations, consist of about 8% to 10% of the prescription volume. "Most businesses could probably keep in operation with that reduction," Andy Troszok, spokesman for the Canadian International Pharmacists Association. "The big concern is ... the rest of brand name pharmaceutical companies will follow." Glaxo maintained yesterday it is "strongly" opposed to the export of its medications, approved only for use in Canada, via the Internet. "This practice presents serious issues for Canada's healthcare system, puts a strain on supply of medicines for Canadians and poses a safety risk for U.S. patients accessing Canadian medications," the statement said. In responding to the Times advertisement, the company said it has responded to concerns about affordability by providing more than \$150-million of medicines free of charge to the most needy and offering discounts through special company programs for consumers who qualify.

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The Ethical Dimensions of the Biological and Health Sciences (Bulger et al)

<http://jama.ama-assn.org/issues/v289n6/ffull/jbk0212-2.html>

Paediatric Cardiology, vols 1 & 2 (Anderson et al, eds)

<http://jama.ama-assn.org/issues/v289n6/ffull/jbk0212-3.html>

Web Site Discontinued: LWWmedicine.com

<http://jama.ama-assn.org/issues/v289n6/ffull/jbk0212-4.html>

Journal of Pain (Gebhart, ed)

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#### Links of the Day

Below are some listservs relevant to pharmacy. If you aren't a member of any, it may be worth it to subscribe. You know, keeping up with Jones's stuff..

[http://www.cis.um.edu.mt/~phcy/virt\\_lib/lists.html](http://www.cis.um.edu.mt/~phcy/virt_lib/lists.html)

<http://www.pharmacy.org/lists.html>

<http://www.pharm.unito.it/itcrs/intlist.html>

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#### Answer of the Day

##### Nalidixic acid

In 1962 George Leshner and his co-workers discovered nalidixic acid in a distillate during synthesis of chloroquine. This marked a new era in medicine, as this was the first completely synthesized antibiotic. Furthermore, nalidixic acid, a topoisomerase inhibitor, has become a key compound in the novel synthesis of many fluoroquinolones antibiotics and undoubtedly saved many lives. Thanks George, now what about Osama?

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