NEW DRUGS

Fortesta Gel for ‘Low T’

Endo Pharmaceuticals has announced the FDA’s approval of Fortesta Gel for the treatment of hypogonadism. Symptoms of low testosterone levels may include erectile dysfunction, fatigue, depressed mood, regression of secondary sexual characteristics, and osteoporosis. Nearly 14 million men in the U.S. are affected, yet only about 1.3 million (9%) are being treated. A boxed warning mentions the risk of virilization if children are exposed to the product.

The clear, colorless, odorless gel is dispensed from a metered-dose pump and is gently applied with one finger to the front and inner thighs.

In a phase 3 trial, 78% of men with hypogonadism who received Fortesta achieved an average serum total testosterone level within the normal range by the 90th day.

Endo acquired the U.S. rights for Fortesta from ProStrakan in August 2009. The gel is sold in Europe as Tostran.

Fortesta is discussed in this month’s Pharmaceutical Approval Update column on page 104.

Sources: Philadelphia Business Journal, December 30, 2010; Endo, December 29, 2010

Fidaxomicin, an Orphan Drug, in Pediatric C. difficile Infection

The FDA has granted an orphan drug designation for fidaxomicin (Optimer Pharmaceuticals) for the treatment of Clostridium difficile infection in children 16 years of age or younger. The infection afflicts more than 700,000 people each year in the U.S.

C. difficile bacteria produce toxins that cause inflammation of the colon, severe diarrhea, and death in the most serious cases. Infection typically results from the use of broad-spectrum antibiotics that disrupt normal gastrointestinal (GI) flora, allowing C. difficile bacteria to flourish.

Fidaxomicin is the first in a new class of antibiotics called macrocycles, which inhibit the bacterial enzyme RNA polymerase, resulting in the rapid killing of C. difficile. The drug’s narrow-spectrum profile eradicates C. difficile selectively with minimal disruption to the normal GI flora; by contrast, antibiotics such as metronidazole (Flagyl, Pfizer) and vancomycin (Vancocin, ViroPharma) tend to disrupt the flora. Fidaxomicin facilitates the return of normal physiology in the colon, perhaps reducing the recurrence of infection.

Some risk factors for infection include the use of broad-spectrum antibiotics (such as cephalosporins and fluoroquinolones), advanced age, and exposure to emerging hypervirulent strains of C. difficile.

Sources: Medical News Today/Optimer, January 5, 2011

Abstral Tablets for Cancer Pain

Fentanyl transmucosal tablets (Abstral, ProStrakan) have been approved for the management of breakthrough pain for adults with cancer. The drug is administered on the soft-tissue surfaces of the mouth, inside of the cheek, gums, tongue, or in the nasal passages or throat, where they dissolve and are absorbed.

Abstral is indicated for patients 18 years of age and older who already use opioid pain medication around the clock and who need high doses of an additional opioid. Breakthrough pain, sudden in onset, is not alleviated by a patient’s usual pain-management plan.

The safety of Abstral was evaluated in 311 opioid-tolerant cancer patients. Only health care professionals skilled in the use of Schedule II opioids may prescribe this drug product.

Abstral is available only through a Risk Evaluation and Mitigation Strategy (REMS) program, which allows appropriate prescriptions to be filled at retail pharmacies and provides access to the drug within hospitals.

Source: FDA, January 7, 2011

Viibryd for Major Depressive Disorder

Vilazodone HCl tablets (Viibryd, PGx Health) have been approved for adults with major depressive disorder (MDD), also called major depression.

Adverse reactions to the medication in clinical trials included diarrhea, nausea, vomiting, and insomnia.

A boxed warning and a patient medication guide are included. The warning describes an increased risk of suicidal thinking and behavior in children, adolescents, and young adults ages 18 to 24 during initial treatment. However, this risk is not increased in adults older than 24 years of age; patients 65 years of age and older who take antidepressants have a decreased risk of suicidal thinking and behavior. The warning also states that depression and other psychiatric disorders themselves are the most important causes of suicide and that close monitoring of patients starting these agents is necessary.

The drug will be sold as 10-, 20- and 40-mg tablets.

Source: FDA, January 21, 2011

Natroba Head Lice Treatment

The FDA has approved spinosad (Natroba, ParaPro) Topical Suspension 0.9% for the treatment of head lice infestation in patients four years of age and older.

This topical drug product should be applied only to the child’s scalp or hair and should be used exactly as prescribed.

The safety and effectiveness of the suspension 0.9% were established in two randomized, active-controlled studies. A
total of 552 subjects received a 10-minute treatment; if live lice were seen a week later, a second treatment was applied. Approximately 86% of subjects were lice-free 14 days after the final treatment, compared with 44% of controls. Adverse events include redness or irritation of the eyes and skin.

This product should not be used in infants. Systemic exposure to benzyl alcohol, one of the ingredients, has been associated with serious adverse reactions and death in neonates and low-birth-weight infants.

Source: FDA, January 18, 2011

**Generic Xodol for Pain**

Boca Pharmacal, Inc. has announced the FDA's approval and launch of hydrocodone bitartrate and acetaminophen 5 mg/300mg, 7.5 mg/300 mg, and 10 mg/300 mg. A generic version of Victory Pharma's Xodol, this agent is indicated for the relief of moderate to moderately severe pain.

Source: Boca Pharmacal, January 27, 2011

**NEW INDICATION**

**Gardasil to Prevent Anal Cancer**

The FDA has approved Merck’s Gardasil vaccine for the prevention of anal cancer and associated precancerous lesions caused by human papillomavirus (HPV) types 6, 11, 16, and 18 in males and females 9 through 26 years of age.

Gardasil is already approved for the prevention of genital warts caused by HPV types 6, 11, 16, and 18 in females. It is also approved for the prevention of oral warts caused by HPV types 6, 11, 16, and 18 in males.

Although anal cancer is uncommon, the incidence is increasing. HPV is associated with approximately 90% of cases of anal cancer.

Gardasil does not prevent the development of anal precancerous lesions associated with HPV infections that already exist at the time of vaccination. The potential benefit is greatest for those who are inoculated before becoming infected with HPV strains contained in the vaccine. Individuals who are screened for anal cancer should not discontinue screening after receiving the vaccine.

The Pharmaceutical Approval Update column on page 104 discusses this new indication.

Source: FDA, December 22, 2010

**NEW FORMULATION**

**Atelvia for Osteoporosis**

Warner Chilcott has announced the FDA's approval of risedronate sodium delayed-release tablets (Atelvia) for the treatment of postmenopausal osteoporosis. This bisphosphonate is a delayed-release formulation of Actonel. The immediate-release form of Actonel is approved for the prevention and treatment of postmenopausal osteoporosis and glucocorticoid-induced osteoporosis (in men and women) to increase bone mass in men and for the treatment of Paget's disease of bone.

Atelvia can be taken immediately after breakfast, allowing patients to follow their morning routines. The new enteric-coated formulation may be more convenient than current oral bisphosphonates. Until now, patients had to wait 30 to 60 minutes after taking Actonel to eat or drink (except water) to ensure the drug's maximum absorption. Many patients are not compliant with these dosing instructions. As a result, bisphosphate absorption is reduced and efficacy is impaired.

The efficacy of Atelvia 35 mg once weekly was shown in a randomized, double-blind, active-controlled trial of approximately 900 patients. Atelvia 35 mg once weekly, taken right after breakfast, was shown to be non-inferior to Actonel 5 mg daily in increasing lumbar spine bone mineral density.


**DRUG NEWS**

**Drug Shortage Grew in 2010**

By December 2010, the U.S. was facing an unprecedented shortage of medications used in cancer treatments, emergency departments, and surgery. Company mergers, unpredictable manufacturing problems, and economic pressures were said to have reduced the supply. In some instances, patients have died because of a lack of the first-tier drug.

A shortage of sedatives used in executions of prisoners has also forced some states to delay the procedure. In January 2011, Hospira announced that it would stop making sodium thiopental. Hospira is the only maker of this drug, which is used in lethal injections.

For the past 12 to 18 months, there have been dire shortages of intravenous (IV) furosemide (Lasix), cisatracurium (Nimbex), chemotherapy drugs, and even morphine and propofol (Diprivan).

Many of the shortages involve generic drugs, which generate less profit than brand-name drugs. The concern is that the shortages are affecting patient safety. Because of industry consolidation, fewer manufacturers are developing these agents. In May 2010, Teva announced that it would stop making sodium thiopental. Hospira announced a shortage of propofol, because it produces little or no profit.

Although the FDA cannot order drug companies to make more drugs, the companies could be encouraged to inform the FDA earlier if a shortage is anticipated so that the agency can alert health care professionals.

New Acetaminophen Limits in Pain Drugs

The FDA is asking manufacturers of prescription combination products that contain acetaminophen to limit the amount of the ingredient to no more than 325 mg in each tablet or capsule. Manufacturers will also be required to add a boxed warning regarding a potential risk for severe liver injury.

Vicodin (Abbott), which contains hydrocodone, and Percocet (Endo), which contains oxycodone, will have limits on acetaminophen content to reduce liver injuries from overdoses. Endo’s version of Percocet with 325 mg of acetaminophen is the most popular strength.

The changes fall short of an advisory panel’s recommendations in June 2009 to ban the prescription combinations and to limit acetaminophen doses in non-prescription drugs. Many patients aren’t aware that the prescription drugs they are taking contain acetaminophen, often abbreviated as APAP on the label.

The FDA is still considering revising rules for over-the-counter cold and pain drugs (e.g., Tylenol, Johnson & Johnson), which usually limit acetaminophen to 500 mg. Extended-release formulations may contain a higher amount.

Acetaminophen was the leading cause of acute liver failure in the U.S. from 1998 to 2003, and almost 50% of cases resulted from an accidental overdose. Many deaths, hospitalizations, and emergency department visits were tied to acetaminophen overdoses each year from 1990 to 1998, according to the FDA.


Autism Vaccine Study Found to Be Fraudulent

The first study to link a childhood vaccine to autism has been widely discredited. It was discovered that a 1998 article by Andrew Wakefield and colleagues was based on false information about the children involved. The article’s conclusions were renounced by 10 of its 13 authors, and the paper was later retracted by the publisher of The Lancet.

A book by Dr. Wakefield (Callous Disregard) also claimed that the medical establishment had ignored the connection between vaccines and autism. The idea that the measles–mumps–rubella (MMR) injection was related to autism frightened parents throughout the world; MMR immunization rates declined and have not yet fully recovered.

Dr. Brian Deer, a British journalist, revealed that Dr. Wakefield and his co-authors had altered facts about their study patients. Although the authors had claimed that the 12 children in their study were normal until they received the MMR vaccine, Mr. Deer discovered that five subjects had already been found to have developmental problems.

In May 2010, Dr. Wakefield lost the right to practice medicine in Britain. Many other studies have shown no connection between the MMR vaccine and autism.

Sources: BMJ (online); Associated Press, January 6, 2011; The Philadelphia Inquirer, January 7, 2011

Avastin Disappointment: Heart Failure In Breast Cancer Patients

Patients with advanced breast cancer who were treated with bevacizumab (Avastin, Genentech), a promising agent in colon cancer, had a fourfold greater risk of congestive heart failure (CHF) compared with placebo treatment. However, the overall risk of CHF was low.

In a meta-analysis involving almost 3,800 patients, those receiving bevacizumab had a 1.6% incidence of high-grade CHF compared with a 0.4% incidence in controls (i.e., a significant relative risk of 4.74). The risk was similar with both low and high doses of bevacizumab.

In December 2010, the FDA began the process of revoking the drug’s accelerated approval status for breast cancer because a review failed to show a survival benefit in those patients.

As an inhibitor of vascular endothelial growth factor (VEGF), bevacizumab carries a risk of adverse cardiovascular effects (e.g., hypertension, proteinuria, thromboembolism). Inhibition of the VEGF pathway is also thought to disrupt cardiac remodeling and to lead to heart failure.

The authors said that asymptomatic cardiac dysfunction can progress to asymptomatic heart failure at a rate of 9.7% per year, with a three-year mortality rate of 16% for those not receiving medical treatment.
Bevacizumab’s association with CHF is not new. The drug’s prescribing information states that the incidence of serious CHF was increased in patients with metastatic breast cancer who received bevacizumab plus paclitaxel (Taxol, Bristol-Myers Squibb), compared with those who received paclitaxel alone (2.2% vs. 0.3%).

Because the evidence is insufficient to state that bevacizumab is associated with an increased risk of heart failure, randomized, prospective trials are needed to determine the magnitude of the risk.

Sources: J Clin Oncol, January 4, 2011; MedPage Today, January 5, 2011; FDA, December 16, 2010

**Diabetes Drugs And Pancreatitis**

Patients with type-2 diabetes may have a higher risk of acute pancreatitis, depending on which medication is used.

A cohort analysis, performed by researchers in Madrid, Spain, and by Novartis in Basel, Switzerland, revealed a statistically significant 77% annual increased risk of acute pancreatitis, or about 23 additional cases for every 100,000 patients with diabetes. However, after adjusting for lifestyle and other variables, the study authors indicated that the risk was reduced to borderline significance.

The study documented 176 cases of acute pancreatitis among 85,525 patients with type-2 diabetes and 243 cases among 200,000 people without diabetes, for an incidence rate of 54 and 30 cases per 100,000 person-years, respectively. Patients with type-2 diabetes also had a 79% increased risk of a first episode of acute pancreatitis.

Metformin (Glucophage, Bristol-Myers Squibb) and sulfonylureas were the most commonly prescribed drugs, followed by insulin. Of the patients with diabetes, 73% were receiving antidiabetic drugs.

Insulin and the long-term use of metformin were associated with a lower risk of pancreatitis, but the long-term use of sulfonylureas seemed to increase the risk. Thiazolidinediones were not associated with acute pancreatitis, although the number of patients who were using them was smaller.

Overall, when the researchers separately analyzed the risk of pancreatitis among treated and untreated patients, they observed that patients not using drug therapy (25% of the study population) had the highest risk. These findings might be a result of the slightly increased risk of acute pancreatitis immediately after a diagnosis of diabetes.

This seems to be the first study suggesting a reduced risk of pancreatitis associated with insulin and metformin. However, it would be premature to suggest potential mechanisms before the findings are replicated.

Source: Diabetes Care 2010;33:2580–2585

**Ondansetron (Zofran) Goes Well With Tramadol (Ultram)**

The aftermath of anesthesia often includes nausea and vomiting. The commonly used analgesic tramadol (Ultram, Ortho-McNeil) tends to be blamed, especially if large doses are injected quickly. Some studies have suggested that ondansetron (Zofran, GlaxoSmithKline) reduces the tramadol-associated effects, but other reports have raised concerns that the combination of ondansetron and tramadol increases emesis and ondansetron failure. The fact that both drugs act on the serotonin (5-hydroxytryptamine) pathway is a possible explanation.

Researchers from Switzerland and Germany found that giving the drugs together did not increase postoperative analgesia consumption or the frequency of emesis. In their study, 179 patients who had undergone major surgery received intravenous (IV) ondansetron, metoclopramide (Reglan, Schwarz), or placebo to prevent emesis. The regimen consisted of intraoperative tramadol load-
Donepezil (Aricept) Benefits Early Alzheimer’s Disease

Donepezil (Aricept, Eisai, Pfizer) may be most beneficial when therapy begins early in the course of Alzheimer’s disease (AD), according to a study from Spain.

The six-month prospective, observational multicenter study involved 403 patients with mild and moderate AD, defined according to baseline Mini-Mental State Examination (MMSE) scores. All patients were evaluated at baseline and six months later.

After six months of monotherapy with donepezil 9.3 mg/day, the patients remained stable overall cognition. Patients with mild AD obtained greater benefits compared with those with moderate AD. The sample as a whole showed significant score increments in memory at six months, probably a result of the increase in mean scores of the mild AD group. By contrast, scores in the group with moderate AD dropped, resulting in a statistically significant difference between the two groups.

There was also a significant difference in orientation and language. Scores rose in the mild AD group but declined in the moderate AD group.

Scores in memory alterations also remained stable, although scores of free and cued recall domains improved significantly. The two groups also differed in temporal orientation and semantic memory, which worsened in the moderate AD patients and improved in the mild AD group.

Scores on the AD Functional Assessment and Change Scale worsened from baseline in the sample as a whole and in each severity group; however, a greater decline was seen in activities of daily living scores in patients with moderate AD.

Although MMSE scores remained stable, the result in this study was not as good as that observed in an earlier Spanish study with donepezil. In that study, MMSE scores improved significantly over baseline. However, more than 60% of those patients were in mild stages, compared with 37% of the patients in the more recent study.

Because of the study’s short duration, the researchers caution that their results should be considered preliminary. They recommend replication with a longer follow-up period.

Nonetheless, they urge making efforts to improve diagnosis in order to identify patients who should receive treatment as early as possible.

Source: Arch Gerontol Geriatr 2011;52:18–22

Some Antibiotics and Hypertension Drugs Don’t Mix

Older adults taking calcium-channel blockers (CCBs) could experience dangerous drops in blood pressure (BP) if they are also taking certain antibiotics. Patients who took CCBs and erythromycin (e.g., E-Mycin) or clarithromycin (Biaxin) were at increased risk of being hospitalized for severe hypotension. Erythromycin and clarithromycin inhibit an enzyme vital to metabolizing CCBs.

A third antibiotic—azithromycin (Zithromax)—was not related to the risk. Azithromycin appears to be the better choice than the other two antibiotics for patients taking CCBs; it does not block the same enzyme. These three agents are macrolides, the most widely prescribed class of antibiotics worldwide.

CCBs are used as long-term medications for hypertension. Examples include amlodipine (Norvasc), felodipine (Plendil), nifedipine (Procardia and Adalat) and diltiazem (Cardizem, Dilacor, and Tiazac).

In a recent study, Dr. David Juurlink and colleagues looked at medical records for more than 999,000 Ontario residents 66 years of age and older who were taking CCBs between 1994 and 2009. During that time, 7,100 patients were hospitalized for severe drops in BP. Of those patients, 131 had been using a macrolide in the week before hospital admission. Erythromycin was linked to a six-fold increase in the risk of hospitalization for low BP; clarithromycin was tied to a nearly four-fold increase.

The team concluded that if a patient needing a macrolide antibiotic is also taking a CCB, it would be best to prescribe azithromycin. Angiotensin-converting enzyme (ACE) inhibitors and beta blockers do not seem to be susceptible to the effects of the two antibiotics.

Older patients are vulnerable to the consequences of severe hypotension. They could become dizzy enough to fall; low BP can also deprive organs of blood and oxygen, leading to shock. Although younger people can usually tolerate a drop in BP, azithromycin would also be the preferred choice for them if they were taking a CCB.

Erythromycin and clarithromycin can elevate blood levels of statins, raising a concern about the risk of muscle dam-
age. It would be wise for people taking statins to take azithromycin instead of the other two macrolides.

Sources: Can Med Assoc J, online/Reuters Health January 17, 2011

Cochrane Reviews
TXA Helps Stop Bleeding In Trauma Patients
A drug used to treat heavy menstrual periods—trianexamic acid (TXA)—might be able to save the lives of many bleeding accident victims and reduce combat deaths, say Cochrane researchers.

TXA (e.g., Lysteda, Ferring) is an inexpensive drug that reduces clot breakdown. It has been used for many years in women with menorrhagia and is often given during planned surgery to reduce the need for blood transfusions.

More recently, TXA has been tested in trauma patients. Of such patients who die in the hospital, nearly half die because of excessive blood loss; most others die from injuries that are worsened by bleeding.

In a new review, TXA reduced the risk of death in injured patients with severe bleeding by about 10%, compared with no treatment. It is estimated that more than 70,000 lives worldwide could be saved each year with TXA. The results were based on one trial involving 20,211 patients and one trial of 240 patients, both carried out since an earlier, inconclusive review in 2004.

A separate Cochrane review showed that TXA effectively reduced blood loss and the need for red blood cell transfusion in patients scheduled for non-urgent surgery.


Benefits of Statins Unclear In Low-Risk Patients
Cochrane scientists warn that there is not enough evidence to recommend the widespread use of statins in people with no previous history of heart disease and that these drugs should be prescribed with caution in people at low risk of cardiovascular disease (CVD).

CVD is the most common cause of death, accounting for nearly one-third of all deaths worldwide. Cholesterol-lowering statins are first-line treatments for heart patients, and the benefits are well established. However, there is less evidence that statins can prevent heart problems in those with no history of CVD. Given that low cholesterol levels can increase the risk of death from other causes, statins may do more harm than good in some patients.

Data from 14 trials involving 34,272 patients were analyzed. Outcomes in patients given statins were compared to outcomes in patients given placebo or usual care. Combined data from eight trials involving 28,161 patients that provided data on deaths from all causes showed that statins reduced the risk of dying from nine to eight deaths for every 1,000 people treated with statins each year. Statins reduced blood cholesterol levels, heart attacks, strokes, and revascularization surgery rates.

However, the researchers say that the conclusions of their review are limited by unclear reporting and that health care professionals should carefully consider each patient’s risk profile before prescribing these drugs. Simply extrapolating the effects from studies in people with a history of heart disease is not considered sufficient, and the decision to prescribe statins in this group should not be taken lightly.

The researchers point out that all but one of the trials they reviewed were sponsored by the pharmaceutical industry. Such trials are more likely to report favorable results for drugs versus placebo, and caution is advised in interpreting the results under these circumstances.

A separate Cochrane review by the same authors considered using counselling to encourage people to change their diets and stop smoking. The authors concluded that combined interventions had little or no impact on deaths or disease caused by CVD.

Despite the existence of multiple prevention strategies, the best intervention for primary prevention in adults at low risk remains unclear.


Fatal Overdose Possible With Benzonatate (Tessalon) Capsules
The FDA is warning the public that accidental ingestion of benzonatate by children younger than 10 years of age can result in death from an overdose. Benzonatate (Tessalon, Forest) is a prescription drug approved for the relief of cough in patients older than 10 years of age. Benzonatate gelcaps are also sold in generic forms. Because it is a non-narcotic, benzonatate is not prone to abuse like other cough medications such as codeine and dextromethorphan.

In December 2010, the FDA strengthened warning labels on Tessalon and other benzonatate drugs concerning the risk of accidental ingestion. Tessalon and Tessalon Perles have a candy-like appearance and may be accidentally consumed by children. Signs and symptoms of overdose can occur within 15 to 20 minutes of ingestion.

Benzonatate is sold in 100-mg and 200-mg liquid-filled spherical capsules. The FDA approved Tessalon in 1958.

Sources: FDA, December 14, 2010; www.drugwatch.com/Tessalon

Exenatide (Byetta) Improves Uncontrolled Diabetes
In a parallel-group, placebo-controlled, randomized trial, adding the twice-daily
injectable drug exenatide (Byetta, Amylin/Eli Lilly) to treatment improved poor glycemic control in patients with uncontrolled type-2 diabetes.

Using insulin with a glucagon-like peptide (GLP-1) analogue improved efficacy in lowering glucose levels. The investigators proposed that the GLP-1 analogue could be used before insulin, especially in older patients already taking metformin (Glucophage, Bristol-Myers Squibb) because the risk of hypoglycemia was minimal. However, the high prevalence of gastrointestinal (GI) adverse effects is a concern.

The goal of the study was to determine whether exenatide would reduce glycosylated hemoglobin (HbA1c) levels more than placebo in patients receiving insulin glargine (Lantus, Sanofi-Aventis). To be enrolled, adults with type-2 diabetes had to have an HbA1c level of 7.1% to 10.5% and had to be receiving insulin glargine alone or with metformin, pioglitazone and had to be receiving insulin glargine to have an HbA1c level of 7.1% to 10.5% enrolled, adults with type-2 diabetes had to have an HbA1c level of 7.1% to 10.5% and had to be receiving insulin glargine alone or with metformin, pioglitazone (Actos, Takeda/Eli Lilly), or both.

Participants received either exenatide 10 mcg twice daily or placebo for 30 weeks. The main study endpoint was the change in HbA1c levels; secondary endpoints were the percentage of participants with HbA1c values of 7% or less and 6.5% or less, seven-point self-monitored glucose profiles, body weight, waist circumference, insulin dose, hypoglycemia, and adverse events.

Average increases in the insulin dosage were 13 U/day with exenatide and 20 U/day with placebo. Both groups had similar rates of minor hypoglycemia.

Adding exenatide to insulin glargine resulted in lower HbA1c values. As in other studies using GLP-1 analogues, blood pressure decreased modestly.

Thirteen exenatide participants and one placebo patient withdrew because of adverse events. The exenatide group had much higher rates of nausea, diarrhea, vomiting, headache, and constipation, compared with placebo patients.

Sources: Ann Intern Med online, December 6, 2010; Medscape, December 29, 2010

**Epilepsy Drugs May Raise Fracture Risk in Older Adults**

In a Canadian study, medications indicated for epilepsy increased the risk of bone fractures in elderly patients. Researchers analyzed the medical records of 15,792 people 50 years of age and older who had non-traumatic fractures between 1996 and 2004. Each person was matched with up to three people who had never had a fracture. A total of 47,289 people served as controls.

The researchers also looked at the participants’ use of epilepsy drugs, including carbamazepine (Carbatrol, Tegretol), clonazepam (Klonopin), ethosuximide (Zarontin), gabapentin (Neurontin), phenobarbital (Luminal), phenytoin (Dilantin), and valproic acid (Depakene, Depakote).

All but one of the drugs (valproic acid) was associated with an increased risk for fractures. Phenytoin and carbamazepine were associated with the highest risk.

The results were similar for people taking just one epilepsy drug and for those taking more than one.


**Tekamlo Lowers BP More Than Monotherapy**

Combining two drugs for the initial reduction of blood pressure (BP) above 150 mm Hg may be more effective than monotherapy alone, according to the ACCELERATE study.

Researchers from the United Kingdom conducted a double-blind, randomized trial of 1,247 patients at 146 primary and secondary care sites in 10 countries between November 28, 2008, and July 29, 2010. The goal was to assess whether a combination of aliskiren (Tekturna, Novartis) and amlodipine (Norvasc, Pfizer) was more effective than either drug alone. Tekamlo (Novartis) combines the two agents.

The researchers randomly assigned patients, in a 1:1:2 ratio, to receive 150 mg of aliskiren plus placebo (315 patients), 5 mg of amlodipine and placebo (315 patients), or 150 mg of aliskiren with 5 mg of amlodipine (617 patients). All enrolled patients had a systolic BP between 150 and 180 mm Hg and a diastolic BP below 110 mm Hg. Patients receiving Tekamlo had a 6.5 mm Hg greater reduction in mean systolic BP (~25.3 mm Hg) compared with the monotherapy groups (~18.9 mm Hg).

ACCELERATE is the first study to test the medium-term efficacy and safety of the two antihypertensive drugs as a first-line treatment for patients with a systolic BP of more than 150 mm Hg.

Sources: The Lancet, January 12, 2011; TriMed Media Group, Inc.

**Chickenpox Vaccine: Two Doses Are Best**

Children may be less likely to get chickenpox if they receive two doses of the chickenpox vaccine instead of just one, according to a study from Yale University. Routine vaccination does not always offer 100% protection; the vaccine might not work the first time, or its effects can wear off.

In 2006, the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics recommended a second dose of the vaccine for children four to six years of age. The first dose is typically given at 12 to 18 months of age.

Despite the effectiveness of one dose of the vaccine, outbreaks occurred. Dr. Eugene Shapiro and colleagues tested the effectiveness of adding the second dose. Starting right after the CDC up-
dated its recommendation through the beginning of 2010, they found 71 infected children four years of age and older from local pediatricians’ offices. For each child, the researchers found two other children who were the same age and whose pediatricians were from the same practice. Then they reviewed their medical records for vaccinations. Of the 71 patients with chickenpox, none of them had received two doses of the vaccine; 66 children had received one dose, and five had received no vaccinations.

Of the 140 children who had never had chickenpox, 22 of them had been vaccinated twice and 117 had been vaccinated once. Only one had never received the vaccine. Based on those findings, the authors calculated that one dose of the vaccine protected 86% of the children, whereas two doses were 98% effective.

For most children, one dose may be enough, but a second dose may be needed to stop the breakthrough cases.

According to the CDC, side effects are more common after the first dose of the vaccine than after the second dose.

The researchers would like to find a natural or dietary agent to deplete the CYP 1B1 enzyme to prevent oral cancer at the precancerous stage. Previous studies had revealed that the CYP 1B1 enzyme sits at the hub of changes that occur in the lungs after smoke exposure. The study found that cells lacking the isoenzyme moved more slowly.

Patients with head and neck cancer are at risk of developing a second primary tumor. Finding a way to reduce subsequent tumors could improve survival. These results may help researchers understand the factors that cause head and neck cancer in addition to the traditional risk factors of tobacco and alcohol exposure. However, because the results are limited to a single premalignant cell line, further studies are needed to validate these findings in humans.


**NEW DRUGS**

**Potato-Based Drug (Immunomax) Fights HPV, Other Conditions**

Immunomax, a novel immunostimulant manufactured from potato sprouts, may bring relief to patients with human papillomavirus (HPV) infections, prostatitis, prostate carcinoma, and other urogenital disorders.

In a study from Moscow, 30 patients being treated for recurrent anogenital warts caused by HPV received six intramuscular (IM) injections of Immunomax (200 U in 20 patients or 100 U in 10 patients) over a period of 10 days. A dermatologist/venereologist examined each patient before the trial, three times during the treatment, immediately after the treatment course, and three months after the end of treatment. At three months, 26 patients (87%) were completely cured, as judged by clinical etiological characteristics. All patients reported that the itching, burning, and other symptoms of inflammation had disappeared. Six patients still had a slight discomfort. Small warts (0.1–0.3 cm) typically disappeared within two to four days after the first injection; large warts were removed simultaneously with Immunomax treatment.

Three months after therapy, anogenital warts reappeared in only four patients. Eight of the 10 patients who received single doses of 100 U were clinically cured of recurrent anogenital warts, similar to the number of cures obtained with single doses of 200 U.

Monotherapy with Immunomax also led to the disappearance of some associated infections: herpes simplex type-2 virus, *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Trichomonas vaginalis*, and *Candida albicans*.

In patients with prostate carcinoma, treatment also produced good results.

Immunomax can also be used to treat purulent surgical processes. Daily injections can speed healing, thereby reducing the need for antibacterial drugs and preventing the formation of rough scars.

Source: *J Men’s Health*, December 2010;7:396–405

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**RESEARCH NEWS**

**Estrogen May Promote Spread of Oral Cancer**

Head and neck cancer is the sixth most common type of malignancy, accounting for 650,000 new cases each year. It is on the rise in some demographic groups, including young women without any known risk factors. Researchers at Fox Chase Cancer Center in Philadelphia report that estrogen may increase the movement of precancerous cells in the mouth and thus promote the spread of the disease within the oral cavity.

It has been recognized that the metabolism of the female hormone changes following smoke exposure in the lungs and may contribute to lung cancer. To learn whether estrogen influences the development of head and neck cancer, the Fox Chase team examined the impact of estrogen on precancerous and cancerous cells. They found that estrogen induced the expression of cytochrome P450 1B1 (CYP 1B1), which is responsible for breaking down toxins and metabolizing estrogen. CYP 1B1 induction, notably, occurred only in precancerous cells, which are neither totally normal nor cancerous. Surprisingly, estrogen did not induce CYP 1B1 in cancer cells.

Depleting the expression of CYP 1B1 diminished the ability of precancerous cells to move and divide, compared with similar cells having normal levels of CYP 1B1. Estrogen also reduced cell death in the precancerous cells, irrespective of the amount of CYP 1B1 present.

The researchers would like to find a natural or dietary agent to deplete the CYP 1B1 enzyme to prevent oral cancer at the precancerous stage. Previous studies had revealed that the CYP 1B1 enzyme sits at the hub of changes that occur in the lungs after smoke exposure. The study found that cells lacking the isoenzyme moved more slowly.

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Patients with head and neck cancer are at risk of developing a second primary tumor. Finding a way to reduce subsequent tumors could improve survival. These results may help researchers understand the factors that cause head and neck cancer in addition to the traditional risk factors of tobacco and alcohol exposure. However, because the results are limited to a single premalignant cell line, further studies are needed to validate these findings in humans.


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**NEW DRUGS**

**Potato-Based Drug (Immunomax) Fights HPV, Other Conditions**

Immunomax, a novel immunostimulant manufactured from potato sprouts, may bring relief to patients with human papillomavirus (HPV) infections, prostatitis, prostate carcinoma, and other urogenital disorders.

In a study from Moscow, 30 patients being treated for recurrent anogenital warts caused by HPV received six intramuscular (IM) injections of Immunomax (200 U in 20 patients or 100 U in 10 patients) over a period of 10 days. A dermatologist/venereologist examined each patient before the trial, three times during the treatment, immediately after the treatment course, and three months after the end of treatment. At three months, 26 patients (87%) were completely cured, as judged by clinical etiological characteristics. All patients reported that the itching, burning, and other symptoms of inflammation had disappeared. Six patients still had a slight discomfort. Small warts (0.1–0.3 cm) typically disappeared within two to four days after the first injection; large warts were removed simultaneously with Immunomax treatment.

Three months after therapy, anogenital warts reappeared in only four patients. Eight of the 10 patients who received single doses of 100 U were clinically cured of recurrent anogenital warts, similar to the number of cures obtained with single doses of 200 U.

Monotherapy with Immunomax also led to the disappearance of some associated infections: herpes simplex type-2 virus, *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Trichomonas vaginalis*, and *Candida albicans*.

In patients with prostate carcinoma, treatment also produced good results.

Immunomax can also be used to treat purulent surgical processes. Daily injections can speed healing, thereby reducing the need for antibacterial drugs and preventing the formation of rough scars.

Source: *J Men’s Health*, December 2010;7:396–405
DEVICES IN THE NEWS

Recalls

Glucose Test Strips. The FDA and Abbott Diabetes Care are recalling 359 different lots of glucose test strips (Precision Xceed Pro, Precision Xtra, Medisense Optium, Optium, OptiumEZ, and ReлиOn Ultima). The strips are used with Abbott’s Precision Xtra, Precision Xceed Pro, Medisense Optium, Optium, Optium EZ, and ReлиOn Ultima blood glucose-monitoring systems.

The strips may give falsely low blood glucose results because they were unable to absorb enough blood for monitoring, possibly because of exposure to warm weather or prolonged storage. The affected strips were manufactured between January and September 2010.

Patients who purchased test strips in retail stores or online may call the company for a free replacement. A different test system should be used to measure blood glucose, or two weeks’ worth of new strips can be purchased in the meantime. If the only test strips available to patients are from affected lots, they should not stop testing their blood glucose, but they should check the amount of time it takes for the meter to start the countdown after blood is first applied to the strip. If the meter takes longer than five seconds to start the countdown, the test strip is defective. If a reading appears lower than normally expected, patients should contact their health care provider.

Source: FDA, December 21, 2010

Unqualified Patients Are Receiving Heart Devices

Many people are receiving implantable heart defibrillators who should not be, resulting in higher costs and risks of complications. As many as 23% of implantable cardioverter defibrillators (ICDs) have been placed in people who did not meet treatment guidelines, said Dr. Sana Al-Khatib of the Duke Clinical Research Institute.

ICDs can restore normal heartbeats, protecting patients from sudden cardiac death, but they are not intended for those who have had a recent heart attack, are recovering from heart bypass surgery, or have severe heart failure.

For the study, Dr. Al-Khatib and colleagues looked only at ICDs used to prevent sudden cardiac death, not at costly devices that include a pacemaker. They found that of more than 111,000 ICDs used between 2006 and 2009, 23% were implanted in patients considered unsuitable candidates because of a recent heart attack or newly diagnosed heart failure. Recipients who did not meet evidence-based criteria were more likely to die or develop a complication that prolonged their hospital stay.

Some hospitals were also more likely than others to follow guidelines. Electrophysiologists, who insert ICDs and pacemakers, tended to follow treatment guidelines more than other doctors who implant the devices.

ICDs cost approximately $20,000 per implant. It remains to be seen whether these findings will hurt sales.


NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

Name: PleuraFlow Active Tube Clearance System

Manufacturer: Clear Catheter Systems, Inc., Bend, Ore.

Approval Date: December 14, 2010

Purpose: PleuraFlow prevents the clogging of chest tubes with blood after heart and lung surgery.

Description: Magnets and a wire loop keep catheters clear and sterile. The system is inserted between the chest tube and the drainage tubing. A guide wire dislodges clots and pulls them toward the drainage system. The wire is advanced and retracted by a magnetic drive that wraps around the outside of the tubing.

Benefit: PleuraFlow minimizes the risks of surgery, avoids complications, and reduces the cost of postoperative care. A tube-clearance system allows a chest tube to be maintained in the postoperative period.

Sources: www.pleuraflow.com; www.pmpnews.com

Name: Arctic Front Cardiac Cryoablation Catheter System

Manufacturer: Medtronic, Inc., Minneapolis, Minn.

Approval Date: December 20, 2010

Purpose: This is the first cryoablation balloon catheter used to treat refractory paroxysmal atrial fibrillation (AF).

Description: Coolant is delivered via the catheter to freeze and kill cells near the entrance to the pulmonary vein, the source of erratic electric signals that cause the abnormal heartbeat in AF.

Benefit: Balloon catheters are considered more efficient and less invasive than other catheters. They can ablate an arc of tissue in one step instead of ablating multiple isolated spots in the pulmonary vein.
with the tip of a radiofrequency catheter. Most ablation catheters deliver radiofrequency heat to destroy cells; the Arctic Front system uses coolant, which enhances catheter stability.

In the STOP–AF (Sustained Treatment Of Paroxysmal Atrial Fibrillation) trial, cryoablation with the balloon catheter left 70% of patients free of AF without the need for further interventions or a new antiarrhythmic drug at one year, compared with 7% of patients who received medical therapy alone ($P < 0.001$).

**Sources:** www.medpagetoday.com; www.dotmed.com; www.news-medical.net

**Name:** Endurant AAA Stent Graft System

**Manufacturer:** Medtrons Inc., Minneapolis, Minn.

**Approval Date:** December 21, 2010

**Purpose:** This system is used to treat infrarenal abdominal aortic aneurysms (AAAs) or aorto-iliac aneurysms.

**Description:** The stent graft is inserted into the body through a catheter. With an endovascular approach, the device can prevent sacs of blood from bursting in the body’s midsection by expanding the walls of the artery and relieving pressure on the bulge. Delivered via catheters inserted into blood vessels in the groin, the Endurant graft conforms to various aortic anatomies, enabling endovascular aortic repair in more patients with AAAs than previously. The flexible wire frame (stent) is sewn onto a woven fabric tube (graft) that is used to create a new path for blood flow in the patient’s aorta, decreasing pressure on the aneurysm and lowering the risk of rupture.

**Benefit:** This device enables precise positioning and ease of access, as well as the safe treatment for patients who might have otherwise been ineligible for endovascular repair.

**Sources:** www.medtronic.com; www.thestreet.com