

■ Adverse Drug Events proliferate

A study to measure the occurrence and preventability of Adverse Drug Events (ADEs) in the July 5, 1995 issue of the *Journal of the American Medical Association* found that slightly more than 6% of adults admitted to the study hospitals surgical units suffered from an ADE of some kind.

Reported incidents were classified by two independent reviewers as ADEs or potential ADEs as well as for severity and preventability

Over a six month period, the study found that out of 4,031 patients admitted, 247 of them experienced ADEs and 194 of the cases were identified as potential ADEs..

1% of the cases were fatal (none preventable), 12% were life-threatening (42% preventable), 30% were serious (also 42% preventable) and 57% were significant. (28% preventable).

Mistakes that resulted in ADEs happened most often when ordering the drug, 56% and giving the drug, 34%. Transcription and dispensing errors made up the remaining 10%.

Reviewing statistics for 1995 reveals ADEs cause:

- \$76.6 billion in medical bills.
- 106,000 – 199,000 deaths.
- 8.8 million hospitalizations.

Statistical data reveals:

- Fatalities due to adverse reactions are greater than those of high-risk sexual behavior, firearms, and motor vehicle injuries – combined.
- Medication errors are the second most frequent and second most expensive malpractice claim.
- Most complications are dose-dependent. Therefore, 70-80 percent of these complications are predictable and preventable. ▲

■ Breast cancer prevention drug increases chances of uterine cancer

Much fuss has been made over a recent study that showed the drug tamoxifen acts to prevent breast cancer. However, a new report issued by the Food and Drug Administration indicates that users of the drug developed uterine cancer at a rate almost twice the norm of non-users.

The FDA report did not go along with the notion that tamoxifen actually prevents breast cancer, only that it **might** help reduce the risk short term. Two studies conducted in Europe and published this summer found **no preventative benefits at all**.

Of grave concern, however, was the fact that women who took tamoxifen developed uterine cancer at twice the rate of those who didn't. Three women in the study died from blood clots that most likely developed from the medication. ▲

■ Steroid therapy continues despite known dangers

The July 15, 1998 issue of the *Journal of Clinical Investigation*, reports that medical doctors continue to prescribe prolonged steroid therapy for millions of Americans despite the fact that research has proven it can lead to serious bone loss (osteoporosis) that weakens the bones.

The study was conducted at the University of Arkansas for Medical Sciences in conjunction with the Central Arkansas Veterans Healthcare System. The researchers said, "Basically, our findings revealed that when animals or humans take high doses of steroids, not only fewer bone-forming cells are made, but they are dying prematurely."

The lead author of the study, Dr. Robert Weinstein says, "Our study shows that steroid-induced osteoporosis arises from changes in the number of bone cells available to maintain bone, causing eventual fractures and, also, collapse of large joints. No bone is spared from the steroid-induced bone loss, but the effects are more dramatic in the spine and in the hip. Unlike common age-and gender-related types of osteoporosis, this form of the disease occurs at any age, even in children. Not infrequently, patients that took steroids for many years end up in a wheelchair."

The researchers pointed out that medicine has known about the long term effects of steroid use for 60 years yet continue to use them more and more often.

Why? Doctors seem to be ignorant of the dangers. Weinstein says. "A recent survey of physicians showed that most underestimated the risk of [steroid]-induced osteoporosis in men and women. Only 25% ranked osteoporosis as one of the top three side effects of high-dose [steroid] therapy in a 45 year-old premenopausal woman and 8% ranked it as one of the top three side effects in a 45 year-old man." ▲

■ Drug ads: good information or marketing gimmick?

The January 27, 1999 issue of the *Journal of the American Medical Association* highlights a debate between Alan Holmer, the president of the Pharmaceutical Research and Manufacturers of America and Dr. Matthew Hollon of the University of Washington in Seattle.

According to Holmer, consumer drug ads "motivate patients to learn more about medical conditions and treatment options." Responding to concerns that drug ads may lead to inappropriate, over-prescription of certain drugs, Holmer goes on to say that "The patient has been empowered with information, not prescribing authority."

Dr. Hollon disagrees and questions the accuracy of the drug ads. One study from 1989, he says, concluded that "standards of [scientific] evidence used to justify [drug] advertising claims are inadequate." A 1993 study found that "important warnings and precautions were missing in half of the 6700 [drug] advertisements surveyed."

In his argument, Dr. Hollon concludes that "for the benefit of patients, physicians, and the public's health, the US Food and Drug Administration should consider stricter – not more permissive – regulations" on the direct-to-consumer prescription drug advertising. ▲

■ Link between heart drugs and suicide

The March 7, 1998 issue of the *British Medical Journal* finds a significant correlation between suicide and the use of calcium channel blockers used to treat high blood pressure.

The study found that patients using calcium channel blockers were five times more likely to commit suicide than those not taking the drug. ▲

■ FDA to increase monitoring of new drugs

The *United States Food and Drug Administration* (FDA) announced that they will be taking steps to reduce the number of deaths caused by approved drugs and medical devices.

One of the steps is to increase surveillance of new drugs and devices after they are introduced and to better analyze the information the FDA collects about adverse reactions. Most drugs are tested on fairly small groups of people and a lot of the problems do not appear until they have been tried out on larger groups after they are put on the market.

Consumer groups have charged that the FDA has approved new drugs too quickly and without proper long-term testing. Studies have reported that about 100,000 people die every year from adverse drug reactions to properly prescribed medications.

FDA Commissioner Jane Henney stressed that no drugs are completely safe saying that adverse reactions can occur from known or unknown side effects, medication errors or defective products. ▲



FDA: Popular heartburn drug causes heart problems

On January 24, 2000, the United States Food and Drug Administration (FDA) issued a warning that the popular heartburn drug Propulsid should only be used as a last resort—and then only after the patient has had an EKG to rule out heart problems.

The warning comes after 70 deaths and 200 reports of irregular heartbeat and other heart disturbances since Propulsid was introduced in 1993.

The FDA warning says that patients should not be given Propulsid if they have: heart disease, valve disease, any history of an irregular heartbeat, abnormal EKG, kidney disease, lung disease, low blood levels of potassium, calcium or magnesium, eating disorders, dehydration or prolonged vomiting.

Propulsid should not be taken with antibiotics, antifungals, drugs for irregular heartbeat, protease inhibitors (taken for AIDS), antidepressants, antipsychotics or grapefruit juice.

■ Doctors still using dangerous acne drug despite warnings

The January 21, 2000 issue of the Morbidity and Mortality Weekly Report from the Centers for Disease Control and Prevention (CDC) says that despite numerous warnings for more than a decade, dermatologists are still prescribing the drug Accutane to women of childbearing age; a practice that has led to severe birth defects in the babies of women using the drug.

The United States Food and Drug Administration (FDA) has approved Accutane for use in patients with severe, disfiguring acne that do not respond to other forms of treatment. In 1988, the maker of Accutane began informing doctors that the drug should not be used in women of childbearing age because of the likelihood of severe birth defects in their children. Inserts with the drug also clearly warn women of the dangers.

The report faulted doctors for not only using the drug in women of child-bearing age but also in women who do not have the severe, disfiguring acne that the drug is approved for. One woman in the study, who ended a pregnancy due to her fears about the drug, was given the drug to prevent menstruation-related monthly acne.

The CDC recommends that doctors fully inform female patients of the risks and precautions associated with Accutane use.

■ Prozac: Drug producer hides suicidal reactions

The May 9, 2000 edition of the *Boston Globe* reports that Eli Lilly and Co. has known for years that Prozac, its best selling drug on the market could cause suicidal reactions in a significant number of patients. Although Lilly has downplayed the danger in the past, the patent for a "new" Prozac promises that the new version will not produce "its more significant side effects," suicidal thoughts and self mutilation.

A review of the company's internal documents, government applications and patents made some interesting findings:

–In 1990, Lilly scientists were pressured by Lilly executives to alter records on physician experiences with Prozac. Mentions of suicide attempts were changed to "overdose" and suicidal thoughts to "depression."

–The German equivalent of the US FDA refused to approve Prozac because Lilly's own studies showed that previously non-suicidal patients who took Prozac were five times more likely to attempt or commit suicide than those on older anti-depressants and three times more likely than those taking placebos.

Lilly has long maintained that an insignificant number of people who take Prozac have attempted or committed suicide and has been very active in trying to discredit researchers who continually prove them wrong.

Dr. David Healy, director of the North Wales Department of Psychological Medicine at the University of Wales is an expert on the brain's serotonin system that Prozac affects. Using his and Lilly's own research he estimates that "probably 50,000 people have committed suicide on Prozac since its launch, over and above the number who would have done so if left untreated."

By way of commentary, 50,000 people (a number Lilly sees as insignificant) are dead over the years as a direct result of using Prozac and the company is still selling it? World-wide last year (1999) Eli Lilly & Co. earned \$10 billion in revenue. Prozac was responsible for more than 25% of that income.

■ Diabetes drug withdrawn from market

The United States Food and Drug Administration (FDA) has requested that the diabetes drug troglitazone, sold under the brand name Rezulin, be withdrawn from the market. The drug has been linked to 63 deaths and 90 confirmed cases of liver failure since entering the market in mid-1997.

Public Citizen, a Washington, DC consumer advocacy group has urged the FDA to conduct a criminal investigation of the maker of Rezulin, Warner-Lambert. Public Citizen says that the company failed to notify the FDA within the 15 day limit required by law when studies showed the drug resulted in liver toxicity. The group says that Warner-Lambert did not inform the FDA of the studies until after the drug was approved for sale.

Rezulin generated Warner-Lambert revenues of \$625 million in 1997 and \$748 million in 1998.

■ Prilosec raises cancer fears

The August, 2000 issue of *Gastroenterology* brings an item that expresses concern that the drug Prilosec, commonly used for acid reflux, may well set up conditions in the stomach that may lead to the patient developing gastric cancer.

Acid reflux is a condition where stomach acid leaks back up into the esophagus through a malfunctioning stomach valve between the stomach and esophagus. Prilosec (generic name omeprazole) is in a class of drugs that are called proton pump inhibiting drugs (PPIs) that turn off the acid producing cells in the stomach.

Researcher Craig Mowat, M.D. says patients who took Prilosec developed "both the altered [internal stomach environment] associated with gastric cancer and the inflamed mucosa. The potential long-term adverse effects of this combination are of considerable concern."



The Drug Report

Various sources report that there's been lots of problems in the world of pharmaceuticals this month. Let's look at a few of the many reports.

The Associated Press reports on November 28, 2000 that the popular drug Lotronex, used for women with irritable bowel syndrome, has been pulled from the market after it was linked with severe side effects ranging from ischemic colitis (an irritable, life-threatening intestinal inflammation) and constipation so severe that many patients had to have portions of their intestines surgically removed. The FDA is aware of 8 deaths and 124 hospitalizations of patients who had been taking Lotronex.

Reuters Health reported on December 14, 2000 that an outbreak of polio, the first in the Western Hemisphere since 1991, appears to be a result of the polio virus used in the oral polio vaccine itself. The virus apparently mutated into a virulent form after it was given to people who had been vaccinated.

The following reports are from the *Alternative Medicine Newsletter*.

The December 7, 2000 issue reports that the acne drug Accutane will receive a special warning label outlining the side effects, including a possible link to suicide in people taking the drug. Soon, patients will be required to sign a waiver stating that they understand the risks.

The move is part of an attempt to counter another problem with Accutane: It causes severe birth defects in children whose mothers are taking the drug. This is not the best of news since Accutane users include teenagers, most of whom think they are invincible, will never die or get pregnant.

The December 12, 2000 issue reports that a study done at the Institute for the Health of the Elderly at Newcastle General Study in England finds that Alzheimer patients are being prescribed drugs that could be making their symptoms worse.

The study estimates that 30,000 people every year are being given the drugs inappropriately. The authors report that the drugs, major tranquilizers, are too often "used as a substitute for good, practical care management."

By way of commentary, we have a pharmacist friend who contends "drugs are for selling, not for taking."



More Than Half Of Americans At Risk Of Drug Interactions

The January 18, 2000 issue of the *Alternative Medicine Newsletter* tells us about a disturbing survey reported by the American Society of Health-System Pharmacists (ASHP) which found that more than half of all Americans are at risk of possible drug interactions.

The survey found that of 1000 American questioned, 46% of them take at least one prescription medicine every day. More than 25% take multiple prescription medicines daily. 56% said that they had taken two over-the-counter medications or supplements in the week before they were surveyed.

Mick Hunt, president of the ASHP says that "as you take more medications [the] opportunity for drug interactions grows."

The survey also found that only 39% of those surveyed tell their doctor or nurse about their drug use. 8% failed to tell them at all. According to Hunt, "healthcare providers need to do a little bit better job at pulling that information out," but ultimately the pharmacist is better qualified at helping patients be better informed on the dangers of the drugs they are taking and how they interact.

Seems to us the safest approach may be to rely less on dangerous drugs and more on a properly functioning body, maintained through Chiropractic Wellness Care.



The Drug Report

The Drug Report highlights recent problems with medications that have been reported in research journals.

A report in the January, 2001 issue of the *Journal of Clinical Psychiatry* reports that SSRI antidepressants are hazardous for patients who experience complex mental illness such as bipolar disorder. Out of 553 patients admitted to Yale-New Haven Psychiatric Hospital in Connecticut, 43 were due to psychosis or mania related to the use of antidepressants. 70% (30) of the 43 patients were taking SSRI drugs such as Zoloft, Paxil, Luvox and Prozac.

The March, 2001 issue of *Epidemiology* reports on a study of 202,000 people who use inhaled steroids for the treatment of their asthma. People over the age of 40 who were heavy users of the steroids were 80% more likely to develop cataracts than those who had not used steroids.

A statement issued on March 12, 2001 by the *European Medicines Evaluation Agency* (EMA) reports that a significant number of patients treated with the new rheumatoid arthritis drug Arava have experienced adverse liver reactions. The agency reports a total of 296 reactions ranging from cirrhosis to liver failure to death. Approximately 200,000 patients have used the drug since it was introduced in 1998.

The March, 2001 issue of the *Archives of Disease in Childhood* reports that the Measles, Mumps and Rubella (MMR) vaccine can cause a rare bleeding disorder in children known as idiopathic thrombocytopenic purpura (ITP). ITP causes bleeding under the skin, giving the appearance of a purple bruise spreading over the body.

This publication has previously reported on the link between the rotavirus vaccine used for diarrhea and a rare form of bowel blockage known as intussusception. The February 22, 2001 issue of *The New England Journal of Medicine* confirms that the vaccine did indeed cause the problem which requires surgery to correct. The rotavirus vaccine was pulled from the market in 1999.



Anti-Seizure Drugs Cause Birth Defects

The April 12, 2001 issue of the *New England Journal of Medicine* finds that anti-seizure drugs given for epilepsy can cause birth defects in the babies of pregnant women who take them.

The study, done at Massachusetts General and Brigham and Women's hospitals, focused on 316 babies whose mothers had taken the drugs while pregnant and 98 whose mothers had taken the drugs but stopped before pregnancy occurred. Babies born to 508 women without epilepsy were used as a control group. The deformities monitored were those of the face and fingers as well as head circumference which is a good indication of brain development.

According to lead author Dr. Louis B. Holmes, 21% of babies whose mothers had taken one anti-seizure drug during pregnancy suffered birth defects. In the group of mothers who took at least two anti-seizure drugs during pregnancy, 28% of their babies suffered defects. 8.5% of babies born to women in the control group had defects

None of the 98 babies whose mothers had stopped the drugs before pregnancy had any major birth defects.

Dr. Ed Dodson, who is past president of the Epilepsy Foundation of America and a professor of neurology and pediatrics at Washington University in St. Louis says, "for a long time I've believed it's the drugs. There are other investigators who don't. I think this helps clarify a complicated issue."

The study also reports that phenobarbital, long considered one of the safest anti-seizure drugs, is just as likely to produce the same problems as other anti-seizure medications.

By way of commentary, this study proves that women taking two anti-seizure drugs while pregnant stand a better chance of producing birth defects than those only taking one. It also proves that not taking drugs while pregnant is a good idea for the developing baby. All drugs are capable of harming an unborn, developing fetus and should be used with the greatest care and discrimination.



Thyroid Drug Concerns FDA

The Wall Street Journal reports on June 1, 2001 that the US Food and Drug Administration (FDA) has told the maker of the thyroid medication Synthroid that its “history of problems” cannot allow the drug to be classified as “safe and effective”.

Synthroid has been a popular drug for thyroid problems for the last forty years. During that time, the drug has never been officially approved for use. Four years ago, the FDA ruled that the makers of thyroid drugs like Synthroid would have to apply for and get FDA approval if they were going to continue marketing them.

Current FDA information on the drug indicates that it may well be taken off the market due to its checkered history of side effects.



Doctors Ignored FDA Warnings On Drug

The August 15, 2001 issue of the *Journal of the American Medical Association* published a letter from Dr. David Graham and his colleagues at the U.S. Food and Drug Administration (FDA). The authors concluded that many doctors ignored FDA letters warning them of dangerous reactions to the recently banned diabetes drug Rezulin.

Four separate letters, from the drug company that produced Rezulin, were sent to U.S. doctors at the request of the FDA warning them of dangerous liver damage that was occurring in patients taking the drug. The letters recommended continuous monitoring of liver enzymes to determine if liver damage was occurring. According to Dr. Graham, the letters and extensive publicity “did not result in sustained or meaningful improvement in the performance of liver enzyme testing of patients taking the drug.”

“Labeling changes and warning letters to physicians cannot be relied upon to effect changes in the way Related Web Sites medicine is practiced,” Graham said.

He went on to say that “even if monthly 1 and type 2 testing had been performed in all patients, it may well have had little effect in terms of preventing acute symptoms associated liver failure with [Rezulin].”

■ Drug Reactions Behind Many ER Visits In Elderly

The December 2001 issue of the *Annals of Emergency Medicine* reports that of all the emergency room visits made by the elderly, nearly 11% of them were because of adverse drug interactions between the drugs they were taking.

Of the 283 patients (between the ages of 65 and 101) whose records were reviewed in the study, 91% of them were taking at least one prescribed or over-the-counter medication.

In a further breakdown of the number of drugs the patients took, the researchers found that 13% of the patients took one drug. 24% took two or three, 23% took four or five, 18% took six or seven and 13% took at least eight different drugs daily. On average, the study patients were taking four drugs on a daily basis.

No surprise to anyone, the number of adverse reactions increased with the number of drugs taken. None of the patients taking only one drug had any medication-related emergencies but 17% of those taking more than six drugs experienced adverse reactions. 12% of those taking two to five medications also experienced reactions bad enough to have to go to the emergency room.

The study also found that half of the patients who came in with drug reactions had another potential drug interaction with their medications that was unrelated to why they came to the hospital in the first place.

Lead researcher Dr. Corrine Hohl from the Sir Mortimer B. Davis-Jewish General Hospital in Montreal, Quebec says “our results suggest that [adverse drug reactions] may represent an underestimated but important [cause of disease] in elderly patients presenting for emergency care.”

In commentary, researchers say that adverse drug reactions account for 23% of hospital admissions, extended hospital stays, additional health problems and in many cases, death.

In our opinion, the saddest part of this story is the fact that the researchers found that even after they had a problem and went to the hospital, the patient’s medication regimens were rarely adjusted to lower the risk of adverse reactions by the time they were discharged.



One third of drug errors in elderly are preventable

A report given on March 24, 2002 at the annual meeting of the *American Society for Clinical Pharmacology and Therapeutics* in Atlanta, Georgia says that one third of all medication errors that happen with elderly patients are preventable.

The researchers collected data on 27,500 patients over the age of 65. They found an error rate of more than 4%, or 1,202 medication errors, by examining such things as doctor, clinic and emergency room notes.

Researchers found that the most errors occurred in emergency room situations. These errors primarily came from mixing blood-thinners such as warfarin with other drugs. Nonsteroidal anti-inflammatory drugs (commonly known as NSAIDS and available over-the-counter) were also identified as a major problem contributing to errors.

Commentary: Aside from recommending that patients simply ask their doctors whether their drugs have any dangerous side effects or interactions, the researchers suggest that the industry use . . . computers! Ever on the cutting edge, the \$1.3 trillion dollar a year medical industry is just now discovering that computerized warning systems should be able to keep track of dangerous drug side effects and interactions. Why, we will even bet that one day computers may replace typewriters and accounting ledgers. Just think!

■ Premature labor drug harms infants

The June 2002 issue of the *American Journal of Obstetrics and Gynecology* finds that a drug given to pregnant women in premature labor can cause damage to their unborn babies.

Since the 1970s doctors have used the drug magnesium sulfate to inhibit uterine contractions in women suffering early labor and is now the most common drug used for this purpose.

This study involved 149 women experiencing early labor. They were randomly given the drug magnesium sulfate or a placebo. Tests for cerebral palsy were performed on the babies immediately after birth and again at 18 months.

Researchers then examined the umbilical cord blood for magnesium sulfate levels in the 165 infants born to the women. 37 of the infants had high magnesium sulfate levels and poor outcomes in the cerebral palsy evaluations.

The data also found that the infant evaluations showed more problems as the dosage of magnesium sulfate given to their mothers increased. The infants whose mothers took the drug were more than three times as likely to have poor outcomes.

■ Aggressive use of cholesterol drug questioned

The June 19, 2002 issue of the *Journal of the American Medical Association* reports that the practice of automatically giving heart attack patients cholesterol-lowering statin drugs may be dangerous.

The problem lies in the fact that many times doctors put heart attack patients on the drugs without checking to see whether or not the patient has high cholesterol. The idea being that this will help reduce the risk of death and prevent second heart attacks.

The study suggests that this approach needs to be re-evaluated. Patients without high cholesterol who took the drugs were found to have a higher risk of death or second heart attack than patients with high cholesterol.

Commentary: More genius research at work here. Who could have guessed that giving sick people drugs they don't need would cause them problems? Previous research has shown that upwards of 80,000 people a year die from drug reactions to properly utilized medications. In our humble opinion, this is not a proper utilization.

■ Most drugs not tested for birth defect risk

The September 2002 issue of *Obstetrics & Gynecology* reports on the disturbing fact that more than 90% of new drugs on the market since 1980 are considered to have an “undetermined” risk of producing birth defects in the fetuses of pregnant women who take them.

All new drugs are tested on animals to see whether or not they produce birth defects. Drug companies then use that information to try and determine whether or not the drug will cause birth defects in humans.

One problem is that while animal testing may give some indications whether a drug is safe for humans, humans do not always respond the same way animals do.

Another problem occurs once a drug gets approval from the FDA. Drug companies then are not usually required to track what happens to humans after they have been taking a drug to check the long-term effects.

The researchers say they recognize that it is unethical to conduct studies in which pregnant women are given drugs to see if they cause birth defects in their children. They then go on to say, “however, almost all drugs are taken by some pregnant women.”

Commentary: The fact that drug companies are concerned about the ethics of drug testing on pregnant women is a good thing. However, once a drug gets FDA approval, turning around and telling pregnant women it’s now OK to take drugs that have not been proven safe is hypocritical at best and dangerous at worst.

■ FDA fees to speed new drug approval tied to drug recalls

On September 24, 2002, *Reuters* news service reported on a government study which found that a law requiring drug companies to pay fees to the U.S. Food and Drug Administration (FDA) to reduce new drug approval times may be linked to a higher rate of drug safety recalls.

According to the Government Accounting Office (GAO), the FDA, in essence, has to match any fees that drug companies pay in order to keep the program fully operational. Various consumer groups say this funneling of money to new drug review programs diverts money from safety monitoring after the drugs are on the market.

The report states that “Our analysis of FDA data found that a higher percentage of drugs has been withdrawn from the market for safety-related reasons since” the enactment of the Prescription Drug User Fee Act (PDUFA).

While the FDA agrees that the law has stretched their resources, they don’t seem to feel it’s a problem.

The facts in the GAO report would seem to disagree. In the early years of the new law, from 1993 to 1996, 1.56 percent of new drugs were withdrawn from the U.S. market for safety reasons. In the years 1997 through 2000, 5.3 percent were withdrawn, a more than 300% increase.

FDA Deputy Drug Unit Director Steve Galson says the numbers are too small to be able to make any conclusions. “They overinterpret tiny, tiny changes in the numbers,” he said.

Commentary: We disagree with Mr. Galson’s opinion which seems to minimize the importance of drug safety monitoring. In this case, “tiny, tiny changes in the numbers” may lead to disability or death for thousands of people from dangerous drug reactions. Easy approval of drugs at the expense of safety monitoring should not be tolerated on any level by anyone.

■ Report: Drug ads continue deception after sanctions

A December 4, 2002 report by congressional investigators from the United States General Accounting Office (GAO) say that some drug companies continue to run deceptive ads and TV commercials, sometimes for years, after being cited for violations by the Food and Drug Administration (FDA).

Drug maker Pfizer, for example, continued to make deceptive claims about its cholesterol drug Lipitor over the last four years despite several letters from the FDA telling them to stop.

In 1997, the FDA revised its guidelines to allow drug companies to do more direct-to-consumer advertising. Since then, consumer advertising has increased almost 150 percent and the FDA issued 88 letters accusing drug companies of ad violations. Some companies, the report said, “have received multiple regulatory letters over time for new advertisements promoting the same drug.”

The drug companies may have found a convenient loophole. New FDA regulations have increased the amount of time it takes for letters to be sent to offending companies by anywhere from 2 to 11 weeks. By limiting their ad campaigns to short periods of time, drug companies can have deceptive ads complete their “broadcast life cycle” and be seen by millions of people before the agency can issue a regulatory sanctioning letter.

Commentary: This report estimates that each year, 8.5 million Americans request and receive prescriptions for specific (and we might add, expensive) drugs after seeing these direct-to-consumer ads. Here’s a tip. Assume the worst about any new drug. Because the FDA has decreased the amount of time for new drugs to be approved many new “miracle drugs” are, in effect, tested on the market. “Caveat emptor” is the Latin phrase for “let the buyer beware.”

■ Hundreds Of Infant Deaths Occur Every Year From Drug Reactions

The November 2002 issue of the journal Pediatrics reports that an average of 243 infant deaths occur each year from prescription drugs, biological products and other therapeutic agents.

The study involved case reviews of more than 500,000 adverse drug events (ADEs) occurring from November 1997 through December 2000. The study was performed by researchers at George Washington University and the University of Maryland. 7,111 of the ADEs reviewed involved children under the age of two.

The Authors found that in the 7,111 cases:

- “only 17 drugs or biological products were a suspect in 54% of all serious and fatal adverse events in drugs administered directly.”
- The drug palivizumab, used in high-risk pediatric patients, accounted for 28% of the adverse events.
- Four drugs accounted for 38% of the reported deaths: palivizumab (15%), nitric oxide (11%), indomethacin (10%) and cisapride (3%). Even though widely used for gastroesophageal reflux in children, Cisapride was not approved for use in infants by the FDA. It was withdrawn from the U.S. market in 2000 because it was found to cause cardiac arrhythmia and sudden death.
- In 24% of all the adverse events, exposure to the drug was from the mother during pregnancy, delivery or breast-feeding.
- 31% of the deaths occurred in the first month of life and 50% between day two and the 12th month.

The authors say drug reactions in children are more likely “because young children have immature detoxification mechanisms and because doses must be individually adjusted for a much wider range of body size and weight.”



Fetal malformations linked to anti-epilepsy drugs

A study in the February 25, 2003 issue of Neurology reports that the children of women who took anti-epileptic drugs during pregnancy have a higher incidence of malformations.

The study followed 970 pregnant women with epilepsy. 740 out of 979 children born to the women were exposed to anti-epileptic drugs during the first trimester (the time when fetal formation and development occurs).

Major malformations were detected in 28 children (3.8%) who were exposed to the drugs. Only 2 children (0.8%) who were not exposed to the drugs had problems.

In an obvious understatement, the authors say, “New [anti-epileptic drugs]...should be thoroughly investigated with regard to their [malformation causing] potential.”



Doctors overusing superdrugs

The April 1, 2003 issue of the *Annals of Internal Medicine* gives us the news that while doctors are finally being more careful about using antibiotics for common ailments, when they do use them they are turning to the most powerful ones available, broad-spectrum superdrugs.

Data from the Centers for Disease Control and Prevention indicates that from 1991 to 1999 doctors wrote 17 percent fewer prescriptions for antibiotics. The problem is that prescriptions for the high-powered broad-spectrum antibiotics doubled from 24 to 48 percent for adults and from 24 to 40 percent for children.

The same data also reports that the superdrugs were being used more and more for bronchitis and respiratory infections, even though they are generally useless against those conditions.

Lead researcher Dr. Michael Steinman of the University of California at San Francisco says, “The more we use [broad-spectrum antibiotics] now for conditions that do not require them, the more quickly bacteria will become resistant to these drugs — and when we really do need them for serious and complicated conditions, they won't be there anymore.”

Commentary: The U.S. government estimates that half of the 100 million antibiotic prescriptions written by doctors each year are unnecessary. That's 50 million unnecessary prescriptions every year. Wow.

■ Prescription drug misuse costs billions annually

In a study presented at an *American Medical Association* science writers meeting, two researchers report that prescription drug related problems cost an estimated \$75.6 billion in medical bills and cause 119,000 deaths every year, the equivalent of a large jetliner crashing every day.

The study was conducted by J. Lyle Bootman, Dean of Pharmacy, University of Arizona, Tucson and co-researcher Jeffrey A. Johnson. They report that 28% (8,8 million) of all hospitalizations are related to problems with prescription drugs, representing \$47.4 billion of the total \$75.6 billion cost.

Side effects range from rashes to death. “Prescription drug-related morbidity and mortality represents a serious medical problem that urgently requires expert attention.” Bootman says. Better prescribing habits by doctors and more counseling by pharmacists could reduce the cost by \$45 billion. ▲

Study: 1 in 5 hospital drug doses in error

A new study focusing on drug “administering errors” was presented in the September 9, 2002 issue of the *Archives of Internal Medicine*. The study reports that nearly 1 in 5, or 20% of drug doses given to hospitalized patients were made in error. 7% of those errors were considered potentially harmful.

In this study, researchers evaluated 36 accredited hospitals, non-accredited hospitals and nursing homes in Georgia and Colorado. Error rates were similar in all of the institutions, accredited or not.

In a typical 300-bed hospital and an average of 10 drug events per patient, per day, these figures translate into two drug errors per patient, every day. Using the previously mentioned 7% harmful rate, that means more than 40 potentially harmful drug errors occur every day in the average hospital.

The researchers said their findings support an earlier report from the Institute of Medicine in 1999 that said medical errors lead to more than 1 million injuries and 98,000 deaths every year.

The Associated Press interviewed Dr. Paul Schyve, the Vice President of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). Oddly, Dr. Schyve did not dispute the findings on the error rates. His concern centered around the finding that accredited hospitals (which his organization accredits) seemed to fare no better than unaccredited hospitals.

He said that accredited hospitals may be more prone to errors because they tend to be larger and take care of the sickest patients.

Commentary: How sick the patient is has no bearing whatsoever on medical staff not checking to make sure they have the right drug or dosage for the right patient anymore than the size of the hospital or its staff does. With this kind of bury-your-head-in-the-sand attitude it doesn't surprise us that there are 1 million injuries and 98,000 deaths a year in the name of health care.

■ Hundreds Of Infant Deaths Occur Every Year From Drug Reactions

The November 2002 issue of the journal Pediatrics reports that an average of 243 infant deaths occur each year from prescription drugs, biological products and other therapeutic agents.

The study involved case reviews of more than 500,000 adverse drug events (ADEs) occurring from November 1997 through December 2000. The study was performed by researchers at George Washington University and the University of Maryland. 7,111 of the ADEs reviewed involved children under the age of two.

The Authors found that in the 7,111 cases:

- “only 17 drugs or biological products were a suspect in 54% of all serious and fatal adverse events in drugs administered directly.”
- The drug palivizumab, used in high-risk pediatric patients, accounted for 28% of the adverse events.
- Four drugs accounted for 38% of the reported deaths: palivizumab (15%), nitric oxide (11%), indomethacin (10%) and cisapride (3%). Even though widely used for gastroesophageal reflux in children, Cisapride was not approved for use in infants by the FDA. It was withdrawn from the U.S. market in 2000 because it was found to cause cardiac arrhythmia and sudden death.
- In 24% of all the adverse events, exposure to the drug was from the mother during pregnancy, delivery or breast-feeding.
- 31% of the deaths occurred in the first month of life and 50% between day two and the 12th month.

The authors say drug reactions in children are more likely “because young children have immature detoxification mechanisms and because doses must be individually adjusted for a much wider range of body size and weight.”

Ritalin Use Linked To Chromosomal Changes

On February 24, 2005, the editors of the journal *Cancer Letters* released an early, online version of their journal. It advises us of a study at the University of Texas Medical Branch at Galveston that found that every one of 12 children treated for ADD/ADHD with methylphenidate, the active ingredient in Ritalin, experienced a threefold increase in levels of chromosome abnormalities of the type typically associated with increased risks of cancer and other damaging health effects.

The researchers were startled to note that all of the children experienced the chromosome damage only three months after taking the drug.

The researchers went on to say that to their knowledge, this is the first study done examining the link between methylphenidate and its potential chromosome-damaging effects.

They decided to do the study because even though methylphenidate has been approved for use in humans for more than 50 years, “there are surprisingly few studies” in either humans or animals “on the potential for serious side effects,” such as chromosome damage and cancer.

In the new study, researchers drew blood from children diagnosed with ADD/ADHD before taking methylphenidate in order to get a baseline level of chromosomal structure. Three months after they began taking normal therapeutic doses of the drug, all 12 children in the study had blood taken again.

“It was pretty surprising that all of the children taking methylphenidate showed an increase in chromosome abnormalities in a relatively short period of time,” said lead researcher Randa El-Zein, M.D., Ph.D. Most of the damage found was chromosome breaks “and a higher frequency of [chromosome] aberrations is reported to be associated with an increased risk of cancer down the line.”

While this does not mean that the children will get cancer, it does expose them to an additional risk factor.

Methylphenidate is the most widely used class of amphetamine-like drugs used to treat ADD/ADHD. Methylphenidate use skyrocketed by more than 500% between 1991 and 1999.

■ Drug Complaints Reach Record High

USA Today reports on March 13, 2005 that the number of adverse drug events (ADEs) reported to the U.S. Food and Drug Administration (FDA) reached an all-time high in 2004.

There were approximately 422,500 ADE reports received by the FDA from pharmaceutical companies, health professionals and patients. This is a 14% increase over the 370,887 reports in 2003.

While the FDA requires the manufacturer to file ADE reports, doctor's and nurse's reports are voluntary, leading government officials to believe that the reported events represent only a portion of the actual number.

Paul Seligman, director of the FDA's Office of Pharmacoepidemiology and Statistical Sciences blames the increase in ADEs on the fact that there are more drugs on the market and use has increased. "Clearly," he said, "when you have more products on the market, you're likely to have more side effects."

Prescription sales cost Americans more than \$235 billion in 2004, a record that beat the 1995 volume by more than 300%.

■ Combining Medicines Makes It Difficult To Predict Adverse Drug Effects

The May 1, 2005 issue of the Journal of Psychiatric Practice reports that patients who take more than one medication rarely were taking the same combination of drugs as other people. Understandably, this makes it difficult for doctors to monitor and predict dangerous drug interactions.

The practice of mixing medicines increased with age, especially among patients taking anti-depressants. More than one-third of patients taking anti-depressants were taking at least 8 other medications.

In his assessment of the finding, Dr. Sheldon Preskorn, professor and chairman of the Department of Psychiatry at the University of Kansas School of Medicine warned that since doctors do not have a complete enough clinical knowledge of all the combined effects of the drugs they prescribe, the result is an increase in the number of adverse drug reactions.