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Health Letter

SIDNEY M. WOLFE, M.D., EDITOR

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Is the U.S. Safe from Mad Cow Disease? Could We Be Safer?

The following are excerpts from a report on the Jim Lehrer Newshour on the epidemic of Bovine Spongiform Encephalopathy (BSE, or Mad Cow Disease) in Europe, and a debate on the same program over the possibility of an outbreak of disease among humans and cows in the U.S., featuring Peter Lurie, Deputy Director of Public Citizen's Health Research Group. The program aired on January 26, 2001.

Paul Miller (Newshour reporter): The fight began in England in the late 1980s when cows acted strangely before dying and autopsies showed their brains looked like sponges. The cause was an abnormal bit of protein called a prion.

Peter Smith (London School of Hygiene and Tropical Medicine): What happens in the disease is that protein becomes malformed, misshapen, and then there seems to be a template effect that works progressively throughout the body, transforming the shape of normal prion proteins into this abnormal form. And eventually this accumulates in the central nervous system and in the brain, leading to death.

Paul Miller: 180,000 head of cattle were infected overall in Britain. And by 1996, scientists discovered that BSE prions could somehow jump species to humans, causing a fatal brain disease known as new variant Creutzfeldt Jakob disease or CJD....An investigation into the epidemic concluded the British government had misled consumers about the extent of the risk to human health. [Variant] CJD has now killed 80 people in Britain. No one is sure how many more have been infected; it can take years for the symptoms to appear. The government report last October blamed the spread of mad cow disease on ground-up bits of infected cattle, fed to herds as extra protein for growth....The bone and animal meal were banned in Britain, but exported to Europe. European countries had banned imports of British beef in 1996, but their own cattle were becoming infected. In November, families of two French [variant] CJD victims blamed British and French officials for the meal exports, and BSE and [variant] CJD in France. A magistrate is now investigating possible manslaughter charges against the officials....Now, the World Health Organization is warning that BSE-infected meat may be in animal and bone meal that has been sold to other parts of the world.

Elizabeth Farnsworth (Newshour Anchor): To discuss the disease and the efforts to prevent its spread to this country, we turn to Dr. Murray Lumpkin,

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MAD COW DISEASE, *from page 1*

senior medical adviser in the commissioner's office at the Food and Drug Administration [FDA]; Dr. Paul Brown, a senior research scientist at the National Institutes of Health—he chairs a committee that advises the FDA On Mad Cow Disease; and Dr. Peter Lurie, deputy director of the Health Research Group for the consumer organization, Public Citizen—he also advises the FDA. Dr. Brown, I want to go back over the science, just briefly, of all this. You have said there is a lot of uncertainty about Mad Cow Disease. What can you say [is known] certainly about its provenance and also about how humans get it?

Dr. Paul Brown: Well, I think the only thing that we can say for absolute certain is that the human disease called variant Creutzfeld—variant Creutzfeld-Jacob Disease is the result of infection with Mad Cow Disease. Everything else about this story is more or less plausible speculation.

Elizabeth Farnsworth: Even that it may come from rendered meat and bone meal products in feed?

Dr. Paul Brown: Yeah, I think we'll never prove the historical origin of this disease, but by far the most plausible explanation is the material that you've heard about, meat and bone meal, which is a product of rendered carcasses. And in the rendering mix, all kinds of things go in it—carcasses from which everything has been removed, livestock, road kill, dying pets, plate waste, it's a great mix of things. Among this—in this mix, would be carcasses from sheep, and sheep have a natural disease called Scrapie, which has been known for at least 250 years. And it's probable that around 1980, because of changes in the rendering process, some of the infectivity of Scrape-infected sheep survived it and got into cattle.

Elizabeth Farnsworth: So cattle get it. Cooking doesn't make any difference in this case; it's not like other diseases that you can get from meat. A human eats it, the protein, the offending protein then spreads to the human's brain. Is that the idea?

Dr. Paul Brown: Yes, that is correct....Beef products go into a lot of things. Gelatin goes into capsules that you swallow as pills. But in the processing of many of these products, any of the infectivity that might have been there would be destroyed. So it's almost surely oral exposure and not, for example, cosmetics.

Elizabeth Farnsworth: What about vaccines?

Dr. Paul Brown: Well, vaccines are a sensitive issue because of course they're given to children. Anything that involves children requires special care. By and large, vaccine exposure to anything that might be infectious is so low as to be almost zero. In other words, when you give a vaccine, the final product does not contain bovine materials. But the viruses, for example, that are used to make the vaccine may have been grown in tissue cultures that were fed with fetal bovine serum. But it is a passing phenomenon that is almost surely diluted to the point of near zero in the finished product.

Elizabeth Farnsworth: Okay. Dr. Lurie, when you look at the situation in Europe, I mean, right now as we speak, slaughterhouses in Portugal are killing 50,000 cattle. Cattle are being killed all over the place. What do you see—big danger, fairly slow spread, hysteria? What do you see?

Dr. Peter Lurie: I think we have a safety net in this country, but my concern is that it has a certain amount of breaches in it and that we aren't as well protected as we really could be. I think the vaccines are perhaps an example of that, not so much in that there is a large risk of that, but the FDA asked the manufacturers to not use materials that came from British cows [since] 1993. But the manufacturers chose to ignore that recommendation from the FDA and they went ahead and did it anyway for at least seven years. So I think there are a number of holes we need to close. Dietary supplements, I think, are another. Here we have an FDA that has practically no authority to adequately regulate dietary supplements. And it is actually possible that one could make a dietary supplement from nervous tissue from a British cow and import it into this country. Now I'm not saying it has happened, but the FDA has so little in the way of regulatory authority over dietary supplements that I think this is a hole we must close immediately....The dietary supplements can be made from extracts from brain, and some people, for reasons unclear to me, seem to find that a worthwhile thing to consume. The problem is that the FDA and the USDA don't have adequate...authority to monitor what is coming into the country. Very few inspections are done. Probably only 1 percent of all material that enters the country is inspected. And companies that are making dietary supplements from cow brain, for example, have every incentive to mislead the United States Government. And it's that that worries me, that these kinds of materials...could enter.

Elizabeth Farnsworth: The problem you mentioned about some of the feed coming into the country, do you think it could be that some cows here could have BSE and it hasn't been recognized yet?

Dr. Peter Lurie: Well, certainly there is no example of a cow in this country that has BSE, nor is there an example of a human with a human version of it in this country. But...we have FDA inspections done very recently that show that firstly they've only inspected about a third of the manufacturers of meal for cows. And secondly, among those that they have inspected up to a quarter of them do not have adequate procedures to prevent the recycling of cow parts into the feed of other cows.

Elizabeth Farnsworth: Dr. Lumpkin, how good do you think the safety net is protecting Americans from Mad Cow Disease?

Dr. Murray Lumpkin: I think it's like any other safety net, it is a safety net that has many components, redundancies that have been built into it, which are obviously quite necessary. I think like any type of an undertaking, it can always be improved. And for a lot of the reasons that you've heard from the other two guests on the show today, we have indeed, been working to do that.

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Still Hard to Swallow

The following article was authored by Morton Mintz who reported on the pharmaceutical industry for The Washington Post *from 1958 to 1988. His books include* "By Prescription Only" (1967) *and* "At Any Cost: Corporate Greed, Women, and the Dalkon Shield" (1985, out of print). *This article was also printed in* The Washington Post *Outlook Section on February 10, 2001 and reprinted with permission of the author.*

What's new about prescription drug pricing is the attention that it's been getting in Congress, thanks partly to busloads of elderly Americans going to Canada and Mexico to buy their medicines at sharply lower costs. What's relatively new is direct-to-consumer television and print advertising of drugs, on which pharmaceutical manufacturers are spending billions of dollars.

What's surprisingly old is the problem of excessively high drug pricing.

In December 1959, the Senate Judiciary Committee's subcommittee on antitrust and monopoly, led by Estes Kefauver (D-Tenn.), launched an unprecedented investigation of the pharmaceutical industry. Over the ensuing 2-1/2 years, the subcommittee exposed pricing practices that repeatedly astonished the public—but may seem all too familiar to consumers today. Some examples from the Kefauver report:

- Eli Lilly was selling 100 tablets of the antibiotic V-Cillin to pharmacies in England for $6.50 and in Australia for $10.75, while charging pharmacies in the United States $18.

- For 100 pills of the steroid prednisone, the production cost was $1.50, tops. Brand name manufacturers were charging pharmacists $18, and the retail price was $30.

- For 100 capsules of the antibiotic tetracycline, Bristol's production cost was $1.67, its price to druggists $30.60. Consumers paid $51.

Then, as now, pharmaceutical manufacturers and their allies claimed that high prices were indispensable to fund the research that produces constant advances in drug therapy. The subcommittee found, however, that the 22 largest pharmaceutical manufacturers were spending 24 cents of every revenue dollar on promotion. This was approximately four times their spending on research.

Kefauver cited specific findings

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MAD COW DISEASE, *from page 2*

Dr. Peter Lurie: ...the fact is that the FDA's own inspection records show that they have not inspected that many plants, and in many cases don't have adequate procedures there. And this week's experience in Texas...is in fact, an example where material that very well might include recycled cow parts appears to have been fed to some cows in Texas. So they have inspection records that show the holes, and now we have actual information from Texas that as best we can tell shows the implications of just that. The FDA is doing a lot of work, but they're simply not doing enough....Remember that that's how the problem began in Britain. It began with some small number of infected cows. Their parts were recycled...through the meal to other cows, and that's how the epidemic grew the way it did. It began with exactly these kinds of breaches in process.

Elizabeth Farnsworth: Dr. Brown, you're advising the FDA on this, too. Where do you come down on the state of the safety net, and what do you think—how do you think we have been successful so far in preventing it, and what more needs to be done?

Dr. Paul Brown: There are really [two] things which have kept the US BSE-free, and ergo variant CJD-free. The first was simply fortuitous. Foot and mouth disease occurs here and there in the world and at the outskirts of Europe. And because of the fear that foot and mouth disease might enter this country, the USDA banned, in large measure, all imports of live cattle from Europe. A few were brought in, but...this was in the '80s. And those cattle have been slaughtered or are now quarantined. That was the first thing. The second thing is that the USDA and the FDA really got on top of this problem very quickly. In point of fact, because of a computing system that is present in this country, the BSE became a notifiable disease in this country before it even became a notifiable disease in Great Britain.

Elizabeth Farnsworth: What needs to be watched out for now? What concerns you now?

Dr. Paul Brown: Well, I think what has been talked about—that is, vigilance in terms of imports of products from other countries. I don't think we need to worry about a lot of products that have been mentioned in passing here. Cosmetics, for example, really are not a problem. Gelatin is really not a problem—not because of where they come from, but because the processing involved in making the products would eliminate the infective agent.

Elizabeth Farnsworth: Okay. Dr. Lurie, on that?

Dr. Peter Lurie: Well, I agree with all of that. I think we also need to expand the testing that we do of potentially infected cows. In this country, we've looked at the brains of about 12,000 cows since the beginning of the epidemic. Now that France has finally recognized its problem, they're looking at 20,000 cows per week. So I think, as a senior...Department of Agriculture official told me, we would like to see an expansion of the ability to test cows in this country. Until we do so, I'm not going to be completely reassured.

DRUG PRICING, *from page 3*
that further undermined the research rationale:

* Schering charged pharmacies $8.40 for 60 tablets of estradiol progynon, a drug for menopausal disorders. Schering bought the drug in bulk from Roussel of France, and therefore had done no research of its own on it. The 60 tablets contained 11.7 cents worth of the drug. Schering's markup was 7,079 percent.

* Rhone-Poulenc of France invented the potent tranquilizers Thorazine and Sparine, and licensed their manufacture to pharmaceutical houses in other countries that had contributed nothing to the invention of either medicine. For 50 Thorazine tablets, Rhone-Poulenc charged pharmacists in France 51 cents; The British licensee charged 77 cents, the West German licensee 94 cents; the U.S. licensee (Smith Kline & French) charged $3.03. For 50 Sparine pills, the U.S. licensee (Wyeth Laboratories) charged 94 cents in Australia but $3 in the United States.

In other words, the problems were the same we see today: medications priced far higher than research and production costs warrant, and priced higher for Americans than for consumers elsewhere.

"What we are confronted with in the [prescription] drug industry," Kefauver concluded in the subcommittee's report, "is the existence of prices which by any test and under any standard are excessive."

The senator urged several reforms. Had they been enacted, consumers would have saved billions of dollars annually for nearly 40 years. But they were not. "Conservative congressmen, responding to industry opposition" gutted the price provisions of the Kefauver bill, *Fortune* magazine reported at the time.

Congress, whether controlled by Democrats or Republicans, has not troubled since the Kefauver investigation to dig deeply into why drug prices are so many times higher than production costs. Nor into the effects on drug prices of the immense cost of promotion. (In the 4-1/2 years ending last June, the industry spent a staggering $54.5 billion promoting its wares to health care professionals and consumers, according to the health care information company IMS Health.)

Congress has failed to investigate the industry's often-repeated claim that it costs up to $500 million, on average, to bring a new drug to market (the figure came from a 1991 paper by four economists with ties to the drug industry). Or where sensible incentives for research end and profiteering begins. Or how to nurture research for therapeutic breakthroughs and to fight great scourges like AIDS, rather than for copycat medicines aimed only at gaining market share or for another drug for baldness.

So, frozen as ever, we begin the 21st century with pricing excesses continuing unabated.

It's unrealistic to expect meaningful, structural pricing reforms from this Congress or this White House. In the 1999-2000 election cycle alone, the pharmaceutical industry made campaign contributions topping $23.4 million, funneled hundreds of millions of dollars to front groups and lobbyists, and reportedly spent more than $40 million on so-called issue ads.

More likely is that last year's canceled bill authorizing re-importation of made-in-the-USA drugs from Canada and Mexico will be repaired and reenacted. But that would treat the symptoms, not the underlying disease of monopolistic drug pricing.

If lasting, reasonable drug pricing is ever to be obtained in this country, one remedy Kefauver advocated should be put back on the table. It's compulsory licensing.

The United States is the only major economic power that allows an inventor to patent a medicine (as opposed to the methods and processes used to produce it). Kefauver's proposal was to give the inventor a three-year monopoly; after that, the company would be compelled to license the medicine to other manufacturers, who would have to pay the inventor royalties of up to 8 percent for the life of the patent. The other manufacturers would have to develop their own production methods, though, since those patents would be unaffected.

When Kefauver's proposal reached the Senate floor, most Democrats and all Republicans allied themselves with the industry in fierce opposition. Kefauver then offered a compromise: compulsory licensing would kick in only for those drugs found by the Federal Trade Commission to have a wholesale price more than five times the cost of production. The compromise, no less ferociously opposed, also died.

Compulsory licensing could still work to encourage profit but not profiteering. But it has little appeal on Capitol Hill, where the Senate came close to passing a bill to add three years to the 20-year life of product patents on the allergy drug Claritin and seven other "blockbuster" brand name medicines. (Schering-Plough's net earnings on Claritin in its first five years on the market were $1.3 billion.) The bill was approved last year by the Senate Judiciary Committee and only faded away in light of the election battle over Medicare drug benefits.

A Congress wanting to take minimal pro-competitive action could consider a proposal from Benjamin Gordon, staff economist of the Senate Small Business Committee's monopoly subcommittee, who worked on an inquiry into the drug industry from 1967 to 1977. Gordon suggested that government authorize the National Institutes of Health or some other federal agency to develop, test and produce—but not sell—new medicines. That agency's experience could provide a yardstick to compare the prices charged by private manufacturers. There is precedent for this in the Tennessee Valley Authority, created during the New Deal, in part to help set standards for the pricing of electric power.

With the aid of such a yardstick, Gordon said in a recent interview, the government could identify which patent-monopoly medicines it bought for programs such as Medicaid were excessively priced. Then the government could contract with other manufacturers to produce and distribute the medicines at a more realistic price.

To do this, the government would invoke a 52-year-old law, Section 1498(a) of Title 28 in the U.S. Code, which empowers it to set the price it will pay the owner of a patent on any invention,

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Product Recalls

January 11—February 12, 2001

DRUGS & DIETARY SUPPLEMENTS

This chart includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs and dietary supplements and Consumer Product Safety Commission (CPSC) recalls of consumer products.

There are no drug recalls to report this month because of a disruption in the production of the FDA Enforcement Report, the weekly publication from which we learn of recalls. The FDA has noted that "Due to a change in staffing, FDA's Office of Public Affairs (OPA) is reexamining the process for publishing the FDA Enforcement Report. As OPA restructures the Enforcement Report over the next few weeks, there will be some disruptions and changes in its production and distribution."

Please continue to report adverse drug reactions to the FDA by calling (800) FDA-1088. The FDA web site is *www.fda.gov*.

CONSUMER PRODUCTS

Contact the Consumer Product Safety Commission (CPSC) for specific instructions or return the item to the place of purchase for a refund. For additional information from the Consumer Product Safety Commission, call their hotline at 1-800-638-2772. The CPSC web site is *http://www.cpsc.gov*.

Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Busy School Bus Toys; On some units, the yellow "awning" piece above the bus door can break loose, posing a choking hazard to young children	Busy School Bus item number 5527 with date codes 91671 through 91883; 12,500 sold nationwide from June 1999 through January 2001; Playskool, Pawtucket, Rhode Island (888) 510-1561 www.hasbro.com/consumer/safety.html
Bicycles; Because pedals are too low to the ground, they fail to meet federal bicycle standards. Children can lose control when a pedal strikes the ground, causing falls and injuries	Model year 2001 Torker Blaster 16-inch Boy's bicycles in red, black, blue, or chrome, and Sunflower 16-inch Girl's bicycles in yellow, pink or florescent green; 1400 sold at bicycle stores nationwide from September—December 2000; Seattle Bike Supply, Kent, Washington (800) 283-2453
Gun Locks; Under certain conditions, these locks can open without the use of a key which can give unauthorized access to a firearm	Locks resemble a bicycle cable lock and have a red cable with a black padlock. Red vinyl bands around the top and bottom of the locks read, "PROJECT" and "HOMESAFE"; 400,000 distributed nationwide by law enforcement agenices from September 1999 through October 2000; Adstar Inc., Merrick, New York (800) 726-6444
Jeans and Overalls (children's); Small decorative metal appliqúes on the legs of the garments can come loose and separate, posing a choking hazard to young children	BABY GUESS and GUESS GIRLS labels sizes 6 months through 6X; 11,000 sold nationwide from October—December 2000; Designer Classics LLC, Keasbey, New Jersey (888) 626-4939
Jumpsuits (Infants); A ribbon that runs through the zipper pull tab can detach, resulting in a potential choking hazard. Consumers should immediately remove and discard the ribbon. The garment then can be worn without the ribbon	100 percent cotton interlock jumpsuits with teddy bear, bunny or puppy embroidery design on the front; or cotton/polyester blend velour jumpsuits with a teddy bear or bunny embroidery design on the front, sold in sizes Small, Medium, and Large; 600,000 sold nationwide from May—December 2000; The William Carter Co. (Carter's), Morrow, Georgia (888) 339-2129 www.carters.com

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Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Kid's Meal Toys; Suction cup on the toy can come off, presenting a choking hazard to young children	"Planet Discovery" plastic disks (about 2 to 3 inches in diameter) with a suction cup (about 1.5 inch in diameter) on the back. The toys depict all of the planets plus the moon and the sun. Toys were distributed with Chick-fil-A kid's meals—nationwide during January 1999 and January 2001; Chick-fil-A Inc., Atlanta, Georgia (866) 736-5914
Lamps; Electronic component inside the plug can overheat, presenting a fire and burn hazard	Floor lamps are sand colored, 4 feet tall and have flexible gooseneck arms to adjust the position of the fluorescent lights. Labels indicate "OTT-LITE TRUECOLOR FLOOR LAMP"; 1560 sold at craft, hobby and fabric stores, including Hancock Fabrics nationwide from November through December 2000; Environmental Lighting Concepts, Tampa, Fla; (800) 842-8848
Miter Saws; Bolts on saws can loosen and the blade could detach, posing a risk of lacerations	12-inch saws, model numbers 3660 TY1 and 3680 TY1; 6,400 sold at home centers and hardware stores nationwide from January 1992 through December 1993; Black & Decker (U.S.) Inc., Towson, Maryland (888) 771-4540
Miter Saws (Recall to repair); Bolts can loosen and the blade could detach, posing a risk of lacerations	12-inch saws, model numbers DW704 TY1 and DW705 TY1; 112,000 sold at home centers and hardware stores nationwide from January 1992 through December 1993; DEWALT Industrial Tool Co., Baltimore, Maryland (888) 771-4540 www.dewalt.com/us/articles/press_release.asp?ID=249
Motocross Motorcycles; Rear brakes on these motorcycles can fail	2001 KX series model numbers KX65, KX85, KX100, KX125, KX250 and KX500; 18,000 sold nationwide from May—November 2000; Kawasaki Motors Corporation, U.S.A., Irvine, California (866) 802-9381 www.buykawasaki.com
Sweatshirts (girls); Children can get entangled and strangle in hood drawstrings that catch on objects	Navy blue Ocean Pacific long-sleeve hooded sweatshirts; 6,600 sold at Upton's, Lamont's, Gottschalks, and Sports Authority stores nationwide from August—October 1999; Trends Clothing Corp., Hialeah Gardens, Florida (800) 7-TRENDS
Tot Rider Walkers; Cover on walker's removable music center can break off, allowing small parts to fall from the product, creating a potential choking hazard to young children	Model 14302; 3,356 sold nationwide from February 2000—January 2001; Kolcraft Enterprises, Inc., Chicago, Illinois (800) 453-7673
Toy Vehicles; Small parts can break off of the toy vehicles, posing a choking hazard to young children	Multicolored plastic airplanes, cars, dump trucks, trains and fire engines sold under the PLAYGO brand name. Each vehicle has a battery-operated, detachable remote control with a 40-inch cord. Enclosed in cab of each vehicle are 1/4 inch multicolor balls; 290,000 sold nationwide from June 1995 through December 1998; Supreme Toys (H.K) Ltd., Hong Kong (800) 567-1774
Tree Wound and Grafting Compound; Pressure can build inside the can and forcibly discharge the compound, which can cause temporary skin irritation	Pint, quart and gallon cans filled from November 11, 1996, through May 5, 1999. Five-digit date (written as year, month, day) is stamped on back of can's label. For example, "81127" means the can was filled on November 27, 1998; 35,000 sold nationwide at hardware and nurseries from November 1996 through August 1999; The Tanglefoot Co., Grand Rapids, Michigan (800) 215-0938 www.tnglfoot@aol.com

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It's the Calories that Count

The desire to lose weight is a near obsession in modern America. And no wonder: 50 percent of Americans are considered to be overweight, a percentage that has been increasing for 30 years. It is therefore no surprise that we are subjected to a daily barrage of quick-fix solutions: diets guaranteed to remove unwanted pounds and transform the couch potato into a supermodel almost overnight. No fewer than 700 weight loss books have been published since 1997 and the combination of book sales, diet pills, nutritional supplements and weight loss programs yields a tidy $33 billion in revenue to often-unscrupulous entrepreneurs.

But is there any science behind the extravagant claims? The U.S. Department of Agriculture (USDA) recently released a report assessing all studies of the major diets in the scientific literature, weighing the reports according to their quality. Their conclusion may sound familiar: the best way to lose and maintain weight loss is to reduce caloric intake and to exercise faithfully.

The USDA report grouped the diets into three categories: high-fat, low-carbohydrate diets (e.g., Dr. Atkins' New Diet Revolution, Protein Power and Life Without Bread); moderate-fat diets (e.g., USDA Food Guide Pyramid, DASH diet and Weight Watchers); and low-fat and very-low-fat diets (e.g., Dr. Dean Ornish's Program for Reversing Heart Disease, Eat More, Weigh Less and The New Pritikin Program).

The report found that one can lose weight with any of these diets, even in the absence of exercise, as long as caloric intake is reduced to about 1,400 to 1,500 calories/day. If that sounds like good news, consider the following: the average American consumes 2,200 calories/day! Of course, you can reduce your caloric intake to less than the 1,400 to 1,500 calories/day and still lose weight if you supplement your diet with even moderate exercise. (A practical approach to weight loss combining a moderate amount of exercise with modest dietary changes is described in the November 1999 issue of the *Health Letter*.)

The USDA's main conclusion is succinct: "Diets that reduce caloric intake result in weight loss." This simple statement directly addresses some of the myths perpetrated by the diet industry. The diets may have more in common than the hype suggests inasmuch as all involve caloric restriction. And if the Atkins diet seems to lead to particularly rapid weight loss, it is probably because in the short term the diet leads to more loss of water than body fat. This water weight is regained as soon as dieting stops. Unfortunately, most of the available data have been gathered from relatively short term studies, so there is little information on how to maintain appropriate body weight.

There are, however, some important nutritional distinctions between the diets. According to the USDA, the only diet that is nutritionally adequate is the moderate-fat diet. In contrast, the other two diets are deficient in various essential vitamins and minerals. High-fat, low-carbohydrate diets are low in vitamins E, A, thiamine, B6, and folate as well as calcium, magnesium, iron, zinc, potassium and dietary fiber. They are also high in saturated fat and cholesterol. Very low-fat diets are deficient in vitamins B12 and E and provide insufficient zinc. Of the three diets, moderate-fat diets have been shown most convincingly to improve cholesterol profiles.

Overall, therefore, the safest and most effective way to reduce weight is to adhere to a moderate-fat diet: consume no more than 30 percent of calories as fat, limit protein to 20 percent of the diet and consume complex carbohydrates, fruits, vegetables and grains in relatively larger quantities.

Many people interested in weight loss hope that there is some simple, comfortable, and quick road to lose the unwanted pounds and keep them off. In reality, the road is blocked by calories. Eating a little less and exercising a little more, on a regular, sustained basis is the only way around the roadblock.

CONSUMER PRODUCTS *cont.*

Name of Product; Problem	*Lot #; Quantity and Distribution; Manufacturer*
Wooden Pull Toys; Wooden pegs can come off of these toys, posing a choking hazard to young children	Dog pull toy is 10 inches long and 5 inches high. Dog's legs are attached to wooden wheels with small pegs. A black string with a large wooden ball on the end is connected to the front of the toy; 2,900 sold at Pottery Barn Kids store in Corte Madera, California, and Pottery Barn Outlet stores in Virginia, Texas, Georgia, Tennessee and Ohio from June 2000 through January 2001; Pottery Barn Kids, San Francisco, California (866) 428-6467

COX-2 Inhibitors Vioxx and Celebrex: Keep Staying Away—It Gets Worse

When Vioxx and Celebrex were approved about two years ago, we were quite skeptical about the claims that they were much safer in the gastrointestinal (GI) tract than other, older nonsteroidal anti-inflammatory drugs (NSAIDs). At the time of approval, neither Merck (Vioxx) nor Pharmacia (Celebrex) had done the comparative long term, higher dose randomized trials in which the newer COX-2 inhibitor drug would be compared to the least dangerous of these older drugs such as ibuprofen (Motrin) to find out if there is a statistically significantly lower amount of serious GI complications such as perforations, ulcers or bleeding with the COX-2 inhibitor drug. In addition, we were worried, as we are about any new drug that does not have an important advantage over existing drugs, about hidden dangers. This is especially true for the COX-2 inhibitors since they affect so many different parts of the body.

GI Toxicity

Prior to recent FDA advisory committee meetings, the two companies submitted new studies which they hoped would convince the FDA to allow the labels of their drugs to state that they were safer, as far as GI toxicity, than the older NSAIDs. Pharmacia played more by the rules and conducted randomized studies in which Celebrex was compared with either ibuprofen or diclofenac, the two NSAIDs with the least GI toxicity. The study failed to show a significantly lower amount of these serious GI adverse effects for Celebrex, compared to the other drugs. Cheating, somewhat, Merck decided that Vioxx would probably appear to have a more favorable safety profile if it was compared to a more-dangerous-than-ibuprofen/diclofenac-NSAID and they chose naproxen as the comparator drug for their study. Although the Merck study did find a statistically significantly lower amount of serious GI complications with Vioxx compared to naproxen, there were several other problems, beyond the wrong choice of naproxen for comparison, which make the findings not really applicable to the general population of people using Vioxx. First, the study was limited to people who had rheumatoid arthritis, a disease for which Vioxx is not even approved. Second, almost 60 percent of the people in the study were simultaneously using steroids such as prednisone as adjunctive treatment for their rheumatoid arthritis. Since steroids themselves can cause ulcers, this distorts the findings.

We agree with the conclusions of FDA's Office of Postmarketing Drug Risk Assessment that the 73 deaths seen with celecoxib [Celebrex](36) or rofecoxib [Vioxx](37) from gastrointestinal bleeding, obstruction, perforation or stenosis show that the current labeling for the two drugs "reflect[s] the risk of fatal gastrointestinal bleeding, obstruction, perforation or stenosis."

Cardiovascular Toxicity

In a recent study published in the *Proceedings of the National Academy of Sciences*, the ability of rabbits to withstand temporary experimental coronary artery occlusion was significantly impaired by treatment with celecoxib which completely blocked the cardioprotective effects of the COX-2 enzyme. The authors of that study concluded that COX-2 enzyme is a "cardioprotective protein." Therefore, it is implied, drugs which block this cardioprotective enzyme, such as COX-2 inhibitors, may neutralize its protective effects.

In Merck's study comparing Vioxx to naproxen, there was a highly statistically significant five-fold increase in heart attacks in the overall Vioxx group (0.5 percent) compared to the naproxen group (0.1 percent). This amounted to approximately 20 heart attacks with Vioxx (out of 4047 patients) compared with 4 with naproxen (out of 4029 patients). This increased number of heart attacks was also accompanied by an increase in other thrombotic (blood clotting) adverse effects such as strokes and blood clots in the legs as well as problems with hypertension in the Vioxx group compared with the naproxen group.

Although the Celebrex study did not find a significantly elevated number of heart attacks in those using that drug compared with those using the older NSAIDs (ibuprofen or diclofenac), there was also cause for concern about heart toxicity with that drug. FDA Cardio-Renal division reviewer Dr. Throckmorton found that "the incidence of adverse events related to cardiac ischemia (decreased blood flow to the heart) was higher in the celecoxib [Celebrex] group...and was most pronounced in the group of patients not taking ASA (aspirin)" as a cardiovascular protective drug. In these patients the rate of myocardial infarction was also highest in the celecoxib group (0.2 percent) compared with users of the other two drugs (0.1 percent). For all patients, on and off aspirin, there was a higher incidence of atrial fibrillation, a cardiac arrhythmia, in the celecoxib group than in either of the other two groups, again more pronounced in the group not taking aspirin. The author concluded by stating that "the data do not exclude a less apparent pro-thrombotic [blood clot forming] effect of celecoxib, reflected in the relative rates of cardiac adverse events related to ischemia."

Once again, a seemingly magic bullet appears to have self-destructed as research reveals the larger context in which it operates—the risks as well as the benefits. The benefits of COX-2 inhibitors as far as reducing GI toxicity appear to have been grossly exaggerated and oversold. Years after the research on these benefits was done, a rapid accumulation of evidence on

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Consumer Product Safety Commission Finally Sees the Light on Lead in Candles

It took two Public Citizen petitions and over a quarter of a century, but the Consumer Product Safety Commission (CPSC) seems finally to have acted responsibly. On February 13, 2001, the Commission voted unanimously to grant Public Citizen's petition (see April, 2000 issue of the *Health Letter*) to ban the sale of candles with lead wicks.

Lead is a known health hazard, particularly for fetuses and young children. Numerous studies have linked the chemical to brain damage, developmental disorders and low IQ. Public health authorities have agreed for decades that any unnecessary exposure to lead should be avoided.

Some unscrupulous manufacturers use lead or other metals in candle wicks to keep the wick upright while manufacturing and burning the candle. In Europe, no manufacturers use metal wicks, so clearly they are unnecessary.

Yet, when Public Citizen first petitioned CPSC to ban candles with lead wicks in 1973, the agency succumbed to the self-serving entreaties of industry and agreed to a voluntary ban. Not surprisingly, before the decade was out, U.S. manufacturers resumed production of the toxic chemical.

In early 2000, Public Citizen did a study documenting the presence of lead wicks in candles sold by major retailers in the Baltimore-Washington area. The study, subsequently published in the *Journal of the American Medical Association* (see the August, 2000 issue of the *Health Letter*), showed that 30 percent of candles had wicks containing metal cores (mostly zinc and tin) and that 10 percent of these had enough lead to produce room air lead levels 10-36 times those permitted by the Environmental Protection Agency. With ongoing exposure, these candles could raise a child's blood level well beyond those established as dangerous by the U.S. government.

It seems the CPSC has finally seen the light. In December 2000, Commission staff recommended that lead wicks be banned and in February the CPSC Commissioners voted 3-0 to grant Public Citizen's petition. The agency now has to go through a public rulemaking process that could take more than a year. In the meantime, Public Citizen is urging consumers to not buy any candles with metal wicks (lead-wicked candles cannot be readily distinguished from wicks made from other metals) and to not burn or return to the store any metal-wicked candles they may have purchased already.

This pattern of events echoes what we have often seen before with other regulatory agencies. All-too-often, agencies fail to exert their legitimate authority and instead fall for empty promises from industry. The lead-wicked candle case is one of the best recent examples of the folly of taking this path—the agency, after removing the accumulated egg from its face, has finally realized that the candle industry could not be trusted and reversed itself. But why must it take 27 years of needlessly exposing children to this toxin to finally bring the agency to its senses?

DRUG PRICING, *from page 4*

with two qualifications: the invention must be used for governmental purposes, and a reasonable royalty must be paid to the patent owner.

That the law could achieve huge savings for the taxpayers was dramatically illustrated in a 1971 speech by monopoly subcommittee chairman Gaylord Nelson (D-Wis.). While the Veterans Administration was buying the tranquilizer meprobamate in Denmark for $1.55 per 500 tablets, he pointed out, Carter-Wallace was charging U.S. pharmacists $26 for the same quantity of meprobamate under the brand named Miltown.

Section 1498(a) could be used to target any brand name medicine with very low production costs but very high prices. A drug manufacturer contending that the government's price is unreasonable can sue the United States. To succeed in court, however, the owner must first establish the patent's validity. This can be extremely difficult, as Carter-Wallace found out. Seeking a generic version of Miltown, the government invoked 1498(a), and the company sued. But after a years-long battle with the Justice Department, a court ruled the patent invalid in 1972.

Only after proving validity can the manufacturer go to the next step: trying to show that the government's price is unreasonable. To do this a drug manufacturer would have to disclose production costs. Brand name medicine manufacturers hate that idea.

A promising new idea came from Rep. Thomas H. Allen (D-Maine), who in 1999 proposed a bill that would allow pharmacies to buy drugs for Medicare beneficiaries at the best price paid by the government. As things stand, the beneficiaries pay retail prices that, on average, are nearly twice those paid by Medicaid, the VA, and big HMOs and hospitals. For example, Allen said, a prescription for Prilosec that cost an average customer $114.56 cost a large-scale buyer $59.10; the figures for Zoloft were $220.45 vs. $115.70.

The GOP-controlled House Commerce Committee held no hearings on the bill, and it died. But Allen, encouraged by having 152 co-sponsors (although none were Republicans), plans to re-introduce it.

His bill aside, the proposals for structural reform of drug prices are old because the structural problems are old. The arguments against the reforms are old, too. But why not a new Kefauver-type investigation? A subpoena-empowered congressional committee could determine where sensible incentives end and profiteering begins. What, exactly, is the case that the leaders on Capitol Hill, Republican or Democratic, might make against such an inquiry? Maybe they should tell us.

COX-2 INHIBITORS, *from page 8*

risks is occurring. For an important enzyme which is close to ubiquitous in the body, it is less than surprising that blocking its activity in one part, the gastrointestinal tract, must be balanced against the apparently harmful effects of blocking its critical functions in other parts of the body.

We strongly urge the retention of the NSAID class-warning label for these drugs, possibly adding that there is no evidence of statistically significant reduction in serious GI toxicity for celecoxib. This should take the form of a box warning (for all the drugs) which should be placed at the beginning of the label.

A second box warning about cardiovascular toxicity needs to be added. It should warn of the lack of platelet aggregation inhibition of the drugs which protects those at risk from an increased occurrence of heart attacks. In addition, the evidence which is rapidly accumulating about the heart damage caused by these drugs must be mentioned in this cardiovascular box warning.

What You Can Do

In light of the above discussion, we continue to advise the patient-protective five-year-rule for these drugs, as we do for all other new drugs that are not breakthroughs. *Do Not Use.*

OUTRAGE, *from page 12*

Charles Gibson: But are you saying that those—that the pictures overstate, in other words the fellow rowing the boat and riding around and stuff, that—that gives an image that the drug will do more than it really can?

Sidney Wolfe: Yes, I think one of the standards that the FDA uses is, is there fair balance between the statement of the benefits of the drugs and the statement of the risks. And in many cases, as you would expect an advertiser to do, they overstate the benefits and understate the risks...and lead people to believe that this drug is going to do much more that it really is and leave...

Charles Gibson: But isn't that awfully subjective when you're saying, "The pictures may tell a better story than the drug really can promise"?

Sidney Wolfe: Well, you have to analyze what the picture is portraying. Of course it's subjective up to a point, but there's also the audio that is going on, often at the same time. It's interesting that the risks usually get the audio treatment, and meanwhile across the screen is flashing the benefit treatment and that, in many cases, doesn't equate to final balance. And it's many big-selling drugs, not just Claritin—an allergy drug which I think you're going to mention in a couple minutes, but lots of drugs have been caught with illegal promotion.

Charles Gibson: Wayne Pines, let me turn to you. I know the FDA oversees this but it's interesting, I find that they can't really punish these drug makers, they can just warn them. Does that give the drug makers, in effect, license to say almost anything?

Mr. Wayne Pines (pharmaceutical industry consultant): No, and I don't think that the companies feel that way. Direct-to-consumer advertising of prescription drugs is the most heavily-regulated advertising on television. Every word, every nuance is looked at by the FDA. It's the only advertising that I know of which lists the risks associated with the products in addition to the benefits. And so I think that the consumer should be assured that what they see on television, generally, is very accurate and very, very balanced. There are instances in which there is a lack of balance, and the FDA moves very, very quickly and steps in and removes those ads from television.

Charles Gibson: Mr. Pines, do the drug manufacturers submit these ads in advance to the FDA?

Wayne Pines: Very often they do. They're not required to, but very

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OUTRAGE, *from page 10*
often they do just to get the FDA's views on the ads. Yes, they do.

Sidney Wolfe: I just wanted to comment on that. They are heavily-regulated except: A, the FDA doesn't have specific regulations just for direct-to-consumer ads. They go for the ones—they're using the ones that were designed for doctors. And, B, their staff is really too small, and, C, they have to submit these things within 15 days of the time they run them. Wayne is right that for at least the TV ads, they often, but not always, submit them in advance. Of the first 25 TV or radio ads that ran after the barrier was lifted in '97, though, 60 percent of them were found to be illegal. So that, obviously, then—maybe it's better now, but still, lots of illegal TV ads are going on which means that they really aren't cleared or sometimes the FDA looks at them and tells them to do something, and they don't pay attention to what the FDA tells them.

Charles Gibson: You should respond. Mr. Pines, go ahead.

Wayne Pines: Well, let me just say that the number of ads that are found violative are a small percentage of the ads that actually run. And once an ad is found to be violative, companies move very, very quickly, the next day, to remove those ads from television...and replace them with acceptable advertising.

Sidney. Wolfe: But then the next month, they'll come back again. The fact that there have been 14 times that ads for Flonase or Flovent, of the same chemical used for either allergy or asthma, 14 times these ads have been found illegal. So they just stop the one when once they're caught, and they come back the next month, do another one. There are no penalties at all for any of this. The FDA doesn't have the ability to put civil monetary penalties. They have rarely, if ever, used criminal sanctions, even for repeat violations. So we've got a real law enforcement problem here.

Charles Gibson: Let me go to Mr. Pines again. Dr. Wolfe mentions 14 times Flonase cited, 11 times Claritin was warned by the FDA, three citations on Celebrex. That doesn't that seem as if the drug manufacturers are sort of skating on thin ice here?

Wayne Pines: Well, I don't think that they are skating on thin ice. I think that the drug companies are being responsive to the FDA. In many cases, as you mentioned earlier, it's a matter of do-whats. It's a matter of image. It's a matter of subjectivity. And in advertising and trying to compress in 60 seconds all the information that a consumer needs about a prescription drug is very, very difficult, and it's very, very challenging. But overall, I just want to say, every single ad, without exception, without exception, contains the risks associated with the products. There have been some ads that have been counterproductive that have annunciated the risks so drastically that consumers have actually been turned off from using the product.

Charles Gibson: Let me play one of these ads. This is a Claritin ad, again that was cited by the FDA. And you mention how difficult it is to get in all the side effects in a short commercial. Take a look here. (Clip shown from Claritin TV Commercial.) They have to squeeze in the side effects there. They do it, sometimes, in almost FedEx commercial speed.

Sidney Wolfe: Charlie, that's a little bit what I was saying before is that the visual is someone that's taking a drug that's so great that they can roll around in hay. I mean, one of the things these ads don't tell about are alternative treatments that may be just as safe or safer and less expensive or prevention, like staying away from things that cause allergies. But you heard—you saw the benefits, and you heard, read as fast as possible, a list of risks. I think that most of the people would come away from that ad—would get the image of the hay and rolling in the hay and taking this drug and probably wouldn't remember very much about the risk. The FDA did a study showing that TV ads are much less likely to convey risk information.

Charles Gibson: Let me give Wayne Pines the last word here.

Wayne Pines: I don't think anybody would think that you can play basketball better or roll in the hay by taking a drug. That's an advertising approach. Every single ad contains the risks. What consumers need to understand is that the advertising is accurate, and, basically, what the advertising is trying to do, is to inform the consumer about the drug and encourage a dialogue with the doctor. Ultimately, it's up to the doctor to decide whether the drug is right for the patient.

Sidney Wolfe: Under pressure from patients. Four hundred and eighty violations of the law in the last four years is really unacceptable. The current status of advertising on television and print of direct-to-consumer ads are unacceptable. Patients should be getting objective information when they get a prescription filled, something the industry stopped.

A Discussion of Misleading Drug Ads

The following is a transcript of Good Morning America, ABC News which featured Dr. Sidney Wolfe, Editor of the Health Letter *in a debate with* Wayne Pines of APCO Worldwide. *The segment was aired on January 3, 2001.*

Charles Gibson, co-host: Well, you see them just about anytime you turn on your TV, prescription drug ads that promise relief from everything from arthritis to postnasal drip, but are they exaggerating their claims? The [Food and Drug Administration] FDA says, in some cases, they are and has warned numerous companies, including the makers, for instance, of the nasal spray Flonase, warned 14 times.

For both sides on this issue, we are joined now from Washington by Wayne Pines of APCO Worldwide, a pharmaceutical industry consultant, and Dr. Sidney Wolfe, director of the Public Citizen's Health Research Group, and I welcome both of you.

If I could, let me start with one of these ads where the FDA has warned the marketers of this drug a couple—three times, actually. This is a Celebrex ad. And then I'm going to come back and ask you about it. Let's take a look.

(Clip shown from Celebrex TV commercial)

Charles Gibson: Sidney Wolfe, let me start with you. That seems fairly benign, what I'm seeing there. Why did the FDA have objection?

Dr. Sidney Wolfe (Director, Public Citizen Health Research Group):

Well, there have been a series of Celebrex ads that have gotten into trouble. I think the main reason for those ads and for most of the ads is that they overstate the benefits, they imply that the drug is much better that it is and with Celebrex, flaunt FDA approval for treating pain, for instance. It's approved for arthritis. But I think that the image that you get, and that's what television ads are, it's an image, overrides the other kinds of information that should be in there. Over the last four years alone, there have been 480 ads that have run for doctors and patients, many of them on television, that have been found illegal, that violate FDA laws or regulations. So this is a very common practice, and the companies just keep repeating.

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