

The Bendectin battle

This year's final chapter in the Bendectin saga is all about inserts — specifically, package inserts. The U.S. Food and Drug Administration proposed in the Dec. 5 *FEDERAL REGISTER* that Richardson-Merrell Inc. of Merrell-National Laboratories in Cincinnati, Ohio, be required to insert consumer information sheets in its packages of Bendectin, a drug used to treat the nausea and vomiting of pregnancy. Those information sheets would remind users of the drug that alternative nondrug treatments, eating soda crackers or drinking hot liquids, for example, are known to relieve mild nausea and that "use of any drug during pregnancy may carry potential risks to the fetus." While the FDA insert proposal — to be finalized in February — actually applies to all manufacturers, distributors and dispensers of any morning sickness drug containing doxylamine succinate (an antihistamine) and pyridoxine hydrochloride (vitamin B₆), the greatest share of that drug-combination's market consists of Richardson-Merrell's Bendectin.

Richardson-Merrell estimates that 25 percent of pregnant women in the United States take Bendectin and that the drug is also popular in other countries such as Germany, Canada and Great Britain. Although this widely used pregnancy drug has been on the market for 23 years, its safety has been questioned in the past two years. Doubts about Bendectin's safety were first brought to the public's attention chiefly through an October 1979 *National Enquirer* article that compared the drug to thalidomide — the early 1960s sedative found to cause severe malformation in limbs of developing fetuses. The article also introduced David Mekdeci of Orlando, Fla., to the general public.

Mekdeci, born in 1975 with a sunken chest and malformations of the right arm and hand, was to be the subject of the first Bendectin lawsuit. His parents were seeking \$12 million from Richardson-Merrell in a damage suit alleging that Mekdeci's birth defects were caused by that company's morning-sickness drug. The trial ended in March 1980 when a federal jury concluded that nothing should be awarded to the boy or his parents for damages but that \$20,000 should be awarded for medical expenses. In May, however, Federal Judge Walter E. Hoffman ordered a new trial, calling the jury's verdict "inconsistent." The retrial is scheduled for January 1981.

If certain lawyers have their way, the Mekdeci trial won't be the only Bendectin-related court case. Lawyers are employing various methods, such as placing ads in newspapers, to seek women who took the drug and bore deformed children to join in lawsuits against Richardson-Merrell. The lawyers in the Bendectin controversy feel the company's past performance is the basis for at least two strikes against it. In 1960, Richardson-Merrell marketed Mer-29, a cholesterol-lowering drug that turned out to cause cataracts. The company was indicted and fined for making false statements to the FDA about Mer-29. In addition, the company marketed thalidomide in Canada in the early 1960s and also tried to introduce it to the U.S. market by distributing free samples to doctors. Later, Richardson-Merrell was successfully sued on behalf of U.S. and Canadian thalidomide children.

Whether the lawyers have more than a company's past record on its side is still unclear. In September, an FDA panel met to review epidemiologic studies of Bendectin. "In 11 of 13 studies of pregnant women who received Bendectin, there was no evidence of an association between the drug and an increased risk of birth defects. None of the studies, however, was large enough to rule out a small increase in risk," FDA officials concluded.

According to FDA statistics, about 2 to 3 percent of children are born with a major birth defect. This risk may be increased if the mother takes drugs or other substances (alcohol, for example) during pregnancy — particularly during the first 8 to 12 weeks when the child's basic body parts develop.

Sharpening the EEG

The brain is abuzz with electrical activity, and for more than 50 years researchers and clinicians have been using the technique known as electroencephalography to record and interpret the brain's electrical activity. During that time the EEG has proved to be an exceptionally useful tool in attempts to understand the workings of the brain. Now, with the aid of computers and mathematical refinement of EEG data, the EEG may become an even more useful tool. Two reports in the Dec. 12 *SCIENCE* conclude that EEG recordings accurately reflect the age and functional status of the brain and can detect learning disabilities and neurological disorders. "With maturation," say the researchers, "the dominant frequency [of brain waves] becomes more rapid, and brain damage, dysfunction or deterioration causes frequency slowing in the brain regions involved."

Previous research has shown that EEG patterns in children change gradually with age. This, say the researchers, "encouraged us to construct regression equations to describe maturational changes in the EEG, to test the accuracy of these equations in diverse groups of children and to evaluate their sensitivity to brain disease or dysfunction." Sixty-second, eyes-closed EEG recordings taken from 140 normal, healthy children who were performing well in school yielded values that fit precisely with those predicted for their ages. In addition, because the observed values were the same in children from different cultures, the researchers suggest those values "may be generally acceptable, independent of cultural, ethnic, socioeconomic, sex or age factors."

Having demonstrated that the set of developmental equations they constructed can be used to accurately correlate EEG values of normal children (up to age 21) with age, the researchers next studied groups of children with neurological disorders and learning disabilities. Such abnormalities result in slowed brain waves, and the researchers found that their method of measuring EEG values "may offer a brief, reliable and economic method of rapid examination of children who, because of consistent behavioral problems or learning difficulties, are considered at risk for brain dysfunction or disorder... [P]ositive findings," they conclude, "would justify referral for more exhaustive evaluations."

The researchers were: E.R. John, H. Ahn and L. Prichep of the Brain Research Laboratories at New York University Medical Center; M. Trepetin of Neurometrics, Inc., in New York; D. Brown of New York State Institute for Basic Research in Mental Retardation; H. Kaye of the State University of New York at Stony Brook; and H. Baird of St. Christopher's Hospital for Children, Temple University School of Medicine in Philadelphia.

Opiates and crime rates

Heroin addicts get blamed for much of the crime committed in our cities, and now an extensive study of persons addicted to heroin and other opiates finds that the blame is well placed. John Ball, Lawrence Rosen and John A. Flueck conducted the study for the Temple University Health Sciences Center in Philadelphia. The data were compiled by David Nurco of the University of Maryland School of Medicine. He found that 243 male addicts in Baltimore committed more than 500,000 crimes during an 11-year period. "The average addict," says Ball, "committed just under 2,000 offenses while on the street in an average 11-year period." Many committed a crime a day while addicted. And "our findings," says Ball, "indicate that it is opiate use itself which is the principal cause of high crime rates among addicts." Crimes were committed at a rate six times higher when the addicts were under the influence of opiates than during periods of nonopiate use.