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Information of importance to physicians and other health professionals

standards and the continuing FDA certification program are intended to bring all digitoxin products to a uniform standard of essentially complete absorption. FDA will continue to monitor digitoxin bioavailability through this program and will bring any significant problems to the attention of the medical community.

References
1. Revised digoxin dosage. FDA *Drug Bull* 6:31-32 (Aug-Oct) 1976.
2. Labeling for digoxin products. *Fed Reg* 41: 17755-17761 (Apr 28) 1976.

Reye's Syndrome: Etiology Uncertain But Avoid Antiemetics in Children

Reye's Syndrome (RS) is now considered by some observers to be among the 10 major causes of death in children aged 1 to 10 years. It was previously considered rare, but the number of cases recognized has increased and milder forms are now also detected.[1,2]

RS is an acute encephalopathy of childhood accompanied by visceral fatty degeneration. The clinical history is generally one of mild prodromal illness followed in 3-6 days by sudden onset of vomiting and CNS disturbance. The age range is from 2 months to adolescence; both males and females are affected.

In one group of 21 patients (5 months to 8½ years of age), only 4 survived. In another series of 16 cases (31% over 10 years of age), 14 were fatal. Currently available therapies are not likely to result in better than 50% survival.[4]

The abrupt clinical picture has suggested a toxic etiology. It has been postulated that chemical toxins in combination with viral infection and genetic predisposition possibly may be involved in production of the syndrome. Concern has been expressed over the possible role of common medications in therapeutic dosage, and suspect drugs have included antiemetics, antipyretics (aspirin and acetaminophen), and antibiotics. This concern has been heightened because of the demonstration that drugs such as acetaminophen can, during the course of their metabolism, yield metabolites which are capable of causing hepatic cell damage.[3,4]

The Center For Disease Control has conducted a surveillance of RS over the past decade. As a result of its studies, the Center now considers influenza B and varicella virus to be the most important etiological factors.

To examine the possibility that drug therapy may also be involved, FDA's Neurologic Drugs Advisory Committee in conjunction with a number of outside consultants, recently reviewed available data. The Committee has concluded that present evidence is insufficient to show that antiemetics, aspirin, and acetaminophen are clearly causally related to RS, although this possibility cannot be eliminated. In view of this, the Committee expressed concern about the widespread use of these drugs, particularly antiemetics, such as phenothiazines and trimethobenzamide (Tigan), for minor indications in children. The Committee recommended against the use of antiemetics, aspirin, and acetaminophen in children whose signs and symptoms (sudden onset of vomiting with CNS disturbance) suggest RS for the following reasons: (1) the possibility remains, although unproven, that these drugs adversely affect the course of the disease, and (2) the extrapyramidal signs caused by antiemetics may be confused with the CNS involvement in RS.

References
1. Reye RDK, Morgan G, Baral J: Encephalopathy and fatty degeneration of the viscera: a disease entity in childhood. *Lancet* 2: 749-752 (Oct 12) 1963.
2. Reye RDK, Morgan G: Encephalopathy and fatty degeneration of the viscera. *Lancet* 2: 1061 (Nov 16) 1963.
3. Stechenberg BW, Keating JP, Koslov S, Schechter M, Chang M, Haymond MW, Feigin RD: Epidemiologic investigation of Reye syndrome. *J Peds* 87: 234-237 (Aug) 1975.
4. Corey L, Haller JS, Rubin RJ, et al: *Reye's Syndrome* (Pollack JD editor). Grune & Stratton, New York, 1974, p 179-187.

Notification of Pacemaker Failures

An FDA-sponsored Pacemaker Registry maintained by three US medical centers monitors and collects data on pacemakers. It recently provided the Agency with a report that evaluates the performance of all registered pacemaker pulse generators.[1] The findings indicate that continued surveillance and long-term evaluation of all varieties of these commercially available generators are essential for identification of causes of unexpected failures.

FDA has found that critical malfunctions may be due to faulty pulse generators, power source failure, lead fracture, and electrode-heart interface alterations. Other malfunctions are caused by dendritic growth on printed circuitry boards, moisture accumulation, inadequate hermetic sealing, and component failure.

Although implantable cardiac pacemakers are effective and reliable devices for treatment of many forms of cardiac disease, system failures and critical malfunctions sometimes occur unexpectedly. Under the Medical Device Amendments of 1976, FDA must insure that both health professionals and the public are notified of such newly identified risks by the most suitable means.

Public notice of pacemaker malfunctions is a sensitive issue involving physicians, their patients,