

merits further study. Certainly there are measurable, although relatively minor, effects on myocardial conduction, demonstrable by in vitro and in vivo animal experiments. Reports of human toxicity that provide cardiac and electrocardiographic commentary (many of these are reviewed in the Lilly Blue Book) strongly suggest that cardiocirculatory disturbances--such as arrhythmias, ventricular fibrillation, and cardiac arrest--arise mainly from severe anoxia, due to respiratory depression and apnea, acidosis, which may be severe, and electrolyte imbalance. Central nervous system depression per se may directly interfere with cardiopulmonary and circulatory function.

The possibility that norpropoxyphene may play a role in cardiac manifestations of severe drug overdose cannot be excluded, but there is no clinical evidence to show that it does. The central nervous system depressant effects of propoxyphene itself (notably anoxia and acidosis) can account for the cardiac effects that have been observed in overdose cases.

Additional Studies

Lilly has indicated consideration of additional studies, including a continuation of the update by Dr. Finkle of those medical examiner offices surveyed in his 1975 study.