Targeted Intervention in the Control of Accidental Drug Overdoses by Children

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CHILDHOOD DEATH RATES have declined remarkably in the United States in the past 50 years—mostly as a result of significant control of infectious diseases. Yet accidental deaths have declined only slightly. In 1975 the death rate for youngsters between 1 and 5 years old was 70 per 100,000 children, and accidents accounted for almost 40 percent of these. In the general population, accidents represent only about 10 percent of the causes of death. Mortality does not fully characterize the problem because it is estimated that severe nonfatal injuries and intoxications outnumber fatal ones by a ratio of 200 to 1.

Poisonings in young children, however, represent a decreasing proportion of accident mortality and morbidity. In 1950 it was estimated that up to 50 percent of all accidents reported to pediatricians were poisonings. Between 1953 and 1963 the U.S. mortality rate for poisoning in preschool children was fairly constant at 2.3 per 100,000 children, but between 1964 and 1967 the rate dropped to 1.7 (*1*). By 1972 the rate had fallen to about 1.4, almost a 40 percent reduction (*2*). Deaths due to aspirin ingestion in children under age 5 declined by 63 percent between 1972 and 1975 (*3*). In a remarkable clinical experiment in Tacoma, Wash., between 1968 and 1970, childhood ingestions of 75-mg flavored "baby" aspirin tablets were reduced by 95 percent (*4*).

Thus, despite the concurrent increase in the toll of childhood morbidity and mortality due to accidents, the portion due to poisonings has declined significantly over the past 15 years. Why?

To answer this question it is necessary to go back to the early 1950s and review the beginning of formal recognition by U.S. pediatricians that their success in the control of bacterial infectious diseases had actually unmasked the accident and poisoning problem that had been "hidden" in the raw statistics all along (*5*). As the result of this emerging awareness, the American Academy of Pediatrics (AAP) established its first Accident Prevention Committee in 1952. The committee instituted a survey of 3,000 AAP members concerning factors associated with childhood accidents. The replies produced interesting data: for instance, it was shown that 30 percent of all serious accidents were related to burns associated with flammable clothing. In this re-

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gard, organized efforts (the first in the nation) pertaining to such product-related injuries were initiated and resulted in many useful recommendations including Federal legislation (the Flammable Fabrics Act).

An unexpected finding in the AAP survey was that about 50 percent of the listed accidents concerned some type of poisoning (*6*). These toxic episodes were usually nonfatal and were caused by common household items such as aspirin, sedatives, petroleum products, cleaning agents, lye, and pesticides. Survey respondents also voiced a need for more information about poison treatment. Eventually the Illinois Chapter of the AAP initiated the first U.S. Poison Control Center in November 1953 in Chicago, under the direction of Dr. Edward Press. It is noteworthy that the American Public Health Association offered cooperation in the venture, and in 1956 recommended that a National Clearinghouse for Poison Control Centers be established. The Secretary of the Department of Health, Education, and Welfare agreed to this, and the clearinghouse operation was assigned to the Public Health Service—where it continues to function. Since 1957 about 500 local centers have been established (*7*).

The combined results of many informational, educational, and treatment endeavors of these centers probably contributed to the proportionate decline in poisoning mortality and morbidity compared with all accidents. They also provided a model for the "crisis center" or special switchboard concept that is presently so popular.

Throughout these early years, aspirin (generally, flavored baby aspirin) was the medicine most commonly ingested—25.8 percent of all cases reported to the Clearinghouse in 1966 (*8*). According to the Clearinghouse, the numbers of children up to 5 years old who were hospitalized because of aspirin ingestion in 1964–65 were as follows:

Age (years)	*Baby aspirin*	*Adult aspirin*
0–1	3	3
1–2	86	18
2–3	483	47
3–4	394	21
4–5	96	12
Total	1,062	101

Subsequently, a number of pediatricians from the AAP and within the Food and Drug Administration encouraged industry and government to marshal all efforts to eradicate the baby aspirin problem.

Hearings were held in Washington by the Subcom-

mittee on Public Health and Welfare (House of Representatives), and all available data on toxicity were presented in testimony. A committee was appointed by the Commissioner of Food and Drugs to assess the situation, and eventually industry and the FDA agreed to limit the number of flavored baby aspirin to 36 tablets per package. The 36-tablet choice was arbitrary and the result of a compromise. The FDA had initially requested a maximum of 25, 1.25-grain tablets. The maximum of 25 tablets per package was accepted in Canada.

The FDA committee also made recommendations regarding childproof packaging, and many of these were incorporated into the Poison Prevention Packaging Act of 1970. Thus, two powerful preventive measures were deployed at almost the same time, and the final attack on aspirin poisoning in toddlers began. In 1977, Dr. Matilda McIntire of Creighton University School of Medicine reviewed in detail the history and results of this attack (*3*). As noted earlier, in 1966 aspirin accounted for 25 percent of all accidental ingestions in children under age 5 (*8*). For this age group, aspirin ingestions declined by 41 percent and mortality reports by 63 percent between 1972 and 1975. By 1974 aspirin accounted for only 4.7 percent of total ingestions reported to the Clearinghouse. A battle had been won.

It is noteworthy that McIntire's review was titled "Safety Packaging: A Model for Successful Accident Prevention." Poisoning in young children is clearly related to developmental achievements (*4*) and behavioral traits (*9*). The adventurous 2-year-old is normally impulsive and can be expected to ingest the contents of any bottle as a simple challenge. No amount of "training" will prevent this and, in fact, the more intelligent toddler is thought to be at greater risk of becoming a victim of accidental poisoning (*9*). Limiting the inevitable environmental hazard to a dose below the minimum lethal concentration will obviously limit mortality. The additional intervention of decreasing accessibility (with a safety closure) limits morbidity (*10*). In the case of baby aspirin, the data clearly reflect the effectiveness of these two discrete interventions and support the conclusion that such a model, with perhaps other specific modifications, can be employed in additional targeted prevention endeavors.

A Model for Poison Prevention

As noted before, reports from the National Clearinghouse for Poison Control Centers have indicated a significant decrease in severe aspirin intoxications in toddlers. It is clear that at least two passive interventions—safety closures and total tablet limitations (*11*)—have contributed the most to this favorable situation. However, if we are to regard the experience with children's aspirin as a model for other preventive programs in poison control, it is necessary to analyze the situation in an epidemiologic manner. Every accidental ingestion by a youngster is the result of a complex net of environmental interactions that include every facet of the child and the world around that child. But certain obvious precursors can be identified, and evaluation of these precursors can guide us to a more logical approach to the selection of useful and specific (targeted) interventions.

Figure 1. Factors that may influence outcome of accidental ingestion of drugs by children

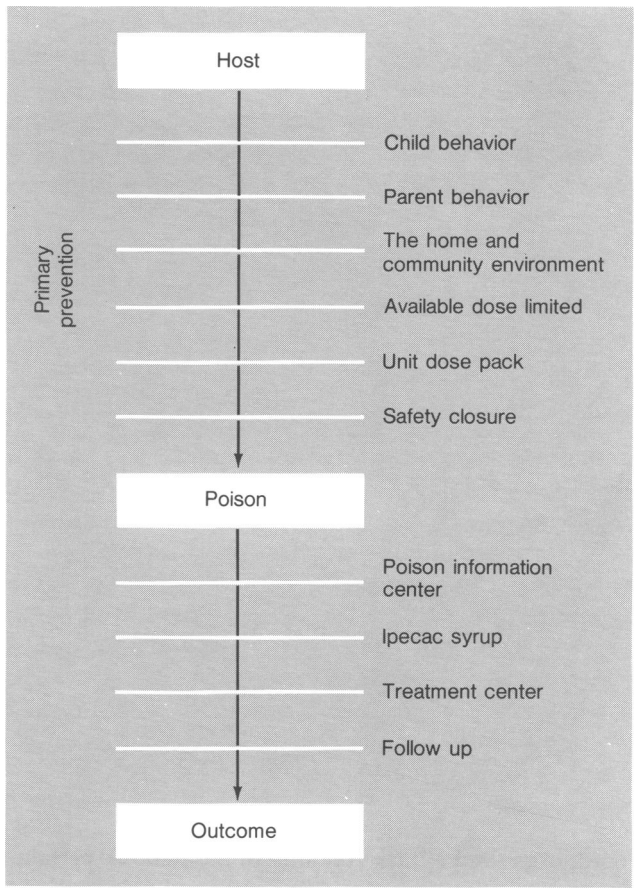
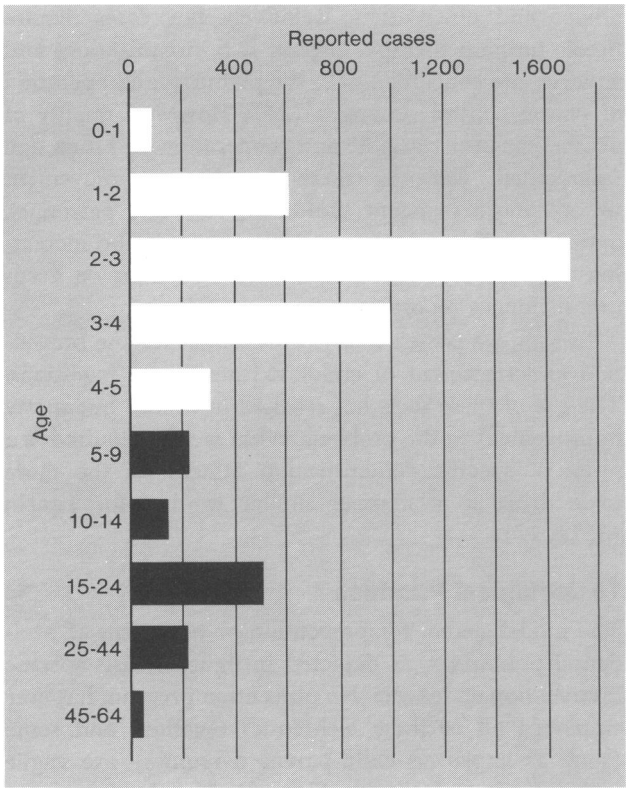


Figure 1 shows elements that influence outcome of accidental ingestion of drugs by children. The host is protected from eventual damage or death by a series of "barriers." Conversely, the child's risk of becoming a victim increases as one or more of these natural or planned protective mechanisms becomes defective or is absent. The barriers (or defects) depicted include the child's behavior, the family's behavior, the community environment, an available dose more or less than toxic, a safety closure, and strip or unit packaging of drugs. These items reflect true primary prevention because if they can be favorably deployed the accident is avoided. Familiarity with the poison information switchboard,

Figure 2. Frequency distribution of all aspirin overdoses reported to the National Clearinghouse for Poison Control Centers, 1976, by age groups



ipecac syrup, other home first-aid measures, or prompt arrival at a poison treatment center all constitute secondary prevention.

Since the incidence of accidental ingestions rises abruptly after age 1 and falls off after age 4 it is quite obvious that motor development and age are risk factors (fig. 2). The child's psychological and personality development are also factors but data supporting this are not as distinct. In 1968, Baltimore and Meyer (*9*) showed a highly significant relationship between daredevilness and the risk of a poisoning accident. An unpublished study by the California Department of Public Health also corollated accident liability with "extraversion, roughhousing, and daring." Wehrle and associates studied 100 children admitted to a hospital in Syracuse, N.Y., for nonfatal poison ingestions. Their sample was chosen randomly and, using a special behavior scale, they described such children as high-strung, impulsive, overactive, and "masculine" (*12*). However, Sobel and Margolis (*13*) compared one-time ingestors with repeaters and controls and concluded that repeated episodes of poisoning were not related to accident proneness or lack of parental supervision.

Because of methodological weaknesses and lack of psychodynamic attention in many of these studies, Sobel conducted an extensive prospective investigation of 1,226 randomly selected children in rural New England (*14*). The 122 cases of poisoning that developed were matched with nonpoisoned children, and all families were subjected to extensive interviews and instruments of psychological and psychosocial measurement. Sobel found that males poisoned themselves more frequently than females. There was no significant graded relationship to age, intelligence, precocious development, or general accessibility of toxic substances in the home. The most remarkable association with repeaters was that of maternal psychopathology—mental illness, poor ego strength, and marital and sexual dissatisfaction. Sobel viewed repeated accidental poisoning as "one of the terminal links in a process which starts with failure of mothering and leads to the frustration of a number of the child's needs. . . ."

In a more recent study, Newberger and associates confirmed the effect of ecological stress on the etiology of accidents, ingestions, failure to thrive, and child abuse (*15*). They recommended a greater focus on the stresses and strengths within the family as a means of identifying and preventing such illnesses (*16*). Simple nonspecific educational campaigns appeared to be unrewarding.

As noted previously, restriction of the total amount of drug per package has contributed to the decline of serious intoxications due to baby aspirin (*11, 17*). It is surprising, however, that a similar strategy has not been employed for other agents, especially the more toxic ones. (The Consumer Product Safety Commission does limit total elemental iron content in over-the-counter vitamin and mineral supplements.)

A somewhat similar but less effective intervention is the use of unit packaging. This method employs plastic strip or blister cells for each tablet (*18*). Although these packages can allow one or more "entries" by the child, the entry operation must be repeated for each tablet thus delaying the possibility of ingesting a large total dose. Indeed, Done has suggested that the strip or blister material be malflavored, thereby decreasing the tendency for the toddler to chew through the package (*18*). Unfortunately, the present interpretation of Federal regulations for poison prevention packaging would regard even a single entry by a child as evidence of a noncomplying package (*19*) since testing standards are designed essentially for safety closures. For certain highly toxic drugs, such as ferrous sulfate, tricyclic antidepressants, digitalis, Lomotil, and narcotics, it would seem prudent to consider the dual use of unit dose barriers plus an outer safety closure. Industry's objections to such suggestions have generally concerned added costs. Yet broad usage would eventually compensate for additional

cost, and the complex packaging would be a clear and needed warning to adults of the real hazards involved in the storage of such dangerous substances. Furthermore, there are many disquieting reports that increasing numbers of adults do not re-secure the safety closure after each use; thus the added protection of an individual tablet barrier, such as strip packs, seems compelling and worth the effort. With such a combination it would be impossible for the child to ingest a handful of loose tablets or capsules in one episode (*18*).

There is now abundant evidence that the Poison Prevention Packaging Act of 1970 has helped to reduce the rate of childhood accidental poisoning. Most of the clinical research supporting the feasibility of this legislation has been reviewed by Scherz (*4*) and the value of testing procedures by Temple (*19*). While there was a significant amount of consumer resistance initially, public education and familiarity with improved child-safe packages have increased acceptance. The biggest current problem concerns mishandling of the container by adults in such a way as to reduce its child-resistant effectiveness (*10, 20*). Physician and pharmacist efforts devoted to adult education programs in the proper use of these containers would probably produce greater (targeted) impact than the present nonspecific safety campaigns so widely employed. Since poor initial performance deters many adults from further acceptance of these containers, Myers believes that Federal testing regulations should reflect a high success rate among adults when they first attempt to open the containers (*20*).

There will always be an irreducible incidence of childhood ingestions. Nevertheless, a number of methods for decreasing the absorption of drugs are available. The value of ipecac as an emetic has been known for more than a century. Adequate directions and labeling for over-the-counter sale in the United States were formalized in 1965 and resulted in the encouragement of campaigns to have this safe and valuable material in all homes with small children (*21*). The proper use of ipecac, in conjunction with professional advice by telephone, can institute early emetic treatment at home and represents rational first-aid therapy. The efficacy, dosage, contraindications, and toxicity of ipecac have been reviewed by Cashman and Shirkey (*22*). Although ipecac syrup should be available in all at-risk homes as a general principle, my previously published targeted recommendation bears repeating—for certain highly toxic drugs, a bottle of ipecac syrup should be dispensed automatically with the initial prescription (*23*).

Any treatment instituted after the accident is termed secondary prevention and is designed to reduce morbidity. Such measures usually require the aid of professionals with knowledge and training in clinical toxicology. Fortunately, most childhood ingestions are relatively benign and require little more than telephone advice and observation. Relatively few cases require heroic hospital therapy. Several U.S. organizations and agencies are concerned with the planning and operation of poison control programs (*24*). However, quality of service has been variable and cooperation and direction fragmented. Recently there has been a movement toward more stringent standards, full-time personnel, and regionalization schemes (*25*). There is also increasing emphasis in larger poison control centers on accurate incidence reporting and patient followup.

In sum, we possess many proved tools for the prevention and treatment of childhood accidental ingestions. The use of these tools has resulted in overall but spotty improvement in the problem. What is now required is a series of specific demonstration attacks on the more toxic drugs in a manner similar to that for aspirin (*3, 11, 17*).

Toxicological Priorities

The model system for prevention or treatment of accidental poisonings, as depicted in figure 1, lists specific intervention endeavors. No prevention program has ever employed all of these techniques together, and some (such as improved child-parent dynamics) are vague and difficult to institute efficiently. Yet the experience with baby aspirin tablets demonstrates that a series of linked and passive interventions can be incredibly successful and acceptable.

From a public health standpoint, another issue must be addressed before additional programs are planned. The thousands of drug preparations on the market encompass a very broad spectrum of toxicological effects. Some items such as antacids, antibiotics, or oral contraceptives produce relatively low intrinsic toxicity when a child ingests as many as 15 to 20 tablets. Other compounds are potentially lethal after absorption of as few as 4 or 5 units (narcotics, ferrous sulfate, and tricyclics, for example). Thus, it is appropriate to evaluate common clinical experience according to a drug's relative potential for producing serious injury. In other words, instead of planning future endeavors to include all drugs, it would be prudent to choose a few compounds of high clinical toxicity and widespread availability.

Such an approach is not unlike the World Health Organization's risk strategy managerial model for the use of limited medical resources in developing countries. The summary phrase, "Something for everyone, more for those in greater need," could be paraphrased as "Concern for all poisonings, but emphasis on those of highest toxicity" (*26*).

Hospitalization due to ingestions of selected drugs by children under 5 years old, 1975–76

Drug	Percent hospitalizations		Total reports	Combined hospitalization data, 1975–76	
	1975	1976		Number	Percent
ExLax	1.57	0.65	1,370	16	1.16
Propoxyphene [1]	6.59	3.94	334	18	5.39
Benadryl	5.68	6.04	325	19	5.84
All iron	16.70	17.01	931	157	16.86
Tricyclics	18.97	18.97	680	129	18.97
Lomotil	25.21	29.16	426	115	27.00

[1] All Darvon and propoxyphene drugs plus mixtures.

SOURCE: National Clearinghouse for Poison Control Centers.

The approximately 500 poison control centers in the United States send individual poisoning reports to the National Clearinghouse. About 150,000 such reports are received yearly, and they are tabulated and summarized in FDA's "Poison Control Statistics." These raw reports generally are not verified, and they do not constitute measures of risk since reporting is incomplete, capricious, and not based on a fixed population. Each specific drug product is tabulated according to age of victim, existence of symptoms, hospitalization, and mortality (*27*). In my attempt to employ these data as rough measures of relative toxicity, I concluded arbitrarily that hospitalization of a patient represented a crude dichotomous measure of severity. (The overall hospitalization rate for all drugs and chemicals in children under 5 years old is about 3 percent.) The combined hospitalization data for 1975 and 1976 for children under age 5 for six arbitrarily selected common drug products are shown in the table. It is recognized that criteria for hospitalization of a poisoned child vary widely among regions, physicians, and economic status of the family, but the similarities in the percentages of patients hospitalized in different years add a measure of reassurance to this approach. It is beyond the scope of this discussion to evaluate the many obvious sources of bias in Clearinghouse reporting methods.

The six drug products (ExLax, propoxyphene, Benadryl, iron salts, tricyclic antidepressants, and Lomotil) represent a group of broadly available pharmaceuticals that may lead to a wide spectrum of acute toxic conditions. Despite 1,370 cases of ExLax overdoses reported for children under 5 years, only 16 (1.16 percent) required hospitalization in the 2-year period. By contrast, 27 percent of the Lomotil ingestions resulted in hospitalization. It is not my intention to profer these crude proportions as equal to standard acute toxicity studies (LD_{50}), but they can represent valuable clinical input for planning risk strategies.

With the use of hospitalization as a measure of clinical toxicity (and recognition of its limitations), it can be seen that overdoses due to iron salts, tricyclics, and Lomotil are regarded as serious matters by local physicians, whereas the other three drugs are considered—on the average—to be much less serious (*28*). Lomotil tablets, used as a remedy for diarrhea, contain diphenoxylate (an addicting narcotic) and atropine in a fixed combination. As few as five tablets can produce life-threatening respiratory depression in a small child (*29*). The proprietory product is listed among the top 50 most prescribed drugs in the United States, and this list may not include all of its generic equivalents (*30*).

Several very similar tricyclic antidepressants are currently available: imipramine, amitriptyline, desipramine, doxepin, nortriptyline, and protriptyline. These drugs are marketed under at least 17 trade names as single entities or combinations. Two preparations, Elavil and Triavil, were listed among the 50 most prescribed drugs in 1977 (*30*). Accidental ingestion of as little as 10 mg/kg of one of these compounds can create a medical emergency; such an overdose would be contained in two 50-mg tablets if ingested by a 22-pound toddler (*23, 31*).

More than 100 iron hematinic products are on the market, but the most commonly prescribed is the 300-mg ferrous sulfate tablet containing 60 mg of elemental iron—as few as 3 or 4 of these can cause severe toxic symptoms in a toddler. Many of the tablets marketed look very similar to the popular "M & M" candy (*32, 33*). Between 1969 and 1973, 543 hospitalizations for iron overdoses were reported to the Clearinghouse for children under 5 years old.

Recommendations

Based on the foregoing, I propose that ferrous sulfate 300-mg tablets, all tricyclic compounds, and all Lomotil formulations be targeted for a special poison prevention attack. These prescription items are already dispensed

in childproof containers under provisions of the Poison Prevention Packaging Act (*34*). However, unlike baby aspirin, limiting the maximum number of tablets to be dispensed per package—because of the small number of units that are toxic for children—would be too inconvenient for consumers. Instead, these three medications could be dispensed as unit doses in opaque plastic strip cells, and the total number of units prescribed could be further enclosed in an appropriate childproof container. Some manufacturers and pharmacists might object to this "double barrier" approach, but the technology exists to produce such packaging, it is practicable, and it would not inconvenience adults. Furthermore, the time taken to open each unit might discourage suicides (*35*). I also recommend that studies be conducted to determine the feasibility of incorporating a malflavored component into the plastic strip material, as suggested by Done in 1971 (*18*).

If our successful experience with the prevention of ingestions of baby aspirin is considered a model (*3*) of targeted intervention in poison control, then we must move toward other compelling targets. My modest proposal for reducing morbidity and mortality from ingestions of ferrous sulfate, tricyclics, and Lomotil could be accomplished easily and soon if manufacturers, pharmacists, physicians, consumers, and regulatory agencies would mobilize to carry it out. No new legislation is required.

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