Accidental Poisoning With Psychotropic Drugs in Children

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• **Seventy-seven (0.24%) of 32,005 admissions to the Massachusetts General Hospital pediatric service during the period 1962 to 1973 were due to accidental poisoning. In 27 cases, mostly involving children less than 6 years of age, psychotropic drugs were implicated. These included sedative-hypnotics in six cases, phenytoin in two, major tranquilizers in five, antidepressants in three, stimulants or hallucinogens in three, and drug mixtures in eight. Toxicologic analyses contributed little to diagnosis and initial management. Except for one child who ingested ferrous sulfate, no patient was seriously intoxicated, and all recovered rapidly without sequelae. Although referral of serious poisoning cases to another hospital may have biased the results, the findings suggest that accidental psychotropic drug poisoning is not a major source of childhood morbidity.**

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More than 50% of all cases of self-poisoning involve accidental ingestion of drugs or other noxious substances by children.[1-3] Psychotropic drugs are implicated in many such cases.[1-5] We investigated the incidence and consequences of accidental psychotropic drug poisoning in children admitted to the Massachusetts General Hospital between 1962 and 1973.

SUBJECTS AND METHODS

The Massachusetts General Hospital is a 1,089-bed general medical center including an 85-bed pediatric service. For all patients admitted from 1962 to 1973, diagnoses were coded descriptively and numerically and stored on magnetic tape.

Patients whose diagnoses were consistent with self-inflicted injury, deliberate or accidental self-poisoning, or attempted suicide were identified by computer. A research nurse (M.D.A.) reviewed the medical records of all such patients under 16 years of age. Pertinent data were recorded on a standardized form. The excerpted summaries were verified against the patient records by a second investigator (D.J.G.) and used to prepare the present report. In patients who experienced central nervous system depression as a consequence of drug ingestion, the severity was rated by the following system of Matthew and Lawson[6]: grade 1, drowsy but responds to verbal stimulation; grade 2, responds to mild painful stimulation; grade 3, minimum response to maximum painful stimulation; and grade 4, no response to maximum painful stimulation.

RESULTS

A total of 32,005 patients were admitted to the Massachusetts General Hospital pediatric service between mid-1962 and mid-1973 (mean ± SD, 2,909 ± 144 per year). Seventy-seven admissions (0.24% of the total) were due to poisoning; in 27 cases psychotropic drugs were implicated. The present report is based on review of the records of these 27 patients. Children treated in the emergency room and discharged without hospital admission are not included.

The patients' ages ranged from 13 months to 7 years (mean, 35 months; median, 24 months); 23 of the 27 were 5 years of age or less. Fifteen (56%) of the children were male. Based on 16 cases for which this information was available, the time between drug ingestion and arrival at emergency treatment facilities ranged from 45 minutes to nine hours (mean, 3.6 hours; median, 2.5 hours). Eight of the 27 cases received treatment at another medical facility before coming to the Massachusetts General Hospital.

Only one patient (No. 27) was ill enough to require resuscitation in the emergency room. Eight children received syrup of ipecac prior to or on arrival at the emergency room, but emesis resulted in only five of these cases. Gastric lavage was performed in 12 children.

A variety of psychotropic drugs were implicated in the 27 cases. These

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Cases of Psychotropic Drug Poisoning

Patient/ Age/Sex	Drug, Quantity Ingested	Highest Blood Concentration, μg/ml	CNS Depression Grade	Duration of Hospital Stay, Days	Comment
1/5 yr 8 mo/M	Glutethimide, 500 mg	6	1	2	...
2/1 yr 7 mo/F	Amobarbital sodium, dose unknown	22	1	1	...
3/2 yr/F	Phenobarbital, dose unknown	32	1-2	3	...
4/2 yr/M	Phenobarbital, 750 mg	36	1-2	1	...
5/3 yr 11 mo/F	Phenobarbital, 360-450 mg	58	2-3	2	...
6/6 yr 11 mo/F	Pentobarbital, 200 mg	12	1-2	4	...
7/3 yr 7 mo/M	Phenytoin, dose unknown	26	1	1	...
8/3 yr 9 mo/M	Phenytoin, dose unknown	49	2-3	3	...
9/1 yr 10 mo/M	Chlorpromazine, 375 mg	...	2	2	Transient hypotension (systolic BP 80 mm Hg) 10 hr after ingestion
10/1 yr 1 mo/F	Chlorpromazine, dose unknown	...	2-3	1	BP 90/35 mm Hg on admission
11/2 yr/M	Chlorpromazine, dose unknown	...	4	3	BP 90/0 mm Hg on admission
12/1 yr 10 mo/M	Chlorpromazine, 200-300 mg	...	1-2	1	BP 75/40 mm Hg on admission
13/unknown/F	Thioridazine, 500-750 mg	...	1-2	1	...
14/3 yr 7 mo/M	Imipramine, 600 mg	...	...	3	Fluctuation between obtundation and agitated delirium Clear manifestations of cholinergic blockade
15/1 yr 7 mo/M	Amitriptyline, 500 mg	...	...	2	Fluctuation between obtundation and agitated delirium Grand mal seizures
16/2 yr 9 mo/F	Phenelzine, 150-225 mg	...	1	2	Lethargy, ataxia Generalized erythematous rash
17/1 yr 3 mo/M	Amphetamine, 75 mg	...	...	1	Tachycardia, agitation, diaphoresis
18/1 yr 7 mo/M	Amphetamine, dose unknown	...	...	1	...
19/2 yr 4 mo/F	LSD, dose unknown	...	...	1	Tachycardia, anxiety, hallucinations
20/1 yr 4 mo/M	Chlorpromazine, 100 mg Benztropine mesylate, 0.5 mg	...	1	1	Drowsiness Hypotension (84/60 mm Hg)
21/4 yr 6 mo/F	Perphenazine, prochlorperazine, trihexyphenidyl, doses unknown	...	...	3	Hyperactivity Acute dystonic reaction
22/7 yr/F	Scopolamine, phenylephrine, doses unknown	...	...	3	Acute toxic delirium
23/3 yr 9 mo/M	Amphetamine, 100 mg Scopolamine, 5.0 mg	...	...	3	Acute toxic delirium
24/1 yr 8 mo/F	Doxylamine, succinate, 200 mg Dicyclomine, 200 mg Pyridoxine hydrochloride, 200 mg	...	...	3	Acute toxic delirium
25/4 yr 9 mo/F	Phenytoin, amphetamine, doses unknown	38 (phenytoin)	...	1	...
26/3 yr 8 mo/M	Phenobarbital, methamphetamine, doses unknown	5.6 (barbiturate)	...	1	...
27/1 yr 9 mo/M	Ferrous sulfate, 1.5-3.0 gm Phenobarbital, 150-300 mg Methamphetamine, 75-150 mg	...	4	Died two days after admission	Death attributable to iron toxicity

included barbiturates, glutethimide, anticholinergics, sympathomimetic amines, and hallucinogens. Drug mixtures were ingested by one third of the patients. Quantitative blood concentrations of barbiturates, glutethimide, and phenytoin were determined by the hospital's clinical chemistry laboratory and recorded in the medical record of patients who ingested these drugs. However, it is doubtful that the results were available rapidly enough to influence clinical management. Methods for identifying other psychotropic drugs were not available or were nonspecific. It appeared in all cases that diagnosis and management were based largely, if not entirely, on history and clinical findings.

The following section summarizes clinical events in each of the 27 cases (Table).

Central Nervous System Depressants

Eight patients (No. 1 through 8) ingested central nervous system depressants alone. These included barbiturates in five cases, glutethimide

in one, and phenytoin in two. Patients 4, 5, 7, and 8 had been prescribed phenobarbital or phenytoin for a seizure disorder, but in the other four instances the drugs were intended for parents' use.

Drowsiness, somnolence, ataxia, and dysarthria were the major signs of intoxication in the six cases of sedative-hypnotic ingestion. Deep coma did not occur. Patients could be aroused at all times, except for patient 5 who was responsive only to deep pain (grade 3) for a period of several hours. Gastric lavage or forced emesis or both were performed in half of the cases.

Two 3-year-old male patients receiving phenytoin for seizure disorders ingested unknown quantities of phenytoin suspension. Patient 7 experienced only drowsiness and ataxia; his blood phenytoin concentration on admission was 26μg/ml. A larger quantity was probably ingested by patient 8; the blood phenytoin concentration was 49μg/ml. This patient had marked ataxia, dysarthria and, bilateral horizontal nystagmus. Prior to admission, he had several episodes of vomiting and his state of consciousness was depressed.

Patients recovered uneventfully with no complications or sequelae. The longest hospitalization was four days.

Major Tranquilizers

Chlorpromazine alone was ingested by four patients and thioridazine alone by one (patients 9 through 13). Drowsiness and somnolence were the major signs of intoxication. Hypotension (systolic blood pressure, 90 mm Hg or less) was noted on admission or shortly thereafter in four cases of chlorpromazine poisoning; treatment other than intravenous fluid and solute was not necessary. In case 11, grade 4 central nervous system depression was transiently reached 15 hours after admission. Other patients remained responsive at all times. Hospitalizations were short, and there were no sequelae of intoxication.

Data on blood concentrations of the implicated drugs were not available. Phenothiazines were identified in the urine of the two patients (No. 11 and 12) whose urine was tested, but the findings were not reported rapidly enough to be of use in diagnosis or clinical management.

Antidepressants

Two patients ingested tricyclic antidepressants, either imipramine hydrochloride or amitriptyline hydrochloride (patients 14 and 15). Both shared the following signs and symptoms: mild pyrexia (37.8 to 38.3 C), tachycardia, dry mouth, flushed facies, and twitching and irritability of skeletal musculature. In both patients, consciousness was noted to fluctuate between a state of drowsiness or obtundation to one of agitation and delirium. Generalized tonic-clonic grand mal seizure activity occurred two hours after admission in case 15. An infusion of phenytoin was begun, but seizures terminated spontaneously and did not recur. Convulsions prior to admission were described by the family of patient 14, but no further seizure activity was noted in the hospital.

Phenelzine sulfate, a monoamine oxidase inhibitor, was ingested by patient 16. Drowsiness and ataxia were the only manifestations.

Stimulants and Hallucinogens

Two male patients (No. 17 and 18) ingested amphetamine preparations. Tachycardia, agitation, and diaphoresis were noted in both patients. Chloral hydrate (750 mg) and diphenhydramine hydrochloride (30 mg) were given to control hyperactivity and agitation in patient 17. A single dose of phenobarbital (60 mg) provided adequate sedation for patient 18. Both patients recovered without sequelae and were discharged after one day of hospitalization.

Patient 19 ingested LSD. The patient was described as "looking scared" and "having an anxious expression" on arrival at the emergency room. One observer noted that the patient seemed to be hallucinating. Tachycardia (160 beats per minute), tachypnea (33 to 40 respirations per minute) and dilated pupils were noted as well. Chlorpromazine (5 mg) was given intramuscularly. The patient recovered and was discharged one day later.

Drug Mixtures

More than one drug was taken simultaneously by the other eight patients (No. 20 through 27).

In the two patients (No. 20 and 21) who ingested mixtures of major tranquilizers and anticholinergic drugs, manifestations of toxicity could be attributed predominantly to the neuroleptic agent. Patient 20 ingested chlorpromazine and benztropine mesylate; he was drowsy and mildly hypotensive on admission, but recovered rapidly without sequelae. Perphenazine, prochlorperazine, and trihexyphenidyl hydrochloride were taken by patient 21. This patient was agitated, irritable, and hyperactive on arrival at the emergency room. Shortly thereafter, signs of an acute dystonic reaction developed including protrusion of the tongue, fixed upward gaze, and opisthotonus. Diphenhydramine hydrochloride (25 mg) was given intravenously and produced substantial improvement.

Three patients were poisoned by drug combinations containing anticholinergic agents (patients 22, 23, and 24). In all three, the major manifestations were consistent with atropine-like toxicity. These included agitation; irritability; hyperactivity; apparent hallucinations; aimless grasping, clutching, or picking movements of the extremities; flushed facies; dry mucous membranes; dilated pupils unreactive to light; apparent inability to focus on moving objects; and tachycardia. Patient 22, a 7-year-old girl, was accidently poisoned when several drops of an ophthalmic preparation containing scopolamine and phenylephrine hydrochloride were instilled into the nose instead of the eye. Signs of "atropine psychosis," as described above, rapidly developed in the patient, including unintelligible speech and irrational behavior. She recovered without specific therapy. Patient 23 accidently ingested approximately 20 tablets of an appetite-suppressant preparation containing amphetamine and atropine. This patient developed

severe tachycardia (200 beats per minute) and became extremely agitated and delirious, requiring intravenously administered pentobarbital (75 mg) for sedation. In case 24, some 20 tablets of a mixture of dicyclomine hydrochloride, doxylamine succinate, and pyridoxine hydrochloride (Bendectin) were ingested, again producing an acute toxic delirium consistent with atropine psychosis. Phenobarbital (100 mg) was administered intramuscularly for sedation. All three of these patients recovered and were discharged after three days of hospitalization.

Unknown quantities of phenytoin and amphetamine were ingested by patient 25. Clinical findings on admission included ataxia, nystagmus, lethargy, and behavior consistent with hallucinations. The findings suggest that both drugs contributed to toxic manifestations. The blood phenytoin concentration (38μg/ml) was in the toxic range. No specific therapy was administered and the patient recovered within one day.

Patient 26 ingested a weight-reducing preparation containing 60 mg of phenobarbital and 16 mg of methamphetamine hydrochloride (Ambar-2) in each tablet. No more than 15 tablets were taken. The parents observed the child being restless and talkative, making repetitive scratching movements, and grinding his teeth. On arrival at the emergency ward, the patient's mental status fluctuated between alertness and lethargy. He received chlorpromazine (8 mg) intramuscularly and recovered sufficiently to be discharged the next day.

The only fatality in the series occurred in patient 27, a 21-month-old boy who ingested five to ten tablets of ferrous sulfate together with several tablets of the phenobarbital-methamphetamine hydrochloride mixture (Ambar-2). The clinical picture was dominated by manifestations of iron poisoning.

COMMENT

The extent to which accidental poisoning contributes to overall morbidity and mortality in children is difficult to assess from the literature. Most published reports do not provide data on the relative contribution of poisoning to total hospital morbidity, nor the extent of the problem relative to a given population base. Reports from large medical facilities or specialized poisoning treatment centers must be cautiously interpreted because cases of poisoning—particularly serious cases—are selectively referred to such centers. In the Boston area, the Children's Hospital Medical Center (CHMC) serves as such a referral center, whereas the Massachusetts General Hospital (MGH) does not. Nevertheless, the pediatric service of the MGH is a major inpatient facility for the Boston-area population. Only 0.24% of pediatric admissions to the MGH in an 11-year period were due to poisoning. The findings from the present series suggest that accidental poisoning is not a quantitatively major cause of serious morbidity in children, although our results may have been biased in this direction because cases of serious intoxication could have been selectively referred to CHMC. Consistent with other reports,[1-5] psychotropic drugs accounted for a substantial proportion of poisoning cases, most of which occurred in children under 5 years of age.

The role of toxicologic analyses of body fluids in the present series was not clear. A variety of screening procedures have been described for rapid identification of psychotropic drugs in blood and urine.[6-13] Obviously, clinicians cannot make use of toxicologic data unless appropriate laboratory facilities are available to perform rapid analyses on a round-the-clock basis.[13] However, even when such facilities are available and used extensively, it is not clear that the results of toxicologic analyses influence patient management.[14,15] At the Massachusetts General Hospital, emergency toxicologic analysis is not available. Our retrospective study suggested that physicians accordingly relied primarily on history and clinical findings to make their diagnoses and to guide initial therapy, although toxicologic findings may have been used in the subsequent assessment of clinical status and prognosis.

Serious intoxication due to psychotropic drugs was not encountered in the present series. With the exception of one fatal poisoning with ferrous sulfate, all patients recovered without sequelae and were discharged after four days of hospitalization or less. Although induced emesis or gastric lavage was performed in many cases, more aggressive methods of drug removal (forced diuresis, dialysis, exchange transfusion)[4,16-20] were not necessary.

Our series does not provide definitive data on whether children are especially "sensitive" to central nervous system depressants.[21] All seven patients who ingested barbiturates or glutethimide experienced a benign clinical course and recovered rapidly. Blood concentrations usually consistent with serious intoxication in adults[22] were not reached in any of the cases.

Clinical manifestations of major tranquilizer intoxication were consistent with the type of phenothiazine ingested.[23] Central nervous system depression predominated when chlorpromazine or thioridazine was involved. Hypotension was also observed in children who had ingested chlorpromazine. Piperazine phenothiazines, on the other hand, produced excitation and dystonic extrapyramidal movements (case 21). Similar findings are reported by Davis and associates,[4] who reviewed 253 cases of phenothiazine poisoning in children.

Tricyclic antidepressant poisoning in children can be serious or fatal.[4,24-34] The incidence of poisoning with these drugs seems to be increasing[33,34] and has been called a "new menace."[34] Only two cases, both nonfatal, occurred in our series. Excitation and toxic delirium were noted in both patients, and seizures occurred in one. Peripheral cholinergic blockade was also apparent. Cardiac arrhythmias[24-34] were not observed.

Poisoning with anticholinergic drugs occurred in three patients, producing peripheral cholinergic blockade and acute toxic delirium. In one patient (No. 22), poisoning was due to scopolamine-containing eyedrops that were mistakenly instilled into the nose. Anticholinergic agents, when components of ophthalmic prep-

arations, are present in high concentrations. Only a few drops can produce serious poisoning in children who accidentally swallow them.[35,36] Such preparations are important household poisons.

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The standardized form used in this study is available from the authors on request.

Nonproprietary Names and Trademarks of Drugs

Amitriptyline hydrochloride—*Elavil.*
Chlorpromazine—*Chlor-PZ, Cromedazine, Promachel, Thorazine.*
Dicyclomine hydrochloride—*Antispas, Bentyl, Dyspas, Spascol.*
Thioridazine—*Mellaril.*

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