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Phenothiazine Poisoning

A Review of 48 Cases

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■ *Of 48 cases of phenothiazine poisoning that were analyzed, 34 were attributed to suicide attempts, nine to accidental ingestion, and five to drug reactions.*

As outpatient treatment of schizophrenia increases, cases of overdose with phenothiazine drugs may be expected to increase also.

The prescribing of multiple phenothiazines and antidepressants is probably contributory to the occurrence of mixed drug ingestions.

The symptoms and signs of phenothiazine poisoning are largely predictable if the atropine-like, alpha-blocking, quinidine-like, and extrapyramidal actions of phenothiazines are appreciated. Unexplainable tachypnea and paradoxical miosis were noted in severe cases.

In one case in the study phenothiazine intoxication was present in the newborn infant of a schizophrenic mother.

PHENOTHIAZINES ARE BECOMING household drugs in California. The closing of state hospitals with the concomitant institution of mass outpatient treatment of chronic schizophrenics through community mental health centers, and recent ques-

tionable advertising campaigns advocating phenothiazines for the treatment of a wide variety of ailments have made these drugs generally available. The high incidence of schizophrenia in young adulthood and the increasing suicide rate in this age group¹ suggest that phenothiazine poisoning will become increasingly common. Two large literature reviews of psychotropic overdose have appeared recently, but the cited case studies were small and seemed largely to involve only severe ingestion illness.^{2,3} An examination

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of the problem of phenothiazine overdosage was therefore undertaken. To that end the presentation, management, and outcome of 48 consecutive cases of phenothiazine poisoning were retrospectively analyzed.

Clinical Material

San Francisco General Hospital, a 1200-bed facility affiliated with the University of California Medical Center, recently instituted a computer card index according to final major diagnosis of all admissions. All charts (except two which were unavailable) coded under "tranquilizer toxicity" from October of 1969 to May of 1971 were studied, and 48 cases involving phenothiazine overdosage as the major contributing event leading to admittance to hospital were selected for further analysis. Included in the cases studied were suicide attempts, accidental drug ingestions, and serious drug reactions. The charts were analyzed for recorded drug type and amount, sex, age, race, marital status, vital signs, eye signs, mental status, treatment, complications, and length of stay. Since many charts were incomplete, complete information was not available on every patient. Because definite toxicology reports were generally not recorded, objective confirmation of the history was often impossible. In all four cases in which it was done, Phenostix testing of the urine was positive—in one case after dilution of the urine.

Results

Sociology (Table 1). Suicide gestures were most common in single, young, white women. Multiple drug ingestion was common (15 of 34 cases). Accidental ingestion seemed to involve the non-white community disproportionately. Phenothiazines of many varieties were involved (Table 2).

Vital signs (Table 3). Phenothiazine poisoning is characterized by a tendency toward hypothermia, tachycardia, tachypnea, and decreased diastolic blood pressure.

Mental status (Table 4). A clear tendency toward greater obtundation was noted in cases of mixed drug overdoses.

Eye signs. No trend was noted in the mixed drug overdoses. However, in the 12 reported cases of pure phenothiazine overdoses in which information was available (the more serious in-

TABLE 1.—General Data on 48 Cases of Phenothiazine Poisoning

	Suicide Attempts	Accidental Ingestions	
Total	34	9	
single drug	19	7	
multiple drug	15	2	
Sex			
male	14	7	
female	20	2	
Race			
white	32	2	
non-white	2	7	
Marital Status			
married	5	—	
single	29	—	
Age (yrs)		Age (yrs)	
Less than 26	21	Less than 5	8
More than 26	13	More than 5	1

TABLE 2.—Phenothiazines Involved in Overdoses

Phenothiazine*	Phenothiazine only	With Other drugs**
Chlorpromazine (Thorazine®)	16	8
Trifluoperazine (Stellazine®)	4	7
Thioridazine (Mellaril®)	3	2
Promazine (Sparine®)	1	0
Unknown	2	0

*in amounts ranging from 200 to 500 mg
 **included Elavil®4, alcohol2, Artane®2, Librium® and 16 other drugs in single instances

TABLE 3.—Initial Vital Signs in 26* Cases of Overdose with Phenothiazine Only

	No. of Patients	No. of Patients
Temperature	98° or less 10	99° or more 5
Pulse	70° or less 2	100° or more 10
Respiration	12° or less 0	25° or more 6
Blood Pressure		
systolic	110° or less 3	130° or more 4
diastolic	70° or less 12	90° or more 1

*Complete data absent in many cases

TABLE 4.—Initial Mental Status of 43 Patients for Whom Data Were Available

	comatose	lethargic semicomatose	awake oriented	hospital stay (days)	intubation
With phenothiazine only	2	14	10	2.2	0
With other drugs	5	9	3	2.8	6

gestions) pupil size in nine cases was "small" (3 mm or less). Only in three cases were the pupils greater than 4 mm in diameter.

Treatment

Treatment included administration of ipecac (15 cases), gastric lavage (nine cases), intravenous hydration (25 cases), and intravenous diphenylhydramine (Benadryl®) in three cases. Methylphenidate (Ritalin®) had been given to two children at other hospitals before they were transferred to San Francisco General. Interestingly intubation was not needed in any case in which only phenothiazine was ingested, but it was required in six cases of mixed overdose.

Prognosis

None of the 48 patients died and half of them needed less than 24 hours in hospital. The average stay of the other 24 was 3.4 days and the longest was 31 days. Potentially serious complications were noted in 17 of the 24 patients with the longer stay in hospital. (Tables 5 and 6).

Discussion

In addition to their antipsychotic activity, the phenothiazines possess significant anticholinergic, alpha-adrenergic blocking, quinidine-like and extrapyramidal activity.⁴ The importance of these modes of action becomes evident in the pheno-

thiazine-poisoned patient. Although unavailability of toxicological data prevented confirmation of the history and the ruling out of mixed, occult ingestions, which are known to occur frequently,⁵ distinct trends were evident in the patients said to have taken only phenothiazines. The hypothermia, tachycardia, and decreased diastolic blood pressure can be directly attributed to alpha-blocking and anticholinergic effects. Hypothermia can be relieved by appropriate covering⁶ while the decreased blood pressure, largely secondary to alpha-blockade, can be easily managed by putting the patient in the reverse Trendelenburg position, by volume expansion, or in more extreme cases by use of direct-acting alpha stimulators.^{2-4,7} Epinephrine with its mixed alpha and beta effect and isoproterenol hydrochloride (Isuprel®) with its largely beta action are therefore contraindicated. The tachypnea noted in these cases has not been noted previously (see reference 4), and an explanation is difficult to formulate. Small pupil size noted in 75 percent of the patients who had taken only phenothiazine was a surprising finding, and it was observed only in the most severely poisoned. This phenomenon may represent an overriding of the atropinic effect by the alpha-blocking effect of phenothiazines and may serve as a clinical clue to the severity of the overdose. This important observation requires further confirmation.

Prolonged QT interval which reverted spontaneously was noted in three cases. Although this is not well documented, persistent widening and QRS changes apparently can be treated effectively with diphenylhydantoin (Dilantin®).⁸ The increased incidence of sudden death in phenothiazine-treated patients may be related to this quinidine-like effect,⁹ and certainly an initial cardiogram is indicated for all phenothiazine-

TABLE 5.—Complications of Phenothiazine Overdose

Phenothiazine	Complication	No. of Cases	Previously reported incidences (percent)
Chlorpromazine (Thorazine®)	seizure	1	1.3
	prolonged QT interval	1	16*
	distended bladder	1	3
	aspiration pneumonia	2	—
Thioridazine (Mellaril®)	ataxia	1	11.8
	aspiration pneumonia	1	—
Prochlorperazine (Compazine®)	ataxia-rigidity	1	33.4
Trifluoperazine (Stellazine®)	athetoid movement	1	1.3
Unknown	rigidity	1	—
	prolonged QT	2	16

*As noted by David, Bartlett and Termoni¹⁰

TABLE 6.—Phenothiazine Reactions

Description of disorder	Tranquilizer
1) Respiratory depression in the newborn of a schizophrenic mother	Fluphenazine (Prolixin®)
2) Photosensitivity reaction-vesicles of hands and face	Chlorpromazine (Thorazine®)
3) Inability to open mouth after treatment of heroin withdrawal	Chlorpromazine
4) Drug fever (105°F), with history of allergy	Chlorpromazine
5) Cogwheel rigidity	Thioridazine (Mellaril®)

poisoned patients. Although it does sometimes occur, death is a rarity in such cases.¹⁰ The low mortality rate may reflect at least in part a tendency to attribute late deaths to other causes. An analysis of potential complications as noted in this study might indicate much more frequent serious sequelae to drug ingestion than are generally reported in other studies.^{11,12} It is of interest, however, that all patients with complications in the present study recovered.

Severe acute extrapyramidal disorders were rapidly reversed with Benadryl® in two of three patients, and this drug is clearly indicated in such situations.³ The case of respiratory depression in a newborn secondary to phenothiazine treatment of a schizophrenic mother (Table 6) indicates that phenothiazines do cross the placental barrier. Similar, but few, cases have been noted previously.^{13,14} The continued persistence of a movement disorder up to 12 months in those cases and the respiratory depression for several days (as occurred in the present case) is disturbing. These little-emphasized side effects of phenothiazines will undoubtedly play a larger role as more young women are treated as outpatients for schizophrenia. The age and sex distribution of patients in the present study in this regard is striking. The increased incidence of phenothiazine overdose in the last nine months of this study (29 cases) as compared with the first ten months (19 cases) is of related interest.

The medical treatment of phenothiazine poisoning was quite satisfactory. Ipecac has been shown to be effective in the presence of these antiemetics.¹⁵ Lavage even long after ingestion is effective since (1) the atropinic effect of phenothiazines delays gastric emptying and (2) phenothiazines are water-soluble and therefore slowly absorbed from the gastrointestinal tract.³ These two factors and the pronounced radiopacity and slow disintegration of most phenothiazine compounds¹⁶ suggest that the diagnosis of phenothiazine ingestion can be made radiographically (see Figure 1).

It should be noted that dialysis is ineffective since phenothiazines are strongly protein-bound.⁴ The use of methylphenidate (Ritalin®) in the treatment of phenothiazine poisoning seems ill-advised since it produces both alpha and beta stimulation⁸ and in the presence of the alpha-blockade of phenothiazines would be expected to lower blood pressure. However, both of two



Figure 1.—Radiograph in a case of chlorpromazine (Thorazine®) ingestion. The patient, a 27-year-old woman, had never received radiopaque contrast material.

patients who were treated with Ritalin® had increased blood pressures for their age upon admission to our hospital.

The high incidence of mixed drug reactions most likely reflects the prescribing habits of physicians. The efficacy of mixing tranquilizers or combining tranquilizers with antidepressants has not been borne out experimentally¹⁷ and indeed may be extremely dangerous (see reference 3, p 96). The increased obtundation in the patients with mixed drug overdose in the present study was striking. The occurrence of aspiration in three cases and in both of two patients said to be taking alcohol is noteworthy for two reasons: (1) the incidence of aspiration should be reducible by attention to position, suction, and careful intubation and (2) since undoubtedly more than two of the 48 patients were taking alcohol, general physicians should be alert to this unreported but important association since alcohol is a synergistic depressant. Certainly, a quick way to identify what drugs have been swallowed would greatly help in the management of all poisoned

patients. A recognition system utilizing mass spectroscopy and a computer link-up is being actively developed at San Francisco General Hospital.

The high incidence of accidental ingestion in non-white children probably reflects poor health education in general. It is likely that the candy-like appearance of phenothiazines plays a role.

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