ORIGINAL CONTRIBUTION
antidepressants, tricyclics, cardiovascular effects;
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Epidemiology of Fatal Tricyclic Antidepressant Ingestion: Implications for Management

Although there is a large body of literature documenting the lethal cardiotoxic complications of tricyclic antidepressant (TCA) overdose, the absence of reliable predictive signs has led to a policy of admitting even trivial-appearing overdoses for inpatient observation. A study of 18 fatal cases revealed that with the exception of two that received clearly inadequate medical care, all fatal ingestions developed major signs of toxicity mandating admission within two hours of arrival at the hospital, and the mean time from arrival to death was only 5.43 hours. All patients who died of direct TCA toxicity did so within 24 hours of arrival. In addition, half the fatal cases presented with only trivial signs of poisoning, but deteriorated catastrophically within one hour. These data lead to an algorithm to guide admission of serious cases. [Callaham M, Kassel D: Epidemiology of tricyclic antidepressant ingestion: Implications for management. Ann Emerg Med January 1985;14:1-9.]

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INTRODUCTION

Tricyclic antidepressants (TCA) are effective antidepressant drugs which also have prominent anticholinergic, adrenergic, and membrane-stabilizing ("quinidine-like") properties.[1] Due to their widespread use in the treatment of depression, they were the fourth most common overdose seen in emergency departments in the United States in 1982, and the third most common cause of drug-related death, after alcohol-drug combinations and heroin.[2] Although clinical features associated with severe poisoning have been identified,[3] no accurate predictor has been developed to identify the trivial ingestion that may be treated on an outpatient basis. As a result, many patients are admitted to the hospital with relatively trivial symptoms for a minimum of 24 hours of observation.[4]

This study was conducted with two goals: to examine the characteristics of a large number of fatal ingestions, and to determine the incidence of fatal outcome in patients with only trivial signs of poisoning over an observation period of at least six hours. The latter concern was stimulated by a previously reported case.[4]

METHODS

The coroner's records of all deaths in Alameda County, California, were examined for a period from January 1974 to July 1982. All deaths identified as involving TCA (by history or toxicology tests) were examined in detail; at a minimum, records examined included the complete coroner's report, autopsy records (including blood, urine, and tissue toxicology screens) and appended suicide notes, investigator interview notes, and hospital records. A toxicology screen (including alcohol, acetone, barbiturate, meprobamate, glutethimide, methyprylon, ethchlorvynol, chlordiazepoxide, diazepam and metabolites, methaqualone, opiates, cocaine metabolites, amphetamine, methamphetamine, methadone, propoxyphene, and TCA) was done on the blood, urine, and usually tissue (especially liver) of all cases examined by the coroner.

Cases were included only if TCA were the primary cause of death; in most, they were the only cause. Cause of death was determined by the coroner (and confirmed by the authors) on the basis of clinical history and find-

TABLE 1. *Type of TCA ingested in fatal overdose*

	Amitrip	Nortrip	Desipr	Imipr	Doxepin	Loxapine	Non-TCA Drugs Present	Total
Male	14	4	4	2	6	1	5	32
Female	30	13	16	5	8	2	6	79
Total	44	17	20	7	14	3	11	111
	(39%)	(15%)	(18%)	(6.3%)	(12.6%)	(2.7%)	(10%)	

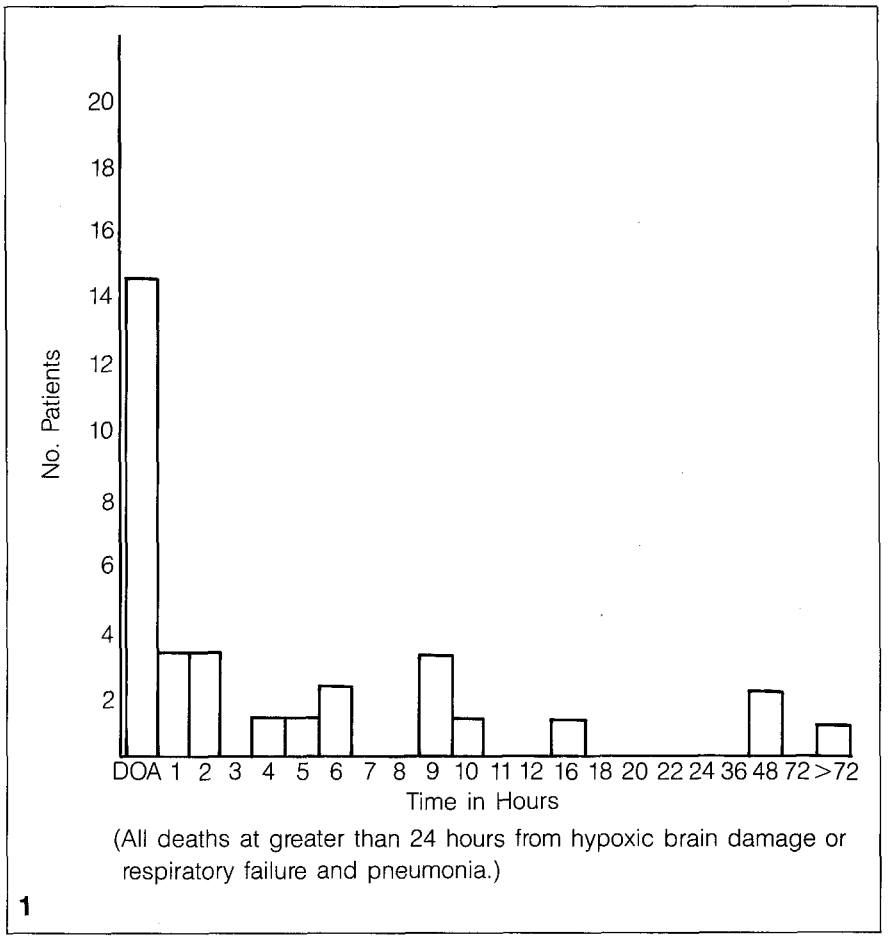

Fig. 1. *Time from arrival to death (N = 32). Excluding DOAs, mean survival time was 19.4 hours (SD = 13.67 hours). Excluding survival for more than 24 hours, mean survival time was 5.43 hours (SD = 4.24 hours).*

ings, autopsy results, and results of the toxicology screen. Cases involving major contributions by other drugs were eliminated even if that drug were not the primary cause of death. The hospital records of all cases that were transported to a hospital also were reviewed by one of the authors; these included ambulance and emergency department records, and inpatient charts. Details of patient presentation and treatment were recorded and tabulated.

RESULTS

Alameda County is a mixed urban, suburban, and rural county with a population of 1,077,339 during this decade. The population is 67% white, 18% black, 8% Asian, and 7% other races, with a median age of 30.7 years. The county had 502,201 emergency department visits in 1980 (personal communication, Art Lathrop, Emergency Medical Service Office, Alameda County, California).

During the 8½ years surveyed, there were a total of 111 fatal ingestions of TCA. The annual incidence of fatal TCA overdose was 1.3 per 100,000, much greater than the 0.8 per 100,000 estimated from Drug Abuse Warning Network (DAWN) statistics.[2] DAWN data include any death in which TCA are mentioned in any fashion, and therefore would be expected to be higher than ours, not lower. Of the patients, 72% were women and 28% were men. The drugs ingested are listed (Table 1). (For this tabulation only, only the drug with the highest level was reported; many patients had levels of several TCA.)

There were three cases of loxapine ingestion, only one of which reached the hospital alive. This patient had no other drugs present, had seizures in the ambulance and coma in the emergency department, had marked hypotension and arrhythmias in the ICU, and died seven days later of ARDS and pulmonary abscess. One patient had primary amoxapine ingestion, which also did not differ clinically from traditional TCA poisoning.

Of the 111 fatal cases, the majority (71%) were found dead at home, in motels, or in parked cars, usually with clear indication of suicidal intent. Many had made previous suicide attempts, often with TCA. Only 32 patients showed signs of life and were actually transported to a hospital, and 14 of these were pronounced dead on arrival (DOA) (Figure 1). The median

TABLE 2. *Prehospital signs of fatal TCA overdoses (12 patients with complete prehospital records)*

Sign	% Patients With Sign	No. Patients With Sign
Comatose	42	5
Seizure	25	3
Slurred speech only	25	3
Alert and awake	25	3
Respiratory arrest	25	3
Tachycardia > 100	25	3
Lethargic	17	2
Hallucinating	8	1
Confused	8	1

TABLE 3. *Initial emergency department signs of fatal TCA overdose (within the first hour, 18 cases)*

Sign	% Patients With Sign	No. Patients With Sign
Comatose	61	11
Tachycardia > 100	55	10
Hypotension	50	9
Respiratory depression	39	7
Seizure	39	7
QRS ⩾ 100 msec	28	5
Alert and awake	17	3
Slurred speech only	11	2
Lethargic	11	2
Hallucinating	11	2
Ventricular arrhythmia	11	2
Confused	5.5	1
Hypothermia	5.5	1
Hyperthermia	5.5	1

age of those who were transported to a hospital was 39 years, and there was no difference in age between those pronounced DOA and those surviving longer.

The patients were treated at a total of 11 different hospitals in urban, suburban, and rural areas. Most were community hospitals with an emergency department volume of around 20,000 to 50,000 per year, but one large county teaching hospital also was included. During this period all were staffed at all times with experienced emergency physicians.

The prehospital and emergency department presentation of cases that survived to the hospital are shown (Tables 2 and 3). Of the 18 patients who survived to hospital, time of ingestion was unknown in ten, of whom seven presented in coma and three, awake. The mean time from ingestion to arrival in the emergency department in the remaining eight patients was 89 minutes, with a range of 15 minutes to 3½ hours and a median of one hour.

The times from arrival to first major sign (Table 4) and to death (Figure 1) are shown. Excluding DOAs, those who developed major signs before they reached the hospital, and two patients who died on the psychiatry ward, the remaining nine patients had a mean time from arrival at the hospital to first major sign of poisoning of only 58 minutes. The mean survival time of the 18 patients who survived to hospital was 19.4 hours (standard deviation = 13.67 hours), but if three cases that lived more than 24 hours are excluded, this dropped to 5.43 hours (standard deviation = 4.24 hours). All three patients had survived the initial complication of TCA overdose and died later of such complications as hypoxic brain damage and respiratory failure. The ingested drug types and plasma levels for the 18 patients who survived to hospital are summarized (Table 5).

A potential weakness in any retrospective study is that treatment was not carried out according to any uniform protocol, and it could be argued that these outcomes were fatal due to improper management. Although retrospective assessment of management from charts is difficult, and particularly so in these complicated and moribund patients in whom major complications and treatments occurred in rapid succession, our impression was that care generally was appropriate and aggressive. Two patients died on the psychiatry ward with essentially no treatment, but of the remaining patients whose charts were reviewed, all were intubated and received manual or mechanical ventilation. All received intravenous (IV) fluids and had arterial blood gas monitoring. Eighty-three percent were lavaged and received charcoal and saline cathartics (in the remaining three cases the charting was not entirely clear on this point); 77% received IV sodium bicarbonate. Every patient received vasopressor therapy; 54% received IV epinephrine and 69% received other pressors (54% received dopamine, 30% isoproterenol, and 15% levarterenol); and 54% received IV physostigmine, with a mixture of beneficial and harmful effects. Thirty-eight percent received IV phenytoin, all but one in a full loading dose.

Eighty-nine percent were defibrillated at some point in their course.

TABLE 4. *Time from hospital arrival to first major sign*

		Signs in These Cases					
	No. Cases	Coma	Seizure	Respiratory Depression	Hypotension	Cardiac Arrest	Arrhythmia
On arrival	6	4	2	1	1		
Within 1 h	8	3	4	2	1		
Within 2 h	1	1	2				
3 h or more*	2					2	

Information not available in one case. Some patients developed more than one sign almost simultaneously.
*Both patients died on the psychiatry ward without close medical observation.

Twenty-three percent were given IV lidocaine, 31% received IV calcium chloride or gluconate, 15% received IV atropine, and one patient received bretylium. In addition one patient had a transvenous pacer and two were hemoperfused with Amberlite XAD resin; these cases all occurred in the last few years.

Of the 18 patients who survived to hospital, 12 died in intensive care and four died in the emergency department. In none of these cases was inappropriate care clearly identified as having led to a fatal outcome; however, the remaining two patients died on the psychiatric ward, one with no medical attention and the other after six hours of monitoring in an emergency department. (This case has been reported in detail elsewhere.[4]) Inadequate medical care probably contributed to the deaths of both. Both presented with minimal findings of poisoning (slurred speech in one, confusion in a chronic psychotic in the other) and died unattended nine hours later.

Nine cases fell into a category we termed catastrophic deterioration (CD). These accounted for 50% of the total fatalities that survived to hospital. These patients presented with few or minimal signs of poisoning (such as slurred speech or tachycardia of 120 or less) and within one hour developed such major complications as seizures, coma, apnea, hypotension, or malignant arrhythmias. Their average time to survival was 5.0 hours, excluding one patient who died seven days later with hypoxic brain damage. One of these patients had CD in the field and presented DOA. Another was lethargic and confused on presentation to the emergency department and rapidly became comatose. The remainder presented with even less alarming signs of poisoning. LC, a 67-year-old woman, took 12 amitriptyline 50-mg tablets and seven flurazepam capsules one hour prior to arriving in the emergency department alert and responsive but with slurred speech. Blood pressure was 110/50 mm Hg and pulse was 108. Within 30 minutes she was apneic, areflexic, and intubated. One-and-a-half hours after arrival she was in ventricular tachycardia, and she died two-and-a-half hours after arrival.

DISCUSSION

This study had two goals: to identify the characteristics of patients with fatal ingestion, and to determine the frequency of presentation with only trivial signs of poisoning in patients with fatal overdose. This information was not obtained with the precision that a large prospective study might have allowed, but clinically useful information was obtained.

The study had certain limitations, aside from its uncontrolled and retrospective nature, the most significant of which is that it did not examine surviving patients. Thus its conclusions may not be valid for an unselected group of patients, for treatment may affect outcome. Although 1,815 hospitalized patients have been reported in 16 major studies (Table 6), no prior series has included more than seven fatal cases. (Fifteen deaths were reported in a survey of telephone consultations.[5] No one has previously reported details of fatal cases.)

Because the average mortality reported in the literature is only 2.6% (Table 6), it would require a case load beyond the capacity of one or even several large hospitals to do a large prospective study of fatal cases. (Only 48 fatal cases have been reported in all the major studies of the last 20 years.) Thus there are no comparable data on fatal ingestions, and the information gathered in our study, although imperfect, is currently the best available basis for clinical decisions.

Our data are clinically useful chiefly in resolving the difficult question of initial management and admission criteria for the TCA overdose patient, particularly in the emergency department.

Management on Arrival

Although the prevalence of most major signs of poisoning is significantly higher on arrival for fatal cases than for TCA overdoses in general (Table 7), there is no one sign that confidently rules out fatal outcome. This is in line with the findings of Petit's study,[3] which similarly correlated such signs as coma, conduction blocks, dysrhythmia, hypotension, and seizures with increased plasma levels of TCA and increased mortality, but also found them present in survivors. There is no prospective study that determines the positive predictive value of a given sign. Thus these complications must be regarded as ominous.

More important, the absence of these complications, either prehospital or on arrival, is not grounds for reassurance. Of our patients who survived to the hospital, 50% fell into a category we termed catastrophic deterioration. These were patients who presented initially with trivial or no signs of poisoning, but went on to develop major signs (coma, seizures, arrhythmias, hypotension, or need for assisted ventilation) in an hour or less.

TABLE 5. *Plasma TCA levels of patients surviving to hospital (all levels drawn postmortem unless otherwise noted)*

Patient	Length of Survival	Drug	Plasma Level	Comments
LC	2 h, 13 min	Amitriptyline Nortriptyline	5,470 ng/mL 870 ng/mL	
AG	5 h, 40 min	Nortriptyline Desipramine Ethchlorvinyl	4,760 ng/mL 1,870 mg/mL 9.8 μg/mL	 Therapeutic 10-20 μg/mL
KN	7 d	Loxapine	1,900 ng/mL	Drawn at admission
DK	2 h, 10 min	Amitriptyline Salicylates	7,400 ng/mL 75 mg%	
RC	50 min	Amitriptyline Nortriptyline	5,700 ng/mL 4,000 ng/mL	
OB	9 h	Doxepin	1,100 ng/mL	
LO	9 h	Amitriptyline Norpropoxyphene	1,100 ng/mL	Present in urine
DP	10 h	Desipramine Salicylates	4,700 ng/mL 67.4 mg%	
TC	48 h	Amitriptyline Nortriptyline	150 ng/mL 299 ng/mL	Drug levels drawn 48 h after ingestion
SE	2 h, 15 min	Nortriptyline Desipramine	8,700 ng/mL 3,100 ng/mL	
CB	5 h, 40 min	Desipramine	8,600 ng/mL	
EB	37 min	Doxepin Desmethyldoxepin	21,800 ng/mL 1,900 ng/mL	
MM	15 h	Amitriptyline Nortriptyline Amoxapine Diazepam Phenobarbital	600 ng/mL 420 ng/mL 1,700 ng/mL 0.13 μg/mL 10.5 μg/mL	
LR	52 h	Amitriptyline Nortriptyline	600 ng/mL 1,340 ng/mL	Drug levels drawn 52 h after ingestion
DI	5 h	Amitriptyline Nortriptyline Phenobarbital	3,510 ng/mL 3,540 ng/mL 8.5 μg/mL	
RJ	4 h	Desipramine	10,100 ng/mL	
PR	6 h	Amitriptyline Nortriptyline Alcohol	5,050 ng/mL 3,420 ng/mL 0.05 mg%	
CC	1 h	Desipramine Imipramine Barbiturates Meprobamate	5,400 ng/mL 6,200 ng/mL 2.5 mg% 2.5 mg%	

Although these CD cases worsened very rapidly, their average time from presentation to death was five hours, not significantly shorter than the 5.92 hours of the non-CD patients. (Standard deviation of the difference between the means = 2.179 hours, t = 0.422.) One CD patient deteriorated at home and was DOA at the hospital. A second presented to the emergency department with intermittent hallucinations but without other signs of poisoning, and 50 minutes later he was in coma. The remaining seven patients had even fewer initial clinical signs of poisoning; 17% were alert and awake, another 11% had only slurred speech, and another 11% were only lethargic (Tables 2 and 3). Only 28% had a QRS duration of 100 msec or greater, a sign that correlates with plasma levels of 1,000 ng/mL or more.[3]

A trivial-appearing TCA patient may collapse very rapidly. Patients who present with any history of TCA ingestion should never be allowed to wait for care.

The First Six Hours

The principles of emptying the stomach and administering charcoal and a cathartic are well established.[1,4] The major decision to be made during this time is whether the patient actually needs admission. When the patient has major signs of poisoning, ad-

TABLE 6. *Clinical signs in published TCA overdose case series*

Ref Study/date	Total No. Patients	% Incidence Coma	Conduction Delays	Supraventricular Dysrhythmias	Hypotension	Respiratory Depression	Ventricular Dysrhythmias	Seizures	Mortality
22 Steel 1967	33	54			30	18	27	48	15
15 Noble 1969	100	51			32			4	0
9 Sedal 1972	26	61	19	19			8	15	7.8
13 Serafimovski 1975	68						57		7.4
3 Petit 1976	40	47	65	30	15	40	17	20	5
23 Thorstrand 1976	153	57	43	0	26	23	3	8	3.3
24 Christensen 1977	158					18	10		0
25 Pall 1977	15	100				20	6	33	0
26 Rose 1977	53	4	17	84			4	4	2
5 Crome 1979*	489	33		3	6	6		13	3.3
27 Woodhead 1979	100	33		1	4		7	6	0
28 Langou 1980	35		40	71	51		34		0
29 Starkey 1980	316	23	.2	22	13	3	.06	4	.06
19 Fasoli 1981	38	34	26	42	0	24	8	3	3
30 Greenland 1981	62	29	13	5				20	3
18 Pentel 1981	129	35	21	45	15	10	8	8	5.4
Total no. with sign	1,815	553	169	250	203	148	133	155	48
Total no. in reporting series†	1,815	1,554	852	1,441	1,433	1,371	1,164	1,554	1,815
Total %	100	35	20	17	14	11	11	10	2.6

Clinical signs as reported and defined by authors. Categories of arrhythmias and conduction blocks very nonuniform and often vague. Sinus tachycardia not included in supraventricular dysrhythmias.
*Series of telephone consultations, not actual managed patients.
†If information unavailable for a given clinical sign in any particular series, patients in that publication omitted from tabulation for that sign.

mission is mandatory. Due to our inability to predict outcome, admission generally has been the practice for most patients with trivial signs also.[4,5] Many of them, however, do not really need inpatient treatment, and thus their admission is unnecessary.

The problem of "unnecessary" admissions is not minor. TCA were the fourth most commonly ingested drugs seen in emergency departments in the United States in 1982, accounting for 7.25% of all drug-related visits.[2] Of all TCA overdoses seen in emergency departments, 67% are hospitalized. This is the highest figure for any drug ingestion; comparable figures for heroin and barbiturates are 27% and 43%. The average admission rate for all overdoses is 39%.[2] Only 12% of TCA ingestions in the emergency department are treated and released.[2] Of patients admitted to the hospital, 65% are awake, 86% have normal blood pressures, 89% have adequate respiration, 80% have normal cardiac conduction, and 83% have normal cardiac rhythm (Table 6). The benign nature of these patients is probably greater than this, for most of the complications occur multiply in a small number of patients.

Our retrospective review of the charts of 40 patients admitted to a county teaching hospital revealed that 50% manifested nothing more than lethargy (not necessitating any airway protection) and tachycardia, and were discharged after two days in hospital. In a study of consultations to a poison control center, 40% of all TCA overdose patients had only minor symptoms, and 73% of pediatric cases had symptoms too minor to warrant treatment. No symptoms were present in 40% of pediatric cases and 14% of adults.[5] The incidence of major complications in our study was similar, suggesting these were typical cases (Table 6). Clearly sizable numbers of patients are admitted for observation only, at considerable cost.

On the other hand, fears of delayed complications and inability to predict outcome have led clinicians to adopt all-inclusive admission guidelines. The best example of the latter was the report of a 38-year-old woman who ingested desipramine and was observed for six hours in an emergency department with no signs of poisoning other than transient slurring of speech and an initial tachycardia of 125 that had resolved by discharge.[4] She collapsed and died 11 hours after ingestion with fatal plasma levels of the drug. She had not, however, received activated charcoal or cathartics, which might

TABLE 7. *Clinical signs in TCA overdose: Comparison of all hospitalized cases to Alameda County fatal cases*

	All TCA Literature (Table 6)	Petit[3]*	Alameda County (First Hour)	
Total no. patients	1,815	40	18	
Coma	35%	47.5%	61%	$P = .05$
Conduction blocks	20%	65%	28%	NS
Supraventricular dysrhythmias	17%	30%	NA	Not tested
Hypotension	14%	15%	50%	$P = .001$
Ventricular dysrhythmias	11%	17.5%	11%	NS
Seizures	10%	20%	39%	$P = .001$
Mortality	2.6%	5%	100%	Not tested

*This study is listed because all patients had plasma levels of drug drawn and the correlation with clinical signs and outcome was determined. Its results were included with the remainder of the TCA literature for statistical analysis by chi-square technique, and were not analyzed separately.

have prevented delayed absorption of the drug, nor was her bowel motility assessed by listening for bowel sounds.

This patient is the only patient in more than 1,800 cases reported in the past 20 years who had a fatal outcome after a long initial observation period with only trivial signs of poisoning. Six cases of delayed complications and fatal outcome were reported in the earlier literature, but all presented with severe major signs of poisoning mandating admission and had their delayed complications after initial improvement.[6-9] Neither these older cases nor the most recent one had the now-standard treatment with activated charcoal.

One of our purposes was to determine whether other patients discharged from emergency departments after observation had fatal outcomes. No such case other than the original one was found in the 111 fatalities reviewed in Alameda County. According to DAWN statistics,[2] the ratio of emergency visits to coroner mentions for TCA is 15.59 to one. Extrapolating these statistics, during the period of our study there should have been 1,730 emergency department visits for TCA, with only one resulting in death after discharge. Both this and the absence of similar reports in the literature suggest that this is a very rare event.

Further support for this interpretation comes from examining the time course of fatal overdoses. Of the 32 patients transported to a hospital, 75% were dead within six hours (Figure 1). Of the 18 cases alive on arrival, 55% were dead within the same period; one third were dead in the first two hours. Even these figures underestimate the rapidity of death. The three patients who died after 24 hours had recovered from the direct toxicity of TCA and went on to die of secondary complications such as hypoxic brain damage and respiratory failure. Excluding these three cases, the mean survival time after arrival was only 5.43 hours, and 66% of those alive on arrival died within six hours. Even more important, 44% of patients developed a major sign of poisoning mandating admission within the first hour. The figure is 53% if the patients dying later of other causes are omitted (Table 4). The mean time from initial presentation to development of first major sign of poisoning was only 58 minutes. With the exception of two patients improperly admitted to the psychiatric ward without medical evaluation or treatment, every fatal case developed a major sign of poisoning within two hours of arrival (Table 4). Similar results have been reported in smaller series.[10] Thus it is clear that the fatal TCA ingestion will declare itself within a matter of hours with major signs mandating admission, or with death.

The reader should note that the statistics citing TCA as the third most common cause of drug-related death in the United States distort the clinical reality.[2] Only 16% of fatalities in our study ever reached a hospital where outcome could potentially be affected by treatment. Correcting for prehospital death relegates TCA a much lower place, not third.

While early series reported mortalities of 7% to 15%, mortality since 1979 has been 12 deaths in 680 hospitalized cases, or only 1.7% (Table 6).

The First 24 Hours

There is concern about the possibility of delayed complications many hours or even days after ingestion. In the 1960s and early 1970s, six such cases were reported.[6-9] All were patients with TCA ingestion who were admitted with major signs, who recovered well, and who then, at 12 to 96 hours after ingestion, unexpectedly collapsed and died. The best documented and most worrisome case involved a 21-year-old woman who was admitted in coma after ingesting nortriptyline and chlordiazepoxide.[9] She recovered well, and at 96 hours after ingestion had a normal ECG. Shortly thereafter she collapsed in her hospital room, became hypotensive, and demonstrated a junctional rhythm. After a long and complicated resuscitation effort, she died. Autopsy reported only a dilated heart with "flabby" ventricle. As with all the other cases during this period, there is no mention of treatment with activated charcoal or cathartics, which are now recommended in the treatment of all TCA ingestions.[1,11,12]

Other studies have documented that some signs of poisoning, such as tachycardia, persist for up to a

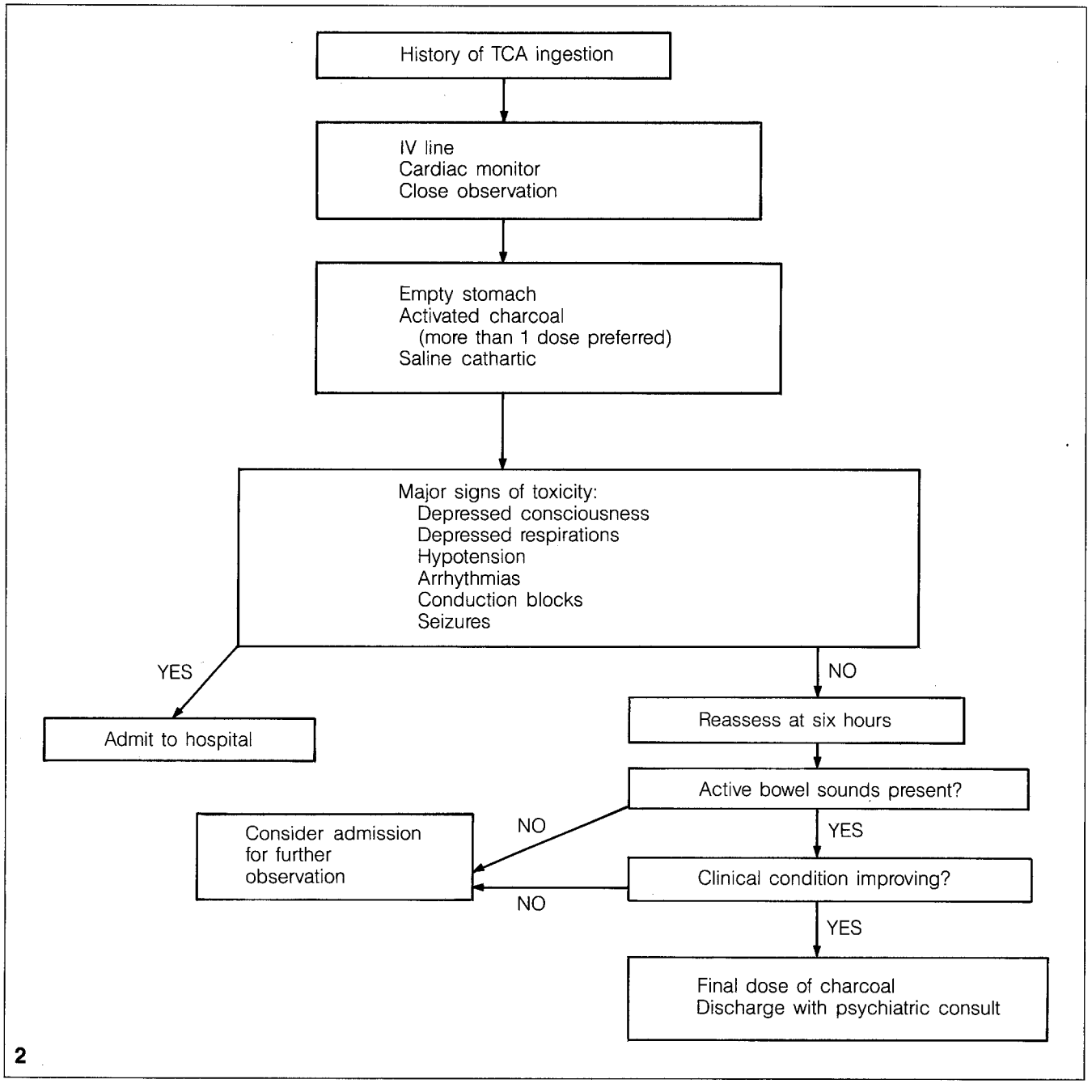

Fig. 2. *Management of TCA ingestion.*

week[13,14] and half of patients have recurring tachycardia 18 to 36 hours after ingestion.[13,15] Such prolonged effects are easily explained by the long and varied half-lives of TCA in overdose, which range from 25 to 81 hours.[16]

These cases raised the justifiable concern of sudden death late in the course of a TCA ingestion, and led to recommendations for monitoring for 48 hours or more after ingestion.[9,17] More recent studies of hospitalized inpatients, however, have allayed fears of serious delayed complications. In a series of 129 patients, all who developed cardiovascular or central nervous system complications did so within an hour of admission. Four of the seven fatalities occurred in the first hour.[18] No patient who had a normal ECG for an hour developed an arrhythmia. A study of 38 cases revealed that there were no arrhythmias more than 24 hours after ingestion.[19] An earlier study of 68 cases revealed the same time course for arrhythmias, and documented that all severe cardiac complications were initially manifested in the first 24 hours.[13]

Our data further support these conclusions. The mean survival time was 19.4 hours. Only 17% survived more

than 24 hours, and these patients had in fact survived the immediate complications of TCA and died later of such complications as infection. If these patients are excluded, mean survival time from arrival was only 5.43 hours. With the exception of two patients who never had proper medical care, every fatality developed major signs of poisoning within two hours of arrival, and none died of late complications after initial recovery.

It is clear from our study and the recent literature that previous fears of unexpected late complications and fatalities have not been realized. Virtually all fatalities attributable to direct TCA toxicity occur in the first 24 hours. No case of relapse and death from direct toxicity later than that has been reported in more than ten years. All such cases that have been reported did not receive the currently recommended treatment of activated charcoal and cathartics.

RECOMMENDATIONS

Any patient who presents for medical care with any history of ingestion of TCU should be placed *immediately* on a cardiac monitor, should have an IV established, and should have his stomach emptied[4,5,20] (Figure 2). He then should receive activated charcoal and a cathartic; multiple doses of charcoal at one-hour intervals are preferred.[21] An ECG should be obtained, and in any patient with altered consciousness arterial blood gases are necessary. The patient should be observed for six hours. If at any time during this period he develops major signs of poisoning (decreased level of consciousness, respiratory depression, seizures, hypotension, arrhythmia, or conduction blocks) he should be hospitalized. If after six hours of observation no major signs develop, the patient should receive a final dose of charcoal and may be discharged to psychiatric evaluation.

Patients who, after six hours, demonstrate only minor signs (such as tachycardia less than 120 or slightly slurred speech) may be discharged if the presence of active bowel sounds suggests that both the ingested TCA and the administered activated charcoal and cathartic are progressing on their way out of the gastrointestinal tract, and if signs of poisoning are decreasing rather than increasing. If bowel sounds are absent or markedly depressed, peristalsis may be inhibited by the anticholinergic effects of TCA, and delayed absorption is more likely.[1,11] In this case, admission for further monitoring and observation probably is prudent.

Management by this algorithm (Figure 2) should allow prompt identification and treatment of seriously poisoned patients. At the same time, the high rate of hospitalization and unnecessary costs for trivial cases will be lowered, while still providing an adequate margin of safety for borderline cases.

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