

# Human Methamphetamine-Related Fatalities in Taiwan During 1991–1996

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**ABSTRACT:** Methamphetamine (MAP) is currently considered to be the major illicit drug in Taiwan, and MAP constitutes the majority of illicit drugs seized by the judicial institutes. Thus, MAP has raised public attention. The purpose of this retrospective study is to observe the trends of MAP-related fatalities in Taiwan with respect to the manners of death so as to determine the epidemiological implications of MAP. Two hundred and forty-four MAP-related fatalities out of a total of 3958 forensic fatalities were collected by the Forensic Medicine Center (Taiwan) during the period of 1991 to 1996. The annual percentages of MAP-related fatalities compared to the total autopsy cases during 1991 through 1996 were 3.4, 10.3, 12.1, 4.2, 4.0 and 5.6%, showing that the number of MAP-related fatalities increased from 1991 to 1993, declined during 1994 and 1995, and rose again in 1996. The mean age of the MAP-related fatalities during this period was 30.7 years and occurred predominantly in males (73%). The manner of deaths included natural, accidental, suicidal, homicidal and uncertain causes of deaths, represented, respectively, by 31 (13%), 143 (59%), 28 (11%), 34 (14%) and 8 (3%) cases. As a consequence of the endemic problem and public hazard created by illicit drug abuse in Taiwan, stronger anti-drug programs and curbs to illicit-drug addiction were required urgently from the government and from the public. The findings of this study represent the results of utilization of an anti-drug program in Taiwan (Support by NSC 85-2331-B-016-092).

**KEYWORDS:** forensic science, methamphetamine, amphetamine, illicit drug abuse, antidrug programs, Taiwan

Crystalline methamphetamine (MAP), one of the most prevalent illicit drugs of the 1990s, has aroused public interest due to its long half-life and potency (1). MAP abuse has become an endemic problem in Taiwan, Asia and other parts of the world (2–4). While the habitual use of amphetamines in the United States has been by oral ingestion (5,6), in Asia the most popular usage is by smoking of MAP. MAP has a greater central nervous system (CNS) effect than does amphetamine, presumably because MAP achieves higher concentrations in the CNS (7). Inhalation of MAP produces a stimulant effect similar to intravenous injection, but inhalation carries an even higher risk of toxicity due to difficulty in controlling the dosage. The smoking of MAP has induced fatalities directly by means of hemorrhagic pulmonary edema (3, 8–10). In addition,

two different effects induced by amphetamine that jeopardize and terrify the Taiwan community (3,11) have been characterized as pathological lesion at high dosage and psychotic behavior at low dosage (12,13). MAP has become an endemic problem in Taiwan with a significant increase in violent behaviors and crimes associated with MAP abusers (14). The increasing incidence of overdoses and the number of victims who died from smoking MAP have aroused public attention (3). The number of MAP-related fatalities increased fourfold from 1991 to 1993 (11). Manners of death and causes of death found by the medical examiner investigations play roles in understanding the behavioral and pathological abnormalities caused by MAP (14). The purposes of this retrospective study regarding the 244 MAP-related fatalities out of the total 3958 forensic fatalities collected by the Forensic Medicine Center, the Public Prosecutor's Office for Taiwan High Court from 1991 to 1996, are to elucidate the epidemiological trend of MAP-related fatalities associated with the trend of illicit drug abuse and to sketch a guideline for Taiwan as well as for the rest of the world.

## Materials and Methods

### Materials

During 1991 through 1996, a total of 3958 forensic cases received autopsy and medicolegal death investigation at the Forensic Medicine Center, the Public Prosecutor's Office for Taiwan High Court (Table 1). Each case was subjected to a thorough forensic investigation including medicolegal autopsy, pathological and toxicological studies, and reports of the investigation following standard procedures (15,16). In order to conclude the manners of deaths and related implications, this retrospective investigation, documents entailed review of reports such as general background resources, past history, testimony of prosecutors' death investigations, the medical examiners' records and reports, as well as age, sex, and endemic distribution.

### Methods

**Toxicological Studies**—Toxicological studies of postmortem body fluids included screening by analyzer (Abbott, USA), Remedi (Bio-Rad), and Toxi-Lab, confirmation by gas chromatography (GC) and quantitative confirmation by gas chromatography/mass spectrometry (GC/MS) following well-established laboratory guidelines (17). MAP-related fatalities were defined as decedents whose body fluid, including MAP blood or urine level, exceeded 0.1  $\mu\text{g/mL}$ . The toxicological methods were constant throughout the study, and the limit of detection was 50 to 100 ng/mL.

In detail, 2.0 mL of each specimen was combined with D<sub>5</sub>-MAP as the internal standard and with 1 mL of 2N NaOH. The drug

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TABLE 1—MAP-related fatalities out of autopsy cases collected from Forensic Medicine Center in Taiwan during 1991 through 1996.

	1991	1992	1993	1994	1995	1996	Total
Amphetamine-related seizures, (kg)	1421	2904	3357	6869	3762	1913	20226
Nonamphetamine-related seizures, (kg)	243	475	1114	680	262	160	2934
Legal charges	14680	28176	47836	43608	31554	26493	192347
Convictions, (%)	13.5	19.1	31.7	30.2	24	20.4	
Autopsy cases	262	390	528	691	930	1157	3958
MAP-related fatalities	9	40	64	29	37	65	244
Percentage MAP-related fatalities	3.4%	10.3%	12.1%	4.2%	4.0%	5.6%	6.2%

was extracted from this sample into 3 mL of chloroform-isopropanol (ratio of 90 to 10). Tubes were capped and mixed by vortex for 8 min, then centrifuged for 5 min at 5000 rpm. The supernatant was transferred to a clear tube and the back extracted with 2 mL of 0.5 N HCl, then the organic layer evaporated to dryness under nitrogen. To form the pentafluoropropionic derivatives, 50  $\mu$ L of pentafluoropropionic anhydrous was added to the dried extract, the samples were mixed by vortexing, heated at 90°C for 30 min in a heating block, dried under nitrogen, and reconstituted in 50  $\mu$ L ethylacetate. A 1  $\mu$ L sample was injected for GC/MS. A Hewlett-Packard (HP) 5890A gas chromatographic with splitless injection, 5970A mass selective detector (MSD) was used. The GC was equipped with a HP-1 fused silica capillary column 25 m  $\times$  0.2 mm i.d./0.33  $\mu$ M film thickness. The carrier gas was helium, and the column flow rate was 1 mL/min. The GC injection pore temperature was 250°C, the transfer line temperature was 280°C, and the oven temperature was held at 60°C for 2 min, then increased by 20°C/min to 280°C, and held at 280°C for 14.78 min. The mass spectrometer was operated in the selected-ion-monitoring (SIM) mode. MAP ions were monitored at *m/z* 204, 160, and 118. Quantity was measured by multiple-point calibration using the ion ratio of each internal standard compared to the same ion ratio in the extracted standard (18).

**MAP-related Fatalities**—Each death was classified according to the manner of death, including either natural, accidental, homicidal, suicidal, or undetermined cause. Natural cause is defined by a predominant pathological illness, even with a finding of a small concentration of MAP that did not appear to influence the illness. Accidental deaths of MAP-related fatalities include two categories: death by taking in a large amount of MAP without intention of death, and other unpredicted fatalities by means other than the toxicity of MAP. Suicides of MAP-related fatalities included two categories: deaths caused by intake of a large amount of MAP with suicidal intention, with or without a suicide note, and deaths caused by self-injury through means other than MAP intoxication. MAP-related homicides are recognized by various forms of violence inflicted upon the decedent as the cause of death. The approach to interpretation of the cases was constant throughout the study.

**Statistical Analysis**—All information and data were recorded and analyzed with an IBM compatible 486 Personal Computer equipped with Excel software. Statistics analyzed were mean, median, mode, variance, standard deviation, coefficient of variances, and student *t*-test to evaluate the significance of sex and age distribution. The data will be presented as mean  $\pm$  standard error of mean (SEM).

## Results and Discussion

### Epidemiological Analysis of MAP-related Fatalities in Taiwan

In Taiwan, a country of about 21 million people with 110 000 deaths each year, about 20% of the cases are reviewed by coroners

(4). From 1991 to 1996, 244 cases were recognized as MAP-related fatalities by toxicological analysis of body fluids including blood and urine (11), and the annual MAP-related cases relative to the total autopsy cases appeared to have increased from 3.4% in 1991 to 12.1% in 1993 (Table 1). The rate of MAP-related deaths declined in 1994 and 1995 to 4.0%, and increased slightly again in 1996 to 5.6% (Table 1). The changing pattern in Taiwan was influenced by the announcement in 1993 of an anti-drug program, by legislation with increased illicit-drug activity enforcement, and by institution of an advanced rehabilitation program for illicit-drug abusers.

During 1991 and 1996, MAP has been the majority (85%) of illicit drugs seized by the Investigation Bureau, Ministry of Justice and the National Police Administration (Taiwan) when compared with other illicit drugs (4,14). Over this time period, the seizure of amphetamine-related substances was 20 226 kg with the greatest amount seized in 1994 (Table 1). Meanwhile, the combined seizure of non-amphetamine-related illicit substances was 2934 kg, with the greatest amount seized in 1993. The combined charges for violation of the Laws for the Control of Narcotics and the Laws for the Control of Illicit Substance totaled 192 347 cases, with the greatest number in 1993 (14). The pattern of illegal activities also showed a large component of MAP-related activities as follows. According to the criminal investigation center attached to the Ministry of Justice (Taiwan), 3670 effective questionnaires of illicit drug-related prisoners showed that 1191 (33.6%) prisoners typically used MAP alone and 670 (18.8%) prisoners typically used both heroin and MAP. Effective questionnaires (1083) of illicit drug traffickers showed that 469 (44.3%) prisoners sold MAP and 58 (5.5%) prisoners sold both MAP and heroin (14,19).

Over the six-year period from 1991 to 1996, there is a chronological relationship between the increased enforcement efforts followed by a decrease in MAP-related mortality (Table 1). Our data suggest that the announcement of the anti-drug program in Taiwan in 1993 did refrain temporarily the endemic popularity of MAP and decreased the numbers of victims.

### Age and Sex Characteristics of MAP-related Victims

The age of the 244 MAP-related victims throughout these six years (1991 to 1996) ranged between 3 and 77 years with an average of 30.7 years (Fig. 1, Table 1). Ninety-four percent of MAP-related fatalities were younger than 51 years of age. The greatest accumulation of MAP-related fatalities (177 cases, 72.5%) was between 21 and 40 years of age (Fig. 1). Statistics showing that young people comprise a significant proportion of MAP-abusers contributed to an urgent reaction to strengthen the anti-drug education and laws. The mean age of death during 1991 and 1996 was 30.7  $\pm$  1.9 years, but changed significantly (*p* = 0.017) during this six-year period. In the initial two years the averages were only 26.9  $\pm$  3.0 and 27.5  $\pm$  2.1 years and only two deaths (4%)

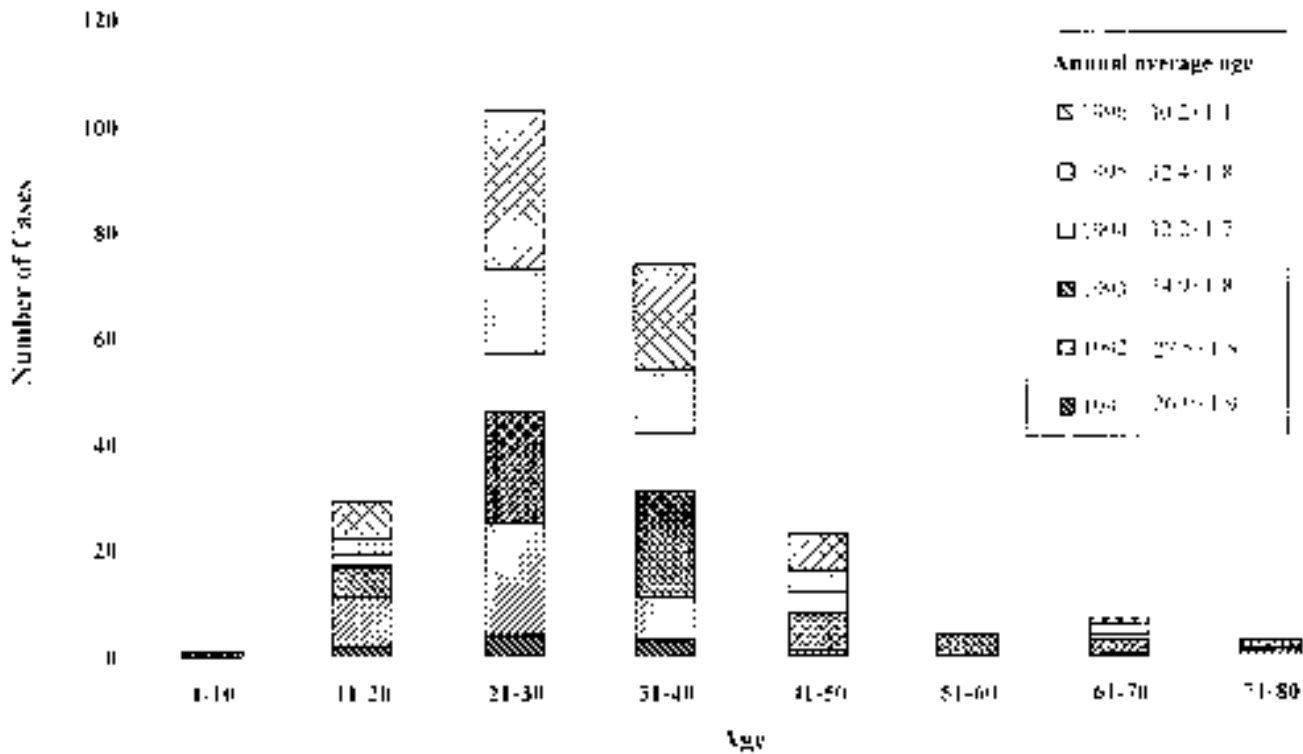


FIG. 1—Age distribution of MAP-related fatalities in Taiwan during 1991 through 1996.

occurred over the age of 40 years. In 1993 in Taiwan, 64 MAP-related autopsy cases had an average age of  $34.6 \pm 1.6$  years and 16 deaths (25%) occurred from age 41 to 80. After 1993, the average age of death declined to  $32.2 \pm 1.9$ ,  $32.4 \pm 1.6$ , and  $30.3 \pm 1.1$  years in 1994 through 1996, with only 5 to 8 cases/year over age 41, representing 14% of deaths.

The majority of the casualties (179 cases; 73%) were males, while only 65 cases (27%) were females during 1991 and 1996. The overall mean ages of MAP-related male and female fatalities were  $32.4 \pm 0.8$  and  $28.8 \pm 1.2$  years, respectively. Over these six years, the average ages of male fatalities were commonly 1 to 3 years older than those of female fatalities, except in 1992 and 1993.

In the peak epidemic year of 1993, an increase in MAP-related deaths over the age 40 (16 cases) was primarily associated with a large increase in deaths among older males (37 cases), raising the average to  $37.7 \pm 2.1$  years of age, as compared to a stable trend of average age of deaths among females ( $27.8 \pm 3.7$ ) ( $p = 0.018$ ). The combination of data showing a much higher incidence of male deaths than female deaths, the older age of male deaths in general and a high proportion of male deaths over age 40 suggests a physical intolerance in males during middle and late adulthood to MAP-induced effects of tachycardia, hypertension, pulmonary congestion, restlessness, etc.

#### Manner of Death

The 244 MAP-related fatalities were categorized as due to: natural causes (31 cases, 13%), accidental causes (143 cases, 59%), homicidal causes (34 cases, 14%), suicidal causes (28 cases, 11%) and undetermined causes (8 cases, 3%) during 1991 and 1996 (Fig. 2). The frequency of manner of deaths among male fatalities are ranked as accidental (61%), homicidal (14%), natural (13%), suicidal (9%) and uncertain (2%) manners of death. In comparison, the

female fatalities are ranked as accidental (52%), suicidal (17%), homicidal (8%) and natural (8%) and uncertain (6%) manners of death.

**Natural Causes**—Thirty-one (13%) of MAP-related fatalities were attributed to a natural cause of death with a minimal level of MAP (usually 0.1 to 0.5  $\mu\text{g/mL}$ ) and most of these deaths occurred at ages between 11 and 40 years (24 cases; 77%) with a mean age of 33 ( $p < 0.01$ , Table 2). Pneumonia was the most obvious finding and was sufficient to result in mortality. Natural manners of death occurred with findings of pneumonitis, pneumonia of natural origin, etc., that are usually combined with pulmonary edema, chronic fibrosis and thickening of the alveolar space typical of chronic MAP abuse. Notable changes were also found in hearts (myocardial fibrosis, granularity, contractive bundle of isolated, clumped myofilaments traversing the myocardial cells with necrosis), livers (fatty metamorphosis, hepatitis), and kidneys (nephritis), as well as central nervous systems (stroke).

The pathology of MAP-related victim's lungs was detected as pulmonary edema with hemorrhage, thickening of the alveolar septum, foreign body granuloma and foreign body reaction of the lung, and has been reported for a subset of these cases (3). In another study of 43 amphetamine-related deaths collected from 1940 to 1975, 31 people died of complications of poisoning including seven people who died of cerebrovascular accidents, six of sudden cardiac deaths, three of hyperpyrexia, eight of uncertain poison-related mechanisms, and seven of medical complications of intravenous injection, while the causes of death were uncertain in the twelve remaining amphetamine-related cases (20). Comparison between the pre-1975 deaths in amphetamine users and the recent deaths in MAP users illustrates a shift from cardiovascular and cardiac pathology to respiratory pathology, which is likely influenced by the change in the route of drug intake. However,

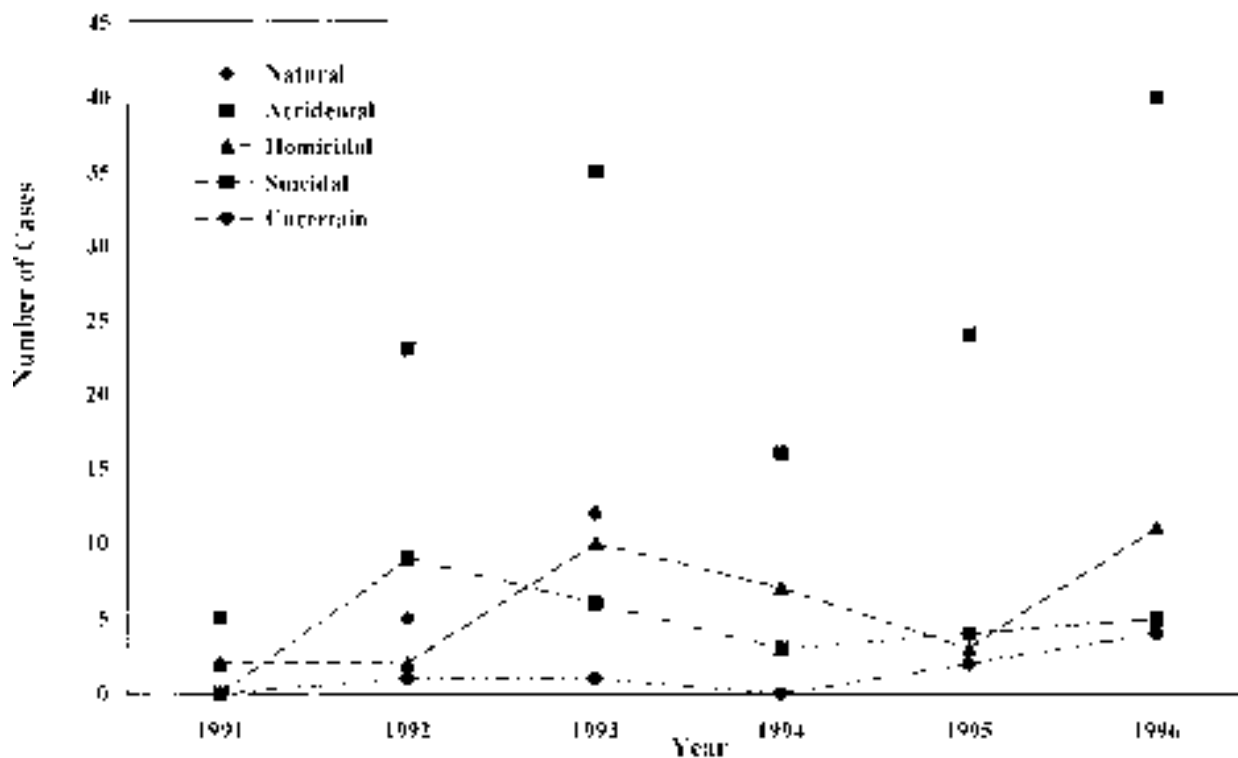


FIG. 2—Annual distribution of causes of MAP-related fatalities collected from the Forensic Medicine Center in Taiwan during 1991–1996.

TABLE 2—Relationship of age distribution and manners of deaths of MAP-related fatalities during 1991 through 1996.

Age	Nature	Accident	Homicide	Suicide	Uncertain	Total
1–10			1			1
11–20	8	14	3	2	2	29
21–30	5	71	12	13	2	103
31–40	11	34	15	11	3	74
41–50	3	15	2	2	1	23
51–60	1	2	1	...	...	4
61–70	2	6	...	...	...	8
71–80	1	1	...	...	...	2
Total	31	143	34	28	8	244
	(13%)	(59%)	(14%)	(11%)	(3%)	(100%)
Mean age	33.1	31.4	30.1	30.7	30.5	30.7
±SEM*	±2.7	±0.9	±1.6	±1.3	±3.4	±1.9
Median	33	29	31.5	29	30.5	...

\* SEM = Standard error of the mean.

another factor that may affect this comparison is improved detection and measurement of MAP, which has a longer half-life, using modern analytical methods.

**Accidental Cause**—Accidents were the most frequent cause of death for 143 (59%) out of 244 MAP-related fatalities, and peak ages were between 21 and 40 years (105 cases; 74%) with a mean age of 31 years (Table 2). Accidental deaths, as all deaths, were mostly in males (109 cases; 76%), whereas accidental deaths in females were fewer (34 cases; 24%). Nevertheless, a high rate among females of more than 50% of deaths as accidents is realized from their overdose by MAP intake (3). These cases mostly resulted from habitual use of MAP and inhalation of poorly controlled dosages.

Fatal overdoses of MAP-related deaths with the MAP concentration higher than 1 µg/mL in the body fluid is essential. Inhalation of the stimulants of abuse is obvious with the greatest number of the reported autopsy cases of pulmonary toxic reaction with necrotic debris in the airway. The pulmonary toxicity in overdose cases is characterized by hemorrhagic pulmonary edema (“Pink Lung”) or so-called neurogenic pulmonary edema due to the centrally-mediated effect that induces increased blood pressure of both pulmonary artery and pulmonary vein. The frequency of severe pulmonary toxic reactions of MAP abusers remains unknown.

**Homicidal Cause**—Thirty-four (14%) out of 244 MAP-related fatalities were recognized as homicides (Fig. 2). Similar percentages of homicides occurred among females (12%) and males (15%), who were mostly aged 21 to 40 years (27 cases; 79%) with a mean age of 30.1 years. This age group with the trend of behavioral sensitization has contributed to fierce arguments or violent fights and even homicide due to MAP-induced neurotoxicity combined with MAP-induced psychosis (13).

Endemic use of MAP has been reported in some parts of Hawaii and California, and 40% of all homicides in San Diego County, California, in 1987 were associated with MAP abuse either through intravenous use or inhalation (2,16,17). Similarly, a high homicidal rate among MAP abusers in Taiwan contrasts with a lower homicide rate among opiate abusers (14), implicating a riotous and violent trend consistent with the amphetamine psychosis in humans, similar to the behavioral sensitization in animals (21).

**Suicidal Cause**—From 1991 through 1996, there were 28 MAP-related fatalities by suicide (11% of autopsy cases) (Fig. 2). These deaths included 17 males and 11 females, representing suicide rates as 9 and 17% of deaths for each gender, respectively. Most deaths (85%) occurred between the ages of 21 and 40.

Suicide might not be easily differentiated from MAP-induced acute toxicity and chronic behavioral sensitization. Although smoking MAP is more hazardous to the addicts' health than other routes of intake (3), it is often difficult to identify the method of drug intake, time of intake and dosage in forensic cases. The complexities of the MAP-related toxicities, including the morphological alteration of the CNS, have led many investigators to study the pathogenesis of amphetamines and MAP (22).

The techniques for illegal manufacture of amphetamine in Taiwan originated from Korea and Japan (23). Ephedrine, the precursor of amphetamine, has mostly been smuggled from China, illicitly manufactured into amphetamine in China, the Philippines, and Taiwan, and exported to Japan and the United States (23). In 1990, the increasing population of amphetamine users in Taiwan had attracted public attention. Amphetamine, therefore, was classified under laws and regulations for control of MAP in October 1990 in Taiwan. The cases of legal charges concerning violation of anti-drug acts increased from about 5000 in 1990 to 43 000 cases in 1994 (14). By comparison with the total number of criminal cases, 13.5% convictions were made in 1991 and the rate increased up to nearly 32% in 1993 (Table 1). The abuse rate of illicit chemicals is estimated to be up to 1.4% of Taiwan's population (14).

In summary, this retrospective study of all 244 MAP-related fatalities during 1991 through 1996 and the trend of illicit drug abuse in Taiwan demonstrates several key epidemiological characteristics, as follows: (a) The majority of MAP-related fatalities were people between 20 and 40 years with a mean age of 30 years and a predominance of males. (b) MAP-related fatalities are most frequently accidental deaths (59%). (c) The number of homicidal cases increased greatly, up to ten cases in 1993 in association with the high rate of drug abuse, and the seven homicides in 1994 represented 24% of MAP-related deaths for that year (Table 1, Fig. 2). After initiation of the 1993 anti-drug program, the homicide rate declined until 1996, with a seven-year average homicide rate of 14%. The majority of the tragedies among young adults reveals the necessity of the anti-drug program to protect the public from the violence of the drug problem in Taiwan. The results of this study illustrate trends of illicit drug abuse for consideration of the endemic problem migrating internationally.

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