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Methamphetamine-Related Deaths in San Francisco: Demographic, Pathologic, and Toxicologic Profiles

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ABSTRACT: A study was undertaken to develop demographic, toxicologic, and pathological profiles of methamphetamine-related deaths. Anatomic and toxicologic findings in 413 deaths where methamphetamine was detected were compared with findings in a control group of 114 drug-free trauma victims. The number of cases per year did not change significantly over the course of the study. Mean age was 36.8 years, but 11% were over the age of 50. Decedents were overwhelmingly male (85.2%) and Caucasian (75%). Blood concentrations of methamphetamine and amphetamine were indistinguishable in cases where methamphetamine was related to the cause of death (MR) and cases where it was not (non-MR) (2.08 vs. 1.78 mg/L, $p = 0.65$, and 0.217 vs. 0.19 mg/L, $p = 0.82$). Coronary artery disease, ranging from minimal to severe multivessel, was identified in 79 of the 413 drug users, but in only six of the 114 drug-free controls ($p = 0.0004$), and MR decedents had enlarged hearts compared with controls. There were also ten cases of subarachnoid and intracranial hemorrhage in the MR group. Abnormalities of the liver (34%) and lungs (24.7%) were frequent. In 65% of these cases, death was due to accidental methamphetamine toxicity. In the remaining cases, methamphetamine was an incidental finding. We conclude that, in our jurisdiction, neither the rate of detection nor the number of methamphetamine deaths has increased significantly in the past 13 years. Decedents are almost all Caucasian males, and many were approaching middle-age. Methamphetamine use is strongly associated with coronary artery disease and with subarachnoid hemorrhage.

KEYWORDS: forensic science, forensic pathology, forensic toxicology, methamphetamine, death, coronary artery disease, myocardial hypertrophy, myocardial fibrosis, subarachnoid hemorrhage

Very little is known about either the pathology or toxicology of methamphetamine abuse (1). There has never been a systematic study of autopsy findings, and only a handful of case reports have been published, mostly in the Japanese literature (2–15). In the United States, the overall prevalence of methamphetamine use, at least when compared with cocaine use, is relatively modest and subject to wide regional variations. San Francisco is one of the regions where methamphetamine-related deaths occur with some regularity (16). During the 13 years from 1985 to 1997, we investigated the deaths of 413 individuals who tested positive for methamphetamine. Our findings suggest a strong association between methamphetamine use, cardiac enlargement, the development of coronary artery disease, and the occurrence of subarachnoid hemorrhage.

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Materials and Methods

Records of all cases where methamphetamine was detected in blood or urine from 1 January 1985 through 31 December 1997 were reviewed. Details were abstracted and entered into a database (StatView™). All of the methamphetamine cases were initially identified by polyclonal EMIT™ urine screening with a 300 ng/mL cutoff. Positive screens were confirmed using gas chromatography with mass spectrometry (GC/MS) on both blood and urine. In our department, the decision to order toxicology screening is made by the forensic pathologist performing the autopsy. The general practice in this department has always been that toxicology screens are performed in all cases of accidental death, and in most cases involving the natural death of young people. Urine drug screening is, of course, routinely done in cases of homicide and suicide. When no urine is available, blood is screened instead. Urine samples were available for testing in 325 of the 413 patients in this study (79%). The number of cases where urine was not available did not change significantly from year to year over the course of the study. The number of cases without urine samples ranged from a low of one case in 1990 to a high of 18 in 1994. Year-to-year variations in the percentage of cases with urine samples did not achieve statistical significance. Alcohol concentrations were measured using headspace chromatography.

Chiral separation was not performed, but none of the case histories or scene investigations gave any indication that either selegeline or Vicks™ inhalers (both sources of l-methamphetamine) had been used by the deceased. The distinction is important, because l-methamphetamine exerts no central nervous system (CNS) effects, and only negligible effects on the heart and great vessels. Its incidental presence in a decedent with a myocardial infarction or stroke could lead to the false assumption that methamphetamine was responsible.

The cause and manner of death in each case was reviewed in order to determine whether death was drug related, or whether the presence of the drug was merely an incidental finding. The recent study of methamphetamine toxicity by Logan et al. followed a similar protocol (35). The manner of death stated on the death certificate cannot be used to make this distinction because, in our jurisdiction, drug-related deaths are considered accidental deaths. Thus the death of a methamphetamine-using passenger in a fatal car accident would be classified as an accidental death, but it would not be a methamphetamine-related death. We defined methamphetamine-related deaths to be those where a direct toxic effect of the drug caused or contributed to the decedent's death. Where such an effect was not evident, the presence of methamphetamine was deemed to be an incidental finding.

In addition to the methamphetamine decedents, a convenience sample of drug-free controls was also studied. The controls were all trauma victims who died in San Francisco from 1988 to 1991.

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There were three criteria for inclusion in the control group: (1) that the decedents died from traumatic injuries, (2) that they were between the ages of 15 and 65, and (3) that complete toxicology testing disclosed the presence of no drugs. At least in our jurisdiction, drug-free trauma victims in this age group are uncommon.

Except in the cases diagnosed with coronary artery disease, the diagnosis in each case was accepted as written in the record. However, the histologic sections were reviewed in each of the 26 cases (25 in methamphetamine users and one in the control) that had been diagnosed with multivessel coronary artery disease. In three of those cases no slides were available, and in four other instances where slides were available, no sections of artery were included on the slide. The fact that reexamination could not be carried out in every case does introduce some possibility for error, but this was a retrospective study, and the initial diagnosis of the pathologist was accepted for the other diagnostic categories. Slides that were reexamined did, in fact, manifest severe coronary artery disease in each instance.

Descriptive statistics were computed for the entire data set. Two-sample t-tests were used to make comparisons between cases where methamphetamine was deemed to be the cause of death, cases where the presence of methamphetamine was an incidental finding, and the control group. Simple logistic regression was used to determine whether variables identified in this fashion could be used to distinguish cases where methamphetamine was the cause of death from cases where it was merely an incidental finding. Chi-square analysis was used to compare the incidence of associated medical disorders in the three study groups.

Results

Demographics—Figure 1 shows the total number of cases seen over the 13-year period. The graph suggests a cyclical pattern with a peak in 1994. However, the number of deaths recorded in 1997 is not significantly different from the number recorded in 1987. As shown in Fig. 2, the mean age was 36.8 years (SE = 0.491, range 16 to 68). Three-quarters of the individuals were under age 42, but 11% were over the age of 50, and 12 were in their sixties. MR decedents were older than non-MR decedents (37.8 vs. 35.1 years, $p = 0.009$). Decedents were overwhelmingly male (85.2%). The sex ratio was the same in MR and non-MR groups. Nearly three-quarters of the decedents were Caucasian (307/413, 74.3%). African-Americans accounted for 14.7% (61/413) of the sample, Asians 4.1% (17/413). Only 7/413 (1.7%) were Hispanic. The composition of the control group was comparable in both race and age. There were 88/114 men (77%), and the mean age was 33 years (SE = 1.1 years, range 14 to 62). The percentage of Asians in the control group was slightly higher than in the methamphetamine users, but the difference was not statistically significant. The manner of death is shown in Fig. 3. Nearly 16% (41) of the 262 accidental deaths were, in fact, trauma deaths unrelated to drug use. Eighteen of the 34 natural deaths were reclassified as having been due to previously unrecognized methamphetamine toxicity. These included patients with myocardial infarction, dissecting aneurysm, and subarachnoid hemorrhage, vascular complications that are now known to be associated with stimulant abuse. Suicide accounted for 13% and homicides for 10% of the deaths. After reviewing all

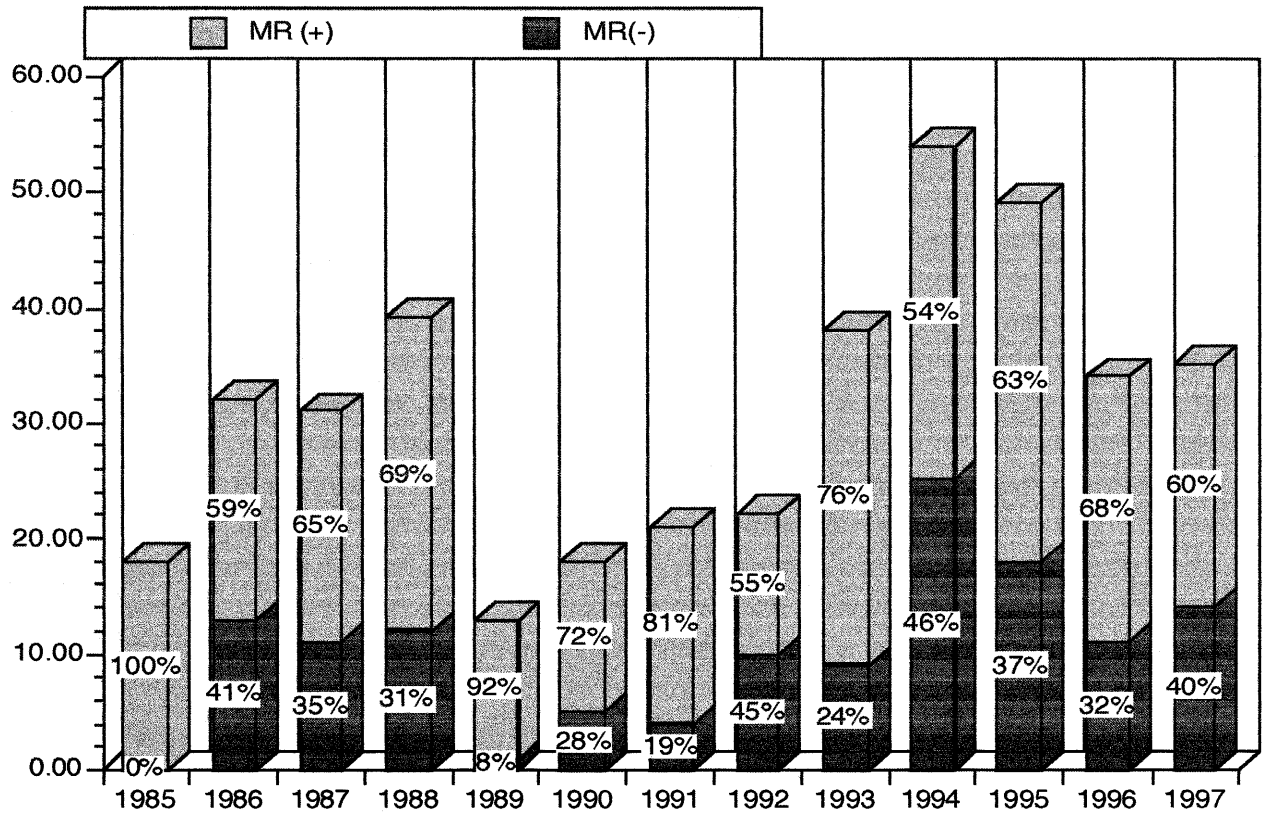

FIG. 1—*Decedents testing positive and negative for methamphetamine. The number of decedents testing positive (MR+ and MR− cases combined) for methamphetamine in 1997 was no greater than the number testing positive in 1986. However, the pattern does appear to be cyclical in nature, with a peak in 1994. It also appears that the percentage of deaths where methamphetamine was an incidental finding is increasing. This increase may simply be a reflection of increased prevalence of use in our jurisdiction.*

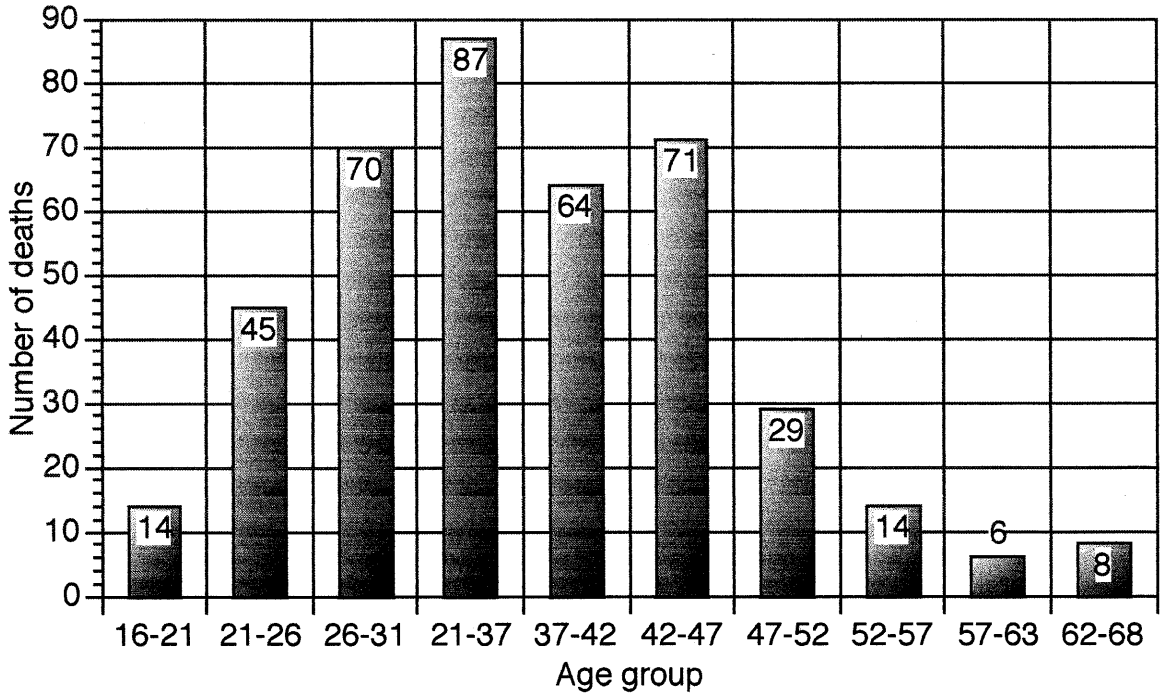

FIG. 2—*Age distribution for methamphetamine-related deaths in San Francisco. The mean age for all decedents testing positive for methamphetamine was 36.8 years. Three-quarters of the decedents were under the age of 43. However, 10% were over the age of 50, and some were in their sixties. This is in agreement with other government surveys suggesting that the population of drug users is aging.*

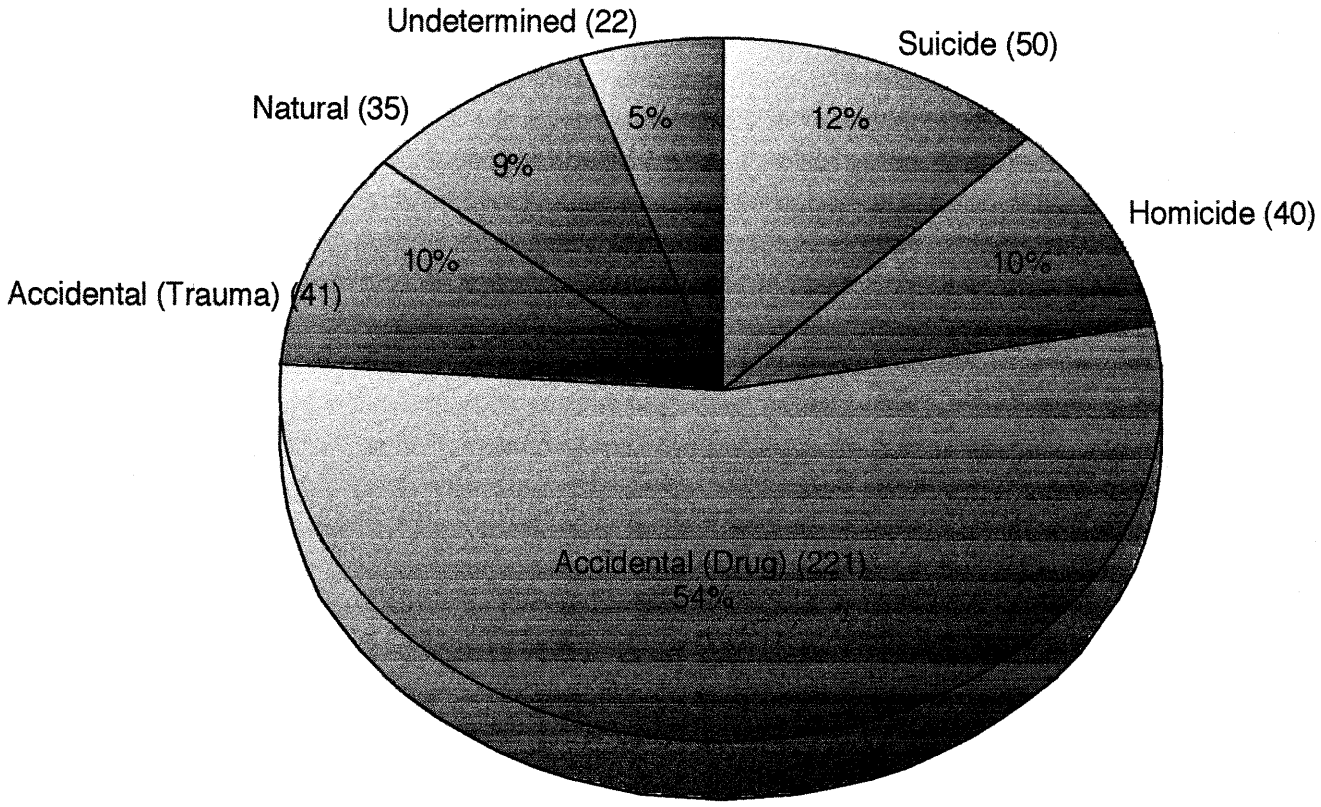

FIG. 3—*Manner of methamphetamine-related deaths (*n *= 413). Accidental deaths have been divided into those where the drug was deemed the cause of death, and those where it was an incidental finding in a trauma victim. Numbers in parentheses indicate the number of cases. In more than half the cases, death was a direct consequence of methamphetamine toxicity. This finding is in contrast to other studies where stimulant-related deaths were attributed mostly to traumatic injuries resulting from homicides, suicides, traffic accidents, and falls.*

TABLE 1—*Comparison of age, body mass index, and organ weights in cases where methamphetamine was the cause of death, cases where it was an incidental finding, and in drug-free controls. Heart weights were significantly greater in both groups of methamphetamine users than in the controls.*

	Methamphetamine, + Unrelated (n = 143)	Methamphetamine, + Related (n = 270)	Control (n = 114)
Age	35 (SD 10.5, SE 0.88)	38 (SD 9.4, SE 0.57)	33 (SD 1.2, SE 1.1)
BMI	22.9 (SD 3.8, SE 0.34)	24.5 (SD 5.6, SE 0.36)	24.7 (SD 5.1, SE 0.489)
Heart	349 g (SD 87, SE 7.0	380 g (SD 107, SE 7.0)	338 g (SD 77, SE 7.0)
Lung	1076 g (SD 417, SE 36.4)	1314 g (SD 398, SE 26.1)	1086 g (SD 453, SE 45)
Lung/ Body wt	0.015 (SD 0.07, SE 0.006)	0.018 (SD 0.06, SE 0.004)	0.016 (SD 0.007, SE 0.001)
Liver	1646 g (SD 419, SE 35.6)	1767 g (SD 468, SE 28.9)	1485 g (SD 427, SE 43)
Spleen	206 g (SD 119, SE 10.0)	266 g (SD 188, SE 12.0)	155 g (SD 179, SE 18)

of the cases, 61% of the deaths were classified as accidental, due directly to methamphetamine toxicity.

Toxicology—Comprehensive toxicology testing was performed in each case. Mean blood methamphetamine concentration was 1.78 mg/L (n = 141, SE = 0.27) in the non-MR group, and 2.08 mg/L (n = 265, SE = 0.46) in the MR group. In 75% of the cases, blood methamphetamine concentrations were less than 1.49 mg/L. Blood amphetamine, a primary metabolite of methamphetamine, was detected in the blood of 65% (271/413), in a mean concentration of 0.22 mg/L (n = 130), SE = 0.04) in the non-MR group, and 0.21 mg/L (n = 249), SE = 0.04) in the MR group. Amphetamine concentrations in the two groups were not significantly different. The median amphetamine/methamphetamine ratio in the 381 cases where both drugs were detected in the blood was 0.19 mg/L.

There were no significant differences between non-MR and MR groups in urine methamphetamine or amphetamine concentrations (37.6, SE 8.4 vs. 26.9, SE 3.5 mg/L and 6.5, SE 1.4 vs. 5.2, SE 1.03 mg/L, respectively). In addition to methamphetamine, other drugs were detected in nearly half of the decedents. Ethanol was present in a quarter of all the cases (105/413), and cocaine or cocaine metabolite in 25.1% of decedents (104/413). The most commonly encountered drug, however, was morphine. It was detected in 30% of the decedents (125/413).

Autopsy Findings—MR decedents had lower body mass indices (BMI) than the controls; 22.9 vs. 24.5 (p = 0.0041). Pulmonary edema, diagnosed by the appearance of the lungs, and lung weight at autopsy, was present in 71% (194/270) of MR decedents versus only 20.9% of the non-MR group (30/143, p = 0.0001). There was evidence of intravenous drug use in more than one-third of the decedents, with needle tracks identifiable in 35% of MR decedents (80/226), but in only 10.6% (14/132), p = 0.0001 of the non-MR group. Other confirmatory evidence for chronic intravenous drug use, in the form of birefringent crystals detectable in the lung or liver, was observed in 10.7% (29/270) of MR cases and in 6.3% (9/143) of the non-MR group (p = 0.234, ns), and in only 1.7% (2/114) of the control group (p = 0.010).

Group means, compared for age, organ, and body weights, are shown in Table 1. Organ weights were uniformly heavier, even after normalizing for body weight. The lung to body weight ratio was significantly higher in MR than in non-MR deaths, and both MR groups were higher than controls (0.018 vs. 0.016 vs. 0.015, $p < 0.0001$). But even though the difference between the groups was very significant, there is so much overlap between the two groups of MR decedents that they cannot be identified by their lung/body weight ratio alone, anymore than they can be identified by their heart, liver, or spleen weights.

TABLE 2—*Anatomic diagnoses in MR and non-MR groups were pooled and tabulated; the ten most frequent findings in the methamphetamine users are listed below. The incidence of the different diagnostic categories was then compared with the incidence of those same categories in a group of 114 drug-free controls. Statistical comparisons showed that only four diagnostic categories—coronary artery disease, myocardial fibrosis, ''triaditis,'' and HIV infection—occurred at significantly higher rates in methamphetamine users.*

Diagnosis	No. of Cases	%
1. Fatty liver	64	15.4
2. Moderate CAD	42	10.1
3. Cirrhosis	37	8.9
4. Pneumonia	32	7.7
5. Myocardial fibrosis	29	7.2
6. ''Triaditis''	25	6.0
7. Severe CAD	24	5.8
8. HIV infection	24	5.6
9. Emphysema	21	5.0
10. Hepatitis	21	5.0

In order to estimate the frequency of medical disorders associated with chronic methamphetamine use, diagnostic categories for the MR and non-MR decedents were pooled, and their frequency compared with the frequency for those same categories in the control group. Obviously, rates for the incidence of medical catastrophes such as subarachnoid hemorrhage and myocardial infarct in methamphetamine users cannot be compared to rates in controls, though the incidence of chronic medical disorders, such as asthma, can be compared.

The ten most commonly encountered medical diagnoses are listed in Table 2. The frequency of these disorders in MR and non-MR groups was also compared. Except for coronary artery disease, myocardial fibrosis, ''triaditis,'' and HIV infection, there was no significant difference in occurrence rates between controls and methamphetamine users. Coronary artery disease, ranging from minimal to severe multivessel, was identified in 79 of the 413 drug users, but in only six of the 114 drug-free controls (p = 0.0004). Decedents with coronary artery disease were older than other MR-related decedents (45.3 $\pm$11.9 years vs. 33.4 $\pm$11.9 years, $p <$ 0.0001). Toxicology testing disclosed that 16 of the 79 decedents with coronary artery disease (20%) had been using cocaine in the immediate perimortem period. Nearly half of the combined methamphetamine/cocaine users with coronary artery disease (9) had also been taking opiates (morphine detected in blood or urine). Except for the age difference, risk factors in the control group were

not significantly different from those of the methamphetamine users with coronary artery disease. Body mass index in the controls was 24.8, SE = 0.45 vs. 24.8, SE 1.5 in the methamphetamine users ($p = 0.50$). Both groups were predominantly Caucasian (53% of the controls and 81% of the MR, $p = 0.40$), and male (77% of controls vs. 87% of the MR, $p = 0.40$). There were no cases of vasculitis, pulmonary hypertension, necrotizing angiitis, or cardiomyopathy; nor were there any cases of endocarditis.

Among the less frequently diagnosed disorders, anatomic changes consistent with asthma were noted in 16 cases (4.1%) versus one in the control group. Intracranial hemorrhage was diagnosed in ten cases (2.4%), myocardial infarction in seven (1.8%), and ruptured aneurysm in five (1.2%), but there were no cases of intracranial hemorrhage, myocardial infarction or aneurysm in the controls. Because of the small numbers the difference in rates cannot be accurately interpreted.

Discussion

In 1995, 488 methamphetamine-related deaths were reported by medical examiners across the United States (16), nearly twice the number that had been reported in 1992. We have not witnessed similar changes in San Francisco. Even though the number of cases doubled, from 24 to 53 in 1993, the rate today is the same as it was a decade ago. Nor has there been any significant change in the age at time of death, or racial pattern of the decedents. Each year, 20 to 40 of the nearly 2000 cases processed by our office test positive for methamphetamine. The reasons for the increase in 1992 and 1993 remain unclear. It is presumably, a consequence of increased drug availability, since there were no changes either in the boundaries of our jurisdiction or our toxicology testing protocols. It is true that the total number of cases has been greater in the second half of the decade than in the first, but the numbers involved are simply too small to accurately predict any trends. The increases in 1992 and 1993 may very well have been a random occurrence.

Demographics—Decedents are overwhelmingly male (87%) and Caucasian (77%). The mean age was 36.8 years. Three-quarters of the individuals were under age 43, but 10% were over the age of 50, some in their sixties. These results mirror exactly those of the Drug Abuse Warning Network (DAWN) survey, which reported that methamphetamine-related death occurred predominately in Caucasian (77%) males (80%), over age 35 (53%) (16), and parallel the findings in a large, recently reported study of postmortem toxicologic findings in Washington State (35). Our findings are also consistent with the results of successive National Household Surveys on Drug Abuse (17). That survey continues to show that the population of drug users is aging.

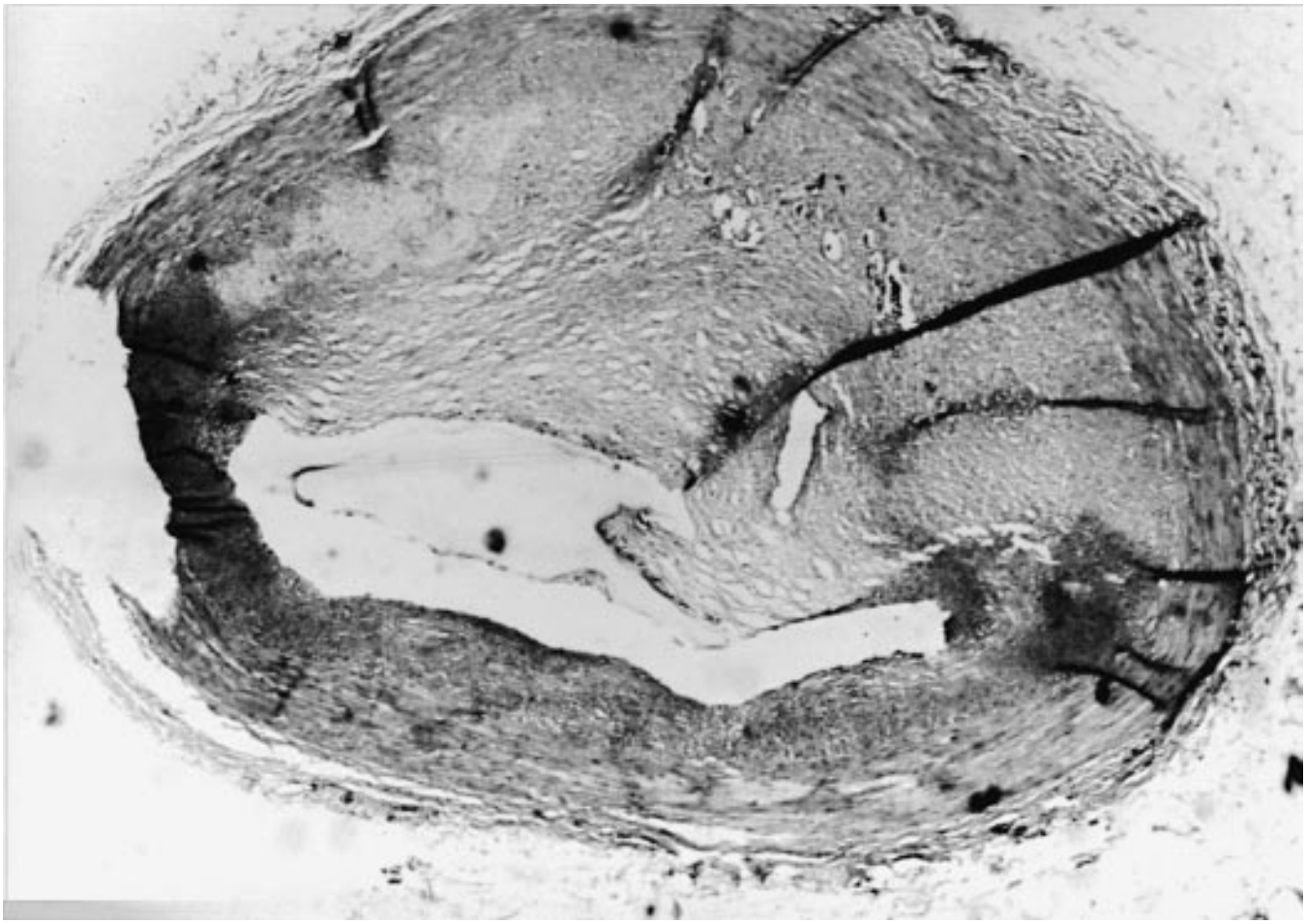

FIG. 4—*Section of epicardial artery from a 44-year-old man with severe, multivessel disease. There is marked luminal compromise and evidence of recanalization. Nineteen of the methamphetamine-related deaths had multivessel disease, compared with only two controls (*p *= 0.003). Hematoxylin and eosin, ×100.*

Many of those who first began using drugs in the 1960s continue to do so today, and the proportion of drug users over age 35 continues to increase (from 10% of users in 1979 to 28% of users > 35 years in 1996). We found that MR decedents were significantly older than non-MR decedents (38 vs. 35 years, $p = 0.009$). This observation, taken with the fact that coronary artery disease was more common, and heart weights greater, in the MR than in the non-MR group, raises the possibility that MR deaths may have a long ''incubation'' period. Increased heart size and multivessel coronary artery disease do not develop overnight. Even though most methamphetamine users are in the younger age groups, years of methamphetamine abuse may be necessary before death occurs.

The manner of death observed here does not support the previously advanced notion that drug-related deaths, particularly those involving stimulants, are more often due to violence than to drug toxicity. In Logan's recently reported series, 43% of the individuals died of homicidal (27%) or suicidal (15%) violence, and only 35% (52/146) of drug-mediated toxicity (35). In a similar study of cocaine-related deaths, two-thirds of the deaths were attributed to traumatic injuries resulting from homicides, suicides, traffic accidents, and falls (18). Violence was clearly a factor in many of the deaths described here—22.8% were suicides or homicides, and 41 (10%) were trauma patients incidentally testing positive for methamphetamine, but more than half of the methamphetamine deaths in our jurisdiction (221/413) were a direct result of methamphetamine toxicity.

The origin of pulmonary edema in cases of drug-related death remains obscure. More than simple heart failure is involved, since the edema fluid usually contains much more protein than the plasma (21,22). Allergic reaction to drug components, with mast cell degranulation, is an old idea that has recently been proposed again as the etiology (23). However, methamphetamine has never been shown to cause mast-cell degranulation, and even if it does, pulmonary edema also occurs in association with the abuse of other narcotics, such as fentanyl, which definitely does not cause histamine release (24).

Toxicology Findings—A detailed analysis of the toxicologic findings is to be reported separately. Mean blood concentrations of methamphetamine were not significantly different in MR cases and non-MR cases (2.08 mg/L vs. 1.78 mg/L, ns) and neither were mean blood concentrations of amphetamine, a methamphetamine metabolite (0.21 mg/L vs. 0.22 mg/L). These findings are in general agreement with the study by Logan et al. that 90% of 142 methamphetamine-related decedents had concentrations of less than 2.20 mg/L (35). The extensive overlap in values, between

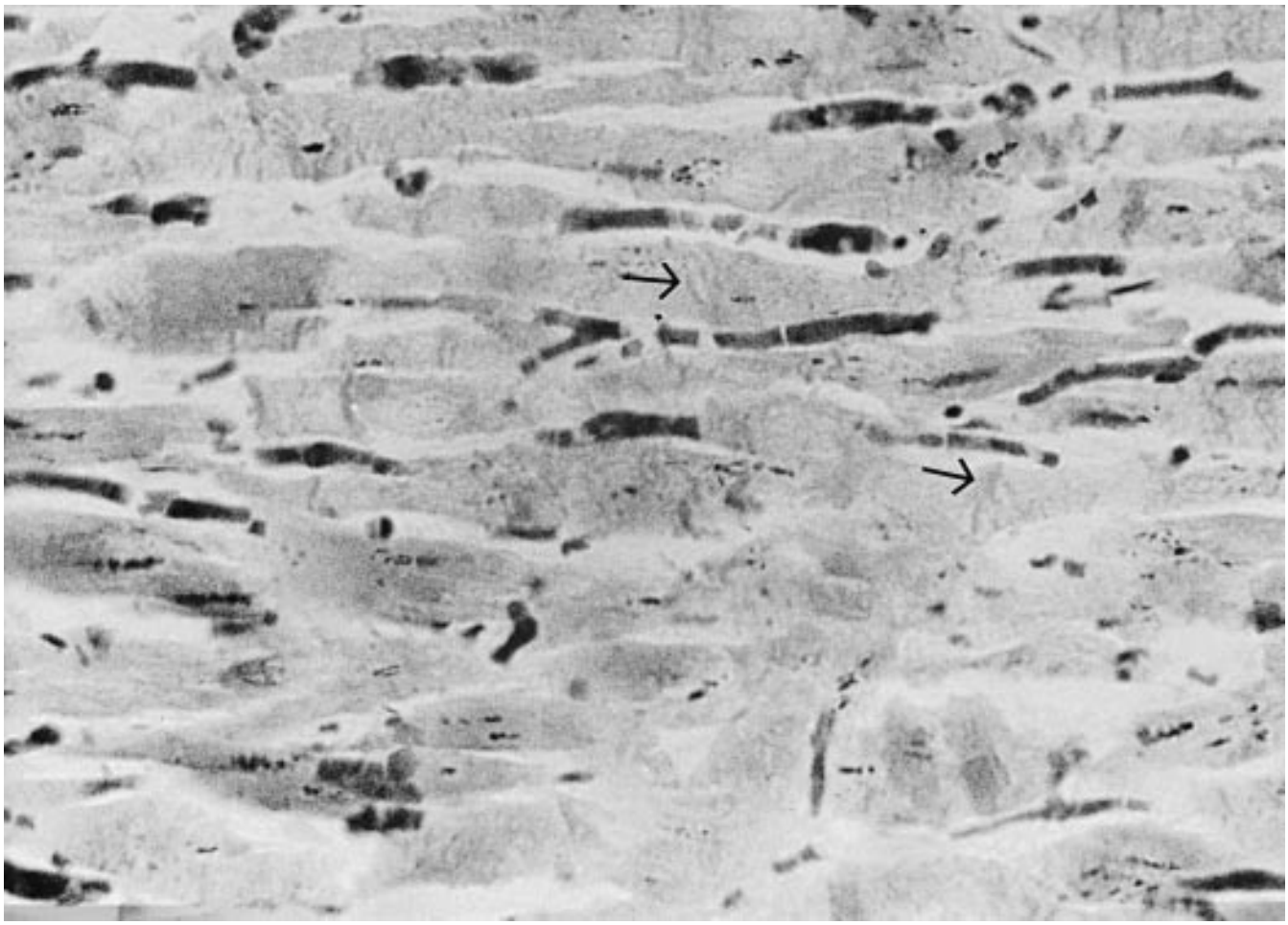

FIG. 5—*Zone of intense contraction band necrosis, similar to the pattern that has been reported in cocaine users. This section of myocardium was taken from the same individual described in Fig. 4. This change is thought to be the result of intense catecholamine stimulation (27) and may account for the patchy fibrotic changes frequently seen in the hearts of stimulant abusers. Patchy myocardial fibrosis was evident in 6.7% of the methamphetamine users, but only 2 (1.7%) of the controls (*p *= 0.003). Hematoxylin and eosin, ×300.*

cases where methamphetamine is the cause of death and cases where methamphetamine is an incidental finding, mirrors the situation in cocaine-related deaths, where blood concentrations of cocaine and benzoylecgonine in cocaine-related deaths are indistinguishable from concentrations in decedents where the drug is an incidental finding (36). The overlap is explained by the phenomenon of tolerance, which occurs rapidly during life, and drug redistribution, which occurs in an unpredictable fashion after death (11).

Vascular Disease—The most striking difference between methamphetamine users and the controls was in the incidence of heart disease: the methamphetamine users had enlarged hearts and they had coronary artery disease. Heart weights in the MR and non-MR groups did not differ significantly, but taken as a group, the hearts of the methamphetamine users were heavier (378 g vs. 341 g) ($p = 0.001$) than the controls. Coronary artery disease, ranging from minimal to severe multivessel, was identified in 79 of the 413 drug users, but in only six of the 114 drug-free controls ($p = 0.0004$). The difference between the methamphetamine users and the controls was especially impressive given that there were no significant differences between the BMIs, sex and racial makeup of the two groups. Because the controls were selected to match the age of the methamphetamine users as a group, and not to match methamphetamine users with a specific disease, controls were younger than the methamphetamine users with coronary artery disease, and age disparity could account for some of the differences. Arguing against that possibility is the fact that heart weights in MR decedents with coronary artery disease were so much greater than in the controls (425 g, SE 13.5 vs. 341 g, SE 7.3, $p < 0.0001$. In adults, increased heart size is abnormal at any age (37). Figure 4 shows a section of coronary artery from a 44-year-old male methamphetamine abuser with multivessel coronary artery disease.

Figure 5 shows contraction bands necrosis in the heart of a 20-year-old methamphetamine user with coronary artery disease. The presence of this lesion usually is an indicator of catecholamine toxicity (27). Contraction bands are commonly seen in the hearts of stimulant abusers, whether cocaine or methamphetamine (25–28). Myocardial infarction is a generally recognized feature of cocaine abuse. Reports of methamphetamine-related myocardial infarction are distinctly rare events (5,28). Given the paucity of reports describing methamphetamine-related myocardial infarction, the finding of so many individuals with such severe disease is something of a surprise and will require additional follow-up. Coronary artery disease is, of course, a very well-known complication of cocaine use, but only 20% of the methamphetamine-using decedents with coronary artery disease were also using cocaine in the immediate perimortem period, and there is no way to determine whether these individuals were regular users or were taking cocaine

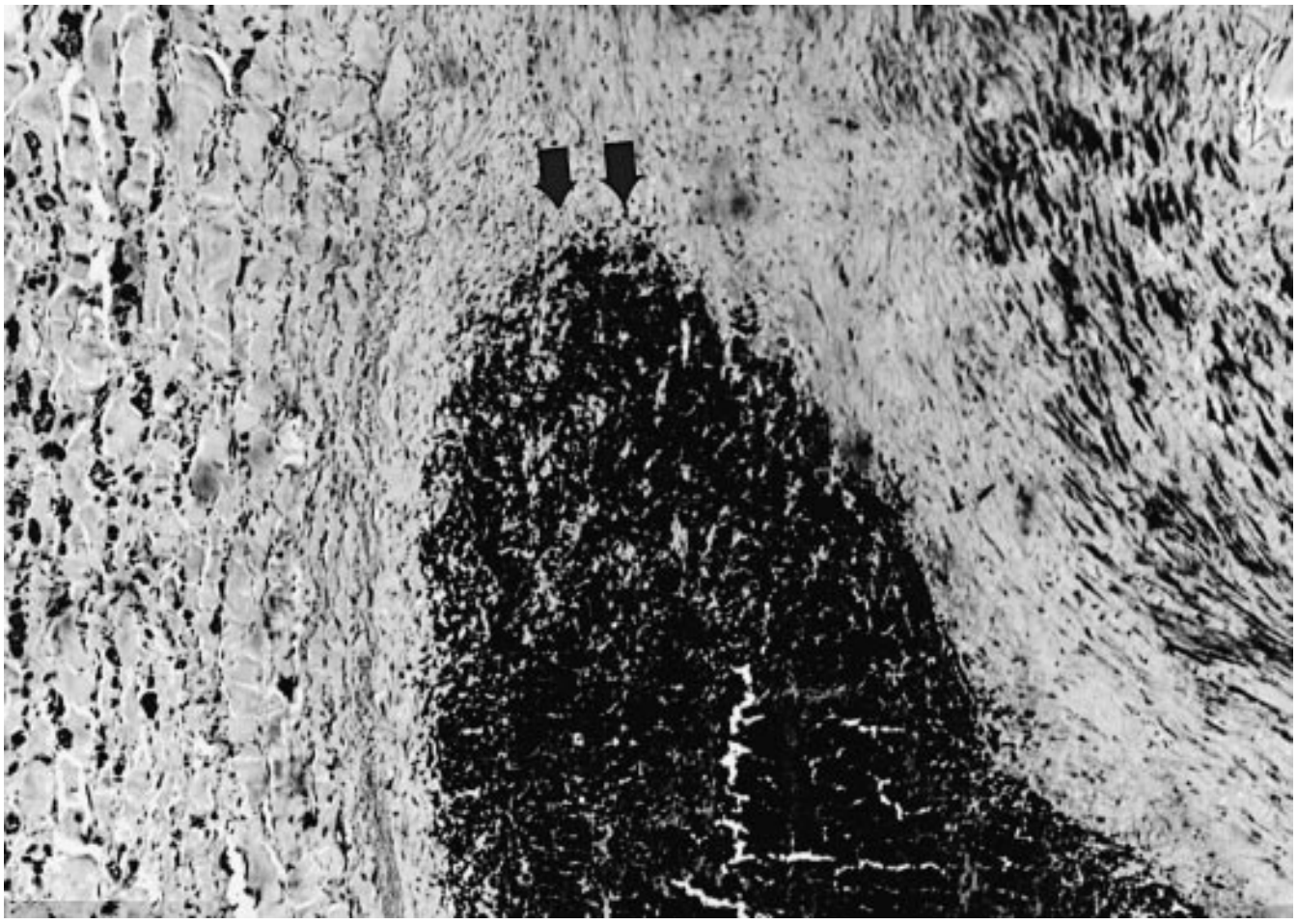

FIG. 6—*Section through the aorta of a 25-year-old man showing blood dissecting into the outer muscular wall and adventitia. Special stains (Van Gieson and Alcian) revealed no specific pathology. Other reports have linked methamphetamine use to acute dissection Van Gieson stain, ×300.*

for the first time. Given the small percentage of decedents with coronary artery disease who were using cocaine, other factors besides cocaine use are obviously involved. If, as the results of the DAWN report and the National Household Drug Survey suggest (16,17), that the population of drug users is aging, there may already be a sizable number of individuals suffering from premature, and unexpected, coronary artery disease.

A possible association of methamphetamine with intracranial hemorrhage and with aortic aneurysm has been reported previously (5,9). The ten additional cases observed in this series suggest that the association is real. Figure 6 shows the edge of an aortic dissection in a 25-year-old man with no known risk factors other than methamphetamine abuse.

Hepatic Disease—Liver disease, manifested by fatty change, cirrhosis, hepatitis, and triaditis, was diagnosed 147 times in 413 patients. Fatty change was equally common in the methamphetamine users and the controls ($p = 0.16$). Hepatitis and infiltration of the portal triads are common findings in intravenous drug users regardless of the drug being injected. Both changes were significantly more common in the methamphetamine abusers than in the controls. Figure 7 shows infiltration of portal triad with lymphocytes and plasma cells (''triaditis'') in a 20-year-old who also had coronary artery disease. This abnormality was present in 6.1% of the methamphetamine cases. Cirrhosis occurred in both MR groups and in controls, but the difference between groups was not significant (35/413 vs. 5/114, $p = 0.12$). This is somewhat surprising, since results of animal studies suggest that methamphetamine, by virtue of its alpha-2-adrenergic activity (30–32), may be intrinsically hepatotoxic. The suggestion is not supported by the findings in this group of decedents.

Lung Disease—Emphysematous changes were observed in both the MR groups and the controls, but the differences were not significant. Even though birefringent crystals were occasionally seen in the lungs of the methamphetamine users, none had evidence of pulmonary granuloma formation or pulmonary hypertension, findings classically associated with intravenous narcotic abuse (20). This observation is also somewhat surprising given the high rate of intravenous drug use in this group of decedents. The absence of granulomas suggests that the expients and adulterants found in methamphetamine may be inherently more soluble, and less toxic, than the substances that are usually mixed with heroin. Pneumonia was relatively common, present in 7.2% (30/413 vs. 4/114,

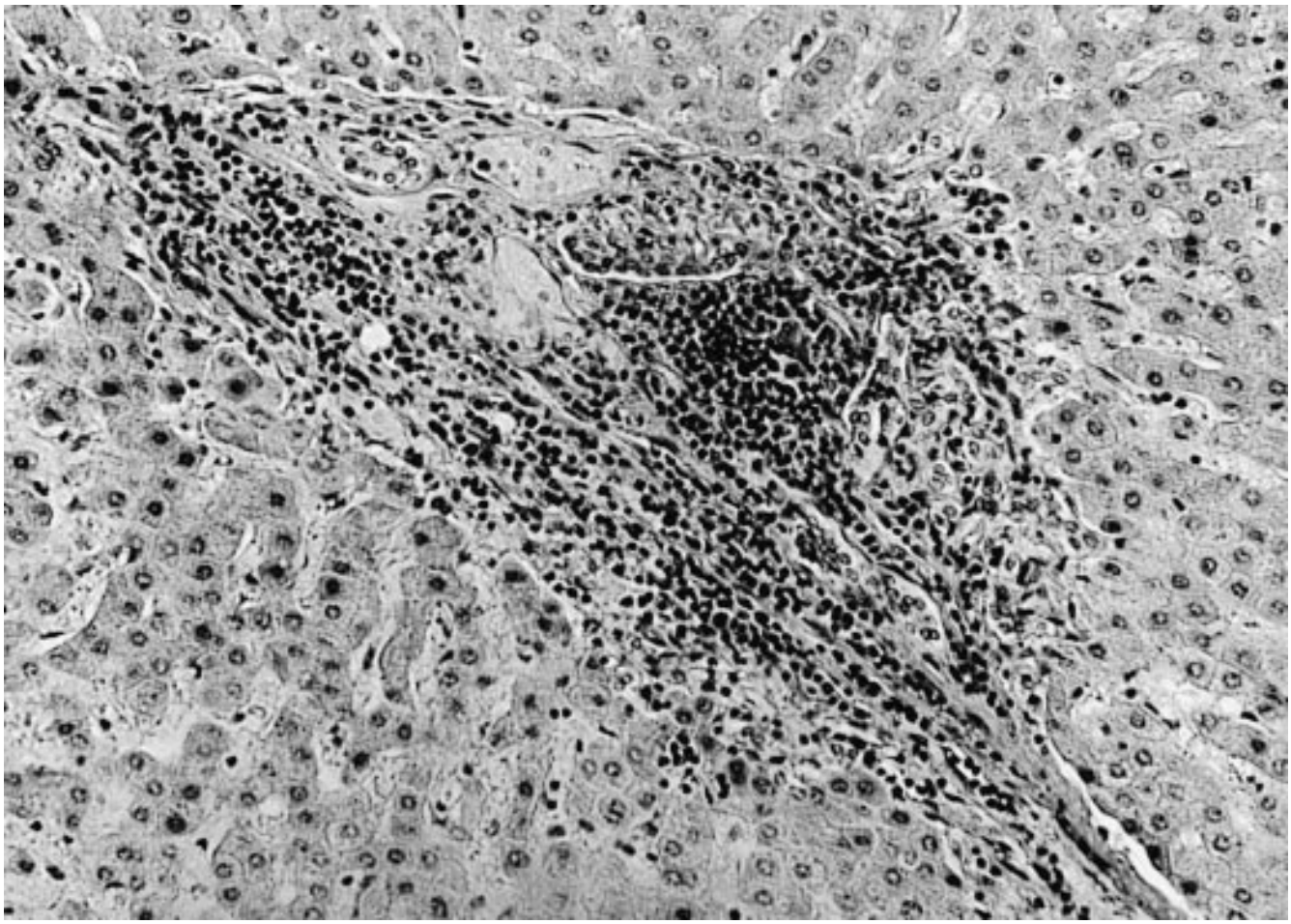

FIG. 7—*Section of liver showing infiltration of portal triad with lymphocytes and plasma cells (''triaditis''). The decedent was a 20-year-old man who also had coronary artery disease. Inflammation of the portal triads is classically associated with intravenous drug abuse, and was first described in the 1960s (19). This abnormality was present in 6.1% of the methamphetamine users, but in only one of the controls (*p = *0.02). Hematoxylin and eosin, ×300.*

$p = 0.015$). Intravenous drug taking is an established, independent risk factor for community acquired pneumonia (33), and that may account for the 30 cases observed in the methamphetamine users. Alternatively, pulmonary hemorrhage and lung destruction are recognized complications of crack smoking (34), and 97/413 (23.4%) of the methamphetamine group were also users of crack cocaine. Given the retrospective nature of our study, causality is impossible to determine.

HIV Infection—A total of 24 cases with AIDS were identified, (either by known clinical history or by the presence of associated disorders such as pneumocystisis pneumonia or Kaposi sarcoma). These cases amounted to 5% of all cases where methamphetamine was detected. The first case occurred in 1990. In 12 of the cases methamphetamine was thought to be the cause of death; in the other cases it was an incidental finding. The rate for HIV-infected MR and non-MR cases in our jurisdiction has remained stable at three to four per year. A number of publications have suggested a link between HIV infection, methamphetamine abuse, and high-risk sexual behavior (1). The observation that 95% of the decedents reported here did not have AIDS tends not to support that suggestion.

Conclusions

Methamphetamine-related deaths are characterized by pulmonary edema and intense visceral congestion. Heart weights are increased, and multivessel coronary artery disease is a relatively frequent finding. Evidence for intravenous drug use is much more frequently present than in controls, as are relatively nonspecific changes in the lungs and liver. Anatomic findings alone cannot be used to distinguish MR, non-MR, and control groups. Toxicologic testing is equally unhelpful. As Logan points out in his analysis of methamphetamine-related deaths: ''. . . methamphetamine concentrations should not be interpreted in isolation, it is important that complete autopsies be performed, in order to understand and properly certify deaths (35).'' Often the clinical history and scene investigation may provide more clues than either the autopsy or toxicologic examination. The reported number of methamphetamine users is rising, but the number of decedents testing positive for methamphetamine in our jurisdiction has not changed during the past decade. As a group, the methamphetamine-related decedents are considerably older than the individuals who are thought to be the most frequent methamphetamine abusers. This suggests that the acute toxicity of methamphetamine is relatively low, and an ''incubation period'' of some years is required before chronic toxicity, with fatal outcomes, becomes evident.

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