

Hepatitis Associated With Illicit Use of Intravenous Methamphetamine

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ABUSE of amphetamine and methamphetamine is widespread in the United States (1-3). In particular, methamphetamine abuse is popular among young drug abusers in San Francisco (4). In 1967, Kramer and co-workers (5) estimated that at least 4,000 persons in San Francisco were regularly taking intravenous amphetamine. Although the majority of the drug users appear to be high school dropouts and hippies, evidence is increasing that high school students are gaining experience with the drug. A 1968 survey of 18,800 high school students in the San Francisco area revealed that 16.3 percent of the students admitted having had experience with amphetamine and more than 6 percent of the students interviewed admitted having used the drug on 10 or more separate occasions (6).

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The psychiatric complications associated with use of methamphetamine have caused much concern, particularly the paranoid state that develops in some users (7, 8). However, except for a few case reports which describe acute overdosage (9, 10), little attention has been paid to the medical complications associated with its use. One medical complication, hepatitis, has been assumed by some authors to be due to serum hepatitis contracted from contaminated hypodermic needles similar to the transmission of serum hepatitis in narcotic addicts (11-13). Barrett and Boyle (14), however, suggest that a toxin in methamphetamine, rather than a virus, is associated with hepatitis.

To investigate the etiology of the methamphetamine-associated hepatitis and the importance of this complication in San Mateo County, Calif., a 3-year analysis of the hospital records of hepatitis patients was undertaken at the county's general hospital. The epidemiologic and laboratory characteristics of hepatitis associated with abuse of intravenous methamphetamine suggest that hepatitis was a frequent complication and that serum hepatitis was responsible for a majority of the cases.

Study Design and Subjects

The 250-bed San Mateo County General Hospital serves the several communities on the San Francisco peninsula. The subjects in our study were methamphetamine abusers with diagnosed

hepatitis who were consecutively admitted to the hospital between July 1965 and June 1968. We reviewed the hospital records of all such patients and interviewed many of those admitted during the final 6 months of the 3-year period. We excluded from the study patients who (a) admitted heavy consumption of alcohol, (b) admitted using narcotics, (c) had heterophile antibodies, or (d) had a close association with a jaundiced friend but did not share hypodermic needles during the 2 months before admission. About 15 percent of the patients were rejected because of these criteria. Three hepatitis patients were admitted a second time during the study period, and the data for each of them were analyzed separately. Thus, for the 3-year period, 75 patients with a total of 78 admissions for hepatitis were studied.

Additionally, serums were collected from 10 hepatitis patients who had a history of methamphetamine abuse and were hospitalized during October 1968 to March 1969. The serums were submitted to Dr. John H. Walsh and Dr. Paul V. Holland at the Blood Bank Department, Clinical Center, National Institutes of Health, for determination of Australia antigen titers by the agar gel diffusion method and the complement fixation method (15). The clinical and laboratory courses of these 10 patients did not differ from those of the patients admitted earlier.

Of the 75 patients studied, all admitted periodic use of intravenous methamphetamine. None reported using the drug for less than 2 months; one patient used it for 7 years—the maximum duration reported. The patients' ages ranged

from 14 through 34 years; the mean was 21.3 years. Males predominated over females, with a ratio of 4 to 1. No difference between sexes was noted in average age. The majority of patients were white. About 25 percent did not graduate from high school, 40 percent had a criminal record, and 7 percent admitted having received psychiatric care previously. Generally, the patients did not know each other, and their residences were scattered throughout the cities served by the hospital. They indicated that they received drugs from a number of different suppliers.

Results

As shown in figure 1, a marked rise occurred after the summer of 1967 in the number of hospital admissions for methamphetamine-associated hepatitis. On the other hand, a comparison of hospital admissions for infectious hepatitis with those for methamphetamine-associated hepatitis clearly showed disproportionate rises for the latter during the study interval (fig. 2). We could not calculate valid attack rates for hepatitis in methamphetamine users because an accurate estimate of the number of users was not available.

The patients with methamphetamine-associated hepatitis generally complained of nausea, vomiting, malaise, and dark urine. These symptoms were present an average of 11 days before hospitalization. The most common physical findings were icterus, 91 percent; hepatomegaly, 65 percent; and adenopathy, 24 percent. As shown in the table, all the patients had elevated serum glutamic oxaloacetic transaminase (SGOT) and

Figure 1. Number of cases of methamphetamine-associated hepatitis in patients at San Mateo County General Hospital, by month of hospitalization

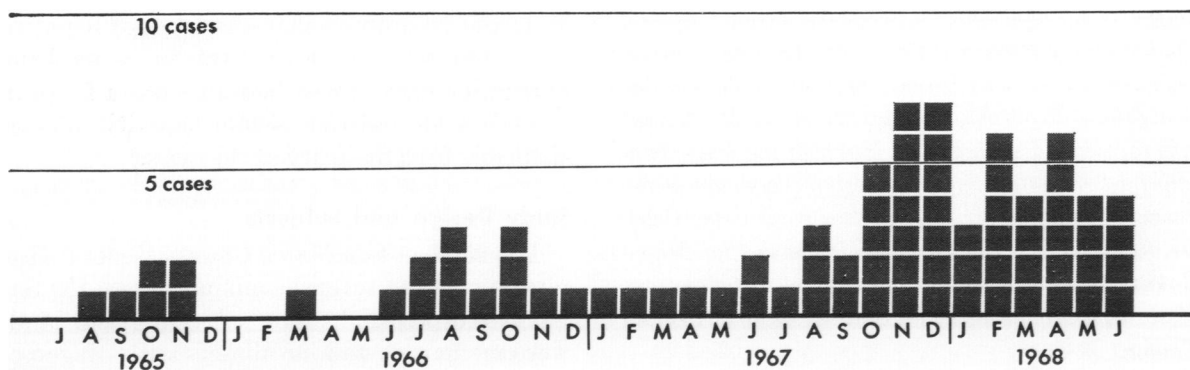
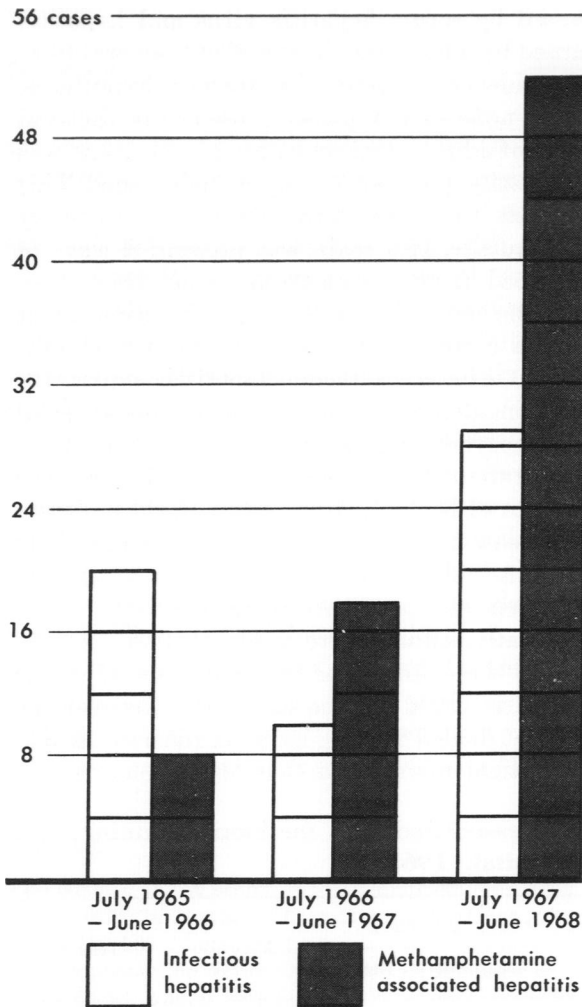


Figure 2. Comparison of number of cases of infectious hepatitis and methamphetamine-associated hepatitis in patients at San Mateo County General Hospital, by year of hospitalization



serum glutamic pyruvic transaminase (SGPT) values with an average SGOT of 1,050 and an average SGPT of 1,425. The average total bilirubin was 6.7 mg. per 100 ml., with the direct bilirubin predominating. An absolute lymphocytosis (more than 3,000 cells per mm.³) was noted for 46 percent of the patients, and 40 percent had atypical lymphocytes on their blood smears.

Twelve patients had percutaneous liver biopsies. The histological picture of nine biopsies was interpreted to be consistent with acute viral hepatitis. Acute inflammatory cells were seen

in the sinusoids and periportal areas. Rare foci of bile stasis were seen occasionally. The parenchymal cells appeared to be swollen and on occasion individual cells were necrotic. Biopsies from three patients indicated that they had chronic active hepatitis; there was cellular infiltration of the periportal areas with occasional extension into the lobules. The infiltrates contained plasma cells, lymphocytes, and eosinophils. Small focal areas of cell necrosis and scattered hyaline necrotic hepatic cells were noted. Some increase in fibrous tissue was noted but frank cirrhosis was not detected.

Of the 10 serums submitted to the NIH blood bank, Australia antigen was detected in six by the complement fixation method and in five by the agar gel diffusion method. One patient was positive by the complement fixation method but not by the agar gel diffusion method.

No deaths occurred among the patients in this series. Chronic active hepatitis was diagnosed by liver biopsy in three patients; examination of their peripheral blood revealed no lupus erythematosus cells. The average time of hospitalization was 14 days, but six patients required more than 1 month. Followup data on the patients were meager because almost all of them failed to keep their followup appointments at the clinic.

Discussion

Hepatitis associated with use of intravenous methamphetamine accounted for almost two-thirds of the hepatitis patients hospitalized at the county's general hospital during the final 12 months of the study (fig. 1). This number undoubtedly represents only a small proportion of the actual cases in the community during that time since many methamphetamine users refused to seek medical treatment during their episodes of jaundice unless they were markedly jaundiced or suffered severe anorexia and nausea.

The sociological composition of the methamphetamine abusers in our study was similar to that of a group of 74 methamphetamine abusers studied in England (16). Both series had similar average ages, age ranges, male-to-female ratios, and criminal records. Although 41 percent of the British group reported a history of childhood neurotic disturbances, only

11 percent received psychiatric care—a percentage comparable to the 7 percent in our group who received psychiatric care.

At least three explanations are possible for the methamphetamine-associated hepatitis: (a) the hepatitis represents an outbreak of infectious hepatitis spreading among the hippie community, (b) the syndrome represents serum hepatitis spread through use of contaminated hypodermic syringes, or (c) the disorder represents toxic hepatitis secondary to either methamphetamine or to an associated contaminant.

Our evidence favors the hypothesis that the illnesses among our study group represent serum hepatitis. The likelihood that they were infectious hepatitis is reduced by the design of the study; patients who associated closely with a jaundiced friend but did not share hypodermic needles were excluded from the study. Second, the absence of clustering of our patients based on residence or drug supplier also mitigates this cause. Third, comparison of hospitalized patients with infectious hepatitis and methamphetamine-associated hepatitis (fig. 2) suggests that although the incidence of infectious hepatitis may be increasing, the incidence of methamphetamine-associated hepatitis is increasing at a disproportionately faster rate. Finally, the Australia antigen was present in the serums of six of the 10 additional patients.

This is a high percentage since it occurs in only one of 1,000 normal people (17). Considerable evidence now suggests that Australia antigen is associated with acute viral hepatitis, usually serum hepatitis (18).

Although distinction between hepatitis caused by serum hepatitis virus and hepatitis caused by a hepatotoxin is difficult, several lines of evidence support the former hypothesis. First, none of our patients used only the oral route of administration, although this route was reportedly popular among female users. This suggests that parenteral usage is a necessary prerequisite. If a toxin was present, it was not absorbed from the gastrointestinal tract. Second, the hepatitis usually had an insidious onset with a clinical and laboratory picture similar to that caused by serum hepatitis. Third, the high incidence of lymphocytosis and atypical lymphocytes suggests a systemic viral illness rather than that caused by a toxin. Fourth, the absence of hematuria and proteinuria indicates that renal toxicity did not occur. Fifth, to date the presence of Australia antigen in serum has not been associated with toxic hepatitis.

Finally, efforts were made to find cases in which the criteria for the diagnosis of serum hepatitis could not be satisfied. However, no patient denied sharing hypodermic needles, and no patient maintained that he routinely steril-

Results of laboratory tests on patients with hepatitis associated with methamphetamine, San Mateo County General Hospital, 1965-68

| Test | Patients | | Average | Range |
|--|----------|---------|---------|--------------|
| | Number | Percent | | |
| SGOT (Sigma-Frankel units)..... | 76 | ----- | 1,050 | 86-4,520 |
| SGPT (Sigma-Frankel units)..... | 59 | ----- | 1,425 | 55-4,520 |
| Alkaline phosphatase (King-Armstrong units)..... | 41 | ----- | 11.6 | 3.0-23.7 |
| Alkaline phosphatase (Sigma units)..... | 34 | ----- | 4.1 | 1.8-7.9 |
| Albumin (gm. per 100 ml.)..... | 55 | ----- | 3.9 | 2.4-5.1 |
| Globulin (gm. per 100 ml.)..... | 53 | ----- | 3.6 | 2.0-5.3 |
| Cholesterol (mg. per 100 ml.)..... | 24 | ----- | 242 | 150-380 |
| Prothrombin time (percent of control)..... | 39 | ----- | 90 | 16-100 |
| Number of patients (less than 50 percent of control)..... | 1 | 2.6 | ----- | ----- |
| Bilirubin (mg. per 100 ml.), total..... | 78 | ----- | 6.7 | 0.5-22.8 |
| Direct..... | 76 | ----- | 5.4 | 0.3-18.8 |
| Indirect..... | 76 | ----- | 1.3 | 0.1-4.2 |
| White blood cell count on admission (cells per mm. ³)..... | 75 | ----- | 7,000 | 2,600-17,900 |
| Less than 5,000..... | 11 | 15.0 | ----- | ----- |
| More than 10,000..... | 8 | 11.0 | ----- | ----- |
| Lymphocytes (cells per mm. ³)..... | 70 | ----- | 3,200 | 810-6,800 |
| More than 3,000..... | 32 | 46.0 | ----- | ----- |
| Less than 1,500..... | 1 | 1.4 | ----- | ----- |
| Atypical lymphocytes..... | 28 | 40.0 | ----- | ----- |

ized his needle and syringe prior to use. Although all three types of hepatitis may be represented in this series of cases, the evidence supports the hypothesis that the majority represent serum hepatitis contracted from use of contaminated "community" hypodermic needles.

Summary

Hepatitis is associated with illicit intravenous use of methamphetamine, and the incidence of this drug complication is increasing in the San Francisco area. The number of admissions of methamphetamine abusers with diagnosed hepatitis increased sixfold during 3 epidemiologic study years at San Mateo County General Hospital and represented two-thirds of the total hepatitis admissions between July 1967 and June 1968.

Records of 75 patients admitted consecutively between July 1965 and June 1968 were reviewed. The epidemiologic data from these hepatitis patients suggest that the syndrome is due to serum hepatitis contracted through the use of contaminated "community" hypodermic needles. The epidemiologic evidence is supported by the presence of the Australia antigen in the serums of six out of 10 patients with methamphetamine-associated hepatitis who were admitted between October 1968 and March 1969.

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Tearsheet Requests

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Program Notes

"Rapping" About Drugs

Visitors to a drug abuse information van of the National Institute of Mental Health, which moves from one area to another in Washington, D.C., are given the opportunity to "rap" about drugs. For 2 weeks in July 1970, it was parked on the sidewalks of Georgetown, an area of the city that attracts a wide cross section of people. This site was the fourth for the drug abuse van, a pilot project of the Institute.

The trailer features film showings, publications, drug referral services, and informal discussions. Starting July 22, it was manned from 10:30 a.m. to 10 p.m. by staff and summer students from the Institute, as well as by volunteers from the local community.

Health Aides for Migrants

The addition of seven health aides to the migrant health project of the Massachusetts Department of Public Health is expected to increase the migrants' use of health services. The aides were recruited on the basis of their familiarity with problems in migrant labor camps. Six aides are natives of Puerto Rico and one is a French-speaking Canadian. Several have worked in migrant camps. The new program, made possible by a grant from the Public Health Service, will be administered through the Massachusetts Health Research Institute.

Most health violations in migrant camps relate to environmental sanitation. In the past, the district sanitarian visited the camps during the day when the workers were in the field. Because of the timing of his visits and language barriers, he was often unaware of the workers' needs. Under the new program, the health aides will spend considerable time with the migrant workers themselves, discussing various needs and problems.

Under the grant for the new project, contracts have been negotiated for the migrant workers to receive prepaid comprehensive care through a group medical practice in Amherst and a similar organization in Chelmsford. These contracts represent the first attempt at providing complete medical care for the migrant population.

Hundreds of migrant farmworkers come to Massachusetts annually to work in the tobacco fields and to pick cranberries, apples, potatoes, and other vegetables. More than 80 percent are natives of Puerto Rico, who come for 4 or 5 months without their families. French Canadians and blacks make up the remainder of the migrant workers—*This Week in Public Health* (Massachusetts Department of Public Health), July 13, 1970.

Genetic Information for All

A genetic information center was established in 1968 by the Connecticut State Department of Health to provide information to participating physicians with a genetic problem. Recently, it broadened the scope of its services because of numerous requests from both State and private agencies. It now fulfills requests from all agencies and also provides direct genetic counseling.

The three subjects on which information has been most frequently requested of the center are cytogenetic services, Down's syndrome, and genetic counseling, followed by mental retardation, microcephaly, and diabetes.—*Connecticut Health Bulletin*, May 1970.

Methadone Treatment

Methadone treatment for heroin addicts in New York State may be administered only by physicians who possess both State and Federal authorization, Dr. Hollis S. Ingraham, State health commissioner, has

cautioned New York State physicians. The drug may not be dispensed by a pharmacist.

In a recent letter to physicians, Ingraham stated that all physicians administering methadone treatment require (a) certification by the State health department for research narcotic privileges, (b) a class VI narcotic registration issued by the Special Tax Section of the U.S. Internal Revenue Service with the approval of the Bureau of Narcotic and Dangerous Drugs of the U.S. Department of Justice, and (c) an investigational new drug license from the U.S. Food and Drug Administration.

A physician who has obtained the three authorizations may administer the medication only by mouth; the patient may be given no more than a 3-day supply and must be maintained under competent medical and social supervision.

Trauma Center Always Manned

A trauma research center of the University of Maryland is staffed around the clock by special teams of physicians. Located in Baltimore, it is funded by the National Institute of General Medical Sciences. According to the director of the center, Dr. R. Adams Cowley, members of the teams are all uniquely trained and equipped to handle crisis patients. A helicopter ambulance service airlifts accident victims from remote parts of the State to the center.

Each year 114,000 Americans die from injuries, and injuries are the leading cause of death among persons aged 1 to 36 years. Better emergency facilities, it is believed, might help prevent some of these deaths. Many U.S. emergency rooms are poorly organized, inadequately staffed, and insufficiently equipped. These discrepancies are especially observed on nights and weekends, said Cowley, when many accidents occur.

Items for this page: Health departments, health agencies, and others are invited to share their program successes with others by contributing items for brief mention on this page. Flag them for "Program Notes" and address as indicated in masthead.