Risk factors for Creutzfeldt-Jakob disease:

A reanalysis of case-control studies

D.P.W.M. Wientjens, MD; Z. Davanipour, DVM, PhD; A. Hofman, MD, PhD; K. Kondo, MD; W.B. Matthews, DM, FRCP; R.G. Will, MD, FRCP; and C.M. van Duijn, PhD

Article abstract—To review the evidence for risk factors of Creutzfeldt-Jakob disease (CJD), we pooled and reanalyzed the raw data of three case-control studies. The pooled data set comprised 178 patients and 333 control subjects. The strength of association between CJD and putative risk factors was assessed by computing the odds ratio as estimate of the relative risk. The risk of CJD was statistically significantly increased for subjects with a family history of CJD (odds ratio = 19.1; 95% CI 1.1 to 348.0). Further, there was a significant association between the risk of CJD and a history of psychotic disease (odds ratio = 9.9; 95% CI 1.1 to 86.1). Although not significantly increased, there was an elevated risk of CJD for subjects with a family history of dementia, a history of poliomyelitis, subjects employed as health professionals, and subjects ever exposed to cows and sheep. No association could be shown with organ meat consumption, including brain. The negative results of this reanalysis reassures the absence of a common risk factor in all CJD patients. However, the ongoing epidemiologic surveillance of CJD in several European countries may provide more evidence to exclude any environmental exposure early in childhood.

NEUROLOGY 1996;46:1287–1291

Creutzfeldt-Jakob disease (CJD) is a transmissible spongiform encephalopathy that may occur in an inherited, infectious, or sporadic form. CJD may be caused by various mutations in the prion protein gene (*PRNP*) on chromosome 20.[1] However, these mutations are found only in familial CJD patients, comprising not more than 15% of all CJD patients.[1] The infectious form of CJD appears to be rare among humans[2] and limited to iatrogenic transmission through neurosurgery and EEG electrode implantation,[3-6] corneal transplantation,[7] and human growth[8-10] and gonadotrophin[11] hormone. For most patients with sporadic CJD, the cause remains unknown. Studies on risk factors for CJD have yielded controversial results and do not show evidence for a common risk factor.[12-17] An increased risk of CJD has been reported for subjects with a history of infection,[12,17] surgery of the head,[13,14] trauma to the head or body,[13,14] tonometry,[14] consumption of pork,[15] and contact with various animals[16,17] in some but not all studies. The recent infection of British bovine cattle through protein supplements derived from animal carcasses has fueled speculations on the possibility of infection of humans through meat consumption and animal contact. Other than the established transmission of Kuru through cannibalistic rituals,[1,2] findings of studies on (organ) meat consumption including brain have not yielded consistent results.[12,15]

Some of the conflicting results may be explained by the small size of the individual studies yielding only limited statistical power to detect an association. To review the evidence for the risk factors previously reported, we pooled and reanalyzed the raw data of three case-control studies of CJD. As no meta-analysis of the existing case-control studies on CJD has been performed earlier, we present our results here.

Methods. All formal case-control studies of CJD were ascertained through MEDLINE search and personal communications. Thus, four studies were identified as eligible for the reanalysis.[12-17] To increase the comparability between studies, we restricted the analysis to the three studies comprising patients diagnosed with CJD according to the criteria of Masters et al.[18] One study was performed in Japan,[13] one in the United States,[14-16] and one in the United Kingdom.[17] The pooled data set comprised 178 patients (mean ± SD age at diagnosis 61 ± 9.5 years; range 26 to 81 years) and 333 control subjects. For each study, ascertainment of patients and control subjects and data collection are discussed briefly.

Japan. The study conducted in Japan comprised 60 cases.[13] According to the criteria of Masters et al,[18] 50%

From the Departments of Epidemiology & Biostatistics (Drs. Wientjens, Hofman, and van Duijn) and Neurology (Dr. Wientjens), Erasmus University Medical School, Rotterdam, The Netherlands; University of Southern California (Dr. Davanipour), Los Angeles, CA; Department of Public Health (Dr. Kondo), Hokkaido University, Sapporo, Japan; University Department of Clinical Neurology (Dr. Matthews), Radcliffe Infirmary, Oxford, UK; and Department of Clinical Neurosciences (Dr. Will), Western General Hospital, Edinburgh, UK.

Supported by the Netherlands Institute for Health Sciences (NIHES), the Slow Virus Infection Research Group Japan, and the Japan Ministry of Health and Welfare.

Received August 21, 1995. Accepted in final form November 1, 1995.

Address correspondence and reprint requests to Dr. C.M. van Duijn, Department of Epidemiology & Biostatistics, Erasmus University Medical School, PO BOX 1738, 3000 DR Rotterdam, The Netherlands.

were classified as probable, 47% as definite, and 3% as transmissible CJD. For this study, neurologic and psychiatric institutions throughout Japan were requested to report patients diagnosed with CJD in the period 1975 through 1977. Patients were compared with 109 age-matched control subjects (± 5 years), including 50 spouses and 59 neighborhood control subjects. In some instances, public health personnel served as neighborhood control subjects. The response rate was 80% in patients, 78% in spouses, and 93% in neighborhood control subjects. Data were collected by a structured interview. For patients, the data were obtained from the spouse. Control subjects were questioned directly.

United States. The study performed in the United States comprised 26 patients, of which 23% were classified as probable CJD, 46% as definite, and 31% as transmissible.[14-16] Patients were ascertained through records submitted to the Laboratory of Central Nervous System Studies of the National Institutes of Health from Pennsylvania, New Jersey, Maryland, New York, and Delaware. Patients were diagnosed with CJD in the period 1970 through 1981. Two control groups were selected: hospital control subjects diagnosed with a nonneurologic disease at the hospital where the patient was diagnosed (n = 22; matching sex and age ± 5 years) and relative control subjects (n = 18; matching sex and age ± 10 years). The response rate was 96% in patients, 85% in hospital control subjects, and 86% in relative control subjects. Data were collected by a structured interview of the spouse (58%), child (27%), sibling (11%), or parent (4%) of the patients. Control subjects were questioned directly.

United Kingdom. The study conducted in the United Kingdom comprised 92 patients, of whom 24% were classified as probable and 76% as definite CJD.[17] Patients diagnosed with CJD in the period 1980 through 1984 were ascertained through neurologic centers in England and Wales and through death certificates of the Office of Population, Censuses and Surveys. For each patient, two age- and sex-matched control subjects were derived from the hospital where the patient was diagnosed (n = 184; matching age ± 4 years). Of the two control subjects, one suffered from a neurologic disorder other than CJD and the other from a nonneurologic disorder. The response rate was 75% in patients and is unknown for control subjects. For patients and control subjects, the data were collected by interviewing an informant. The relationship to the informant was matched in 87% for patients and control subjects. In 78% of subjects, it was the spouse, in 16% a child, and in 6% a sibling.

Analysis. This reanalysis was based on the original raw data of the three studies. We only included risk factors assessed comparably in at least two out of three studies. The risk factors studied were family history of CJD, dementia, and Parkinson's disease; medical history, including head trauma, hospitalization for psychotic disease, history of poliomyelitis, hepatitis, jaundice, allergy, and blood transfusion; employment as health professional; exposure to animals; living in a rural area; and consumption of organ meat. Exposures of patients, relatives, and spouses may be similar for family and occupational history, animal exposure, place of residence, and diet, due to the shared environment. As this may bias the results toward the null hypothesis, relative and spouse control subjects were excluded in the analysis of these putative risk factors. Thus, the number of subjects included in the study may vary according to the number of studies and control subjects included, as well as to the missing values within a study. For each risk factor, we report the number of subjects exposed and the total number of subjects for whom data on the risk factor were available.

The strength of association between CJD and putative risk factors was assessed by computing the odds ratio (OR) as an estimate of the relative risk.[19] Relative risks were estimated by maximum likelihood methods and the 95% CI were based on the asymptotic SEs. Confounding by age, sex, and study center was taken into account by including these variables into the logistic regression model.

Results. Family history of CJD, dementia, and Parkinson's disease for patients and control subjects are reported in the table. A positive family history of CJD was found only in CJD cases. Seven patients (4%) had a relative with CJD. An increased risk of CJD was also observed for patients with a positive family history of dementia in any relative, which was borderline significant (OR = 1.9; 95% CI 0.9 to 4.1). When restricting the analysis to first-degree relatives, the OR remained increased (OR = 1.8; 95% CI 0.8 to 4.0; not shown in the table).

With regard to the medical history (table), significantly more CJD patients than control subjects had a history of hospitalization for psychotic disease. Three of five CJD patients were hospitalized 15 years or more before the onset of CJD. No association was found with head trauma, hepatitis, jaundice, allergy, or blood transfusion. The risk of CJD associated with poliomyelitis was increased (OR 3.9; 95% CI 0.3 to 43.4). However, the significance is difficult to interpret as the number of exposed subjects is very small. Fewer CJD patients than control subjects had a history of surgery. The difference was statistically significant for abdominal surgery.

A nonsignificantly increased risk of CJD was found for subjects exposed to patient tissue through their employment as a health professional (i.e., medical doctors, nurses, dentists, laboratory workers, ambulance employees) (OR 1.5; 95% CI 0.5 to 4.1) (table). Exposure to cows and sheep was associated with a borderline significant increased risk of CJD (OR 1.7; 95% CI 0.9 to 3.1 and OR 1.6; 95% CI 0.9 to 2.9, respectively). Also, there was a nonsignificant increased risk of CJD for subjects who lived in a rural area at diagnosis (OR 1.4; 95% CI 0.8 to 2.4; not in table). Consumption of organ meat, including brain, liver, and kidney, was not associated with an increased risk of CJD (table).

Discussion. In this reanalysis of case-control studies, the risk of CJD was statistically significantly increased for subjects with a family history of CJD. We also found a statistically significant association between the risk of CJD and the patient's history of psychotic disease. No statistically significant association could be shown for medical history other than psychosis or with organ meat consumption. Although not significantly increased, more CJD patients than control subjects had a family history of dementia, a history of poliomyelitis, an occupational history as

Table *Risk factors for Creutzfeldt-Jakob disease (CJD)*

	Patients*	Control Subjects*	Odds ratio [95% CI]	
			Crude	Adjusted†
Family history				
CJD[13-17]	7/166	0/285	18.8 [1.0–341.2]‡	19.1 [1.1–348.0]‡
Dementia[14-17]	15 /126	17/212	1.6 [0.7–3.2]	1.9 [0.9–4.1]
Parkinson's disease[14-17]	7 /117	7/194	1.7 [0.6–5.0]	1.7 [0.6–5.0]
Medical history				
Psychotic disease[13-17]	5 /111	1/219	10.3 [1.2–89.8]‡	9.9 [1.1–86.1]‡
Head trauma[13-17]	27 /176	55/329	0.9 [0.6–1.5]	0.9 [0.5–1.5]
Poliomyelitis[13-17]	2 /168	1/332	4.0 [0.4–44.6]	3.9 [0.3–43.4]
Hepatitis/jaundice[14-17]	9 /118	18/222	0.9 [0.4–2.2]	0.9 [0.4–2.1]
Allergy[13-17]	39 /174	64/330	1.2 [0.8–1.9]	1.2 [0.8–2.0]
Blood transfusion[13-17]	17 /174	45/328	0.7 [0.4–1.2]	0.6 [0.4–1.2]
Surgery				
CNS[13-17]	0 /149	10/301	0.3 [0.1–1.2]	0.3 [0.1–1.2]
Eye[13-17]	6 /176	23/332	0.5 [0.2–1.1]	0.5 [0.2–1.1]
Abdominal[13-17]	39 /176	96/331	0.7 [0.5–1.1]	0.7 [0.4–1.0]‡
Tonsillectomy[13-17]	13 /171	32/331	0.8 [0.4–1.5]	0.7 [0.4–1.4]
Occupational, animal, and dietary exposure				
Health professional[14-17]	8 /119	7/206	1.5 [0.6–4.2]	1.5 [0.5–4.1]
Cow exposure[13-17]	26 /95	26/145	1.7 [0.9–3.2]	1.7 [0.9–3.1]
Sheep exposure[13-17]	26 /171	25/262	1.6 [0.9–2.9]	1.6 [0.9–2.9]
Organ meat				
Brain[13-17]	14 /177	33/261	0.6 [0.3–1.2]	0.6 [0.3–1.8]
Liver[13-17]	104 /117	179/206	1.2 [0.6–2.5]	1.3 [0.6–2.6]
Kidney[13-17]	61 /86	135/179	0.8 [0.4–1.4]	0.8 [0.3–1.4]

* Number of subjects with a positive history or subjects exposed/total number of subjects in analysis.
† Adjusted for age, sex, and study site.
‡ $p < 0.05$.

health professional, history of exposure to cows and sheep, and had lived in a rural area.

The internal validity of this reanalysis depends on the validity of the individual studies. Selection bias may have occurred through nonresponse in patients and control subjects in the individual studies. Further, control selection differed considerably across studies. However, to distort the findings, nonresponse and control selection should be associated with the risk factors studied. This seems unlikely for most risk factors. However, in the case of medical history, risk factor exposure may have been associated with control selection in the largest study conducted in the United Kingdom,[17] which was hospital based. The use of hospital control subjects may have led to high exposure frequencies for medical disorders, surgery, and blood transfusion. This may explain the lower frequency of surgery in CJD patients than control subjects. Unfortunately, the a priori statistical power of an analysis limited to the two small studies from Japan[13] and the United States[14-16] was too low to yield a meaningful solution to this problem. Another source of information bias might have been biased recall of putative risk factors. Also, the data collection through informants for patients and personal interviews for control subjects might have biased the data in two of three studies. To take this bias into account, we restricted the analysis to exposures not easily forgotten by control subjects and informants. For this reason, family history of dementia was restricted to first-degree relatives and the patient's history of psychotic disease to those requiring hospitalization. Further, we checked whether the association with a risk factor was found consistently across studies. In each of the studies, a family history of dementia, history of psychotic disease, employment as a health professional, and exposure to cows and sheep was associated with an increased CJD risk. This suggests that if bias occurred, it must have occurred in all studies similarly despite the differences in the design among studies.

Another issue is that the statistical power of our analysis may have been limited for rare exposures. Although we pooled the data of all case-control stud-

ies in which the patients met the criteria for CJD by Masters et al.,[18] the number of patients included in this reanalysis was still small, which is reflected in the width of the 95% CIs. Given an exposure frequency in control subjects of 10%, a significance level of 5% (two-sided), and statistical power of 90%, the smallest detectable relative risk in a study of 200 patients and 200 control subjects is 2.5.[19] If the exposure frequency is only 1%, the smallest detectable relative risk under these conditions is 8.0,[19] which is a strength of association seldom observed in epidemiologic research.

Despite the limitations, our analysis showed a significant association between history of psychotic disease and the risk of CJD. Whether psychotic disease is a risk factor for CJD or is merely an early symptom of CJD pathology is undetermined. Future studies on the relationship between CJD and psychotic disease may be relevant. Our study shows familial aggregation of CJD, which may be explained by mutations in the *PRNP* gene that segregate in the families.[1,20] Also, homozygosity at codon 129 of *PRNP* may be associated with an increased susceptibility to prion diseases.[21,22] Our reanalysis showed a borderline significant association between CJD and family history of dementia. In a number of patients with familial forms of dementia, there have been *PRNP* mutations,[23] and the familial aggregation of CJD and dementia may therefore be related to *PRNP* mutations segregating in these families. However, other genetic factors (e.g., the apolipoprotein E gene [associated with both the risk of CJD[24] and Alzheimer's disease[25]] or nongenetic factors) may underlie the relationship; studies of families in which CJD and dementia aggregate may be of interest.

Our reanalysis did not support a number of previously reported associations. When pooling the data of the three studies, there was no association of the CJD risk with head trauma or the consumption of organ meat, including brain. The latter was associated with an increased risk of CJD in the study of Bobowick et al.,[12] which is not included in the present reanalysis. Based on our findings, blood transfusion did not increase the risk of CJD in the period studied. There was no significant evidence in our study of transmission of CJD among humans or from cattle to human. However, there was a nonsignificant increase in risk of CJD for subjects employed as health professionals, subjects ever exposed to cows and sheep, and living in a rural area. In our reanalysis, the power to assess a statistically significant relationship for exposure to patients and exposure to animals was low. Data on the presence of prion disorders in patients or animals to which patients were exposed were not available. Further, the individual studies were performed in the 1970s and early 1980s when information in particular on inherited prion diseases among humans and animals was not yet available, which has limited the possibility to separate genetic and nongenetic patients in the present reanalysis. The negative results of our reanalysis are important in the light of public health to reassure the population that there are no common risk factors for CJD.

Our data cannot exclude an environmental source of infection that might have occurred early in childhood. The ongoing systematic epidemiologic surveillance of CJD in several European countries might provide evidence of such exposure as residential histories throughout life are studied.[26] These extensive studies with similar design will be highly comparable and therefore will be able to resolve the problem of selection bias and of the limited statistical power of our reanalysis.

Acknowledgment

This research was carried out under the auspices of Concerted Action on the Epidemiology of CJD, by means of a grant of the European Community. We would like to thank Hanneke den Breeijen and Michael Koenders for their help in data management and data analysis and Jane Mackenzie and Wakana Sakurai for their technical assistance.

References

1. Prusiner SB, Hsiao KH. Human prion diseases. Ann Neurol 1994;35:385–395.
2. Brown P, Cathala F, Raubertas RF, et al. The epidemiology of Creutzfeldt-Jakob disease: conclusion of a 15-year investigation in France and review of the world literature. Neurology 1987;37:895–904.
3. Masters CL, Richardson EP Jr. Subacute spongiform encephalopathy Creutzfeldt-Jakob disease: the nature and progression of spongiform change. Brain 1978;101:333–344.
4. Will RG, Matthews WB. Evidence for case-to-case transmission of Creutzfeldt-Jakob disease. J Neurol Neurosurg Psychiatry 1982;45:235–238.
5. Thadani V, Penar PL, Partington J, et al. Creutzfeldt-Jakob disease probably acquired from a cadaveric dura mater graft. J Neurosurg 1988;69:766–769.
6. Bernouilli C, Siegfried J, Baumgartner G, et al. Danger of accidental person to person transmission of Creutzfeldt-Jakob disease by surgery. Lancet 1977;1:478–479.
7. Duffy P, Wolf J, Collins G, et al. Possible person to person transmission of Creutzfeldt-Jakob disease. N Engl J Med 1974;290:692–693.
8. Powell-Jackson J, Weller RO, Kennedy P, et al. Creutzfeldt-Jakob disease after administration of human growth hormone. Lancet 1985;2:244–246.
9. Gibbs CJ, Joy A, Heffner R, et al. Clinical and pathological features and laboratory confirmation of Creutzfeldt-Jakob disease in a recipient of pituitary-derived human growth hormone. N Engl J Med 1985;313:734–739.
10. Brown P, Gajdusek DC, Gibbs CJ, et al. Potential epidemic of Creutzfeldt-Jakob disease from human growth hormone therapy. N Engl J Med 1985;313:728–731.
11. Cochius JI, Mack K, Burns RJ, et al. Creutzfeldt-Jakob disease in a recipient of human pituitary gonadotrophin. Aust NZ J Med 1990;20:592–593.
12. Bobowick AR, Brody JA, Matthews MR, et al. Creutzfeldt-Jakob disease: a case-control study. Am J Epidemiol 1973;98: 381–394.
13. Kondo K, Kuroiwa Y. A case-control study of Creutzfeldt-Jakob disease: association with physical injuries. Ann Neurol 1982;11:377–381.
14. Davanipour Z, Alter M, Sobel E, et al. Creutzfeldt-Jakob disease: possible medical risk factors. Neurology 1985;35:1483–1486.
15. Davanipour Z, Alter M, Sobel E, et al. A case-control study of Creutzfeldt-Jakob disease: dietary risk factors. Am J Epidemiol 1985;122:443–451.
16. Davanipour Z, Alter M, Sobel E, et al. Transmissible virus dementia: evaluation of a zoonotic hypothesis. Neuroepidemiology 1986;5:194–206.
17. Harries-Jones R, Knight R, Will RG, et al. Creutzfeldt-Jakob

disease in England and Wales, 1980–1984: a case-control study of potential risk factors. J Neurol Neurosurg Psychiatry 1988;51:1113–1119.
18. Masters CL, Harris JO, Gajdusek DC, et al. Creutzfeldt-Jakob disease: patterns of worldwide occurrence and the significance of familial and sporadic clustering. Ann Neurol 1979;5:177–188.
19. Schlesselman JL. Case-control studies. New York: Oxford University Press, 1982.
20. Collinge J, Brown J, Hardy J, et al. Inherited prion disease with 144 base pair gene insertion. 2. Clinical and pathological features. Brain 1992;115:687–710.
21. Collinge J, Palmer MS, Dryden AJ. Genetic predisposition to iatrogenic Creutzfeldt-Jakob disease. Lancet 1991;337:1441–1442.
22. Palmer MS, Dryden AJ, Hughes JT, et al. Homozygous prion protein genotype predisposes to sporadic Creutzfeldt-Jakob disease. Nature 1991;352:340–341.
23. Collinge J, Owen F, Poulter H, et al. Prion dementia without characteristic pathology. Lancet 1990;336:7–9.
24. Amouyel P, Vidal O, Launay JM, et al. The apolipoprotein E alleles as major susceptibility factors for Creutzfeldt-Jakob disease. Lancet 1994;344:1315–1318.
25. Strittmatter WJ, Saunders AM, Schmechel D, et al. Apolipoprotein E: high avidity binding to beta-amyloid and increased frequency of type 4 allele in late-onset familial Alzheimer's disease. Proc Natl Acad Sci USA 1993;90:1977–1981.
26. Alperovitch A, Brown P, Weber T, et al. Incidence of Creutzfeldt-Jakob disease in Europe in 1993. Lancet 1994; 343:918.

Intracranial hemorrhage associated with cocaine abuse:

A prospective autopsy study

Kurt B. Nolte, MD; Lawrence M. Brass, MD; and Carol F. Fletterick, MS

Article abstract—*Objectives:* To determine the incidence of cocaine abuse in cases of fatal intracranial hemorrhage and to examine potential pathophysiologic mechanisms. *Design:* Prospective clinical, autopsy, and toxicologic evaluation of all cases of fatal non-traumatic intracranial hemorrhage examined during 1 year (April 11, 1989 to April 10, 1990) at the Connecticut Office of the Chief Medical Examiner. Autopsy examination included exhaustive histologic evaluation of cerebral vessels and parenchyma for vasculitis and other vasculopathies. *Results:* Ten of 17 (59%) of all non-traumatic intracranial hemorrhages were associated with a positive toxicology for cocaine. Seven (70%) of these were parenchymal hemorrhages, and the remaining three (30%) were subarachnoid hemorrhages (ruptured berry aneurysms). No vasculitis or other vasculopathy was identified. *Conclusions:* These findings implicate cocaine use as a significant risk factor for fatal brain hemorrhage and may explain, in part, the increased incidence of hemorrhagic stroke in some drug-using cohorts. The lack of specific pathologic findings suggests that cocaine-associated intracranial hemorrhages are a consequence of the pharmacodynamic effect of cocaine and not a cocaine-induced vasculopathy.

NEUROLOGY 1996;46:1291–1296

Cocaine abuse is associated with adverse effects on cardiac and skeletal muscle, cerebral vessels, uterus, and placenta.[1-3] Cerebrovascular complications of cocaine abuse include ischemic infarcts, intracranial hemorrhages, transient ischemic attacks, and anterior spinal artery and lateral medullary syndromes.[4,5] Several controversial and unproven mechanisms for cocaine-generated strokes have been hypothesized, including cocaine-associated vasculitis and transient hemodynamic effects mediated by the pharmacologic action of cocaine.[4,6-10] Although many clinical reports of cocaine-related strokes have appeared over the past few years, toxicologic documentation is poor, and there are few autopsy studies.[4,10,11] In addition, the incidence of the association between cocaine use and stroke is unclear. We describe the results of a prospective autopsy-based investigation into the epidemiology, clinical manifestations, and pathology of cocaine-associated intracranial hemorrhage.

Methods. All individuals with fatal non-traumatic subarachnoid or parenchymal brain hemorrhage autopsied between April 11, 1989, and April 10, 1990, at the Connecticut Office of the Chief Medical Examiner were studied. In each case, information was sought regarding the circumstances of death, history of cocaine and other drug use (including route of administration), temporal sequence of clinical symptoms, past history of hypertension, sickle cell disease, vasculitis, renal or hepatic failure, and family history of intracranial hemorrhage or stroke. Available hospi-

From the Office of the Medical Investigator (Dr. Nolte), University of New Mexico School of Medicine, Albuquerque, NM, Formerly: Office of the Chief Medical Examiner, State of Connecticut, Farmington, CT; the Department of Neurology (Dr. Brass), Yale Stroke Program, Yale University School of Medicine, New Haven, CT; and the Office of the Medical Examiner (Ms. Fletterick), State of Connecticut, Farmington, CT.

Received July 6, 1995. Accepted in final form October 16, 1995.

Address correspondence and reprint requests to Dr. Kurt B. Nolte, Office of the Medical Investigator, University of New Mexico School of Medicine, Albuquerque, NM 87131-5091.

