

K-28126 (405)

inhibition test was negative for echinococcosis, cysticercosis, and toxoplasmosis.

Hemagglutination inhibition and flocculation tests for filariasis were done on the possibility that the hemoptysis and eosinophilia (Löffler syndrome) might be explained. Positive results were reported—hemagglutination titer, 1:200-800; flocculation, 1:5. The second (1:200) and third (1:800) hemagglutination titers were positive. Identification of microfilaria in the patient's blood or in the blood of her pet dog was not made. A presumptive diagnosis of infestation with *Dirofilaria immitis* was made.

Comment

Despite the absence of microfilaria in the blood or demonstration of a

nematode, Adolph et al¹² have indicated that serologic tests for filariasis (hemagglutination and bentonite flocculation) were useful in arriving at a clinical diagnosis of filariasis. On the basis of presumptive diagnosis, a therapeutic trial was undertaken with the use of diethylcarbamazine citrate, (2 mg/kg/day for one week). The dose was increased over three weeks to 18 mg/kg/day.

Follow-up examination after three weeks of therapy showed no untoward effects and no signs of meningeal irritation. Diethylcarbamazine citrate therapy was discontinued after two weeks at the dosage of 18

mg/kg/day (five weeks of treatment). Chills, nausea, and malaise were complaints during the final week of therapy.

The patient had no further hemoptysis. Chest x-ray film was normal four months after treatment. The peripheral blood no longer showed increased eosinophils. There have been no recurrences of the patient's complaints of hemoptysis. There has been no eosinophilia during the nine years of follow-up.

The hemagglutination inhibition and flocculation tests were performed at the Public Health Service Communicable Disease Center, Atlanta.

References

1. Phillips JH: Studies of the transmission of *Dirofilaria immitis* in Massachusetts. *Am J Hyg* 29:121-129, 1939.
2. Beaver PC, Orihel TC: Human infection with filariae of animals in the United States. *Am J Trop Med Hyg* 14:1010-1029, 1965.
3. Harrison EG, Thompson JH: Diminution of human lung. *Am J Clin Pathol* 43:224-234, 1966.
4. Tucson RA, Firestone P, Blaustein AU: Human pulmonary dirofilariasis manifesting as a "coin" lesion. *JAMA* 199:45-46, 1967.
5. Spear HC, et al: Solitary pulmonary lesion due to *Dirofilaria*. *N Engl J Med* 278:832-833, 1968.
6. Lewis JF, Williams RW, Tinsley E: Pulmonary coin lesion due to *Dirofilaria immitis*. *Arch Surg* 99:385-390, 1969.
7. Goodman ML, Gore I: Pulmonary infarct secondary to *Dirofilaria* larvae. *Arch Intern Med* 113:702-705, 1964.
8. Donoghue DL: Tropical eosinophilia: An etiologic inquiry. *N Engl J Med* 269:1357-1364, 1963.
9. Pande RS: Filarial encephalitis. *J Assoc Physicians India* 10:469-471, 1962.
10. Alajouanine T, et al: Encephalite pur endocardite fibroblastique d'origine filarienne. Read before the Société Française de Neurologie, Nov 5, 1959.
11. Harrison EG, Thompson JH: *Dirofilaria immitis* in pathology of protozoal and helminthic infection. Marcial-Rojas (ed), Baltimore, Williams and Wilkins Co, 1971.
12. Adolph PE, Kagan JG, McQuay RM: Diagnosis and treatment of *Acanthocheilium perstans* filariasis. *Am J Trop Med Hyg* 11:76-88, 1962.

PLAINTIFF'S
EXHIBIT

DOW 49

ST0095845

Asbestos-Like Fibers in Duluth Water Supply Relation to Cancer Mortality

Thomas J. Mason, PhD; Frank W. McKay; Robert W. Miller, MD

Asbestos-like fibers in industrial waste first entered the water supply of Duluth in 1955. In the next 14 years, no carcinogenic effect was apparent in the patterns of cancer mortality among persons of all ages, nor among children. The period of observation is short relative to the latent period for occupationally induced carcinogenesis from asbestos.

(*JAMA* 228:1019-1020, 1974)

HIGH concentrations of asbestos-like fibers have been reported recently in the drinking-water supplies of Duluth, Minn., and other communities on the shores of Lake Superior. Officials of the Environmental Protection Agency stated that these fibers probably came from mine-tailings or mill-

waste from taconite ore, which has been emptied into Lake Superior since 1955.^{1,2} This pollution has caused concern because occupational exposures to asbestos are known to induce mesothelioma of the pleura and peritoneum, as well as cancer of the lung, esophagus, and stomach, after a latent period usually of 20 to 40 years.³ Asbestos fed experimentally to rats has passed through the gastric and intestinal mucosa into the bloodstream. Fibers were lodged in gut

wall, lungs, brain, omentum, and other organs.⁴

To determine if the fibers present in the drinking water of Duluth were related to cancer mortality, we have studied data abstracted from death certificates for all persons who died of cancer in the United States, from 1950 to 1969.

Methods

The data were made available to us by the National Center for Health Statistics. We have tabulated the numbers of deaths ascribed to cancer among whites, according to age, sex, and five-year intervals, as well as the age-adjusted cancer death rates for Duluth (1960 population, 105,759), for comparison with data for the state

From the Epidemiology Branch, National Cancer Institute, Bethesda, Md.
Reprint requests to A-521 Landow Building, National Cancer Institute, Bethesda, MD 20014 (Dr. Miller).

Sites With Risk Ratios Significantly Different From Unity In at Least One Five-Year Interval								
Site (ICD)*	White Men				White Women			
	1954- 1954	1955- 1959	1960- 1964	1965- 1969	1954- 1954	1955- 1959	1960- 1964	1965- 1969
Esophagus (150)								
State†	1.42	2.26‡	2.20‡	1.30	1.80	0.07‡	0.10‡	0.16
County‡	1.04	1.79	1.58	1.05	1.79	0.06‡	0.06‡	0.14
	(181)	(23)	(25)	(14)	(6)	(2)	(3)	(6)
Stomach (151)								
State	1.14	1.58‡	1.30	1.48‡	0.92	1.02	1.40	1.17
County	1.13	1.61‡	1.37	1.57‡	1.04	1.02	1.77‡	1.41
	(90)	(101)	(70)	(61)	(38)	(34)	(43)	(30)
Large intestine, excluding rectum (153)								
State	1.04	1.39	0.95	0.83	0.98‡	1.06	1.04	1.18
County	0.98	1.31	0.87	0.73	0.52‡	0.96	1.02	1.10
	(47)	(60)	(47)	(45)	(27)	(54)	(53)	(67)
Rectum (154)								
State	1.25	1.26	1.80‡	1.60	0.86	1.17	1.20	1.97‡
County	1.37	1.10	1.63‡	1.88‡	0.66	1.07	1.16	1.94‡
	(31)	(30)	(40)	(34)	(13)	(18)	(17)	(25)
Total digestive tract (150-154)								
State	1.10	1.48‡	1.30‡	1.22	0.79	1.06	1.18	1.30‡
County	1.11	1.44‡	1.25‡	1.16	0.78	0.99	1.22	1.28‡
	(184)	(214)	(182)	(154)	(84)	(108)	(118)	(128)
Biliary passages and liver (155, 156A)								
State	0.65	1.12	1.45	1.14	0.84	1.62	0.74	0.88
County	0.60	1.08	1.19	1.11	0.94	1.94‡	0.84	0.79
	(9)	(16)	(20)	(14)	(19)	(32)	(15)	(12)
Pancreas (157)								
State	1.26	1.43	1.39	1.40	0.96	1.90‡	0.71	1.41
County	1.18	1.16	1.34	1.35	1.00	2.12‡	0.68	1.43
	(35)	(38)	(44)	(44)	(16)	(38)	(17)	(35)
Lung (162, 163)								
State	1.15	1.58‡	1.35	1.49‡	0.78	1.76	1.39	1.31
County	0.90	1.16	1.14	1.25	0.59	1.63	1.30	1.15
	(60)	(103)	(109)	(150)	(9)	(23)	(22)	(29)
All malignant neoplasms (140-205)								
State	1.11	1.39‡	1.18‡	1.29‡	0.93	1.26‡	1.10	1.20‡
County	1.01	1.28‡	1.08	1.18‡	0.88	1.22‡	1.10	1.17‡
	(519)	(854)	(594)	(648)	(377)	(525)	(465)	(527)

*International Classification of Diseases for World Health Organization numbers.

†State of Minnesota.

‡Hennepin County, Minnesota.

§Number of deaths in Duluth.

||Risk ratio differs significantly from 1.0 ($P < .01$).

of Minnesota and Hennepin County, which includes Minneapolis (1960 populations, 3,371,603 and 825,986, respectively). The number of deaths from cancer and the age-adjusted death rates were examined for each cancer site, as coded according to the International Classification of Diseases.

Results

For 21 cancer sites, risk ratios were calculated from age-adjusted mortality rates for Hennepin County and the state, and tested for statistical significance, assuming an underlying Poisson distribution. The risk ratios (Duluth/comparison group) for eight individual sites that differed significantly ($P < .01$) from unity for either

sex are given in the Table. If the asbestos fibers had induced cancer at a particular site, one would expect the mortality rates for that site to have increased in males and females over time, especially in the most recent five-year period studied (1965 to 1969). As shown in the Table, the only site that fell into this category was cancer of the rectum.

Comment

The question arises, is the excess of rectal cancer attributable to the fibers, or is it one observation among many, which by chance fits the pattern sought? Other human experience, from occupational exposures, revealed that among 17,000 asbestos installation workers in the United

States and Canada in the 1967 to 1971 period, there were 26 deaths from cancer of the colon or rectum as compared with 17.5 expected, not a very large excess.* An important feature of this study was that cancer of the upper gastrointestinal tract showed far greater excesses than were observed for cancer of the colon or rectum. There were 13 deaths from cancer of the esophagus vs 3.2 expected and 16 from cancer of the stomach vs 6.6 expected. Thus, in Duluth, one would expect a greater excess of cancer in the esophagus and stomach than in the rectum, but this did not occur. It appears that the high rate of cancer of the colon in the 1965 to 1969 period in Duluth was observed by chance.

To determine if young people were especially susceptible to the carcinogenicity of asbestos in the drinking water of Duluth, we examined cancer mortality data for persons who died before 20 years of age, during the period of 1950 through 1969. Through the use of Hennepin County and state data, risk ratios were calculated for leukemia (ICD 204), cancer of the nervous system (ICD 193), and all other cancers. No significant excesses were found.

The delayed effects of asbestos in drinking water are unknown, and the extent to which asbestos has accumulated in the water with the passage of time has not yet been reported. A longer period of follow-up than was possible in this study will be necessary before one can conclude that there is no cancer hazard related to the drinking water supplies of Duluth and neighboring communities.

References

1. Findings of Fact: Conclusions of Law and Order for Judgment. Reserve Mining Company, Minnesota Pollution Control Agency, Dec 15, 1970, p 8.
2. Environmental News. Environmental Protection Agency, June 15, 1973.
3. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Lyons, France. International Agency for Research on Cancer, 1973, vol 2, pp 17-47.
4. Pontefract RD, Cunningham HM: Penetration of asbestos through the digestive tract of rats. *Nature* 243:252-253, 1973.
5. Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, ed 7. Geneva, World Health Organization, 1957.
6. Hammond EC (ed): Combined Clinical Staff Conference held at the Clinical Center, National Institutes of Health by the National Institute of Environmental Health Sciences, Bethesda, Md. *Ann Intern Med*, to be published.