DLE - The fight goes on! DAC

Letters to the Editor

Readers are invited to submit letters for publication in this department. Submit to Doris Flournoy, Publisher, Journal of Occupational Medicine, 1845 W. Morse, Chicago, IL 60626. Letters should be typewritten, double spaced and should be designated "For Publication."

RECD.

Conclusions Questioned in Brain Tumor Excess Study

To the Editor — We are greatly concerned about errors in the recent article: "Diagnostic Sensitivity Bias-An Epidemiologic Explanation for an Apparent Brain Tumor Excess" by Dr. Peter Greenwald et al (*JOM* 23:690-694, 1981). These errors, we feel, invalidate the conclusions drawn and suggest alternative explanations. Since the authors correctly state that demonstration of this type of bias could have far-reaching effects on all occupational epidemiology, proof of its demonstration must be scrutinized in detail.

The basic problem appears in Table 3 where the frequency of record availability, incorrect diagnosis, clinical diagnosis, and pathologic confirmation is compared between brain tumor cases involving Kodak and non-Kodak employees identified by death certificate. Hospital records were not available for nearly 18% of the Rochester Area tumor comparison group, as opposed to 4.7% of the Kodak group. Cases for whom records were unavailable were then included in the denominator while calculating frequency of incorrect diagnosis, clinical diagnosis and pathologic confirmation. This amounts to assuming that all cases for whom records could not be obtained either did not have pathologic confirmation or did not die of brain cancer. We do not find this to be a reasonable assumption.

Recalculation of these frequencies and p values when record-not-available cases are omitted shows that all significant differences between the Kodak group and the tumor comparison groups disappear. Only results for the Rochester Area group are shown in the table, but results for the statewide group were similar.

Thus, a death certificate diagnosis was just as likely to be incorrect for Kodak employees as for Rochester Area residents (11.4% versus 14.4%). The data show that the only major difference between a death certificate indicating brain tumor for a Kodak employee and one for a Rochester Area or New York State resident is that the Kodak employee was more likely to have obtainable hospital records. This fact itself may be explained by the special relationship of the study authors to Kodak employees and perhaps, their physicians.

Further down in Table 3, the frequency with which certain diagnostic techniques were used is compared. Brain scans and pneumoencephalograms were used more often for the Kodak employees. We suggest that these differences are irrelevant when the frequency of craniotomy and autopsy, the definitive procedures for diagnosing brain cancer, were performed at similar rates in Kodak employees. An alternative explanation for these data is that patients with comprehensive medical insurance are subjected to a greater number of diagnostic procedures.

Finally, the article's assertion that brain tumors are difficult to diagnose relative to other fatal disease must be questioned, except perhaps when referring to the very elderly. In the population under study, which was all presumably under retirement age, there is little reason to believe that brain tumors remain undiagnosed. The proportion of death certificates in this study, confirmed by records or by pathology, was in accord with data from The Third National Cancer Survey which showed that 89% of death certificate brain tumors were confirmed by hospital records as opposed to only 82.7% for all cancer sites combined.[1] If the diagnostic sensitivity bias really exists as a problem in occupational epidemiology, it was not demonstrated by this study.

Peter Gann, M.D., M.S.
Chief, Occupational Medicine
Kenneth D. Rosenman, M.D.
Director, Occupational and Environmental Health Services
New Jersey Department of Health
Trenton, New Jersey 08625

Frequency of Record-Availability, Incorrect Diagnosis, and Pathologic Confirmation Among Kodak and Rochester Area Brain Tumor Cases Identified by Death Certificate

	Kodak Cases			Rochester Area Cases			
	Total	No.	%	Total	No.	%	p (2-sided)
No hospital records available	64	3	4.7	84	15	17.9	0.036
Metastatic cancer or non-cancer	61	7	11.4	69	10	14.4	0.798
Cases with records available, clinical diagnosis	61	3	4.9	69	7	10.1	0.430
Cases with records available, pathologic confirmation	61	51	83.6	69	52	75.4	0.345

Reference

1. Percy C, Stanek E, and Gloeckler L: Accuracy of cancer death certificates and its effect on cancer mortality statistics. *Am J Pub Health* 71:242-250, 1981.

Authors' Response

Substracting study subjects not having hospital records from the denominator in the upper part of Table 3 *increases* the difference between cases and the Rochester tumor comparison group with respect to misdiagnosis and clinical diagnosis. The effect is the opposite of that asserted by Gann and Rosenman. This can be seen by comparing the percentages in their table to our Table 3, reproduced on the next page.

The Gann and Rosenman distortions of the death certificate denominator for purposes of calculating rates of pathological confirmation are invalid. The total number of death certificates noting brain tumors is the correct denominator for all four upper rows of Table 3, since the basic question was about coding on death certificates. Verification of pathologic confirmation generally does not depend on availability of hospital records, as hospital pathology departments have their own filing systems. Pathology files as well as hospital records were searched in this study.

It is suggested by Gann and Rosenman that we, perhaps because of "a special relationship" with employees and physicians, were in a better position to obtain hospital records of Kodak employees than controls. This implication is incorrect. The study was designed so that the investigators could not have affected the record retrieval process and therefore the availability of records. The hospital records were sought directly by the New York State Department of Health by persons unaware of cases/tumor comparison group status. Study cases and controls were dispersed in many different hospitals in Upstate New York.

Drs. Gann and Rosenman are in error when they presume the study group was all under retirement age. In fact, approximately 25% of the cases were retirees and thus cross the spectrum of "the very elderly," a group in which our critics agree that brain tumors are difficult to diagnose and thus are vulnerable to the diagnostic sensitivity bias. The potential for such a bias is clearly shown in a recent report of experience in Rochester, Minn., where the mean annual incidence of primary central nervous system neoplasms in individuals over age 55 is dramatically influenced by autopsy results – with most cases being first diagnosed after death.[1] The total excess in our study was in the population over age 55, with cases being diagnosed up to age 81.

During the study period, brain scans and pneumoencephalograms were important diagnostic procedures, with reported diagnostic sensitivity of 82% and 94% respectively.[2] We agree that craniotomy with biopsy and autopsy often may be definitive. We agree that craniotomy with biopsy and autopsy often may be definitive. We note again that all eight procedures were more commonly performed in cases than in Rochester area controls and that seven of eight were more commonly performed in cases than in statewide controls. This pattern of 94% (15/16) of the diagnostic comparisons showing higher degrees of testing for Kodak employees provides evidence of a diagnostic sensitivity bias.

Gann and Rosenman cite the Percy et al[3] reference, but neglect to describe these investigators' comments about death certificate coding of brain tumors. To quote from Percy et al, "Word choice is critical for determining the correct code. For example, when malignant brain tumors such as astrocytoma or glioma were diagnosed in the hospital, the physician frequently signed out the death certificate as 'brain tumor.' This cause of death is coded to category 238.1, neoplasm of unspecified nature of the brain and is therefore not recorded as a cancer death." It is difficult to see how our critics missed this message, since even the brief article abstract states: "Other misclassification problems were found for cancer of the uterus, *brain*, and buccal cavity, including most of its sub-sites." Because of this potential bias, in our study the 238.1 category was included in death certificate searches.

In the Percy et al study, cancers metastatic to the brain were the most common group misclassified as primary brain tumors (personal communication from C. Percy). Thus, coding rules and difficulties that coders have in applying them in a uniform and consistent manner also can lead to artifacts in brain tumor rates.

We hope this clears up any confusion that may result from the Gann and Rosenman letter. The possibility of a diagnostic sensitivity bias remains an important consideration in this type of investigation, particularly where the study population has liberal access to high quality diagnostic testing, employee insurance coverage,

Contined on page 432

Table 3. — Frequency of Pathology Confirmation and Diagnostic Procedures on Cases and Tumor Comparison Groups.

	Eastman Kodak Cases			Rochester Area Tumor Comparison Groups				Statewide Tumor Comparison Groups			
	Total	No.*	%	Total	No.*	%	p	Total	No.*	%	p
Coded as Brain Tumor on Death Certificate											
No hospital records available	64	3†	4.7	84	15	17.9	0.036	100	13	13.0	0 166
Not cancer or metastatic cancer	64	7	10 9	84	10	11.9	0.623	100	17	17.0	0 170
Clinical diagnosis (no pathology)	64	3	4.7	84	7	8.3	0 381	100	10	10 0	0 219
Pathologically confirmed‡	64	51	79.7	84	52	61.9	0.019	100	60	60 0	0 008
Pathological or Clinical Diagnosis of Brain Tumor											
Craniotomy, brain surgery or biopsy	54	48	88 9	59	49	83.1	0.373	70	53	75.7	0 061
Brain scan	54	33	61 1	59	25	42.4	0 046	70	21	30 0	0.0005
Angiogram	54	41	75.9	59	40	67 8	0 338	70	45	64 3	0 163
EEG	54	20	37 0	59	20	33 9	0.727	70	23	32 9	0 627
Pneumoencephalogram	54	19	35 2	59	9	15 3	0 014	70	12	17 1	0 021
Autopsy	54	28	51 9	59	28	47 5	0.782	70	24	34 3	0 049
Skull x-ray	54	50	92.6	59	50	84.7	0 191	70	67	95 7	0 455

*Number that hospital records indicated procedure was performed

†Two of these are included with the 54 pathologically or clinically diagnosed cases for the study of exposures, giving the 56 cases shown in Table 1 (see text for details)

‡Of the pathologically confirmed cases, slides could be obtained for review on 51 cases, 46 Rochester area matched controls, and 44 Statewide matched controls as shown in Table 2

p = Significance levels for differences in proportions having procedures between Kodak cases and comparison groups

occupational medical service referrals, and the impact of neurologic and neurosurgical specialists in a university school setting.

Peter Greenwald, M.D.
National Cancer Institute
Bethesda, MD 20205
Barry R. Friedlander, M.D.
Charles E. Lawrence, Ph.D.
Terry Hearne, M.S.
Eastman Kodak Company
Rochester, NY 14650
Kenneth Earle, M.D.
Armed Forces Institute of Pathology
Washington, DC 20306

References

1. Annegers JF, Schoenberg BS, Okazaki H, et al: Epidemiologic study of primary intracranial neoplasms. *Arch Neurol* 38:217-219, 1981.
2. Witcofski RL, Maynard CD, and Roper TJ: A comparative analysis of the accuracy of the technetium-99m pertechnetate brain scan: followup of 1000 patients. *J Nucl Med* 8:187-196, 1967.
3. Percy C, Stanek E, and Gloeckler L: Accuracy of cancer death certificates and its effect on cancer mortality statistics. *Am J Pub Health* 71:242-250, 1981.

Best Medical Care at Reasonable Cost

To the Editor: I was distressed to read the political advertisement (JOM 24:191, 1982) entitled "Think of Your Prescription as a Vote." If this was paid advertising, it would be clearly marked as such and it should contain the advertiser's name. If this was an editorial, I am appalled.

The patent laws of this country give the "innovator" 17 years without competition to reap a fair profit from an innovation. The insinuation that one cannot rely on generic drugs is outrageous. All drugs, brand name and generic, must meet the same federal standards for quality.

As physicians, our first duty is to our patients. The drug manufacturers can make a fair profit under the present laws. Our concern should be that our patients receive the best medical care available at reasonable cost.

Katharine C. Rathbun, M.D., M.P.H.
Director of Health
City of Pasadena
Pasadena, TX 77502

Editor's Note: The indicated material was sponsored by Rolf Werner Rosenthal, Inc., an advertising agency, representing a number of pharmaceutical companies.