

specific exposure estimates used in the paper under consideration here.

With regard to the criticism that the half-life for 2,3,7,8-TCDD (6.9 years) used in the estimation was derived from a subset of the cohort ($n = 48$), it is important to note that this estimate is in agreement with results from other cohorts (5–7).

Dr. Swaen's second criticism concerns the appropriateness of the comparison group. Because the validity of all inferences from epidemiologic data depend on the comparability of groups compared, we adopted two comparison strategies in the current paper and a third in a previous paper (a standardized mortality ratio (SMR) analysis with mortality of the German population as reference (8)). One comparison involved a cohort of gas workers, and the other used an internal comparison within the cohort of chemical workers. The two lowest exposure quintiles served as the reference group. We outlined the advantages and disadvantages of each comparison in detail in the paper. Our conclusions were not based on one comparison alone, as Dr. Swaen suggests.

With respect to the gas worker comparison, Dr. Swaen mentions the different minimum duration of employment between the chemical worker cohort (3 months) and the gas worker cohort (10 years). Because of this difference, we adjusted the Cox regression models for duration of employment. In addition, our first SMR analysis (8) had shown that the elevated cancer risk in the chemical workers cohort is mainly due to an elevation in the subgroup with long duration of exposure (≥ 20 years). Thus, restricting the chemical worker cohort to workers with duration of employment of ≥ 10 years increases, rather than decreases, the relative risks in the comparison with the gas worker cohort. Finally, the explanation for the selection process in the gas worker cohort is that in the Cox regression analysis only gas workers actively employed on January 1, 1952 (the start of the follow-up for the chemical worker cohort) were included, leaving 2,528 out of 3,120 male workers.

The last issue that Dr. Swaen raises is that of the statistical analysis. He mentions that the relative risks presented in table 3 for total mortality are very high compared with the SMR in relation to the Federal Republic of Germany (FRG) population reported in 1991 (8). However, one should compare the relative risks in table 3—derived from a proportional hazard model including the cohort of gas workers as unexposed controls—with the SMR for the gas worker comparison in the 1991 paper, not with the SMR in relation to the FRG-population mortality. For the lower exposure categories, the magnitude of the gas worker-related estimates reported in 1991 and in the current paper are very similar. With regard to the estimate in the highest exposure category, it is important to stress that no comparable exposure category was identified in the earlier paper. Further-

more, the relative risk for total mortality was significant and substantial not only in the comparison with the gas workers, but also in the internal comparison (relative risk = 1.55, 95 percent confidence interval 1.06–2.26, table 5 (2)).

In summary, within the constraints which are inherent to retrospective mortality studies in an occupational setting, we see strong indirect evidence against a serious bias in the exposure estimates. Furthermore, the results derived from comparisons with different groups using statistical techniques that adjust for basic differences between groups corroborate each other. Thus, we stand by our conclusion that these data are evidence of a dose-response relationship between estimated dioxin levels and risk of all-cause, cancer, and cardiovascular mortality. Our findings support the hypothesis that TCDD is a human carcinogen.

REFERENCES

1. Swaen GMH. Re: "Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany." (Letter). *Am J Epidemiol* 1997;146:361–2.
2. Flesch-Janys D, Berger J, Gum P, et al. Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany. *Am J Epidemiol* 1995;142:1165–75.
3. Flesch-Janys D. Quantifizierung der Exposition gegenüber Dioxinen in einer epidemiologischen Berufskrebsstudie. Dissertation. (In German). Heidelberg: Universität Heidelberg, 1992.
4. Flesch-Janys D, Berger J, Konietzko J, et al. Quantification of exposure to dioxins and furans in a cohort of a herbicide producing plant in Hamburg, FRG. Chlorinated dioxins and related compounds 1991—Part 2. *Chemosphere* 1992;25:7–10:1021–8.
5. Pirkle JL, Wolfe WH, Patterson DG, et al. Estimates of the half-life of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in Vietnam Veterans of Operation Ranch Hand. *J Toxicol Environ Health* 1989;27:165–71.
6. Michalek JE, Pirkle JL, Caudill SP, et al. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 10-year follow-up. *J Toxicol Environ Health* 1996;47:209–20.
7. Poiger H, Schlatter C. Pharmacokinetics of 2,3,7,8-TCDD in man. *Chemosphere* 1986;15:1489–94.
8. Manz A, Berger J, Dwyer JH, et al. Cancer mortality among workers in a chemical plant contaminated with dioxin. *Lancet* 1991;338:959–64.

Dieter Flesch-Janys
 Freie und Hansestadt Hamburg
 Behörde für Arbeit, Gesundheit und
 Soziales
 Tesdorpfstrasse 8
 20148 Hamburg
 Germany

RE: "A NEW PERSPECTIVE ON JOHN SNOW'S COMMUNICABLE DISEASE THEORY"

Dr. Winkelstein (1) has to be commended for describing again in great detail how John Snow's investigations on the spread of cholera were based on strong a priori reasoning. Snow's ideas derived from his insight into the etiology of infectious diseases. As an historical example, it remains important to remember that Snow's theory on the communication of cholera was not derived from his epidemiologic

observations, but preceded them.

Previously, I had called attention to this often neglected aspect of the history of Snow and cholera, and I had based my argument on the first edition of Snow's book *On the Mode of Communication of Cholera* (2), which was written before he made his observations on water companies and the Broad Street pump (3, 4). Others in the recent literature

had already called attention to this interpretation of his work (5). The first persons who clearly stated that Snow had specified his hypothesis before collecting the facts were his contemporary friend and biographer, Sir Benjamin Ward Richardson (6), and also Wade Hampton Frost, who wrote the introduction to the 1936 reprint of the second edition of Snow's work (7). Both described how Snow already had his theory "in mind" when he looked for suitable observations to test it.

The historical part of Dr. Winkelstein's paper is beautifully researched. It will remain a cornerstone in the literature about John Snow. However, his perspective is less new than the title of his contribution implies. This perspective is simply repeatedly forgotten, and equally often rediscovered.

REFERENCES

1. Winkelstein W. A new perspective on John Snow's communicable disease theory. *Am J Epidemiol* 1995;142(Suppl):S3-S9.
2. Snow J. On the mode of communication of cholera. London: J Churchill, 1849.
3. Vandembroucke JP. Which John Snow should set the example

for clinical epidemiology? *J Clin Epidemiol* 1988;41:1215-16.

4. Vandembroucke JP, Eelkman Rooda HM, Beukers H. Who made John Snow a hero? *Am J Epidemiol* 1991;133:967-73.
5. Cameron D, Jones IG. John Snow, the Broad Street pump and modern epidemiology. *Int J Epidemiol* 1983;12:393-6.
6. Richardson BW. John Snow, MD, a representative of medical science and art of the Victorian era. In: Frost WH, ed. *Snow on cholera* (reprint). New York: The Commonwealth Fund, 1936:xxv-xlvii.
7. Frost WH. Introduction. In: Frost WH, ed. *Snow on cholera* (reprint). New York: The Commonwealth Fund, 1936:ix-xxi.

Jan P. Vandembroucke
 Department of Clinical Epidemiology
 Leiden University
 P.O. Box 9600
 2300 RC Leiden
 The Netherlands

Editor's note: In accordance with Journal policy, Dr. Winkelstein was given the opportunity to reply to the above letter, but he chose not to do so.

RE: "FAMILY HISTORY OF CANCER AND RISK OF LUNG CANCER AMONG LIFETIME NONSMOKING WOMEN IN THE UNITED STATES"

We read with interest the report of a deficit of digestive tract cancers in the first-degree relatives of nonsmoking female lung cancer patients (1). We have noted a similar deficit in the first-degree relatives of patients with squamous cell carcinoma of the head and neck (SCCHN) in two separate case-control studies. In the first study of 754 cases of SCCHN and 1,507 age- and sex-matched hospital controls carried out in southern Brazil (2), we found a reduced risk for colorectal cancer in association with a family history of SCCHN (adjusted relative risk (RR) = 0.60, 95 percent confidence interval (CI) 0.20-1.77). In a second study (3), we found a deficit of colorectal cancer in 1,429 first-degree relatives of 242 cases of SCCHN compared with 934 relatives of 156 spouse controls ascertained at one hospital in Montreal (adjusted RR = 0.49, 95 percent CI 0.18-1.21).

Wu et al. (1) note the deficit of lung cancer in hereditary nonpolyposis colorectal cancer families. Several population-based studies have shown significant (4, 5) or nonsignificant deficits (6, 7) of second cancers of the colon and rectum after lung cancer (and vice versa).

It appears that there may be an inverse relation between colorectal cancer and both SCCHN and lung cancer. Environmental and genetic aspects of this phenomenon deserve to be explored further.

REFERENCES

1. Wu AH, Fontham ETH, Reynolds P, et al. Family history of cancer and risk of lung cancer among lifetime nonsmoking women in the United States. *Am J Epidemiol* 1996;143:535-42.
2. Foulkes WD, Brunet J-S, Kowalski LP, et al. Family history of cancer is a risk factor for squamous cell carcinoma of the head

and neck in Brazil: a case-control study. *Int J Cancer* 1995;63:769-73.

3. Foulkes WD, Brunet J-S, Sieh W, et al. Familial risks of squamous cell carcinoma of the head and neck: retrospective case-control study. *BMJ* 1996;313:716-21.
4. Teppo L, Pukkala E, Saxen E. Multiple cancer—an epidemiologic exercise in Finland. *J Natl Cancer Inst* 1985;75:207-17.
5. Lynge E, Jensen OM, Cartensen B. Second cancer following cancer of the digestive system in Denmark 1935-1982. In: Greenwald P, ed. *Multiple primary cancers in Connecticut and Denmark*. NCI monograph no. 68. Washington, DC: US GPO, 1985:277-308.
6. Enblad P, Adami H-O, Glimelius B, et al. The risk of subsequent primary malignant diseases after cancers of the colon and rectum. A nationwide cohort study. *Cancer* 1990;65:2091-2100.
7. Hoar SK, Wilson J, Blot WJ, et al. Second cancer following cancer of the digestive system in Connecticut 1935-1982. In: Greenwald P, ed. *Multiple primary cancers in Connecticut and Denmark*. NCI monograph no. 68. Washington, DC: US GPO, 1985:49-82.

William D. Foulkes
 Montreal General Hospital
 1650 Cedar Avenue
 Montréal, Québec
 Canada H3G 1A4

Steven A. Narod
 Breast Cancer Research
 Women's College Hospital
 Toronto, Canada M5G 1N8

Editor's note: In accordance with Journal policy, Dr. Wu and her coauthors were given the opportunity to reply to the above letter, but they chose not to do so.