

Letters to the EditorCorrespondence re: C. Byrne *et al.*, Predictors of Dietary Heterocyclic Amine Intake in Three Prospective Cohorts. *Cancer Epidemiol. Biomark. Prev.*, 7: 523–529, 1998Letter**Steven R. Tannenbaum¹**

Division of Bioengineering and Environmental Health, Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

The paper by Byrne *et al.*, “Predictors of Dietary Heterocyclic Amine Intake in Three Prospective Cohorts” (1), continues the trend toward estimation of carcinogen intake by dietary questionnaire. They seem to have missed the one paper that combined both analytical chemistry and dietary information (Ji *et al.*; Ref. 2).

The take-home lessons are:

(a) Until the analytical chemistry in the 1994 study was completed (2), the role of bacon and sausage as a source of heterocyclic amines was not known.

(b) Ethnic practices in cooling and food selection are important. How valid could it be to compare individuals from Sweden to African-Americans in Los Angeles?

(c) Byrne *et al.* (1) can keep manipulating the minute quantity of real analytical data currently available, but the sample is too small to be meaningful.

(d) If Byrne *et al.* (1) want to improve the questionnaires, they should invest the time and effort in getting more data on real populations, not on a chef’s idea of how to cook chicken.

(e) Had Byrne *et al.* (1) read the paper by Ji *et al.* (2), they might actually have been able to test their model questionnaire.

References

1. Byrne, C., Sinha, R., Platz, E. A., Giovannucci, E., Colditz, G. A., Hunter, D. J., Speizer, F. E., and Willett, W. C. Predictors of dietary heterocyclic amine intake in three prospective cohorts. *Cancer Epidemiol. Biomark. Prev.*, 7: 523–529, 1998.
2. Ji, H., Yu, M. C., Stillwell, W. G., Skipper, P. L., Ross, R. K., Henderson, B. E., and Tannenbaum, S. R. Urinary excretion of 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline in white, black, and Asian men in Los Angeles County. *Cancer Epidemiol. Biomark. Prev.*, 3: 407–411, 1994.

Reply**Celia Byrne,¹ Rashmi Sinha, Elizabeth A. Platz, Edward Giovannucci, Graham A. Colditz, David J. Hunter, Frank E. Speizer, and Walter C. Willett**

Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital, and Harvard Medical School, Boston, Massachusetts 02115 [C. B., E. G., G. A. C., D. J. H., F. E. S., W. C. W.]; Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892 [R. S.]; and Departments of Epidemiology [E. A. P., G. A. C., D. J. H., W. C. W.] and Nutrition [E. A. P., E. G., W. C. W.], Harvard School of Public Health, Boston, Massachusetts 02115

We were aware of the article by Ji *et al.* (1) that Dr. Tannenbaum mentions in his letter (2) commenting on our paper (3). Because the study by Ji *et al.* (1) compared frequency of intake of 11 foods with urinary levels of MeIQx² among 76 participants who provided both urine and food data and did not measure the HCA concentration in the food (1), the results were not directly related to our study (3).

In response to Dr. Tannenbaum’s “lessons”:

(a) Ji *et al.* (1) did provide information on the association between reported frequency of bacon consumption and urinary concentration of MeIQx. However, metabolic studies have shown that urinary MeIQx levels reflect short-term (within 12 h) and not long-term intake of MeIQx (4). Thus, only if there is little variation in daily intake will one measure of urinary MeIQx reflect the relevant long-term usual exposure. Consistent intake of HCA is unlikely, given that recent analytical studies (4–7) showed significant variation in HCA levels in different foods and in the same food, depending on how the food was cooked (cooking methods) and the degree of doneness (outside appearance).

(b) We agree with Dr. Tannenbaum that ethnic differences in cooking and food selection are important. This point was emphasized in the discussion of our paper (3), in which we indicated that, “in other populations, different questions may be necessary to measure the variation in dietary HCA exposure.”

(c) Concerns regarding the appropriate use of real analytical data and meaningful study size are central to any epidemiological study. We sought to identify an alternative method to existing food frequency questions to better assess variation in HCA intake. We agree with Dr. Tannenbaum that larger studies are needed to determine whether HCA intake is related to risk of developing specific cancers. For this reason, we have included the relevant questions we identified from our study of 673 randomly selected participants in subsequent question-

Received 7/23/98; accepted 10/14/98.

¹ To whom requests for reprints should be addressed.

² The abbreviations used are: MeIQx, 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline; HCA, heterocyclic amine; NHS, Nurses’ Health Study; HPFS, Health Professionals Follow-up Study.

Received 6/17/98; accepted 7/28/98.

¹ To whom requests for reprints should be addressed.

naires mailed to the entire NHS and HPFS cohorts. With future follow-up, we will be able to ascertain whether differences in reported HCA intake are associated with risk of specific cancers.

(d) The more than 280,000 participants in the NHS, NHS II, and HPFS are not a representative sample of the United States population, although they are, indeed, "real populations." The dedication and commitment to the research effort by these participants provides meaningful information to many people beyond those in the studies themselves. We asked participants to report how the food they usually eat was cooked and its appearance. The database for HCA levels was created by cooking and testing multiple samples of each meat/method/doneness combination.

(e) As indicated in response (a) above, the results from the study by Ji *et al.* (1), although very interesting, did not provide the information necessary for us to conduct our study. However, our study results help to explain why Ji *et al.* (1) found that urinary MeIQx levels were associated with reported intake of bacon but not with other foods. If they had ascertained information about cooking methods and degree of doneness for other foods, they may have noted an association (4). Our study found that, to estimate the intake (not excretion) of HCA from bacon in these three United States cohorts, we needed to ascertain only frequency of consumption (3). For other foods, additional information regarding cooking methods and degree of doneness was necessary to assess variation in HCA levels (3).

References

1. Ji, H., Yu, M. C., Stillwell, W. G., Skipper, P. L., Ross, R. K., Henderson, B. E., and Tannenbaum, S. R. Urinary excretion of 2-amino-3,8-dimethylimidazo[4,5-*i*]quinoxaline in white, black, and Asian men in Los Angeles County. *Cancer Epidemiol. Biomark. Prev.*, 3: 407–411, 1994.
2. Tannenbaum, S. R. Correspondence re: C. Byrne *et al.* Predictors of dietary heterocyclic amine intake in three prospective cohorts. *Cancer Epidemiol. Biomark. Prev.*, 7: 523–529, 1998. *Cancer Epidemiol. Biomark. Prev.*, 7: 1153, 1998.
3. Byrne, C., Sinha, R., Platz, E. A., Giovannucci, E., Colditz, G. A., Hunter, D. J., Speizer, F. E., and Willett, W. C. Predictors of dietary heterocyclic amine intake in three prospective cohorts. *Cancer Epidemiol. Biomark. Prev.*, 7: 523–529, 1998.
4. Sinha, R., and Rothman, N. Exposure assessment of heterocyclic amines (HCAs) in epidemiologic studies. *Mutat. Res.*, 376: 195–202, 1997.
5. Sinha, R., Rothman, N., Brown, E. D., Salmon, C. P., Knize, M. G., Swanson, C. A., Rossi, S. C., Mark, S. D., Levander, O. A., and Felton, J. S. High concentrations of the carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP) occur in chicken but are dependent on the cooking method. *Cancer Res.*, 55: 4516–4519, 1995.
6. Sinha, R., Rothman, N., Salmon, C. P., Knize, M. G., Brown, E. D., Swanson, C. A., Rhodes, D., Rossi, S., Felton, J. S., and Levander, O. A. Heterocyclic amine content in beef cooked by different methods to varying degrees of doneness and gravy made from meat drippings. *Food Chem. Toxicol.*, 36: 279–286, 1998.
7. Sinha, R., Knize, M. G., Salmon, C. P., Brown, E. D., Rhodes, D., Felton, J. S., Levander, O. A., and Rothman, N. Heterocyclic amine content of pork products cooked by different methods and to varying degrees of doneness. *Food Chem. Toxicol.*, 36: 287–296, 1998.