Cancer Cluster Investigation within the Mission Memorial Hospital Laboratory

Final Report

March 31, 2006

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Executive Summary

This investigation was conducted in response to concerns expressed by employees of the Mission Memorial Hospital (MMH) Laboratory that they were experiencing a high incidence of cancer. The investigation resulted in an initial report prepared by the Occupational Health & Safety Agency for Healthcare in BC (OHSAH) and released for comment in March, 2004 (Attachments 2 & 3). The associated presentation is included as Attachment 4. In addition, Attachments 5, 6 and 7 are supportive documents from the initial investigation. Subsequently a new breast cancer case was identified and errors in staffing levels were corrected. A re-analysis of the breast cancer incidence rate was completed in April, 2005 (Attachments 8 & 9) and a revised Draft Report was released in September, 2005. The revised Draft Report still did not address all of the concerns raised by the MMH Laboratory employees and resulted in a set of critical questions being posed which were presented to the Fraser Health Authority (FH) and OHSAH in November of 2005 (Attachment 10). The responses to these questions for which OHSAH was responsible were sent to FH and the Health Sciences Association (HSA) in January, 2006 (Attachment 11) and were presented at MMH on February 8th, 2006 to representatives of FH, HSA, the BC Nurses' Union (BCNU) and the Hospital Employees' Union (HEU). Some of the questions posed by the Laboratory employees were responded to by FH and are included as a separate document. This Final Report is therefore a compilation of the investigation of cancer incidence at the MMH Laboratory and the results of an extensive consultation process with the employer, labour representatives, and the individuals involved.

The results of this investigation are presented in three parts: a comprehensive review of the literature, an epidemiologic cluster analysis, and an occupational exposure investigation. The investigation procedures followed the established guidelines by the BC Cancer Agency (BCCA) for cancer cluster investigations[1]. These guidelines are in keeping with international approaches[2].

In summary, 64 individuals were identified as having worked in the laboratory between January 1, 1970 and December 7, 2004. Information on health status and diagnosis of cancer were obtained through personal interviews with employees. One person was diagnosed with cancer

[1] Guidelines for the Investigation of Cancer Clusters in BC. BC Cancer Agency, Cancer Control Research, November 1998.
[2] Guidelines for Investigating Clusters of Health Events. US CDC, July 27, 1990.

prior to working in the MMH laboratory and was excluded from the analysis. Of the remaining employees, ten employees reported a cancer diagnosis, of which seven were breast cancer. A total of 974 person-years of observation were available for the data analysis after excluding one subject because of diagnosis of cancer prior to start of employment. Based on the age and calendar-year adjusted rates for the BC population, the expected number of breast cancer cases in the women was 0.8 and the expected number of all cancers for all employees was 2.3. The Standard Incidence Ratios (SIR), which is the observed number of cases divided by the expected number, was found to be 8.4 for breast cancer among women at the MMH Laboratory, and 4.7 for all cancers among both men and women at the lab. In other words, the risk for breast cancer was over 8 times the expected rate; and the rate of all cancers was over 4 times the expected rate. The 95 percent confidence intervals indicate that both findings were significant. It can be concluded that the perception of the laboratory workers that they were experiencing an excess in cancer was confirmed – i.e. this is truly an observed cancer cluster.

The risk of developing breast cancer was also analyzed by the age at first employment at the MMH Laboratory, the subjects' length of time at work prior to diagnosis and by their job title. The most important result was that no association was found between breast cancer risk and either the age of first employment or the duration of exposure. However, there was a non-significant increase in risk by job title with 'technician' being at greater risk than the grouping 'aid, clerk, or ECG technician'.

A walk-through survey of the laboratory in its present state did not identify any potentially hazardous exposures for which control measures are not in place. Review of indoor air quality records and chemical assessment of carcinogens in the workplace also did not show any obvious and extreme exposures in the past (based on current scientific literature), which could be related to the increase in risk. Assessment of radiation exposure in the laboratory was also found to be at typical natural background and would not contribute measurably to increased cancer risk. Thus, while it can not be ruled out that workplace factors played some role in the complicated process of carcinogenesis that led to this tragic outcome for laboratory workers and their families, the exact relationship between workplace exposures and the cancers that resulted remains elusive.

The evidence collected to date does not allow us to reach scientific conclusions to support the association between work-related exposures and breast cancer in this cluster. However, this

report has confirmed that this is indeed a statistical significant cluster. This usually points to the need to follow up with an etiological study with the required statistical power to investigate for this association while controlling for other non-work related exposures. Prior to embarking on such a study however, there is a need to establish an etiological hypothesis based on scientific evidence that provides proposed mechanism(s) for breast cancer causation. Our review of the literature was unable to establish the basis for such a hypothesis, as we did not find any scientific evidence for the plausibility of a laboratory work-related etiological hypothesis regarding breast cancer. While dioxins from the incinerator stack emissions have been implicated with other cancers, these did not include breast cancers; despite the potential exposure of MMH Laboratory workers to these emissions. Moreover, the number of people who worked in the Mission Hospital Laboratory is not sufficiently large to provide an adequate sample size for an etiological investigation.

Thus, it is recommended that this specific cancer cluster investigation be closed and the analysis updated in five years. If new evidence emerges to support a disease causation hypothesis for laboratory work-related breast cancer, and a larger study with an adequate sample size can be designed, then this subject could be investigated further at that time.

It is important to understand that human beings are exposed to carcinogens in almost all environments, at home, at work, and even walking in the sunshine. Every effort should be made, in this and all workplaces, to ensure that the workplace remains as safe and free of carcinogenic exposures as possible, and that the workforce is able to pursue safe and healthy choices in all aspects of their lives.

Forward

This report is the culmination of work conducted by numerous individuals, either on staff at OHSAH, serving as an OHSAH consultant or as a UBC trainee on rotation at OHSAH. Key personnel include the authors, Phil Bigelow, Shicheng Yu, Trevor Corneil, Victor Omelchenko, Malcolm Steinberg, and George Astrakianakis. We acknowledge the strong support and assistance of the BC Cancer Agency (Drs Nhu Le, Greg Hislop, and Malcolm Hayes), the School of Occupational and Environmental Hygiene at the University of British Columbia (Dr. Paul Demers), the Fraser Health Authority (Mr. Dave Keen and Ms. Rosemary Nemanishen), and the Health Sciences Association (Mr. Marty Lovick and Ms. Bev Banfield).

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March 31, 2006

Table of Contents

Executive Summary ii
Forward v
Table of Contents vi
Introduction 1
Methods 1
Review of Literature 2
Analysis of Cancer Incidence Data: Epidemiology and Statistics 2
Field Investigations: Possible Exposures to Potentially Carcinogenic Substances or Physical Agents 4
Literature Review 4
Breast Cancer Epidemiology 4
Breast Cancer Risk Factors 8
Sociodemographic Factors 8
Inherited Risk Factors 10
Breast Conditions 11
Hormone Factors 11
Prevention of Breast Cancer 16
Occupational and Environmental Factors in Breast Cancer 17
Breast Cancer Risk among Laboratory Workers 21
Incinerator Emissions and Cancer 25
Cancer Cluster Investigations 28
Investigating Cancer Clusters: Methods and limitations 29
Analysis of Mission Memorial Hospital Laboratory Cancer Incidence Data 33
Events in the Mission Memorial Health laboratory cancer cluster investigation 33
Cancer Cluster at the Mission Memorial Hospital Laboratory 33
Field Investigations: Potential Exposures to Potentially Carcinogenic Substances or Physical Agents 36
Conclusions 37
Summary 37
Recommendations 39
References 41

- *Attachment 1:* Field Investigations: potential exposures to potentially carcinogenic substances or physical agents (conducted in August 2003)
- *Attachment 2 and 3:* Initial epidemiological and statistical analysis of the cancer incidence data (March 2004).
- *Attachment 4:* presentation to the MMH Laboratory employees and staff (March 2004)
- *Attachment 5:* Indoor air quality assessment (November 2004)
- *Attachment 6:* Radiation exposure assessment of laboratory area for 70 days (June-August 2004)
- *Attachment 7:* Chemical assessment of Carcinogens (June 2004)
- *Attachment 8:* Research update (March 2005)
- *Attachment 9:* Presentation to the MMH Laboratory employees and staff (May 2005)
- *Attachment 10:* Critical questions posed by MMH Laboratory personnel (November 8, 2005)

- *Attachment 11A:* OHSAH responses to critical questions (January 9th, 2006)
- *Attachment(Separate Document):* FH responses to critical questions

same rate of cancer as the BC population. The computation of expected numbers of cases is adjusted for both the age of each individual as well as the calendar years that they were at risk. The findings from the statistical analyses are presented in Table 3.

Table 3: Observed and expected cases and age/calendar-year adjusted standardized incidence ratios (SIRs) for breast cancer (females only) and all cancers.

Cause	Person-years	Number of subjects	Expected cancers	Observed cancers	Standard Incidence Ratio	95% Confidence Intervals
Breast Cancer (females)	856.28	57	0.83	7	8.43	3.39 – 17.38
All cancers (females only)	856.28	57	2.18	10	4.59	2.20 – 8.44
All cancers (all subjects)	973.49	63	2.34	11	4.70	2.35 – 8.41

Data Presented as frequency, mean(standard deviation)

A finding of a SIR of 8.4 for breast cancer with 95 percent confidence intervals exceeding 1.0 indicates that the expected number of breast cancers was significantly elevated. The SIR of 8.4 indicates that the women in the MMH Laboratory were experiencing breast cancer incidence at approximately eight times the rate than women in the BC population. The 95 percent confidence intervals suggest that, the true SIR (since this is just a statistical approximation) was expected to be between 3 and 17 with 95 percent certainty. Therefore, statistically speaking, this is a true cluster of breast cancer cases that exceeds what is expected among women in BC. Similarly, the standard incidence rates for all cancers in both men and women were significantly elevated as compared to the rates in BC. However, given the large proportion of cancers that were of the breast, the excess in the total cancer SIRs was driven by the high number of reported breast cancers in the employee cohort.

Cox proportional hazard modeling showed that the variables Age at start of work at MMH Laboratory, Job Position (Technician vs. Aid, Clerk or ECG), and Job Status (Part time vs. Full Time) were not related to the hazard rate. The hazard rate is defined as the probability per time unit that a person who has not developed cancer to the beginning of the respective interval will develop cancer in that interval (Table 4). This is a very important finding. It suggests that there is

- Past exposures were likely much higher as a number of procedures have been modified due to technological advances

    - A major change was in the preservation of tissue samples, tissue staining, and glucose measurement. These procedures, in the past, required open use of solvents and reagents which included formalin, xylene, and *o*-toluidine. Most of these procedures were performed in a separate area of the laboratory, which was removed when the procedures were modified. It should be noted that *o*-toluidine, which was discussed in the literature review, is a rat mammary carcinogen, and formaldehyde (the major component in formalin) is a known human carcinogen.

    - Other areas of the laboratory also were renovated due to changes in laboratory procedures. Remnants of a local exhaust ventilation system are present in one area where open chemicals were once mixed and dispensed.

- Poor indoor air quality was a common complaint in the past but appears to be less of a problem currently. An incinerator at the hospital was a source of very odorous and potentially hazardous compounds (likely acid gases and possible combustion products of PVC (monomers of vinyl chloride) and other plastics (halogenated organics)).

Previous air quality studies have been performed at MMH Laboratory; however investigators did not have access to the historical findings. In discussions with occupational health and safety professionals at FH, it was mentioned that previous studies were standard IAQ surveys and all measured concentrations of air contaminants were below regulated limits.

Conclusions

Summary

- The incidence of **breast** cancer among MMH Laboratory employees (SIR=8.4) statistically exceeds the expected incidence rate of breast cancer among women. Therefore this is a true cluster of breast cancer cases.

- We conclude, based on a proportional hazards analysis, that this increase is not statistically related to age at start of work or duration of exposure. The risk of breast cancer by job

position (technician vs. aid or clerk), is elevated but this increase is not statistically significant.

- On observation and literature review, no current occupational chemical exposures, or records of past occupational exposures were found that might relate working in the MMH laboratory environment to elevated breast cancer risk, or cancer in general. No significant findings were found during radiation testing in the laboratory, or on basic air quality testing.

- We conclude that this investigation be closed and an update to the analysis conducted in five years time. Should a larger cohort study be conducted that suggests an increase in breast cancer in laboratory workers, or if a hypothesis is generated based on new scientific knowledge, the concerns of the employees of MMH laboratory should be reviewed at that time.

In our study we did not gather personal information pertaining to known risk factors for breast cancer. The reason for not gathering this information was that this is a preliminary epidemiological study and information on risk factors is difficult to interpret without a comparison population where the prevalence of risk factors is available. For example, in our study if we had detailed information about reproductive factors, family history of breast cancer, socioeconomic factors, alcohol consumption, physical exercise, and obesity, we would only be able to compare the prevalence of those factors with those within the general population. Thus, such data would provide clues as to the possible reasons for the elevated risk – if the prevalence of these risk factors were the same as the general population it would suggest that occupational factor(s) predominate. Only a full-scale etiologic investigation would have the capability of clearly identifying occupational factors as attributable to the increased breast cancer risk.

A full-scale epidemiologic study is not an appropriate action to take despite the increased rates of cancer MMH Laboratory employees have experienced. The major goal of cluster investigations is to identify risk factors so that action can be taken to reduce exposures and risk. Air quality studies and reviews of procedures indicate that current exposures to carcinogens are minimal. Past exposures to chemicals like *o*-toluidine may have resulted in some increased risk for employees, but these exposures appear to have been eliminated.

Another issue that discourages a major epidemiologic investigation pertains to the statistics of clusters themselves. Cluster research has shown that elevated rates occur by chance at some geographic locations and times. In fact, clusters always occur and it is a statistical phenomenon – even when there is no causal factor that is responsible for the increased incidence (this is why so few cluster investigations uncover any new risk factors). So, if we look around at many geographic areas and times we will find some clusters; if a specific cluster is related to statistics and not an etiologic agent, it is most likely that in the next time period at this location the rate will not be significantly elevated. Thus, it would be very prudent to continue to evaluate the incidence of breast cancer in MMH Laboratory employees to see if the rate comes closer to what is expected.

In summary, this study confirmed that the perceived cluster was an observed cluster and that MMH Laboratory employees were experiencing an elevated rate of breast cancer. The factors associated with this increased incidence could not be determined but may have been due to: (1) a cluster of reproductive and other known, non-occupational, risk factors, (2) past exposures to chemical carcinogens and less likely to ionizing radiation, and (3) a statistical anomaly.

Recommendations

Our recommendations for action to be considered are:

(1) provide education to all employees about risk factors for breast cancer and the importance of self exams and mammography, with assistance provided to ensure access to mammography if needed;

(2) continue to collect information on the incidence of breast and all cancers in the future so that standardized incidence ratios (SIRs) can be re-calculated in five years time;

(3) a new investigation can be considered at a future time if larger cohort studies suggest a link between breast cancer and hospital work, or laboratory work in particular, and/or if new scientific knowledge allows for a hypothesis on work-related causation to be generated for testing; and .

(4) Every effort should continue to be made, in this and all workplaces, to ensure that workplaces remain as safe and free of carcinogenic exposures as possible, and that the workforce is able to pursue safe and healthy choices in all aspects of their lives.