Volume 2 Issue 1
November 2002

Dedicated to the prevention of occupational illness and injuries, and promoting the well-being of all workers

Occupational Medicine Clinical Update

Occupational Health Clinics for Ontario Workers Inc, Sarnia-Lambton

Beware the "Double Cohort"

There's nothing like playing some "old-time hockey" to take your mind off the pressures of office practice. No distractions, no being pulled in all directions at once - just you, the puck, and five guys trying to kill you.

Well, almost no distractions. As you rest up for your next shift you become aware of the unmistakably pungent odor of the player next to you. Turning your head to find some uncontaminated air you muse that it's no wonder Lemieux and Koivu ended up with lymphomas. A lifetime of exposure to these fumes could cause cancer in the most robust body.

Hmmm...could there be something to this? If autoimmune diseases, solvents and pesticides are suspected of causing lymphomas, why not eye-watering b.o.? Immune suppression and stimulation theories course through your brain. Maybe it's the molds in the equipment? What self-respecting Canadian ever washes his (or her) hockey equipment?

An hour later you are searching PubMed for studies on hockey players and hematologic malignancies. You can see it now: fame, fortune and a name in history with the likes of Pasteur, Osler, or at least the Hanson brothers, are a few mouse clicks away.

You find a few case-control studies that have indeed found increased risk of lymphoma in professional hockey players. So far, your hypothesis stands.

At last you find what you really want: a big cohort study - Lymphoma and Exposure to Volatile Emanations from Hockey Equipment in a Multinational Cohort of More Than 55,000 Professional Hockey Players. Perfect, but alas, your Dionysean fantasies are ripped to shreds as you read the results. No increased risk.

Big study, no increased risk. So much for your theory, right?

Covert Cohorts

Occupational epidemiological studies can be basically looked at as either *hypothesis-generating* (case reports, case series, proportionate mortality studies) or *hypothesis-testing* (case-control or cohort studies).

The case reports of two pro hockey players with lymphomas generates a hypothesis: Is there an association between rotting hockey gear and lymphomas? The cohort study above showing no elevation in risk would appear to refute the hypothesis.

Pivotal to the question is the quality of the study itself. This is a function of a number of factors, with one of the most fundamental questions being that of exposure.

Factors Affecting Study Quality
- Bias
- Confounding
- Exposure assessment
- Diagnostic accuracy
- Statistical power
- Appropriate analysis and interpretation

Two case studies will help illustrate this point.

Case Study #1 - Cohort Within a Cohort

Vinyl chloride is a known human carcinogen causing angiosarcoma of the liver. Union Carbide published mortality data for 88,000 of its workers employed between 1974-1983 [Teta et al, 1990]. Of note, there was no overall excess mortality. In fact they showed a deficit SMR (standardized mortality ratio) of 89 amongst all their workers, from biliary/liver cancer (see table 1, page 2).

This might lead to the conclusion that there is no risk of cancer from working with vinyl chloride. Even amongst hourly male employees there was no *statistically significant* excess (SMR = 129).

However, on looking within one chemical division there was a statistically significant excess of biliary/liver cancer (SMR = 288), and at one facility it was nearly six times expected (SMR = 592).

Even within these latter two groups there would likely be significant numbers of employees who never had appreciable exposure to vinyl chloride, thus underestimating the risk to exposed workers even further.

(Continued on page 2)

O H C O W

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(Continued from page 1)

The authors concluded "This (cause of death category) also exemplifies the dilution of important effects that can occur when the at-risk population is overwhelmed by persons not exposed to the risk factor."

"...dilution of important effects can occur when the at-risk population is overwhelmed by persons not exposed to the risk factor."

Thus a key question in any cohort (or case-control) study is always: did the workers actually have the exposure? All the other factors that define a high quality study are for naught, if accurate exposure estimates are not determined in some way. ?

Table 1: Malignant Neoplasms of the Biliary Passages and Liver in Union Carbide Workers (1974-1983)

Group	n	SMR (standardized mortality ratio)	95% Confidence Interval
Overall Company	88,289	89	51 - 144
Hourly Males	34,795	129	64 - 230
Hourly Males Chemical/Plastics	7,901	288*	132 - 547
Hourly Males Chemical/Plastics, South Charleston Facility	Not provided	592*	217 - 1289

* statistically significant

Case Study #2 - A Tale of Two Cohorts

In 1997, the National Cancer Institute (NCI) published a cohort analysis of 74,848 Chinese benzene workers [Hayes et al]. The NCI study found an elevated risk in a spectrum of hematologic neoplasms, including non-Hodgkin's lymphoma (NHL).

In apparent contrast, the American Petroleum Institute (API) sponsored a multinational cohort analysis of 308,199 petrochemical workers and mortality from NHL [Wong and Raabe, 2000] ostensibly in relation to benzene exposure. This was a meta-analysis of 26 cohorts with data supplied by petroleum companies, and showed no increase in risk of death from NHL.

So which study is correct? They may both be, as long as you understand the question they are actually capable of answering.

The key difference between the two studies is the question of exposure. The NCI study had detailed assessments of exposure and hence was able to answer the question it was asking: Is benzene exposure associated with hematologic malignancy, like NHL? The API study answered the question: Did this group of workers have increased mortality from NHL? However, it couldn't answer the question of whether benzene is associated with NHL because there was no actual benzene exposure data.

As we saw in Case 1, this point isn't merely academic. Cohorts without valid assessment of actual chemical exposure can obscure huge rates of increased risk amongst a large group of exposed workers, with very little difficulty. ?

After reviewing "Lymphoma and Exposure to Volatile Emanations from Hockey Equipment in a Multinational Cohort of More Than 55,000 Professional Hockey Players" you make several key discoveries.

First, the study was funded by the Hockey Equipment Manufacturers Association (HEMA). Second, HEMA has been charged with suppressing information advising washing of hockey equipment as it prolongs wear-life, thus decreasing replacement of equipment. Third, the study had a huge proportion of Swedish players and almost no Canadians.

You write a letter to the editor of the journal. "Obviously the authors have produced a study which cannot possibly answer the research question. Without substantial numbers of Canadian hockey players (who traditionally never wash their hockey equipment) and an overrepresentation of Swedes (who are fastidiously clean and arguably don't play hard enough to sweat), the study includes a large proportion of players without the exposure in question.

You call for more representative studies that include accurate assessments of exposure with odorimetry.

References

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Additional references available on request but not provided due to space constraints.