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ENDOTOXIN EXPOSURE AMONG SOFTWOOD LUMBER MILL WORKERS IN THE CANADIAN PROVINCE OF BRITISH COLUMBIA

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Abstract: An increased prevalence of respiratory problems among softwood lumber mill workers has been observed in a number of studies. These workers are potentially exposed to a variety of respiratory hazards including wood dust, abietic or other resin acids, monoterpenes, and fungi, as well as endotoxins. The objectives of this study were to determine if lumber mill workers were exposed to hazardous levels of airborne endotoxin and to identify the factors contributing to high exposures. Personal endotoxin samples (n = 216) were collected in four lumber mills in the Canadian province of British Columbia. The mean personal exposure concentration was 2.09 ng/m^3 and 9% of the samples were above 5 ng/m^3. Factors related to the personal endotoxin exposure were type of job, use of compressed air, the percentage of time spent in a booth or cab during a shift, and dust concentration. Log storage practices were also suspected of playing a role. The levels of exposure observed in this study were low compared to the levels reported for populations with respiratory problems attributed to endotoxins.

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INTRODUCTION

The prevalence of respiratory symptoms and decreased lung function among softwood lumber mill workers has been observed to be significantly higher than unexposed control groups [4, 5, 7, 12, 14]. Lumber mill workers are potentially exposed to a variety of respiratory hazards, including wood dust, the chemical constituents of wood, moulds, and bacteria. In order to institute appropriate preventative measures it is important to determine which of these exposures are responsible for the respiratory problems. A relationship between exposure to endotoxins, a component of the cell membranes of Gram-negative bacteria, and acute and chronic changes in lung function and respiratory symptoms has been reported in other occupational settings with exposure to organic dusts [13, 17, 21]. But, to date, there are no reports of respiratory disease among lumber mill workers due to endotoxins.

Exposure to endotoxin has been assessed in a number of industries, but relatively little data is available regarding endotoxin exposure in lumber mills. Dutkiewicz *et al.* [9, 10] reported the presence of Gram-negative bacteria and endotoxin in samples taken from stored timber logs. Dahlqvist and colleagues [4] reported levels of airborne endotoxin were 1.5–2.5 ng/m^3 among Swedish wood trimmers exposed to relatively low levels of wood dust (mean = 0.26 mg/m^3). A pilot study to characterise respiratory hazards in a Canadian lumber mill, showed the presence of both endotoxins and viable Gram-negative bacteria in accumulated dust on workplace surfaces; however, airborne concentrations of endotoxins and Gram-negative bacteria were not measured in the Canadian study [6].

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The objectives of this study were to determine if lumber mill workers were exposed to hazardous levels of airborne endotoxin and to identify the factors contributing to high exposures. To meet these objectives, personal exposure to endotoxins was assessed in four Canadian lumber mills. This study was a part of a large cohort study of lumber mill workers designed to examine the health effects of fungicides, wood dust, and other hazards [22].

MATERIALS AND METHODS

Study population and sampling strategy. Samples were collected in four lumber mills in the Canadian province of British Columbia. Each mill was located in a different region of the province; Northern interior, Southern coast, Vancouver Island, and Southern interior. Sampling was conducted over a two week period in each mill, respectively in May, June, July and August of 1997. The interior mills mainly processed Engelmann spruce (*Picea engelmannii*) or white spruce (*Picea glauca*), lodgepole pine (*Pinus contorta*), and sub-alpine fir (*Abies lasiocarpa*). The coastal mills primarily processed Western hemlock (*Tsuga heterophylla*). The logs processed in the two coastal mills had a much larger diameter than those processed in the interior mills. Log storage prior to processing also varied. The Southern coastal mill stored the logs in salt water whereas the mills in the Southern interior and on Vancouver Island used fresh water storage of the logs. Following debarking, the Southern interior mill stored logs on land for a short time while the Northern interior mill stored logs in fresh water as well as on land.

The goal was to sample all production and maintenance jobs, with the exception of administrative jobs, at least once in each mill. Individuals were randomly selected from all available job title/shift combinations. Full shift samples (8 or 12 hours) were collected for the majority of samples. The minimum time for samples included in the analyses was 4 hours. At the end of the sampling period, participants were questioned about work tasks performed during the shift that may have influenced exposure to endotoxin. This included compressed air use to remove wood dust from machinery and surfaces, and the percentage of time spent in a booth or cab.

Endotoxin sampling and analysis. The airborne samples were collected using a GSP-sampler (Deha-Haan & Wittmer GmbH, Friolzheim, Germany) for inhalable dust. Inhalable dust is the mass fraction of total airborne particles that can be inhaled through mouth and nose [1]. Teflon (polytetrafluorethylene) filters, 0.45 µm pore size, 25 mm diameter, were used (Costar, USA). Filters were preconditioned in a climate-controlled room (temperature 22 ± 2ºC, relative humidity 65% ± 5%) and weighed in triplicate on a Sartorius microbalance (Sartorius M3P, Germany). Personal air sampling pumps (SKC model 224-44XR, Eighty Four, PA, USA) were calibrated to a flow rate of 3.5 litres per minute. After sampling, the filter was immediately refrigerated at 4ºC. Before weighing to determine dust concentration, the filters were desiccated at 4ºC for approximately 48 hours and then re-equilibrated in the climate-controlled room for 48 hours at 22ºC. After equilibration, the filters were again weighed in triplicate and stored in 50 ml pyrogen-free centrifuge tubes until extracted for endotoxin [8].

Endotoxin levels were determined using the BioWhittaker kinetic turbidimetric Limulus Amebocyte Lysate (LAL) assay. This is an *in vitro* biological assay, which is based on the reaction of LAL circulating amoebocytes of the horseshoe crab, *Limulus*, with lipopolysaccharide. The endotoxin was extracted from the filters for the analysis. Teflon filters were chosen for their hydrophobic properties and their ease of manipulation for extraction procedures [20].

All glassware was baked at 180ºC for 4 hours to render it endotoxin free (depyrogenation). The buffering salts were also depyrogenated before use as described by Milton [18]. For the extraction of endotoxin from the filters, 20 ml of a buffer solution (0.05M Na_2HPO_4-0.01% triethylamine in pyrogen-free water, pH 7-7.5) was added to the 50 ml centrifuge tube containing the filter. The tubes were shaken for 1 hour, sonicated for 60 minutes at 20ºC, and centrifuged at 1000 × g for 10 minutes. Two pyrogen-free vials were filled with 2.5 ml extraction solution from each tube. One vial from each sample was refrigerated until analysis (within 24 h) and the other vial was stored frozen at –20ºC for reference.

Samples, blanks (pyrogen-free water) and standards were dispensed in 100 µl aliquots in a 96-well microtitre plate (Costar). Each assay plate included a standard curve in duplicate of *E. coli* 055:B5 endotoxin (Biowhittaker) ranging from 0.01–1 ng/ml. Samples were tested at full strength, 1:10 and 1:100 dilutions. All dilutions were made in pyrogen-free water. The plate was pre-incubated at 37ºC to bring the samples to this temperature before adding 100 µl LAL reagent to each well using an eight-channel micropipettor. The turbidity of the samples was measured at 1 minute intervals at 340 nm wavelength (λ) using a Molecular Devices ThermoMax plate reader at temperature controlled to 37 ± 0.5°C. Spectrophotometric measurements were analysed using Molecular Devices SoftMax® pro software.

The kinetic turbidimetric assay measures the time of onset of increasing optical density indicating increasing turbidity. If there is no endotoxin present there is no "time of onset" and samples are not assigned a numeric value by the software (e.g. below the limit of detection of the method). In this series of samples there was interference from the sample matrix in the undiluted samples. This interference disappeared in the 10-fold diluted samples. The endotoxin content was diluted beyond the sensitivity of the assay for the 100-fold diluted samples. Therefore, all calculations were performed on the 10-fold diluted samples. This served to increase the limit of detection of the extracted samples.

Table 1. Endotoxin concentrations (ng/m^3) by lumber mill.

Lumber mill (samples)	Arithmetic mean	Geometric mean	Geometric Std. Dev.	Range
Southern coast (n = 56)	1.24	0.50	2.82	<0.25–16.92
Vancouver Island (n = 50)	1.00	0.55	2.52	<0.25–9.32
Southern interior (n = 60)	2.51	1.15	3.04	<0.25–34.75
Northern interior (n = 50)	3.60	1.52	3.73	<0.25–32.86
All four mills (n = 216)	2.09	0.83	3.30	<0.25–34.75

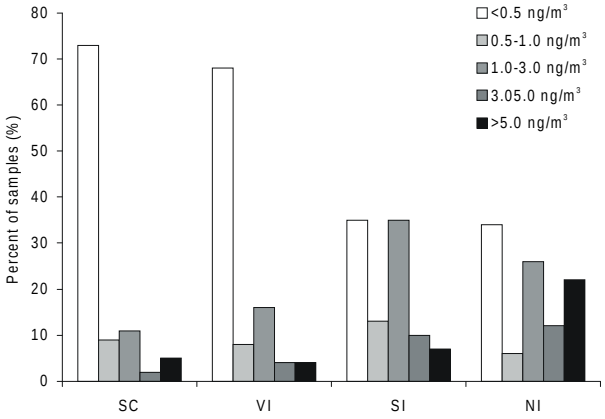

Figure 1. Frequency distribution of percentage of endotoxin samples by mill. SC – Southern coast, VI – Vancouver Island, SI – Southern interior, NI – Northern interior.

Results were expressed as the nanograms of the standard endotoxin *E. coli*: B5 per cubic metre of air (1 ng equal to approximately 10 Endotoxin Units, EU). Field blanks were pre-weighed filters taken to the field and treated identically to sample filters, except that no air was drawn through the filter. Twenty-one field blanks were extracted and analysed in parallel with the sample filters. The interference effect was present in the field blank filter extracts in the undiluted samples and was overcome in the 10-fold dilution. The 1:10 dilution of field blank extracts was identical to the pyrogen-free water blanks. The limit of detection (LOD) of the method was calculated from the lowest value of the standard curve. The LOD for samples up to 8 hours was 0.400 ng/m^3, and for samples up to 12 hours was 0.250 ng/m^3.

Statistical analysis. Samples were divided into the following job groups for analysis: front sawmill, other sawmill, planer mill, clean-up, maintenance, and miscelaneous jobs. The "front sawmill" group consisted of jobs responsible for cutting logs to usable lengths, removing the bark, and removal of the rounded outer portions of the log. The "other sawmill" group consisted of jobs responsible for cutting the lumber to the dimensional widths and lengths as well as grading and sorting. Sawmill workers were separated into two groups based on the *a priori* hypothesis that potentially higher levels of endotoxin could be present in the front end of the sawmill because this is where whole logs or slabs (parts of the outside of the log) are handled. The two interior mills and the Vancouver Island mill each had a separate planer mill where the surfaces of boards were smoothed. Clean-up and maintenance jobs (including saw filers, welders and industrial mechanics) were also placed in separate groups. The remaining jobs, primarily those in the yard and on the water where logs and/or lumber are stored, were included in the "miscellaneous" group.

Non-parametric tests were used to assess the impact of potential determinants of exposure. A difference was considered statistically significant when the p-value was 0.05 or less. The correlation between the endotoxin concentration and the dust concentration was also calculated using the log-transformed concentrations.

RESULTS

General characteristics. There were 223 samples collected. Six samples were excluded because the sample time was shorter than 4 hours and one sample was excluded because the worker performed jobs in different groups during the shift. The total number of analysed samples was 216.

Eleven plates were used for the determination of the 216 endotoxin samples. A standard dilution series was made in duplicate on every plate. Based on the 11 duplicates of the 0.1 ng/ml endotoxin standard, the coefficients of variation (relative standard deviation) were 1.6% (within plate), 6.8% (between plates), and 8.4% (total).

Of the 216 samples, 51% were below the LOD. The personal mean endotoxin exposure ranged from the LOD to 35 ng/m^3, with a geometric mean of 0.83 and a geometric standard deviation of 3.30. 20 samples (9%) were above 5 ng/m^3 and 9 samples (4%) were above 10 ng/m^3. The distribution of the exposure measurements appeared to be log-normal.

Endotoxin concentration by mill. The endotoxin concentration in each mill is presented in Table 1. A frequency distribution by mill is presented in Figure 1. The difference between the endotoxin concentrations in the interior (Northern and Southern interior, combined) and in the coastal mills (Southern coast and Vancouver Island, combined) is statistically significant ($p = 0.001$, Wilcoxon two sample test). The differences between the two coastal mills and between the two interior mills were not significant. The Northern interior sawmill had the highest number of samples above 5 ng/m^3; 24% of samples compared to 5%, 4%, and 7% samples in the Southern coastal, Vancouver Island, and Southern interior mills, respectively.

Table 2. Mean endotoxin concentrations (ng/m^3) by job group.

Job group (samples)	Arithmetic mean	Geometric mean	Geometric Std. Dev.	Range
Front sawmill (n = 23)	1.51	0.71	3.32	<0.25–8.50
Other sawmill (n = 46)	2.59	0.90	3.81	<0.25–34.75
Clean-up (n = 8)	6.23	4.77	2.29	1.09–14.39
Planer mill (n = 27)	0.87	0.59	2.30	<0.25–3.71
Maintenance (n = 62)	2.88	1.12	3.42	<0.25–32.86
Miscellaneous (n = 50)	0.90	0.53	2.34	<0.25–7.96

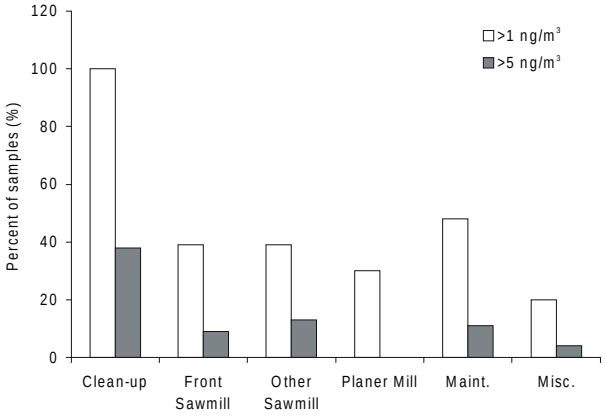

Figure 2. Percentage of samples above 1 and 5 ng/m^3 endotoxin by job group. Maint. – Maintenance, Misc. – Miscellaneous.

Endotoxin concentration by job group. The mean endotoxin concentrations in each job group are presented in Table 2. The exposure to endotoxin in the planer mill was very low as was the exposure in the miscellaneous jobs. The clean-up workers had clearly the highest exposure to endotoxin. This mean is based on 8 samples while the numbers of samples for the other work groups were larger. Maintenance workers and "other sawmill" also had a relatively high exposure. The percentage of samples above 1 and 5 ng/m^3 in each work group are presented in Figure 2.

Endotoxins are expected to be mainly present on the outside of the log. Thus, it was predicted that endotoxin exposure among front sawmill jobs would be higher than other sawmill jobs. However, the mean concentration in the other sawmill group was slightly higher (0.71 compared to 0.90 ng/m^3 endotoxin). On closer examination it was found that 83% of front sawmill and only 28% of other sawmill workers spent more than 50% of their shift in an enclosed booth. Among workers who spent less than 50% of shift in an enclosed booth, the geometric mean exposures were 2.96 ng/m^3 and 1.11 ng/m^3 endotoxin among front and other sawmill workers, respectively. Among workers who spent more than 50% of shift in an enclosed booth, the corresponding geometric means were 0.53 ng/m^3 and 0.52 ng/m^3 endotoxin, respectively.

Table 3. Mean endotoxin and dust concentrations by lumber mill.

Lumber mill	Endotoxin (ng/m^3) Geometric Mean	Dust (mg/m^3) Geometric Mean	Correlation Coefficient
Southern coast	0.50	0.48	0.80*
Vancouver island	0.55	0.52	0.53*
Southern interior	1.15	1.21	0.62*
Northern interior	1.52	2.14	0.52*

* $p < 0.001$

Dust concentration and endotoxin concentration. Table 3 presents the geometric mean dust concentrations and endotoxin concentrations in each lumber mill. The dust concentrations were significantly lower for the coastal mills in comparison with the interior mills ($p = 0.001$, Wilcoxon two sample test). The difference between the coastal mills was not significant. The dust concentration was significantly higher for the Northern interior mill compared to the Southern interior mill ($p = 0.0034$, Wilcoxon two sample test). Endotoxin concentration was correlated with dust concentration (Fig. 3). The correlation coefficient from the log-transformed endotoxin concentration and the log-transformed dust concentration was 0.69 ($p < 0.0001$).

Use of compressed air and endotoxin concentration. Compressed air was used in all four lumber mills to remove accumulated dust from machinery and other workplace surfaces. An *a priori* hypothesis was that accumulated dust would provide a medium for the growth of Gram-negative bacteria and that the use of compressed air would result in increased exposure to endotoxins.

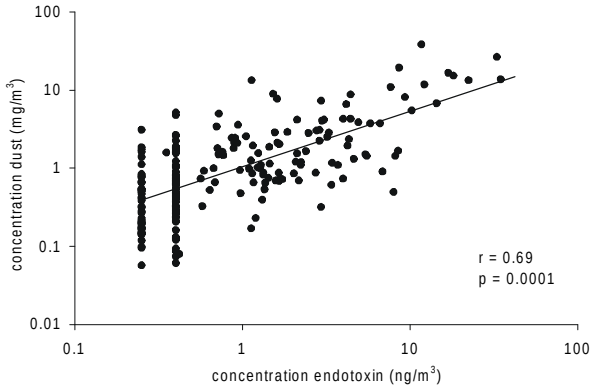

Figure 3. Relationship between the endotoxin and dust concentration. Both endotoxin and dust concentrations are presented on logarithmic scales.

Overall, 32% of all sampled workers reported the use of compressed air for clean-up. The geometric mean exposure among workers reporting the use of compressed air was 1.18 ng/m^3 and for those reporting no use was 0.68 ng/m^3. This difference was statistically significant ($p = 0.0005$, Wilcoxon two sample test). The clean-up workers had the highest exposure of all the work groups. However, only 50% of the clean-up workers reported the use of compressed air and those who did had similar exposures to those who did not (6.0 vs. to 6.5 ng/m^3 endotoxin, respectively).

DISCUSSION

In this study, the highest endotoxin concentration observed was 35 ng/m^3 and 9% of the samples were above 5 ng/m^3. Significant factors related to increased endotoxin exposure were level of dust exposure, use of compressed air for clean-up, and employment in jobs responsible for clean-up and maintenance. Work in an enclosed booth appeared to have a protective effect within the highest exposed areas of the sawmills.

The mean level of exposure varied considerably between lumber mills. The Northern interior lumber mill, with fresh water and dry land storage of logs, had the highest endotoxin concentrations. The southern coastal lumber mill, with salt water log storage, had the lowest concentrations of endotoxin. Because immersion in water may inhibit the growth of some forms of Gram-negative bacteria on logs, it was hypothesised, *a priori*, that log storage techniques may be an important factor in the variability of endotoxin levels between lumber mills. In addition, fresh water may be more conducive to bacterial growth than salt water. While the mean exposures in the four lumber mills fit this general pattern, there are too few mills in this study on which to base firm conclusions. Additional differences between the regions, such as temperature extremes, relative humidity, age of the logs and length of storage time may also play a role.

There are some limitations that should be borne in mind when interpreting the results of this study. Each lumber mill was sampled in a consecutive month from May through August and all endotoxin extractions and analyses were performed in September. The filters were stored at 4ºC. A study by Douwes *et al.* [8] showed that storage at refrigerator temperatures for a period of 1 year had no effect on endotoxin levels. The Northern interior mill, which was sampled first and where the filters were stored for the longest time, had the highest endotoxin concentration of the four mills. The next mill to be sampled was the Southern coastal mill, which had the lowest endotoxin concentration of the four mills. This would argue against time of storage being responsible for apparent regional differences between endotoxin concentrations.

It has been noted by other researchers that interfering substances can be present in samples which may result in under or over estimation of the endotoxin concentration [15]. In this study, the filter media used were found to introduce interference with the kinetic turbidimetric LAL assay. It was possible to negate the effect of the interfering substance by diluting the samples, but this also served to raise the level of detection, and may have obscured some sample values that would have been measurable using another filter medium.

Table 4. Endotoxin concentrations (ng/m^3) from different studies.

Study [Reference]	N	Arith. Mean	Geom. Mean	Range
Grain industry [Kennedy *et al.*, 1997]	376	369	12.65	<LOD–17,653
Pig farmers [Preller *et al.*, 1995]	350	130	92	6–1,503
Potato processing industry [Zock *et al.*, 1995]	195	130	20	1–2,908
Animal feed industry [Smid *et al.*, 1992]	530	25	n/a	0.2–470
Sawmill industry [present study]	216	2	0.83	<0.25–35

LOD = limit of detection, n/a = not available

The endotoxin concentrations observed in this study are relatively low compared to the concentrations found in studies where adverse health effects have been observed [19, 21, 23]. The endotoxin concentrations from other studies in which a large number of personal samples were collected are presented in Table 4. It is important to be cautious when comparing studies where endotoxin concentrations have been analysed in different laboratories. There is no internationally accepted and standardised method for extraction and analysis of Gram-negative bacterial endotoxins from environmental samples. The most commonly accepted method is based on the lipopolysaccharide-induced clotting mechanism of Limulus amoebocyte lysate due to the sensitivity of this reaction. The lipopolysaccharide-induced reaction can be measured turbidimetrically or chromogenically, either kinetically or by endpoint assay. Due to the variation in measurement methods, results from different studies are difficult to compare. Based on the results of an inter-laboratory round robin endotoxin assay, Chun *et al.* [3] concluded that the results from different laboratories can vary by as much as an order of magnitude, but that intra-laboratory variations were small. Therefore, the most valid comparison may be made with the grain industry study by Kennedy *et al.* [16] whose endotoxin analyses were performed in the same laboratory but using different filter medium (depyrogenated glass fibre). The results of that study showed mean endotoxin concentrations 10 times higher than the highest concentrations observed in the current study.

There is no standard occupational exposure limit for endotoxin, but the Dutch Expert Committee on Occupational Standards (DECOS) of the Health Council of the Netherlands has proposed an exposure limit of 50

Endotoxin Units/m^3 (equivalent to approximately 5 ng/m^3 endotoxin) for personal inhalable dust exposure measured as 8 hour time weighted average [11]. A decrease in FEV_1 (forced expiratory volume in 1 second) is the most consistent parameter that has been reported to be affected by endotoxin exposures [11]. There has been a wide range of estimates of the level at which no decrease in FEV_1 would be observed. Based on the results of an experimental study of short-term exposure to endotoxins, Castellan *et al.* [2] showed no effects at 9 ng/m^3. A study by Smid *et al.* [21] of animal feed workers suggested a threshold of 3–7.5 ng/m^3. Other studies have also observed effects at levels below 20 ng/m^3, such as the study of pig farmers by Heederik *et al.* [13] and cotton workers by Kennedy *et al.* [17].

CONCLUSION

Workers in softwood lumber mills are potentially exposed to a variety of respiratory hazards, including wood dust, abietic or other resin acids, monoterpenes, and fungi, as well as endotoxins. The levels of exposure to endotoxins among lumber mill workers observed in this study appear to be low in comparison to other populations in which respiratory problems have been attributed to endotoxins. However, a small number of samples were within the range in which health effects have been observed in other studies. While it is unlikely that exposure to endotoxin is solely responsible for the respiratory problems observed among lumber mill workers, it may be a contributing cause.

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