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MUSCULOSKELETAL AND RESPIRATORY DISEASE IN ALUMINUM SMELTER WORKERS: THE KITIMAT STUDY

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ABSTRACT

A study was carried out on 1 242 smelter workers to examine the impact of exposure to various toxic substances at work on the respiratory and musculoskeletal systems of the workers.

A risk index for each worker was developed which estimated the impact of all major substances to which workers were exposed on each major target organ system. It considered the intensity of exposure, the toxicity of each substance for the major target organ system and the multiplicity and duration of exposure each worker to each group of substances.

A significant relationship was found between increasing levels of exposure to fluoride and other pulmonary irritants, and obstructive pulmonary changes as measured by the one second vital capacity (FEV_1/FVC). This was true when the groups were standardized for cigarette smoking and age. Large numbers revealed FVC and chest X-ray abnormalities suggesting fibrosis but which did not correlate with exposure level.

Highly significant relationships were found between exposure to fluorides and a history in workers of surgery on the back and neck, fractures of bones and a history of musculoskeletal diseases and conditions in the absence of X-ray changes of "classical fluorosis." Some of these analyses in addition to being statistically significant showed stepwise increases in the rate of abnormality or surgery with increase in exposure as measured by musculoskeletal risk index suggesting progression with increasing dose and with effects even at moderate exposure levels.

Thus, it would appear that fluorosis is a disease of multiple organ systems, particularly the musculoskeletal and respiratory systems and that the dense bone found in early studies represents a single manifestation of far advanced disease. A more appropriate name for this disease which may appear before such bony changes and affects multiple organs might be systemic fluorosis.

Since 1932, when Moller and Gudjonsson[18] first reported X-ray bone changes in humans due to occupational fluoride exposure, it has been known that workers exposed to this material may suffer negative health effects. These have been summarized in a number of review documents[3,11,20,22,27,29]. Roholm

confirmed these findings in a study of the health status of cryolite workers in 1937 in his classic monograph[22]. Since that time, other scientific workers have reported additional groups of cases of bone abnormalities, in some instances with crippling effects, in men exposed to fluorides in aluminum smelters[1,14,25,28].

The respiratory system has also been identified as a major target organ affected by fluorides. Reports include findings of an abnormally increased prevalence of inflammation of the larynx or pharynx, "asthma" and bronchitis, as well as large numbers with abnormal chest X-rays[1,6,7,10,17].

The Canadian Association of Smelter and Allied Workers (CASAW), which represents the workers at the Alcan Smelter in Kitimat, British Columbia, became concerned about the increasing numbers of workers requiring back and neck surgery and the possible excessive exposure to fluorides and other toxic materials, and undertook support of a health effects study in this population.

The overall objective was to determine, by epidemiologic means, whether exposure to materials in the smelter had adversely affected the health of the workers. This paper will limit itself to the examination of the effects of exposure on the respiratory and musculoskeletal system.

METHODS AND SUBJECTS

The Alcan aluminum smelter which was studied is in Kitimat, British Columbia, a town of 12000 people located along the coast in northern British Columbia, Canada.

Production started in 1954. The smelter produces approximately 820 tons of aluminum per day, and emits approximately 4–5 kg of fluoride per ton of aluminum into the ambient air. Aluminum is produced by the Söderburg process with vertical studs. The anodes are made at the smelter's carbon plant from green coke. The refined aluminum is cast into ingots and bars, and shipped out.

Virtually all of the smelter workers live in Kitimat. The work force is composed of approximately 2000 hourly workers who rotate every two weeks in 8-hour shifts around the clock. Maintenance workers work only day shift.

The cohort was selected using a seniority list of hourly employees as of November, 1976. There were 1936 persons on this list, which excluded office staff, management, and foreman. Also excluded from the study were those on disability leave, and those who had worked at the smelter for three months or less. Eighty-five percent of those eligible by these criteria participated. An appointment system was set up which allowed each eligible person to come in on a day off after at least 12 hours away from the plant.

Each individual filled out a self-administered questionnaire, which provided name, birthdate, ethnic and racial background, previous work record, and marital status. An interviewer-administered questionnaire collected information on past medical history, symptoms, and smoking history. Those categorized as having had back or neck surgery following employment answered "yes" to one or more of the following questions:

Have you ever had spinal fusion? What year?

Have you ever had low back surgery? What year?

Have you ever had neck surgery? What year?

Individuals having surgery at multiple sites or more than once were counted only once. Those categorized as having had one or more fractures of the bone following employment were also counted once.

The pulmonary function testing was done by a trained nurse using the Hewlett-Packard 982A system which utilizes a pneumotachometer, a desk top computer, and a printer. The equipment was standardized daily. Three tests were carried out and the best selected for use by the computer. The Morris nomogram[19] was used to generate predicted volumes.

The actual forced vital capacity as a percent of the predicted vital capacity (FVC) was considered to be abnormal if less than 80%. The actual forced expiratory volume after one second as a percent of the actual forced vital capacity (FEV_1) was considered abnormal if less than 70%. The actual forced expiratory flow between 25% and 75% of the total flow as a percent of the predicted forced expiratory flow between 25% and 75% of the flow (FEF) was considered abnormal if less than 70%.

A PA chest X-ray and an AP lumbar spine were done and were read by a board certified radiologist in Chicago, who knew only the age and sex of the patient. He used a modified ILO U/C 1971[12] format for reading the chest X-rays, and a limited category checklist form for reading the spine X-ray. Fifty X-rays of each type were re-read by him without his knowledge, and his results were well reproduced.

For the bone X-rays those categorized as "abnormal" included: increased density, whiteness, cortical thickening, hyperostosis, blurring of margins and calcification of ligaments. Those categorized as "possibly abnormal" included fracture(s), evidence of bone surgery, renal calculi, other soft tissue calcification, "other" abnormalities, scoliosis and lipping of vertebral bodies.

For the chest X-ray, those categories considered "abnormal" were: small, rounded opacities 2/2 or greater any zone(s), small irregular opacities 1/1 or greater any zone(s), any large opacities, any pleural thickening, all "other symbols" except "TB inactive" and pleural calcification. Those considered as "possibly abnormal" were: small, rounded opacities (1/1) any zone(s), "TB inactive", ill defined diaphragm and ill defined cardiac outline.

An organ system specific risk index was developed for each worker which took into account the intensity of exposure to a toxic material, the duration of exposure, the multiplicity of exposures, and the level of toxic impact of the material on the organ system in question.*

For purposes of analysis, the frequency distributions of both the pulmonary and musculoskeletal risk indices were used to categorize the entire cohort into low, medium and high exposure groups.

* This is discussed in another paper titled "Assessment of exposure and risk through the use of a Personal Cumulative Organ Risk Index" by S. Conibear and B. Carnow, to be published in Vol. 4 of these Proceedings.

Workers were then divided into four age groups. The first, 18–30, the second, 31–40, the third, 41–50, and the fourth, 51 years or older. The group ages 18–30 were used because there were very few individuals under the age of 20 and these were, therefore, included. The same is true of 51 or older, that is, there were very few individuals in the 60+ range. In regard to smoking, three groups were used: those who never smoked cigarettes or quit more than one year before entering the study, those who smoked less than one pack of cigarettes a day or quit less than one year before the start of the study, and the third group, those who smoked pack of cigarettes per day or more.

RESULTS

Relationship between occupational exposure to pulmonary stressors and prevalence of abnormal chest X-ray and pulmonary function test findings

Criteria for abnormal and possibly abnormal chest X-ray categories are described above. The prevalence of abnormality among those subjects having low, medium, and high occupational exposure to pulmonary stressors was examined. Differences among exposure groups with respect to these prevalences were not significant.

A comparison of mean values of FEV_1/FVC for the three pulmonary risk groups was made using an analysis of variance, and is shown in Table 1. A statistically significant inverse relationship was found between level of pulmonary risk and $FEV_1\%$ when adjusted for age and smoking. Cigarettes and age also were significantly related when adjusted for the other two parameters.

Relationship between occupational exposure to musculoskeletal stressors and abnormal bone X-rays or history of selected musculoskeletal disorders

Musculoskeletal diseases

Workers were classified into three musculoskeletal risk groups, categorized as low, medium and high risk by the Organ Risk Index Method which examines intensity, multiplicity, toxicity of material, and the musculoskeletal system as target organ. Most of the risk to bone related to fluoride exposure. A small rating was given to those few workers exposed to cadmium and lead. The same four age groups, 18–30, 31–40, 41–50, and 50+, were considered.

Workers were asked if they had ever been told that they had arthritis, gout, back trouble, slipped disc, and "other" musculoskeletal problems. Workers were counted once if they answered yes to one or more of these five questions. The results are noted in Table 2. The Mantel-Haenzel chi-square test was used to examine relationships between those in the highest compared to lowest, highest compared to medium, and medium compared to lowest categories of exposure. As can be seen, comparison of high and low exposure groups revealed marked differences in every age group. In the 18–30 group, 50% reported a history of musculoskeletal disease as compared to less than 10% of those in the lower

TABLE 1

A comparison of the mean values of FEV_1/FVC actual for the low, medium, and high pulmonary risk groupings with adjustment for age and cigarette smoking. N = 1189 (only male workers), grand mean = 77.11%.

			Mean (%)	
		N	Unadjusted	Adjusted
Pulmonary risk	Low	370	79.77	78.22
	Medium	416	77.67	76.96
	High	403	74.09	76.25
Age (years)	18–30	462	80.36	79.81
	31–40	292	76.54	76.50
	41–50	269	75.50	76.05
	51 +	166	71.66	72.40
Smoking history	Never or quit more than 1 year prior to testing	438	77.58	77.74
	Smokes less than 1 pack or quit less than 1 year prior to testing	210	78.65	77.87
	Smokes more than 1 pack a day	541	76.13	76.30

	Sum of squares	DF	Mean square	F	Significance of F
Main effects	117813312.000	7	16830464.000	22.577	0.000
Pulmonary risk	4951344.000	2	2475672.000	3.321	0.036
Age	46236080.000	3	15412026.000	20.674	0.000
Smoking history	6431090.000	2	3215545.000	4.313	0.014
Explained	117813504.000	7	16830496.000	22.577	0.000
Residual (unexplained)	880393216.000	1181	745464.188		
Total	998206720.000	1188	840241.313		

exposure groups. Looking at the older age groups, a similar stepwise increase is noted in the comparison between medium and low exposure groups, and high and medium exposure groups. As shown in the table, all differences were significant.

Musculoskeletal symptoms

The symptoms included joint pain, back or neck pain, stiffness in the back, stiffness in joints, and swollen joints. The responses were scored as zero for never, one, if they occurred 1–3 times per month, two if more than three times

TABLE 2

Comparison of the frequency of a history of musculoskeletal diseases commencing after employment in the smelter among those with a history of high, medium, and low exposure to bone stressors.

Exposure groups	Age groups								Mantel-Haenzel χ^2
	18 – 30		31 – 40		41 – 50		51 +		
	Negative history	Positive history	Negative history	Positive history	Negative history	Positive history	Negative history	Positive history	
High	10	5	51	27	96	96	64	68	42.90
Low	249	19	82	8	33	5	8	3	$\alpha < 0.001$
Medium	154	46	104	30	29	20	18	14	37.43
Low	249	19	82	8	33	5	8	3	$\alpha < 0.001$
High	10	5	51	27	96	96	94	68	5.00
Medium	154	46	104	30	29	20	18	14	$0.05 > \alpha > 0.025$

TABLE 3
Comparison of the frequency of complaints of musculoskeletal symptoms in the past one year summarized as a score among those with a history of high, medium, and low exposure to bone stressors.

Exposure groups	Age groups								Mantel--Haenzel χ^2
	18–30		31–40		41–50		51+		
	Low	High	Low	High	Low	High	Low	High	
High	15	0	74	4	159	30	115	13	1.954
Low	238	5	83	6	37	1	11	0	$\alpha > 0.05$
Medium	176	23	122	12	44	5	28	4	14.92
Low	238	5	83	6	37	1	11	0	$\alpha < 0.001$
High	15	0	74	4	159	30	115	13	0.159
Medium	176	23	122	12	44	5	28	4	$\alpha < 0.10$

per month but less than daily, and three, if they occurred daily or were present all the time. These were applied to each of the five categories and the score is the sum of these responses. The results are shown in Table 3 and reveal significant differences between the medium and low groups. Since a comparison of the high and low exposure groups did not reveal significant differences the positive findings are difficult to interpret.

Musculoskeletal surgery

The questions used to elicit a history of surgery of the spine are listed above. Those having a history of surgery of the back or neck or spinal fusion after starting work at the smelter were reported as positive. Workers were counted once even where multiple surgical procedures were performed, such as on the back and neck. The results shown in Table 4 were strikingly positive. A comparison of the high to low risk groups revealed no surgery in the younger age groups, but as the age groups increased, surgical intervention in those at high risk due to exposure increased remarkably to almost 25% in the 51+ category as compared to zero percent in this age group with little or no exposure. A similar increase is noted when medium and low categories are compared. Where high and medium exposures are compared, the results were not significant, although in the older age group almost 25% had surgeries compared to 10% in those moderately exposed.

History of fracture since commencing work at Kitimat

The workers giving a history of having one or more fractures since beginning work at the smelter were counted only once. As can be seen in Table 5, the results when high and low exposure groups, and medium and low exposure groups were compared, were significant at α less than 0.001 level. The results of a comparison of the high to medium exposure groups did not achieve a significant level of association. The biggest differences were seen in the groups from 31–40 and 41–50.

X-ray abnormalities of bone

A comparison of the groups high to low, medium to low, and high to medium revealed no significant differences in bone X-ray abnormalities between groups when standardized for the four age groups 18–30, 31–40, 41–50, and 51 years or older, when comparing abnormal and possibly abnormal to normal. The results are shown in Table 6.

DISCUSSION

Concern by the workers and considerable effort by the CASAW Union resulted in 85% of the workers participating in the study. Two hundred and sixteen did not participate and of these only 46 were due to refusals. The study

TABLE 4

Comparison of the frequency of back and neck surgery performed since commencing work at the smelter among those with a high, medium, and low history of exposure to bone stressors.

Exposure groups	Age groups								Mantel-Haenzel χ^2
	18–30		31–40		41–50		51+		
	No surgery	Surgery	No surgery	Surgery	No surgery	Surgery	No surgery	Surgery	
High	15	0	71	7	173	19	107	25	10.62
Low	268	0	89	1	38	0	11	0	$\alpha > 0.001$ $\alpha < 0.005$
Medium	194	6	131	3	43	6	29	3	11.12
Low	268	0	89	1	38	0	11	0	$\alpha < 0.001$
High	15	0	71	7	173	19	107	25	1.57
Medium	194	6	131	3	43	6	29	3	$\alpha > 0.10$

TABLE 5

Comparison of the frequency of a history of one or more fractures occuring since employment at the smelter among those with a history of high, medium, and low exposure to bone stressors.

Exposure groups	Age groups								Mantel-Haenzel χ^2
	18–30		31–40		41–50		51+		
	No fractures	Fractures	No fractures	Fractures	No fractures	Fractures	No fractures	Fractures	
High	14	1	66	12	158	34	110	22	15.50
Low	254	14	90	0	38	0	9	2	$\alpha < 0.001$
Medium	171	29	126	8	40	9	28	4	19.52
Low	254	14	90	0	38	0	9	2	$\alpha < 0.001$
High	14	1	66	12	158	34	110	22	0.99
Medium	171	29	12	8	40	9	20	4	$\alpha > 0.10$

TABLE 6
Comparison of the frequency of boney X-ray abnormalities among smelter workers with a high, medium, and low history of exposure to bone stressors.

Exposure groups	Age groups								Mantel-Haenzel χ^2
	18–30		31–40		41–50		51+		
	Abnormalities	No abnormalities	Abnormalities	No abnormalities	Abnormalities	No abnormalities	Abnormalities	No abnormalities	
High	2	13	32	46	142	50	121	11	1.12
Low	55	213	26	64	23	15	11	0	$\alpha > 0.10$
Medium	48	152	44	90	32	17	31	1	1.11
Low	55	213	26	64	23	15	11	0	$\alpha > 0.10$
High	2	13	32	46	142	50	121	11	0.71
Medium	48	152	44	90	32	17	31	1	$\alpha > 0.10$

was cross-sectional, that is, it examined healthy workers and was, therefore, a study of a survival population. Thus any abnormal findings represent a most conservative estimate of the problem. Further, internal controls were used because the community is relatively isolated and most able bodied men work in the smelter. Since even the "controls" had some degree of exposure, differences would tend to be minimized so that when they appear the problems are at least as serious as found.

The personal organ risk index, which takes into account the duration, nature, intensity and organ toxicity of each major material to which men are exposed represents an attempt to quantitate cumulative exposures to a single toxic material as well as multiple exposures to materials which may affect a particular target organ. Our results suggest that it may be a very useful method for quantitating risks in workers who, in today's industries, are often exposed to multiple insults and are moved because of production needs or seniority to different operations in a single plant.

Respiratory system

That fluoride as a gas and as particulate is extremely irritating to the mucous membranes, bronchial mucosa and other tissues of the respiratory tract has long been known[3,11,20,22,27,29]. Additionally, it has been shown that the lungs concentrate fluoride when inhaled and even when it enters the body through ingestion. Roholm performed an autopsy on an exposed worker and found ten times the concentration of fluoride in the lungs as compared to the stomach tissues[22]. Knaus found the same ten-fold increase in concentration of sodium fluoride in the lungs as compared to other organs following an infusion into rats[15].

Numerous studies have documented the acute inflammatory and broncho-spastic effects of the inhalation of fluorides. Mangold and Becket observed immediate upper respiratory irritation following exposure[16]. Others have found inflammation of the nose and throat resulting in sinusitis, pharyngitis, laryngitis and atrophic rhinitis, frequently accompanied by cough, hoarseness, sore throat and epistaxis[8,9,15,21,24]. A number of investigators have reported acute bronchospastic effects from exposure to fluorides following a workday in smelters in addition to increased problems with asthma as a result of chronic exposure[6,7,10,17]. Midttun reported 54 cases of asthma in 400 workers. He noted increased eosinophile counts during these attacks[17]. Two of his cases developed severe status asthmaticus following recurrent exposure.

Studies reporting chronic effects on lungs have also appeared in the literature. Agate reported cough in almost 13% of workers exposed to fluorides as compared to 4% of those minimally exposed[1]. A report from Great Britain by His Majesty's Chief Inspector, revealed that workers exposed to high concentrations of fluorides developed bronchitis and emphysema, with deaths due to cor pulmonale[9]. In these workers, diffuse fibrosis was found in addition to fluorosis of the bones.

Many of the findings in the reported studies were indicative of advanced and, in many cases, irreversible disease. This study, therefore, concentrated on examining pulmonary function in apparently healthy workers exposed to fluorides and other pulmonary irritants in the smelter, in the hope that it might reveal early signs of abnormalities if they were present. In that event, measures could then be taken to prevent progression of disease and perhaps such procedures could be used to monitor unaffected workers. The pulmonary function abnormalities found in this study confirm that fluorides particularly, and perhaps other pulmonary irritants present in the smelter may seriously affect the respiratory tract. The decreasing mean FEV_1 and the increasing percentage of those with abnormal FEV_1's in those with increasing exposure reflect the development of early obstructive pulmonary changes in workers considered to be healthy and actively working in the smelter. The stepwise increase in the rate of abnormality of the FEV_1 from little or no exposure to heavy exposure is significant also in that it suggests that workers exposed to moderate levels of fluorides are also affected although not yet to the same degree as those heavily exposed.

A number of other studies have evaluated pulmonary function in smelter workers. Johnson and co-workers, found FEV_1 to be negatively correlated with exposure as did our study[13]. Kaltreider and co-workers, on the other hand, found normal FVC's in workers that he examined[14]. In his study, however, there was no standardization for cigarette smoking and the pulmonary function unit used was the McKesson Vitalor, a hand held unit which has only a 6 second tracing time, and produces results of very questionable value. Discher and Breitenstein also carried out examinations of pulmonary function in smelter workers[5]. They found no difference in the percentage of abnormalities when exposed workers were compared with controls. Some of the differences, between our study results and theirs may be explained by the fact that in Discher's study, 30% of the workers were nonrespondents and an even larger number of controls refused to participate. The tested group was, therefore, highly selective. Further, on the one hand "new hire" workers who had little exposure were included as exposed workers while those controls who did participate appeared to have greater than normal exposure to other respiratory irritants. Also in that study, workers in the potroom were separated into a high exposure "anode" workers group and a medium exposure group consisting of potroom operators and others in the potroom. If potroom operators are actually a high exposure group, as certainly appears to be the case in our study, the relative abnormalities might not reveal themselves.

Chest X-rays of a large majority of the workers in this study were read as possibly abnormal by the roentgenologist while only 82 workers or 6.6% of the total were in the definitely abnormal category. It should be remembered that the ILO method of classifying X-rays requires reporting any and all abnormalities, not just those considered to be clinically significant, which is generally the method used in reporting abnormalities in clinical medicine. In fact, many other studies report a greater frequency of findings of workers with definitely

abnormal chest X-rays, variously characterized as "increased markings," "reticulum pattern," and "increased reticulum markings." In Roholms study, for example, 50% of the chest X-rays were found to be abnormal with incipient or moderate signs of pulmonary fibrosis[23]. Tourangeau noted that 15% of the workers he examined had X-ray findings of increased pulmonary markings and reticulum[26]. Bowler found no differences in vital capacity when compared with controls but reticulation was reported on the chest X-rays of 36% of those examined[2]. Derryberry noted "increased pulmonary changes" on X-ray in 14.9% of exposed workers as compared to 6% of controls[4]. Popyan and Demirchoglyan found 20% of those examined to have plural thickening[21]. The large number of possible or definitely abnormal X-rays in the absence of correlation with exposure suggests possible overreading of films or a wide range and variety of changes in all groups as a result of a generally dusty environment.

Musculoskeletal systems

The classic cases of fluorosis described by Moller and Gudjohnsson and Roholm, and the epidemics of fluorosis found in India are not seen very often today although Kaltreider examined 79 potroom workers and found that 96% of them had varying degrees of skeletal fluorosis. There is, however, considerable evidence in the literature that fluorides affect the back and neck. Moller and Gudjohnsson, and Roholm in their studies remarked on the stiffness of the back and complaints of the workers of rheumatic pains. Agate and co-workers, found abnormal X-rays in more than 25% of heavily exposed potroom workers with symptoms of musculoskeletal disease but without the classical signs of fluorosis[1]. Vischer and co-workers examined 17 heavily exposed potroom workers and found 9 of them with increased density of the pelvis and lumbar spine on X--ray[28]. All 17, however, showed ossification of spinal ligaments and "outgrowths of bony spurs on the vertebrae." All of the workers except one complained of pain and stiffness of the extremities, shoulders, neck and lower back. Similar findings of musculoskeletal changes without classic signs of fluorosis in workers exposed to high levels of fluorides have appeared in a number of other studies. Of special importance is a large prospective study by Zislin and Girskaya[30]. They followed 2 738 workers from the time they first came to work in the smelter and compared them with 1 770 workers employed in a non-fluoride industry. They found that non-specific bone changes, musculoskeletal symptoms and other findings antedate the classic changes of fluorosis in the bones by 5 to 7 years, and concluded that the changes of fluorosis described by Roholm represent the late stages of the disease. Our findings of a highly significant relationship between frequency of fractures and back and neck surgery and a high musculoskeletal risk index in the absence of so-called "classic fluorosis" X-ray findings supports the findings and conclusion of these other studies that fluorosis is a disease complex and much more than merely the appearance of dense bone. This conclusion is also supported by our findings of a very strong stepwise, significant correlation between a past history of other bone and joint diseases and a high musculoskeletal risk index.

The most striking finding was the relationship between back and neck surgery following employment and an increased musculoskeletal risk index as a measure of exposure to fluorides. This was highly significant when standardized for age using Mantel-Haenszel chi-square analysis. Again, the findings revealed a stepwise increase with exposure, suggesting abnormally increased frequency of disease even in those moderately exposed. Comparison of definitely or possibly abnormal bone X-rays as defined in Table 2 failed to reveal differences between risk groups. In the older age groups the great majority showed abnormal findings in all risk groups. The effect of the fluoride on bony changes if present was not seen possibly because all changes including those primarily due to age were given equal weight. The absence of classic changes of fluorosis in the presence of significant relationships between exposure and history of disease, fractures and bone surgery also mandates that the disease complex be regarded as more than "bone density" changes.

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