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# Fatal Asthma From Powdering Shark Cartilage and Review of Fatal Occupational Asthma Literature

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**Background** *Work-related asthma (WRA) is the most common work-associated respiratory disease in developed countries.*
**Method** *We report shark cartilage dust as a new potential cause of occupational asthma (OA) in the context of other fatal OA case reports.*
**Results** *A 38-year-old white male worked for 8 years in a facility which primarily granulated and powdered various plastics. Sixteen months prior to his death, the plant began grinding shark cartilage. After 10 months of exposure, he reported chest symptoms at work in association with exposure to shark cartilage dust and a physician diagnosed asthma. Six months later, he complained of shortness of breath at work and died from autopsy-confirmed asthma. The latency from onset of exposure to symptoms and from symptom onset to death was shorter than 10 previously reported OA fatalities.*
**Conclusion** *Recognition of occupational causes and triggers of asthma and removal of affected individuals from these exposures is critical and can prevent progression to irreversible or even fatal asthma.* Am. J. Ind. Med. 42:50–54, 2002. *© 2002 Wiley-Liss, Inc.*

***KEY WORDS: occupational asthma; fatal asthma; shark cartilage; work exposure***

## INTRODUCTION

Fatal asthma is an uncommon but well recognized occurrence [Greenberger et al., 1993; Hannawa, 2000]. In many countries, mortality associated with asthma progressively increased since the 1970s, but may have improved somewhat in recent years [Pearce et al., 1995; Mormile et al., 1996; Campbell et al., 1997; Taylor et al., 1997; Mannino et al., 2002]. In contrast, less is known about mortality associated with work-related asthma (WRA). WRA is the most common work-associated respiratory disease in developed countries [Malo, 1990; Axon et al., 1995]. It is more common than is generally recognized, can be severe and disabling, and is subject to primary, secondary, and tertiary preventions. WRA has been subclassified into work-aggravated asthma (WAA), characterized by exacerbation of pre-existing asthma at work; irritant-induced asthma, also known as reactive airways dysfunction syndrome (RADS); and sensitizer-induced occupational asthma (OA) [Friedman-Jimenez et al., 2001]. OA is generally associated with a latency period of months to years between first exposure to an agent and development of immunologic sensitization and asthma. Prognosis is better among workers with shorter durations of exposure after symptom onset (irrespective of the agent) suggesting that early removal from exposure can actually cure OA [Chan-Yeung and Malo, 1995]. In contrast, failure to implement exposure reduction or control can lead to irreversible asthma after an affected worker leaves the industry, or death as reported below.

## CASE REPORT

A 38-year-old mill worker died of asthma while at work. He had been employed for 8 years in an industrial mill

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engaged in the reduction of various bulk plastics and other materials into granular or powdered form using attrition mills, knife mills, and hammer mills. Sixteen months prior to his death, the plant began grinding and milling shark cartilage into a fine powder for use in natural remedies. The processing of the material into the desired powder size involves milling and cycling the powder through a series of mesh screens. Powder of the desired size is conveyed to a station where drums are filled and weighed prior to storage and shipment. The most significant sources of dust generation were identified as feed hoppers, damaged gaskets and ductwork, filling stations, and weighing stations. Personal dust sampling performed during shark processing showed that co-workers had exposures to respirable dust ranging from 0.92 to 5.14 mg/m$^3$ in comparison to the permissible exposure limit for ''non-toxic'' respirable dust of 5 mg/m$^3$. Exposures for total dust ranged from 26.4 to 44.7 mg/m$^3$, as compared to the applicable permissible exposure limit of 15 mg/m$^3$. Samples were also analyzed for endotoxin content. Levels of endotoxin were less than 1.6 endotoxin units (EU) per milligram of dust.

After 10 months of exposure, the worker developed wheezing, coughing spells, and episodes of dyspnea during exertion at work. The symptoms were triggered on several occasions by exposure to shark cartilage dust. A physician diagnosed asthma. Personal history was unremarkable for asthma and other respiratory conditions. Records made no mention of any unusual exposures away from work. He smoked one pack of cigarettes per day for 22 years.

The symptoms worsened over time. He began wearing a disposable respirator (paper mask) at work, but it did not improve his symptoms. At some point during this time, he was removed from grinding operations and assigned to other duties. However, he continued having respiratory symptoms associated with exposure to shark cartilage dust. About 3 weeks before death, he developed an acute episode of dyspnea, chest pain, and hoarseness at work attributed to the inhalation of shark cartilage dust. He sought treatment for acute asthma at a hospital emergency department. On the day of his death, he again complained of shortness of breath at work. His supervisor granted him permission to go home because of asthma symptoms. However, he was subsequently found by co-workers in an unresponsive state. Aggressive efforts at cardiopulmonary resuscitation by emergency medical personnel were unsuccessful.

The autopsy findings confirmed asthma as the cause of death. Grossly, white–yellow thick mucous casts were noted throughout the tracheobronchial tree. Multiple emphysematous blebs were reported in the upper lobes bilaterally and in the right middle lobe. In addition, severe sub-pleural emphysema was observed. Microscopic examination of the bronchi showed edema with eosinophilic infiltration, thickening of the basement membrane, hypertrophy of the submucosal mucus glands, and hypertrophy of the smooth muscle. The airway lumen contained copious mucoid material with numerous eosinophils.

## DISCUSSION

This case report suggests shark cartilage dust as an asthma-inducing agent. Shark cartilage has not been previously reported to cause immunologic sensitization nor adverse reactions. The latency after first exposure, development of asthma symptoms in close temporal association with exposure to powdered cartilage, and increasing severity with continued exposure support shark-cartilage associated dust as the etiologic agent for OA. Whether sensitization occurred to cartilage or other bioaerosols generated during milling cannot be established posthumously. Autopsy findings of this case are consistent with changes found in other reported cases of fatal asthma [Sobonya, 1984; Dunnill, 1986; Klenerman and Adelson, 1987]. These findings include the presence of thick mucus casts in the airways, eosinophilic infiltration of the bronchial walls, and hypertrophy of the submucosal mucus glands as characteristic features of asthma death. In addition to the mucus, the plugs characteristically contain sloughed epithelial clumps (Creola bodies), remnants of eosinophils (Charcot-Leyden crystals), and mucus casts (Curschman spirals)[Sobonya, 1984; Dunnill, 1986; Klenerman and Adelson, 1987]. Structural changes in the bronchial mucosa among subjects with fatal OA are similar to abnormalities in non-OA cases [Saetta et al., 1991].

Fatal OA has been documented in previous reports (Table I). Responsible agents have included flour in one case [Ehrlich, 1994], isocyanates in three cases [Anonymous, 1985; Fabbri et al., 1988; Carino et al., 1997], green coffee dust in two cases [NIOSH, 1995], printing sprays containing gum arabic in one case [Groetschel and Wiesbaden, 1958], bicycloheptadine dibromide in two cases [Murray and Fink, 1962], and papain dust in one case [Flindt, 1978]. Where reported, the latency between initial occupational exposure and onset of OA ranged between 1½ and 15 years. Reported intervals between onset of OA symptoms and death ranged between 2 and 20 years. Relative to these reported time intervals, the current case had onset after a shorter exposure latency (10 months) and early mortality after only 6 months of asthma symptoms.

In most cases of fatal OA, evaluation for specific IgE-sensitization and/or responses to specific inhalation challenge were not undertaken or were negative. In only two cases was specific IgE-sensitization demonstrated, in both cases by skin prick test. In one of these cases, papain was the etiologic agent [Flindt, 1978]. In a case where flour was the responsible agent, skin prick test to flour itself was negative, but tests to wheat and maize were positive. Interestingly, specific inhalation challenge with flour was strongly positive despite the negative skin test with this agent. The total IgE

**TABLE I.** Reported Cases of Fatal Occupational Asthma (OA) at Work

| Age | Atopy | Sensitizing agent | Industry | Tenure at work | Time from OA symptoms onset to death | Specific IgE | Inhalation challenge test | Confirmed autopsy | Reference |
|---|---|---|---|---|---|---|---|---|---|
| 52 | NA | Gum arabic | Printing | 20 year | 12 year | NA | NA | Yes | Groetshcel |
| 26 | NA | Bicycloheptadine | Pharmacology | >3 year | 3 year | NA | NA | Yes | Murray |
| 26 | No[a] | Dibromide[e] | Lab | >2 year | 2 year | NA | NA | Yes | |
| 45 | No[a,b] | Papain powder | Laboratory | $3\frac{1}{2}$ year | 2 year | Positive[c] | NA | Yes | Flindt |
| NA | NA | Green coffee dust[e] | Food processing | NA | NA | NA | NA | No | NIOSH |
| 40 | NA | Isocyanates | Autobody painting | NA | NA | NA | NA | NA | Anonymous |
| 43 | Yes[b] | Toluene diisocyanates | Autobody painting | >20 year | 20 year | NA | (TDI) $FEV_1$ 60% fall | Yes | Fabbri |
| 34 | No[b] | Diphenylmethane diisocyanate | Steel foundry | >6 year | 6 year | Negative[d] | (MDI) $FEV_1$ 44% fall | Yes | Carino |
| 42 | No | Flour | Bakery | 20 year | 5 year | Negative to flour, positive to wheat and maize[c] | (flour) $FEV_1$ 73% fall | No | Ehrilch |
| 38 | NA | Shark cartilage | Milling | 8 year | 6 month | NA | NA | Yes | — |

NA indicates not available; —, current report.
[a]Atopy was defined by history.
[b]Atopy was defined by a positive skin prick test (SPT) to common allergens.
[c]SPT was used.
[d]RAST was used.
[e]Two cases.

level was 822 IU/ml [Ehrlich, 1994]. In a case where toluene diisocyanate (TDI) was the etiologic agent, demonstration of IgE-sensitization was not attempted but specific inhalation challenge test was strongly positive [Fabbri et al., 1988]. In a case where 4,4′-diphenylmethane diisocyanate (MDI) was the responsible agent, specific inhalation challenge test was strongly positive despite a negative radioallergosorbent test (RAST) for serum specific IgE [Carino et al., 1997].

For isocyanate asthma, detection of IgE sensitization has not been consistently found [Mapp et al., 1997]. The absence of sensitive and specific serological and skin prick tools for demonstrating sensitization makes attribution of asthma caused by isocyanates more challenging. The gold standard for diagnosis, specific inhalation challenge, is not generally available [Ortega et al., 2002]. Findings reported in fatal OA are consistent with findings in non-fatal OA, where tests for specific IgE-sensitization to high molecular weight agents are more likely to be positive than those to low molecular weight agents [Chan-Yeung and Malo, 1995; Weissman and Lewis, 2000]. Many factors may contribute to poor test performance for IgE-sensitization to low molecular weight agents, including methodologic considerations and lack of a proven etiologic role for specific IgE in OA induced by many of these agents.

Identification of severe asthma and subsequent increased risk for fatal asthma pose a major challenge in management of both occupational and non-OA. The magnitude and frequency of symptoms—the most commonly used indicators—are unsatisfactory for estimating asthma severity as these often do not correlate with objective measures of pulmonary function. Patients may complain of severe symptoms of asthma, yet have normal spirometry and bronchial reactivity to methacholine. Conversely, other patients may report no symptoms of airways obstruction until it is far advanced [Rubinfeld and Pain, 1976]. Such individuals may only be identified as being at risk for severe asthma or even death by obtaining objective measures of spirometric performance and bronchial hyperreactivity.

Frequently, adverse outcomes result from underestimation of asthma severity, underuse of objective measurements to assess disease activity, and underuse of therapeutic drugs. It is possible that in the near future assessment for genetic polymorphisms will facilitate identification of cases at increased risk for fatal asthma. Particularly in OA, early identification and removal from exposure to environmental agents causing asthma (including those not traditionally recognized as sensitizers) can be of critical importance.

In the current report, despite the lack of objective measurements of specific IgE-sensitization or work-related changes in pulmonary function, the case history supports shark cartilage dust as the etiologic agent both for the induction and exacerbation of this individual's fatal OA.

The prognosis of OA is poor in workers who continue to be exposed to the sensitizing agent. Conversely, cessation of

exposure can minimize, or even cure OA [Tarlo et al., 1995]. Thus, diagnosis and treatment of workers with OA represent an opportunity to prevent recurrences in those workers (tertiary prevention), to prevent clinical asthma in sensitized but asymptomatic individuals (secondary prevention), and to prevent sensitization in co-workers and those in similar jobs (primary prevention) [NIOSH Alert, 1998]. Identification of sentinel cases of OA should trigger a series of preventive measures that might include substitution of non-asthmagenic materials in manufacturing processes, limitation of exposure by removal from exposure, and engineering controls. This is particularly important since previous reported fatalities occurred two or more years after onset of symptoms. Even in reported cases of fatal OA, a window of opportunity to prevent disease progression and death by removal from exposure to offending agents existed for a period of months to years after the onset of symptoms.

Respirators are the least preferred method of controlling worker exposures and should not be used as the only control for routine operations, but may be protective as other controls (such as engineering controls) are put in place. If a respirator is recommended, selection must be based on the hazard to which the worker is exposed. Choices could include cartridge-containing negative pressure respirators or powered air-purifying respirators, which allow better comfort and communication. The workers must be fit-tested and trained in the correct use of the respirator as well as its limitations [ATS, 1996]. Particularly for sensitizing asthma, disposable paper mask respirators are unlikely to be sufficiently protective, as was the case in the current report. Thus, respirators should not be used as the sole intervention for reducing exposure to agents causing OA. Removal of affected workers from exposure must be considered when clinically appropriate.

Many of the particulates generated by grinding and milling activities, including shark cartilage, are among the ''particulates which are not otherwise classified or regulated'' (PNOC/R). Setting new or lower regulatory controls have many obstacles and many ''non-toxic'' respirable dusts likely contribute to chronic obstructive respiratory disease [Becklake, 1998]. For asthma-causing agents, existing permissible exposure limits are rarely protective, even when substance-specific, since standards are not designed to protect the susceptible. Thus, physicians cannot assume that there is a safe workplace for their asthma patients even when applicable laws exist and employers are compliant. Efforts to document presence or absence of work-related patterns are critical to patient management, consideration of respiratory protection and counseling. Recognition of occupational causes and triggers of asthma can result in prevention of progression to irreversible asthma and death if further exposure is avoided. Exposure reduction may require work restriction, job change, effective respiratory protection, and enlisting public health authorities to recommend engineering controls, screen co-workers at risk, and explore exposure-response relations as a basis for hazard recognition and control.

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