Cobalt asthma in metalworkers from an automotive engine valve manufacturer

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Background
Cobalt asthma has previously been described in cobalt production workers, diamond polishers and glassware manufacturers.

Aims
To describe a case series of occupational asthma (OA) due to cobalt, identified at the Birmingham Heartlands Occupational Lung Disease Unit, West Midlands, UK.

Methods
Cases of cobalt asthma from a West Midlands' manufacturer of automotive engine valves, diagnosed between 1996 and 2005, were identified from the SHIELD database of OA. Case note data on demographics, employment status, asthma symptoms and diagnostic tests, including spirometry, peak expiratory flow (PEF) measurements, skin prick testing (SPT) and specific inhalational challenge (SIC) tests to cobalt chloride, were gathered, and descriptive statistics used to illustrate the data.

Results
The natural history of presentations has been described in detail, as well as a case study of one of the affected workers. Fourteen metalworkers (86% male; mean age 44.9 years) were diagnosed with cobalt asthma between 1996 and 2005. Workers were principally stellite grinders, stellite welders or machine setter-operators. All workers had positive Occupational Asthma SYStem analyses of serial PEF measurements, and sensitization to cobalt chloride was demonstrated in nine workers, by SPT or SIC.

Conclusions
We have described a series of 14 workers with cobalt asthma from the automotive manufacturing industry, with objective evidence for sensitization. Health care workers should remain vigilant for cobalt asthma in the automotive manufacturing industry.

Key words
Cobalt; hard metal; metalworking fluid; occupational allergy; occupational asthma; occupational respiratory disease.

Introduction
Occupational cobalt exposure confers an increased risk of sensitizer-induced asthma [1–6] as well as allergic dermatitis and hard metal lung disease [7–9]. Cobalt asthma has been reported in diamond polishers [10–14], cobalt and hard metal production workers [4,5,15,16] and a glassware factory worker [17] but is rarely described in metalworkers [18] or welders. We describe a case series of cobalt asthma in metalworkers from an engine valve manufacturing company encountered at the Birmingham Heartlands Occupational Lung Disease Unit between 1996 and 2005.

Methods
Cases of cobalt asthma from a manufacturer of stellite-tipped steel engine valves, confirmed between 1996 and 2005, were identified from the Midland Thoracic Society’s Rare Respiratory Disease Registry Surveillance Scheme of Occupational Asthma (SHIELD) database, a voluntary reporting scheme for occupational asthma (OA) in the West Midlands, UK [19]. For each worker, case note data regarding demographics (age, gender, ethnicity, co-morbidity, atopy, smoking status), employment duration, asthma symptoms at diagnosis and work effect were gathered, along with details of diagnostic tests: (i) skin prick testing (SPT) to common aeroallergens and to 1–10 mg/ml cobalt chloride, (ii) urinary cobalt concentration (μg/l), (iii) two hourly peak expiratory flow (PEF) measurements analysed using Occupational Asthma SYStem (OASYS) [20], (iv) non-specific bronchial responsiveness (NSBR) to methacholine challenge tested using the Yan method [21], (v) spirometry measured according to European Respiratory Society/
Results

Illustrative case: Worker 2

A 39-year-old worker was referred by the company occupational health service, with an 18 month history of chest tightness, breathlessness on exertion, wheeze, blocked nose and runny nose. His symptoms became progressively worse throughout the working week and were better away from work on holiday. He had no past medical history. There was no family history or prior history of asthma, hay fever or cat allergy and he had never smoked cigarettes regularly. He used a 100 μg salbutamol metered-dose inhaler infrequently for asthma symptoms. The worker had been employed at the company for 4 years on day shifts as a machine setter-operator, which included grinding and polishing of stellite valve seats. Clinical examination and chest radiograph were normal. Spirometry revealed FEV₁/forsed vital capacity (FVC) = 78%, FEV₁ = 3.41 l (78% predicted) and FVC = 4.38 l (82% predicted) with normal gas transfer measurement (diffusing capacity = 11.95 ml CO/min/mmHg; 98% predicted). He was moderately hyper-reactive to methacholine while still exposed at work (PD₂₀ = 713 μg). SPTs revealed a 6 mm wheal to histamine control, 6 mm to dermatophagoides pteronyssinus and 4 mm to cat dander. Analysis of two hourly PEF monitoring revealed definite OA, with an OASYS score of 4.0 (Figure 1). Total serum immunoglobulin E (IgE) measured 932 kU/l (reference range 0–200 kU/l), urine cobalt concentration was 3 μg/l suggesting occupational exposure (UK population reference range 0.12–1.9 μg/l) [24], white blood cell count was 9.7×10⁹/l (normal range 4.0–11.0×10⁹/l) and eosinophil count 0.03×10⁹/l (normal range 0–0.44×10⁹/l). The worker underwent SIC to nebulized 1 mg/ml cobalt chloride solution in a buffered solution to pH 6.8 (three active challenges totalling 5 min). At 11 h post-challenge, he experienced wheeze and chest tightness, resembling his symptoms at work, and a late fall in FEV₁ from 4.00 l by 20%, to 3.21 l (Figure 2). FEV₁ continued to drop to 3.17 l/min (−21%) at 12 h post-challenge. The worker underwent three control exposures to nebulized 0.9% saline, lasting 5 min in total, with an immediate but non-sustained fall in FEV₁ of 11.6% accompanied by a brief episode of light headeness, but no asthma symptoms, and then no change in FEV₁ over 12 h following the challenge. Additionally, he experienced a 3-fold increase in NSBR from a baseline PD₂₀ of >4800 μg to 1500 μg 24 h post-challenge to cobalt chloride. The worker was diagnosed with OA due to sensitization to cobalt and was moved to quality control inspection. However, his bench was situated within 10 m of stellite grinding machines, and serial PEF monitoring and urine cobalt measurements at 12 months after diagnosis indicated ongoing exposure. The worker was granted ill-health retirement and found alternative work as a postman.
Figure 1. Serial PEF measurements from Worker 2 were analysed using OASYS. The plot showed OA and OASYS score was 4.0. The top part of the chart shows the diurnal variation (DV) for each day. The middle of the chart shows the maximum, mean and minimum peak flow for each day. Workdays are shaded (diagonal slash bars are afternoon shifts, diagonal backslash bars are morning shifts) and the rest days are blank. The horizontal lines containing numbers in this part of the chart are scores for the work–rest–work and rest–work–rest complexes (seven complexes in total in this record). The bottom of the record shows the days, dates and number of readings per day for the record.

Figure 2. SIC to nebulized 1 mg/ml cobalt chloride from Worker 2. The FEV₁ fell by 20%, from a baseline of 4.1 l to 3.21 l at 11 h post-challenge. After control challenge with nebulized 0.9% saline solution, FEV₁ remained within 15% of baseline.
Case series

Fourteen workers were diagnosed with OA due to cobalt, including the illustrative case. One further worker had OA with a positive SIC to used MWF but negative SIC to cobalt chloride 1–10 mg/ml. The demographics and diagnostic characteristics of the 14 workers with cobalt asthma are shown in Table 1. Twelve employees worked directly with stellite (six machine setter–operators, five stellite grinders, one stellite welder) and two indirectly (one packer and one electrician). All cases were diagnosed between 1996 and 2005, with a peak incidence of five cases diagnosed in 1999 (see Figure 3). The median duration of employment prior to onset of symptoms was 8 years (IQR = 2.5–17.8) and median symptom latency prior to diagnosis was 30 months (IQR = 24–48). Cough (93%) and wheeze (93%) were the most commonly reported symptoms and 43% of workers had work-related rhinitis symptoms at diagnosis. All 14 workers reported symptoms that were better away from work at the weekend or on holiday. Seven out of 10 (70%) workers tested in clinic had urine cobalt concentration >2 μg/l, the level associated with occupational exposure (median = 2.6 μg/l; IQR = 1.7–8.5). OASYS analysis of serial PEF readings from all 14 workers demonstrated OA (OASYS score range 3.0–4.0). Nine workers had evidence of sensitization to cobalt, either by positive SIC to 1–10 mg/ml cobalt chloride (n = 6) or positive SIC to nebulized cobalt chloride 1–10 mg/ml (n = 7), or both. The details of positive SICs are shown in Table 2; there were three immediate, three dual and one late asthmatic reactions to cobalt chloride. The remaining five workers were diagnosed with cobalt asthma on the balance of probability, based on positive PEF records, clinical presentation and exposure patterns. Following diagnosis, eight cobalt workers were relocated within the company (three of whom remained exposed), two were retired, two made redundant and two remained exposed in the same job.

Discussion

Fourteen metalworkers from a single manufacturing company were diagnosed with OA due to cobalt between 1996 and 2005. Principally, workers were stellite grinders, stellite welders or machine setter–operators. All workers experienced asthma symptoms that were better away from work, either on days off or on holiday, and many showed features of occupational rhinitis (43%). All workers had positive OASYS analyses of serial PEF measurements, and sensitization to cobalt chloride was demonstrated in nine of those workers by SPT or SIC.

Since 1989, new cases of OA in the West Midlands, UK, have been prospectively reported to the Midland Thoracic Society's SHIELD voluntary surveillance scheme, by regional respiratory and occupational physicians. Thus, the strength of this study is that we were able to identify all cases of cobalt asthma from a single employer. SHIELD receives notifications when OA is demonstrated in nine of those workers by SPT or SIC. One additional worker (machine setter–operator) had a negative SIC to cobalt chloride and positive challenge to contaminated MWF, so there is the potential for attributing asthma to the incorrect agent.

We have provided evidence for a sensitization mechanism in nine workers, with positive SICs and SPTs.
to cobalt chloride, accompanied by a mean latency of exposure of 8 years (IQR = 2.5–17.8) prior to symptom onset. This is consistent with documented reports of sensitization to cobalt in asthma [1–6] and dermatitis [25,26] in occupational settings. Both IgE-dependent [15] and non-IgE-dependent mechanisms have been implicated [16]. The workers in our series were predominantly atopic (64%), with positive SPTs to cobalt chloride (75%), and six of seven positive SICs to cobalt chloride were immediate (including dual) asthmatic reactions. This is suggestive of a predominant IgE-mediated response, although the measurement of serum-specific IgE to cobalt would have been helpful in this regard.

Figure 3. Timeline of incident cases of cobalt asthma, by occupation. The index case was diagnosed with cobalt asthma in 1996, nine further cases were identified between 1998 and 2001, along with a case of contaminated MWF-related OA, and four further cases of cobalt asthma were diagnosed between 2003 and 2005. Grey-shaded boxes represent night-shift workers, unshaded boxes represent day-shift workers.

Table 2. Characteristics of all SIC tests undertaken

<table>
<thead>
<tr>
<th>Worker</th>
<th>Pre-SIC PD_{20} (μg)</th>
<th>Post-SIC PD_{20} (μg)</th>
<th>Nebulized control challenge</th>
<th>Active nebulized challenge</th>
<th>% Max immediate reaction</th>
<th>% Max late reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>260</td>
<td>140</td>
<td>MWF (1% solution); 15 min</td>
<td>Cobalt chloride 10 mg/ml; 3 min</td>
<td>−34.8</td>
<td>−31.4</td>
</tr>
<tr>
<td>2</td>
<td>&gt;4800</td>
<td>1500</td>
<td>0.9% saline; 5 min</td>
<td>Cobalt chloride 1 mg/ml; 5 min</td>
<td>−9.5</td>
<td>−20.7</td>
</tr>
<tr>
<td>3</td>
<td>&gt;4800</td>
<td>&gt;4800</td>
<td>Aluminium chloride 10 mg/ml; 5 min</td>
<td>Cobalt chloride 10 mg/ml; 5 min</td>
<td>−17</td>
<td>−20</td>
</tr>
<tr>
<td>4</td>
<td>&gt;4800</td>
<td>&gt;4800</td>
<td>Clean MWF (1% solution); 15 min</td>
<td>Cobalt chloride 1 mg/ml; 10 min</td>
<td>−26.8</td>
<td>−18.3</td>
</tr>
<tr>
<td>5</td>
<td>3235</td>
<td>2609</td>
<td>0.9% saline; 20 min</td>
<td>Cobalt chloride 5 mg/ml; 20 min</td>
<td>−17</td>
<td>−10</td>
</tr>
<tr>
<td>6</td>
<td>709</td>
<td>272</td>
<td>Aluminium chloride 5 mg/ml; 12 min</td>
<td>Cobalt chloride 5 mg/ml; 17 min</td>
<td>−22.9</td>
<td>−10.9</td>
</tr>
<tr>
<td>7</td>
<td>4800</td>
<td>2400</td>
<td>Clean MWF (1% solution); 5 min</td>
<td>Cobalt chloride 10 mg/ml; 5 min</td>
<td>−19.2</td>
<td>−16</td>
</tr>
<tr>
<td>Other worker</td>
<td>&gt;4800</td>
<td>&gt;4800</td>
<td>Cobalt chloride 10 mg/ml; 5 min</td>
<td>Used MWF (2% solution) for 10 min</td>
<td>−18.4</td>
<td>−12.6</td>
</tr>
</tbody>
</table>

PD_{20}, provocative dose that decreases FEV\textsubscript{1} by 20%, methacholine reactivity by the Yan method [21].

aGreater than 1 h and up to 12 h post-challenge.
Although we have previously reported a single case of cobalt asthma from the automotive manufacturing industry [18], this is the first case series in metalworkers described in detail. Cobalt asthma has been reported in cobalt production workers [7–9], diamond polishers [10–14] and a glassware factory worker [17]. Cobalt production workers have higher exposures [4,16] compared with other cobalt industries [27], and exposure from production work confers a 5-fold risk of asthma over non-exposed workers [5]. Our workers showed modest increases in urinary cobalt concentration (median = 2.6 μg/l) in keeping with non-production work exposures. We postulated that workers’ cobalt exposure increased significantly, firstly when a common sump for used MWF was installed, widely distributing cobalt-contaminated oil mist, and secondly when ventilation systems were switched off overnight to decrease noise.

We have described a case series of 14 workers with cobalt asthma from the automotive manufacturing industry, with objective evidence for sensitization in the majority of cases. Hard metal-tipped machine tools and stellite alloys are in common usage in automotive manufacturing, and so health care professionals should remain vigilant for cobalt asthma in this industry.

Key points
• This study describes a case series of cobalt asthma in stellite grinders, welders and machine setter-operators from a manufacturer of engine valves.
• Sensitization to cobalt chloride was demonstrated in the majority of workers by skin-prick testing or specific inhalational challenge.
• Cobalt asthma occurs in the automotive manufacturing industry, where carbide-tipped machine tools and cobalt alloys are commonly used.

Conflicts of interest
None declared.

References
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**Neurological memories**

One of my pleasures in reading journals is the stirring of memories, as when I read Dr Sealy’s informative paper on the management of dizziness [1]. It started with a pithy quote from Dr WB Mathews’ book, *Practical Neurology*, published in 1963. How well I remember it! At that time, as a young medical registrar, I was attracted to a career in neurology and obtained a post that gave me a great deal of practical experience of the subject. Indeed, there was rather more than I would have wished for, as my consultant’s main interest was in his private practice and he expected me to do his clinics with the help of the house physician. I was familiar with the standard large textbooks of neurology but quickly found they were deficient in practical advice on management. Dr Mathews’ book was a lifesaver, as it dealt with presenting symptoms rather than anatomical syndromes—headache, dizziness, blackouts, etc. I quickly became an adequate substitute for my boss.

Why did I not become a neurologist? It would certainly have become progressively easier as modern diagnostic techniques displaced carotid and vertebral angiograms, air encephalograms and frequent lumbar punctures, but it was not to be. I finally lost patience with my boss when he refused to come to his clinic to help me when my wife ran into difficulties in labour and I got my revenge by starting my outpatient letters with ‘I saw your patient in the unexpected absence of Dr X’. It worked—he got a curt message from the professor of medicine, but I was instructed to change the format of my letters and when I refused he said: ‘Don’t ever ask me for a reference, Seaton!’ So I went into cardiology then chest medicine and later added occupational medicine. In contrast, the house physician decided that medicine was not for him and became a knighted president of a surgical Royal College.

In my day one didn’t train formally in medicine. It was necessary every year or so to apply for the jobs one thought appropriate, while in one’s spare time (before study leave) one wrote papers, passed exams, tried to do research and taught medical students, activities which in that very competitive world increased one’s chances of obtaining the jobs one wanted. My knowledge of cardiology led me to propose a hypothesis to explain the cardiac effects of air pollution and to delve into the effects of inhaled nanoparticles. My experience of chest medicine led me to propose an explanation for the increase in asthma in relation to maternal diet during pregnancy. My interest in neurology led me to studies of neurological effects of chemicals and to propose that significant exposures to solvents may have diverse effects on the nervous system depending on the genetic susceptibilities of the individual. And Dr Mathews’ book inspired me to write with my colleagues a similar book for trainee occupational physicians, *Practical Occupational Medicine*. I hope you have a copy.

**Anthony Seaton**

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**Reference**