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EDITORIAL

Justification for screening for chronic beryllium disease: closer to reality

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Chronic beryllium disease (CBD) appeared to be waning 30 yrs ago [1]. In 1980, less than one case per year was reported and the incidence rate per ton of beryllium produced had declined from between five and 10, to less than 0.001. CBD appeared to be heading toward the medical archives as a success story of environmental control in the absence of understanding of the pathogenesis of the disease. However, in 1982, an immunological test performed on lymphocytes recovered from the bronchoalveolar lavage fluid demonstrated a marked increased in the number of beryllium-sensitive cells in the lung compared to the blood, strongly suggesting that CBD was a hypersensitivity to beryllium [2]. The findings of that initial study were confirmed in larger studies [3] and by different investigators [4, 5]. Around 10 yrs later, an immunological test (the beryllium lymphocyte proliferation test (BeLPT)) was initially used in cross-sectional studies and later in the surveillance and screening of current and former beryllium workers [6–8]. Those studies demonstrated that CBD was not heading for the medical archives, but that the disease was present in much greater numbers than previously reported due to misdiagnosis of overt cases and the detection of early and asymptomatic cases through immunological testing.

There are several aspects of beryllium disease that could account for this phenomenon. First, there is a long latency from exposure to the onset of the disease, thought to be ~10 yrs, although cases have been diagnosed as long as 40 yrs after initial exposure [1]. Secondly, the minimal amount of exposure necessary to cause the disease is not known, and the amount of exposure that was known to cause the disease is incredibly low. Reports from around the world now demonstrate that beryllium disease can result from processes that were thought to be safe, *i.e.* use of metal alloys with low concentrations of beryllium (<2%) [9].

Beryllium's ability to make metals easier to work with and more durable has led to its use in alloys (along with copper), dental bridges and crowns, and jewellery. Jewellers in France [10], dental technicians in Germany, Israel [11, 12] and the USA [13], and workers in metal reclaiming processes [14] have all been found to be at risk. In addition to current and former beryllium workers, community residents living near beryllium processing plants have been shown to be a risk for beryllium disease, both as a result of beryllium taken into the home on workers' clothes (para-occupational) and due to contamination of the ambient air. In the 1940s and 1950s, cases were reported in Loraine (OH, USA) [15] and Reading (PE, USA) [16], but until now, no new cases have been reported in the medical literature. In a recent issue of the *American Journal of Respiratory and Critical Care Medicine* [17], eight cases of newly diagnosed and recognised beryllium disease were reported in individuals who lived within 1 mile of a beryllium processing plant. The exposures of all these individuals dated from the 1950s. These reports suggest that beryllium disease is certainly much more frequent than suspected and involves populations that were not previously thought to be at risk or were thought to be at extremely low risk for the disease.

The continuing presence and lifetime risk for the development of beryllium disease raises the question as to whether medical screening is useful. For medical screening to be useful, three criteria must be met. First, there must be a test that can detect the disease or process before it manifests clinically. Secondly, the disease process detected should cause significant impairment. Thirdly, there should be a treatment available that can arrest or prevent the manifestations of the disease. There is no question that BeLPT can detect beryllium disease before it becomes manifest. However, many individuals that develop a positive BeLPT may never develop clinical disease. A previous study suggests that one-third of individuals identified with only a hypersensitivity reaction to beryllium may develop granulomatous lung disease within 5 yrs [18]. Whether they will develop physiological impairment is not clear.

In this issue of the *European Respiratory Journal*, MARCHAND-ADAM *et al.* [19] address the issue of whether there is a treatment that can prevent or control the disease. The late 1950s' report by SEELER [20], which summarised the beryllium case registry experience with treatment, strongly suggested that corticosteroids were only effective if used early in the disease. As a result, corticosteroids and other immunosuppressive medication are considered to be the standard of treatment, and there never have been nor will there ever be controlled trials. The study by MARCHAND-ADAM *et al.* [19], which is the best report of treatment in patients with a confirmed immunological diagnosis of CBD, confirms the earlier report of SEELER [20] and describes computed tomography (CT) findings that appear responsive to corticosteroids. Eight patients with immunologically confirmed CBD were treated with corticosteroids; a 26% improvement was noted in

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vital capacity and a 15% improvement was seen in diffusion capacity of the lung for carbon monoxide. In six of the eight patients, the treatment appeared to stop progressive fibrosis. The study by MARCHAND-ADAM *et al.* [19] confirms the earlier report by SEELER [20] and strongly suggests that cases of beryllium disease that could be detected through medical screening programmes would benefit from corticosteroid therapy.

Nevertheless, the role of immunological screening for chronic beryllium disease will remain controversial [21, 22]. The identification of populations at risk potentially includes not only current workers but also former workers, contract workers who visit beryllium plants to perform construction or repairs, inspectors of beryllium plants (such as National Institute for Occupational Safety and Health inspectors) and, finally, community members who live near plants where air pollution is known to occur. The individuals with potential exposure to beryllium, the practitioners who care for them, and the industries and the insurers who will have to pay for the costs of screening will continue to struggle with the question as to whether immunological screening should be performed and if so, how frequently.

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