Raynaud’s Phenomenon and other serious health risks from laboratory work with solvents

Gordon L Purdie, Dianne J Purdie and Andrew A Harrison

Because Raynaud’s Phenomenon (RP) appeared to be common in a cytology department, where it was thought of as a normal part of growing old for women, we suspected something in the work environment or a work practice might be causing RP. RP is associated with many conditions and is normally seen as colour changes in fingers in cold, typically white and blue. When considering conditions associated with RP and possible work-related causes we thought that, if there is a high rate of RP among cytology department workers, it might be caused by solvent exposure. There is evidence that solvent exposure causes scleroderma (1,2), an autoimmune connective tissue disease with RP being a common symptom. The solvent xylene is normally used in cytology and histology. We conducted a postal survey of scientists, technicians and laboratory assistants from cytology, histology and transfusion medicine departments. It was hoped that most of those from transfusion medicine would have not worked with solvents.

Raynaud’s Phenomenon and solvents

We found that laboratory workers who had worked with solvents had more than double of the rate of severe RP and have published the survey in the Journal of Rheumatology (3). Eight percent of those who had worked with solvents had severe RP compared with 3% among those who had not worked with solvents. After adjusting for age and sex, those who had worked with xylene or toluene and either acetone or chlorinated solvents had an almost nine times greater risk of severe RP. Higher rates of severe RP were associated with longer durations of working with xylene or toluene.

Given the evidence that solvents might cause scleroderma and undifferentiated connective tissue disease (signs, symptoms and laboratory abnormalities that suggest a connective tissue disease, but which do not meet criteria for any specific rheumatic disease) (4,5), these increased rates of severe RP could be early preclinical scleroderma or another connective tissue disease. Other signs of early scleroderma include antibodies and nail-fold capillary abnormalities. RP, with some of these signs, is predictive for scleroderma (6,7). Our findings could be of serious concern since scleroderma and some another connective tissue diseases have high morbidity and mortality.

Other solvent related diseases

As well as this evidence linking solvent exposure to RP and connective tissue diseases and there is also some evidence linking solvent exposure to multiple sclerosis (8). Solvent exposure also causes central neurotoxicity, peripheral neuropathy, acute poisoning and contact dermatitis (9). Solvent exposure has also been linked to renal failure, reproductive disorders, multiple chemical sensitivity, and several cancers, particularly laryngeal, naso-pharyngeal, bladder, leukaemia, non-Hodgkin’s lymphoma and multiple myeloma (9).

Minimising solvent exposure

There is no known safe level of solvent exposure. Solvents are absorbed though our lungs and skin. Skin absorption occurs from the air and from direct contact (10). The Department of Labour also produces Workplace Exposure Standards (WES) (11). Its levels are not upper limits of safe exposure. We do not know what vapour levels have been in medical laboratories. However, there are historical references to high levels in medical laboratories. One study reported xylene concentration in the atmosphere at a hospital laboratory well above the Threshold Limit Value (12). Another found, with no extraction fans operating, a xylene level of 75 ppm, above the WES of 50 ppm, and a formaldehyde level of 13 ppm (the WES has a ceiling of 1 ppm) (13). For xylene the WES does not consider skin contact. It also does not consider interactive effects of simultaneous exposures. Ketones interfere with the metabolism of several solvents (14). Acetone is a ketone that is used in medical laboratories. In rats and mice, blood concentration of xylene was higher with simultaneous acetone exposure and its decline slower than without acetone exposure (15). This was a large effect and suggests the WES should be considerably reduced when both these solvents are used. Xylene is not cleared within 24 hours, hence with daily exposure there will be increasing body levels (16).

In our survey 81% of people working in histology or cytology departments had handled wet slides without gloves. Skin absorption models have been developed (10), showing that when air levels are low skin contact with xylene could be the main exposure source. For example, they suggest that there is similar absorption of xylene from having 100cm² of skin exposed for 10 minutes to inhaling vapour for 8 hours at one fifteenth of the WES.

In 1992 the Department of Labour produced guidelines for the safe use of organic solvents (17). These recommend elimination, if not practicable isolation, and if exposure was unavoidable then minimisation.

Wearing appropriate gloves is a simple way to reduce one source of exposure. At the time of our survey, mid 2006, 49% of people working in histology and cytology had worked with xylene or toluene wet slides without gloves during 2006. The 1992 Department of Labour guidelines recommend the use of viton gloves for xylene and toluene as it provides excellent protection. Nitrile gloves provide fair protection from xylene and toluene and are not recommended. Nitrile is permeable to some organic solvents, including xylene and toluene which come through the gloves after about an hour and half an hour respectively (18). Different solvents require different gloves, for example, viton and nitrile are rated as poor for acetone and butyl excellent.

When to go the doctor

RP is common. Our research has confirmed a prevalence in New Zealand comparable with countries with a similar climate; about 20% of women and 5% of men (19). In most cases it is a relatively benign complaint. Cold hands and colour changes are the most common symptoms, but in some cases pain and numbness can interfere with daily activities. In rare cases it may be severe enough to cause digital ulcers and even gangrene. RP is sometimes associated with chilblains, especially in younger people, causing transient localised red plaques, itch and a burning sensation in the affected areas. People with RP should see their general practitioners if the symptoms are easily provoked, occur in warm temperatures, impinging on function or causing concern or significant discomfort. Investigations may be performed if the history and examination suggest that RP may be a symptom of a more generalised autoimmune condition, particularly in cases of new-onset RP in adults.
Medical advice should be sought in all cases where the onset of symptoms follows exposure to solvents. This is because solvent exposure can, in rare cases, lead to the development of connective tissue diseases, of which RP may be an early manifestation.

**When to eliminate exposure**

If you are concerned that solvent exposure is giving rise to problems with your health, or may do so in the future, you may wish to eliminate your exposure to solvents. We do not know if solvent exposure only initiates these diseases or whether continued exposure makes them worse. Cancers might be initiated, and neurotoxicities made worse. Magnant et al found some differences in patients with scleroderma between those occupationally toxically exposed and others, suggesting that the exposures influence the severity of scleroderma (20). They hypothesized that toxic agents may amplify the cellular response rather than the humoral response and that people with scleroderma should stop continued exposure. If you have signs or symptoms that could be early CTD a precautionary approach would be to eliminate your solvent exposure.

**Author information**

Gordon Purdie, BSc, Senior Research Fellow
Dianne Purdie (nee Stanley), CT(ASC) CT(IAC)
Andrew Harrison, MB ChB FRACP PhD, Rheumatologist and Associate Professor

1Dean's Department, University of Otago Wellington, New Zealand
2Wellington, New Zealand
3Department of Medicine, University of Otago Wellington, New Zealand

**Corresponding author**

Gordon Purdie, Department of Public Health, University of Otago Wellington, PO Box 7343, Wellington South, New Zealand. E-mail: Gordon.Purdie@otago.ac.nz

**References**