



Could exposure to methyl bromide cause motor neurone disease?

There is significant speculation about the role that exposure to the fumigant, methyl bromide (MeBr) might have played in the incidence of motor neurone disease (MND; also termed amyotrophic lateral sclerosis [ALS]) in Nelson port workers. There are two important considerations in determining whether MeBr could be responsible. The first is, do the cases represent a cluster?—i.e. is the observed incidence in the exposed workers greater than the incidence in the general New Zealand population? And secondly is there a mechanistic rationale for MeBr initiating the neurodegeneration that leads to MND? It is the latter of these two considerations that I will address here.

MND is the common endpoint of a multifactorial pathway. It is known to be familial in some cases and therefore can have genetic origins—9.5% of MND sufferers have a family history of the disease.¹ It involves free radical toxicity (resulting from exogenous chemical exposure or endogenous free radicals such as superoxide via the xanthine uric acid pathway) to the spinal cord leading to irreversible damage and consequent neurodegeneration.² Indeed, defects in the superoxide dismutase (SOD) gene with consequent low SOD activity and reduced superoxide free radical detoxification have been shown to occur in sub-groups of MND patients.^{3,4} The risk of developing the disease is likely to be greater with coincidence of a multiple risk factors. The disease is relatively rare with a world incidence of 2/100,000 population and therefore to find 5 cases since 2002 in a sub-population of Nelson (total population 87,000) is high especially as they all worked in the same port.

Exposure to free radical generating chemicals is a likely risk factor in MND; at low doses such exposure is unlikely to induce MND in people with 'normal' free radical detoxifying mechanisms such as SOD and glutathione (GSH). However excessive exposure could overpower such mechanisms allowing survival and consequent interaction of highly reactive free radicals with neurones in the spinal cord so initiating neurodegeneration.

MeBr is a free radical generator. It generates the highly reactive methyl ($\bullet\text{CH}_3$) and bromine ($\bullet\text{Br}$) free radicals.⁵ It is possible that workers regularly exposed to MeBr could receive a sufficiently high free radical insult to overpower neuronal cellular protection mechanisms. We should, therefore, not rule out the Nelson workers exposure to MeBr as a factor in their development of MND.

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