

# Editorial

## Solvents and the brain

Probably the first indication that an organic solvent might affect behaviour (and by inference, the brain) was given by the French physician August Delpech in 1856. In that year Delpech published a report on a series of 24 patients whom he had seen suffering from insomnia, frightening dreams, extreme irritability, sexual difficulties, and outbursts of ferocious rage. The patients had all been exposed to carbon disulphide during the cold curing of rubber in small, poorly ventilated workplaces which had sprung up in Paris to satisfy the demand for balloons made from the newly introduced rubber coated fabric. Some of those who had been exposed to the carbon disulphide vapour had become so agitated that they had thrown themselves to their deaths from the windows of the rooms in which they had worked. Cases of carbon disulphide psychosis continued to be reported in France during the 1870s and 1880s after which time they were also reported in Germany and in America. At the turn of the century, the process of making viscose rayon was introduced. This process required the use of carbon disulphide and, among those exposed to it during the first half of the present century, psychiatric symptoms were relatively common; the syndromes noted were described in a classic paper by Braceland in 1942.<sup>1</sup>

After Delpech's original observations, there was no room for doubt that exposure to some solvents might result in the appearance of a toxic organic psychosis, but the number of such cases in industry has tended to fall in the wake of improvements in occupational hygiene and the general lowering of exposure levels. In the early 1970s, however, carbon disulphide was again in the news when Hänninen reported that exposed workers performed significantly less well in a battery of psychological tests than men who were not exposed, although their performance was somewhat better than that of men who had been diagnosed as having carbon disulphide poisoning.<sup>2</sup> Hänninen considered that carbon disulphide could induce a sub-clinical organic psychosis, and her investigations set in train a series of others in which similar effects were looked for in other groups of solvent workers.

In 1976 Axelson and his colleagues added a further dimension to this problem when they published the results of their case-referent study in which they showed that workers who retired early because of minor psychiatric disorders were about twice as likely to have been exposed to solvents than workers who took early retirement on other medical grounds.<sup>3</sup> This observation was confirmed in Denmark by Olsen and

Sabroe a few years later.<sup>4</sup> Shortly afterwards attention was focused particularly on house painters who were said to have an enhanced risk for the development of presenile dementia.<sup>5</sup>

Since then, the extent to which exposure to organic solvents may result in disabling symptoms caused by damage to the central nervous system has been a matter of considerable debate. For example, although many such cases have been described from the Nordic countries, especially in Denmark where many hundreds of solvent workers obtain compensation for occupationally induced neuropsychiatric disorders, there have been relatively few from other countries; a large study of painters in the United Kingdom found no adverse neuropsychological effects that could not be ascribed to their pre-exposure ability.<sup>6</sup> Because of these international discrepancies, a working group on the chronic effects of organic solvents on the central nervous system was convened in Copenhagen by the World Health Organisation; the report of this group has now been published.<sup>7</sup>

One of the difficulties highlighted at that meeting was that the chronic syndrome said to be produced by long term exposure to solvents has been called different things by different authors. In fact about 20 names have been given to the syndrome, which makes comparison more than a little difficult. As the report notes, the lack of a standardised approach "... impairs the interpretation of studies performed in different countries as well as international collaborative activities."

The new report describes two disorders of the central nervous system that may be caused by long term exposure to solvents, an organic affective syndrome and a chronic toxic encephalopathy that may be mild or severe. In the first syndrome disorders of mood predominate whereas the second is characterised by a change in personality, which is accompanied by core symptoms of fatigability, bad memory, difficulties in concentration, and loss of initiative. The two syndromes are not to be thought of as stages through which an individual must necessarily pass, and the severity of the symptoms varies considerably although most are mild. The core symptoms of the chronic toxic encephalopathy may be accompanied by others, including depression, dysphoria, emotional lability, headache, irritability, paraesthesiae, sleep disturbances, and vertigo.

The WHO report also gives some guide lines on the diagnosis of the syndromes which are described. Essentially, the diagnosis has to be one of exclusion since none of the symptoms is specific to solvent poisoning and even in a patient in whom no cause other than exposure to solvents can be postulated it is by no means certain that the solvent is the causative agent.

During the meeting it became clear that the chronic

effects of exposure to solvents are related to the degree and duration of exposure and that they are likely to declare themselves only after heavy (this is not defined) and prolonged (at least ten years) exposure. To what extent the symptoms are reversible once exposure is discontinued is as yet unclear, but in some cases an improvement has been noted.

The workshop made some progress towards the clarification of the nature of the chronic effects of solvent exposure—it appears that the syndrome affects a small number of those exposed to solvents (although Danish authorities may dispute this) and that the symptoms are usually mild and may be at least partially reversible. Many other issues remain unresolved, however. Thus it is not at all clear why there is such a discrepancy between the number of cases reported (and compensated) in Denmark and other countries. And what is the underlying pathological process? Is there a loss of neurones in those affected by the condition or are the symptoms the consequence of some alteration in the action of neurotransmitters? Are they the result of an effect on neuronal membranes? Nor is it clear which solvents are capable of causing the symptoms, although most attention is now being given to white spirit as being the most likely industrial solvent to do so. To what extent are the symptoms reversible? This is also not known with any degree of certainty but is clearly of importance when deciding safe levels of exposure and the extent to which the condition should attract compensation, if at all. There is an obvious and urgent need to find a suitable animal model in which this condition may be studied.

The WHO report is to be welcomed as a step towards the better understanding of the effects of solvents on the brain, and it should at least spur occupational physicians and psychiatrists to work together to find the true prevalence of the syndromes described. Those who read it, however, should be forewarned that this is by no means the last word. At a meeting held in North Carolina in October 1985 the effects were again reviewed and yet another classification was suggested and further guidelines for diagnosis put forward. Under the North Carolina scheme (which has yet to be published), the effects are grouped into three types with no reference to syndromes or encephalopathy. In type 1 the patient complains of non-specific symptoms such as fatigability, bad memory, difficulties in concentration, and loss of initiative; these symptoms are reversible if exposure is discontinued. In type 2a there is a pronounced and sustained change in personality denoted by fatigue, emotional lability, and alterations in impulse control and general mood and motivation. In type 2b there are difficulties in concentration, impairment of memory, and an impairment in the capacity to learn. These symptoms (unlike those in 2a) may be accompanied by objective evidence of impairment (as mea-

sured in psychological tests) and there may also be minor neurological signs. The complete reversibility of type 2b is questionable. Type 3 is characterised by dementia with pronounced global impairment in intellect and memory and is often accompanied by neurological signs. It is at best poorly reversible but may not progress once exposure has ceased. Types 1 and 2 are most likely to result from occupational exposure and type 3 from repeated, severe intoxication or from deliberate abuse. In recent Swedish publications type 1 would be equivalent to the so called neurasthenic syndrome and type 2 would be equivalent to the psycho-organic syndrome. In Danish publications type 2b has been referred to as "mild dementia." Types 2 and 3 correspond to the categories of "mild" and "severe" toxic encephalopathy in the WHO report.

The fact that the nomenclature could be revised—by much the same group of people—in four months tends to imply that the condition is still not as well defined or understood as one would like. Probably the North Carolina nomenclature is to be preferred, although by the time the proceedings of that meeting are published (and we are promised them soon) yet another revision may have taken place. If multicentre studies are to be carried out, and these hold the best prospect of obtaining enough cases to study, then a proper operational definition of a "case" must be arrived at. The best evidence that exposure to solvents can induce chronic effects on the brain, however, will come when they can reliably be produced in an animal model and the pathophysiology adequately shown. There is much to be done still, a century after Delpech first drew attention to the problem, to determine to what extent solvents truly are "a foul and pestilent congregation of vapours."

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