Routine diagnostic procedures for chronic encephalopathy induced by solvents: survey of experts

van der Hoek, J.A.F.; Verberk, M.M.; van der Laan, G.; Hageman, G.

Published in:
Occupational and Environmental Medicine

DOI:
10.1136/oem.58.6.382

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)
Routine diagnostic procedures for chronic encephalopathy induced by solvents: survey of experts

J A F van der Hoek, M M Verberk, G van der Laan and G Hageman

doi:10.1136/oem.58.6.382

Updated information and services can be found at:
http://oem.bmjjournals.com/cgi/content/full/58/6/382

Rapid responses
These include:
You can respond to this article at:
http://oem.bmjjournals.com/cgi/eletter-submit/58/6/382

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Topic collections
Articles on similar topics can be found in the following collections
Diagnostics (393 articles)

Notes

To order reprints of this article go to:
http://www.bmjjournals.com/cgi/reprintform

To subscribe to Occupational and Environmental Medicine go to:
http://www.bmjjournals.com/subscriptions/
Routine diagnostic procedures for chronic encephalopathy induced by solvents: survey of experts

J A F van der Hoek, M M Verberk, G van der Laan, G Hageman

Abstract

Objectives—To study the routine diagnostic procedures used in different countries for chronic toxic encephalopathy (CTE) induced by solvents.

Methods—By means of a postal questionnaire selected international experts were asked about the methods they use to diagnose patients suspected of having CTE induced by solvents, the number of patients, entrance criteria, and the results of these diagnostic procedures.

Results—18 Experts working in 18 diagnostic centres responded. Most of them agreed that a diagnostic procedure for CTE induced by solvents should contain an interview and neurological, physical, and neuropsychological examinations. However, the tests used were very different, as were the classifications for CTE. Depending on the institute, a diagnosis of CTE was made in 6%–70% of the referred patients. The proportion of patients with CTE stage I ranged from 0% to 33%, stage II from 5% to 100%, and stage III from 0% to 95%.

Conclusion—The intentions of the two 1985 conferences that aimed at clarity and uniformity of diagnosis of CTE induced by solvents are far from reached. It is possible, now the conditions are more favourable, to aim at this important goal and to propose some refinement of the then proposed criteria.

Keywords: solvents; chronic toxic encephalopathy; diagnostic criteria; classification

Material and methods

We designed a concise questionnaire (five pages, 15 questions) on the routine diagnostic investigation of patients suspected of having CTE induced by solvents. The questions investigated the number of patients referred, referral, entrance criteria, disciplines involved, applied examinations, assessment of exposure, the classification used, and the diagnoses...
made; a neuropsychological protocol was asked for. Experts were selected on the basis of authorship of articles and editorials on CTE induced by solvents. More or less worldwide coverage was intended. Twenty five questionnaires were sent out in April 1999, including five to Swedish centres because they are all involved in this field. A reminder was sent out in August 1999. All questionnaires referred to the situation in 1998.

Results
Eighteen experts in 18 different institutes returned a completed questionnaire; three experts brought up that they and the institutes where they were employed were not or no longer involved in assessing patients for CTE. So the response was 82% (18/(25−3)) at least: among the non-respondents there may be non-involved experts as well. Questionnaires were received from Sweden (five), United States (three), Denmark (two), and one each from Belgium, Croatia, Finland, France, Germany, the Netherlands, New Zealand, Norway, and Switzerland.

Referral
The number of patients referred to the 18 centres in 1998 varied from four to 142 (mean 40 patients). Patients were mainly referred by general practitioners (GPs) or occupational physicians; their contribution, however, varied greatly (fig 1), even among the five centres in one country (Sweden), where the referral by the GP ranged from 10% to 60%. Fourteen centres did not have entrance criteria with a minimum duration of exposure. The other four centres had such criteria, ranging from minimally 1 year to minimally 10 years of exposure, but exceptions were made for patients with very intensive exposure. Eight centres did not require specific symptoms or signs, five centres required cognitive or mood changes reported by the patient, and four centres required a psychometric evaluation before entry. One tertiary referral centre required that an occupational physician had already diagnosed CTE; the main function of this centre was to verify whether the disease was of occupational origin to satisfy social security requirements for financial compensation.

Diagnostic Procedure
In most centres, an occupational physician or occupational specialist and a neuropsychologist examined the patients (table 1); occupational hygienists, neurologists, or psychiatrists were usually consulted when necessary. A chemist or toxicologist was seldom involved. An interview was part of the diagnostic procedure in all centres, a physical examination in 16, neurological examination in 15, and psychological tests in 14. In most centres, blood tests, electroencephalogram (EEG), imaging of the brain, electroneuromyography (ENMG), or evoked potentials were used on indication only (table 2). Thirteen centres used one set of core tests and two used two consecutive sets of core tests with the second set being used only when the first set showed defined impairments. Three centres did not use a set of core tests.

Ten centres sent us their neuropsychological protocol. Various tests were used to evaluate

![Figure 1](http://www.occenvmed.com)
Our survey shows that there is broad agreement that a routine diagnostic procedure for CTE induced by solvents should contain an interview, and neurological, physical, and neuropsychological examinations. However, there was a large variation in the tests used in the diagnostic procedure, and it is amazing that in four centres psychological tests were not a part of the diagnostic procedure.

Most centres assessed the extent of exposure by interview and about half assessed the work-life exposure by means of an exposure index, but all but one centre also took the possibility of malingering into account at all. Of the referred patients, between 6% and 70% of them were diagnosed with CTE. Of these patients 0%–33% were diagnosed with CTE type I/1, 5%–100% with type II/2, and 0%–95% with type III/3 according to the WHO or Raleigh classification (fig 2).

Discussion

Our survey shows that there is broad agreement that a routine diagnostic procedure for CTE induced by solvents should contain an interview, and neurological, physical, and neuropsychological examinations. However, there was a large variation in the tests used in the diagnostic procedure, and it is amazing that in four centres psychological tests were not a part of the diagnostic procedure.

Most centres assessed the extent of exposure by interview and about half assessed the working life exposure by means of an exposure index. We think that earlier exposure should be assessed by means of an exposure index and that the same method should be used by each centre to calculate the exposure index, which

---

**Table 1** Disciplines involved in the examination of patients suspected of having CTE in 18 specialised centres in 12 countries

<table>
<thead>
<tr>
<th>Disciplines</th>
<th>Always</th>
<th>If indicated</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Neuro)psychologist</td>
<td>11</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Occupational specialist</td>
<td>11</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Occupational physician</td>
<td>9</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Occupational hygienist</td>
<td>6</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Neurologist</td>
<td>6</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Toxicologist</td>
<td>2</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Chemist</td>
<td>2</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>1</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social worker</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist in internal medicine</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vision physiologist</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist in medicine</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2** Examinations used to evaluate patients suspected of having CTE in 18 specialised centres in 12 countries

<table>
<thead>
<tr>
<th>Examinations</th>
<th>Always</th>
<th>If indicated</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interview</td>
<td>18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Physical examination</td>
<td>16</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Neurological examination</td>
<td>15</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Psychological tests</td>
<td>14</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Laboratory</td>
<td>7</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>CT/MRI</td>
<td>5</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>EEG</td>
<td>5</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>ENMG</td>
<td>3</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Evoked potentials</td>
<td>2</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rCBF (1)</td>
<td></td>
<td>SPECT-PET (1)</td>
<td></td>
</tr>
<tr>
<td>SPECT (1)</td>
<td></td>
<td>Biomonitoring (1)</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2** Distribution of final diagnoses according to WHO or Raleigh (% of referred patients) among the centres. Centres are numbered as in figure 1.
was not the case. The fact that the solvents involved were recorded individually or categorised in groups offers the chance to study possible specific effects of a solvent or a category of solvents.

Many of the neuropsychological tests in use are not internationally accepted. Clearly they are not of the same standard as those used in other centres where patients enter the procedure to obtain financial compensation. We can only assume that the diagnostic procedures used in other centres where patients suspected of CTE are diagnosed will probably not be of the same standard as those used in the centres that participated in this study. This is because our respondents are experts who are not only involved in routine diagnosis of patients but were chosen because they are also active in the field of science.

The distribution of diagnoses of CTE across the centres differed strikingly. This can be explained by several factors: the variety in indications for referral; in the assessment of the exposure; assessment of the signs and symptoms; and in the different classifications used. The use of different classifications is important: WHO type II requires only one of four selected cognitive domains (speed, attention, dexterity, and short term memory) to be impaired. By contrast, Raleigh type 2B requires impairment of all three selected cognitive domains (concentration, memory, and learning capacity), although later in the workshop proceedings it is stated that “type 2B most likely shows mild-to-moderate impairments in the following three functions: psychomotor functions, sustained attention/concentration, and verbal and non-verbal memory”. Even so, the WHO and Raleigh classifications, allowing for assessment of the degree of impairment, are more informative than general classifications such as ICD-10 and DSM-IV. For instance, DSM-IV only recognises “inhalant-induced persistent dementia (292.82)” and “inhalant-induced mood disorder (292.83)”, however the equivalent of CTE type II or 2B “inhalant-induced cognitive disorder” is not recognised. If a more general classification for a case is required—for example, for statistics or financial compensation, we suggest that such a classification should be used in combination with a specific CTE classification. The fact that the WHO or Raleigh classifications are used by only three of the 18 centres indicates that they have their drawbacks. The most important drawback in our opinion is the lack of well described criteria. Other reasons for why the 1985 Raleigh and WHO meetings had little success may be that in those days the awareness of the potential effects of chronic solvent exposure on the CNS was limited and that the existence of the “Scandinavian solvent syndrome” was controversial. Nowadays there is little doubt that long term occupational exposure to solvents can result in a chronic encephalopathy: most nations of the European Union recognise CTE in their official list of occupational diseases. So the need for a univocal classification system will now be recognised more widely. For these reasons we think that activities to attain international consensus are more likely to succeed now than in 1985. Such a classification system is also necessary for international comparison of incidence, and neurological studies of CTE and its treatment. The improved classification should contain an approach for the assessment of exposure. Also, the relevant neuropsychological domains based on internationally validated neuropsychological tests should be defined and distinct criteria for the required extent of impairment in these domains should be formulated. We think that a new CTE classification that meets these requirements would be advantageous and better than the two current classifications.

We express our gratitude to the following people for their much appreciated cooperation: Dr R Akila, Helsinki, Finland; Professor O Axelsson, Linköping, Sweden; Dr L Barregård, Göteborg, Sweden; Professor M-A Boissat, Lausanne, Switzerland; Professor S Dally, Paris, France; Dr E W Dryson, Penrose, New Zealand; Dr P Gustavsson, Stockholm, Sweden; Dr H L Leira, Trondheim, Norway; Dr S Mikkelsen, Copenhagen, Denmark; Dr L Morrow, Pittsburgh, USA; Professor P Ørbaek, Lund, Sweden; Dr K Rasmussen, Herning, Denmark; Professor G Trehg, Heidelberg, Germany; Dr M Vane, Leuven, Belgium; Dr A Vrica, Zagreb, Croatia; Professor R F White, Boston, USA; and Dr G Wieslander, Uppsala, Sweden. We are also indebted to Professor Bassuzy for his stimulating ideas about this study.