Survey of solvent related chronic encephalopathy as an occupational disease in European countries

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Abstract

Objectives—To obtain information about solvent related chronic encephalopathy (SRCE) in the countries of the European Union (EU).
Method—A survey was conducted in 1998 and 1999 among medical experts, authorities for health and safety, and social security institutions.
Results—SRCE is an acknowledged occupational disease in most of the participating countries. However, the numbers of compensated cases differ considerably. This is mainly a consequence of national social law rather than of differences in the criteria of diagnosis. In countries with relatively high reported incidences—such as Denmark, Finland, Norway, and Sweden—the number of acknowledged cases has declined over the past 5–10 years, although the most important criteria of diagnosis and causality, according to expert opinion, equivalent diagnostic procedures, and measures for prevention within the EU are not comparable.
Conclusions—There is a need for common guidelines for early diagnosis and the evaluation of causality. Actual figures of SRCE are not suitable to estimate prospective numbers of cases. For this reason a multicentre study in EU states is necessary after a consensus of diagnostic procedure. It is likely that the number of cases will decrease as a result of changes in legislation and preventive measures—such as substitution or reduction of solvents in the products, improvement of technical equipment, and regular health surveillance. Future research activities should focus on follow up studies of prognosis, randomised clinical trials of treatment, investigation of neurotoxic mechanisms, and of the interaction of solvent mixtures.

Keywords: organic solvents; encephalopathy; occupational disease

Effects on the central nervous system (CNS) in workers exposed to organic solvents have become an important issue over the past decade. Early knowledge of neurotoxicity involved in occupational exposure was acquired by clinical observation. One of the first authors was the French physician Delpech who in 1856 reported workers exposed to carbon disulfide with severe mental impairment.2 3

Around 80 years later, Knabenhans and Borbely published monographs with several hundred references to the neurotoxic effects of various solvents.4 5

According to Bleuler (1943)6 those mental changes were summarised as psycho-organic syndrome. It has to be noted however, that many case studies describe additional neurological and psychiatric symptoms which do not correspond well with present knowledge.

After these reports there were few further publications. One exception was the study by Grandjean et al (1953)7 of workers in Switzerland exposed to trichloroethylene.

A new appraisal of neurotoxicity was initiated in the 1970s as a consequence of Danish, Finnish, and Swedish reports. Several investigators found an increased frequency of neuropsychiatric symptoms and signs of impaired performance in neurobehavioural tests among painters, lacquerers, printers, workers exposed to jet fuel and others.8–14

The controversy in the discussion which emerged and seems to continue has to do with the former Danish practice of classifying and reclassifying the neuropsychiatric symptoms as presenile dementia.15

In many countries dementia was understood to be a progressive, non-reversible process of a much more severe type than what had been found among the working populations studied. There was, however, no uniform psychiatric practice for classifying less severe brain disorders at the time.16 As a consequence, no direct comparison of diagnosis and diseases was possible in retrospective studies.

Another problem was the superficial and to some extent incorrect reporting of findings in the media as “disease of the paint can” or “Danish painter’s disease” and resulted in considerable uncertainty about health risks in occupational groups in contact with organic solvents.

Numerous studies were undertaken in the 1980s reflecting the widespread use of organic solvents in industry and handicrafts. The results of these studies have been published in the scientific literature.17–22 Various aspects of the disease have been discussed at several international conferences and agreement was reached with respect to diagnostic methods, clinical pictures, and the need for further research.22–26

According to the International Workshop on Neurobehavioral Effects of Solvents in Raleigh, North Carolina in 1986, the clinical manifestations of an SRCE were classified into four types.24 A brief summary follows: patients with type 1 complain only of non-specific symptoms such as fatigue, difficulties in concentration,
Table 1  Classification and number of cases of occupational solvent related chronic encephalopathy (SRCE)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Occupational SRCE</th>
<th>Period</th>
<th>Notified</th>
<th>Acknowledged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>± (since 1998)</td>
<td>1994–98</td>
<td>No answer</td>
<td>No answer</td>
</tr>
<tr>
<td>Belgium</td>
<td>DSM IV or ICD-9</td>
<td>1997–98</td>
<td>−600</td>
<td>0</td>
</tr>
<tr>
<td>Denmark</td>
<td>ICD-10</td>
<td>1978–98</td>
<td>−9100</td>
<td>−5500</td>
</tr>
<tr>
<td>Finland</td>
<td>ICD-10</td>
<td>1980–97</td>
<td>No answer</td>
<td>486</td>
</tr>
<tr>
<td>France</td>
<td>± (since 1998)</td>
<td>1997–98</td>
<td>No answer</td>
<td>No answer</td>
</tr>
<tr>
<td>Germany</td>
<td>± (since 1997)</td>
<td>1980–98</td>
<td>No answer</td>
<td>139</td>
</tr>
<tr>
<td>Italy</td>
<td>DSM IV or ICD-9</td>
<td>1980–98</td>
<td>No answer</td>
<td>532</td>
</tr>
<tr>
<td>Netherlands</td>
<td>± (since 1970)</td>
<td>1980–87</td>
<td>No answer</td>
<td>936</td>
</tr>
<tr>
<td>Norway</td>
<td>ICD-9 or ICD-10</td>
<td>1989–91</td>
<td>632</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1994–96</td>
<td>289</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>ICD-10</td>
<td>1980–98</td>
<td>7203</td>
<td>4355</td>
</tr>
<tr>
<td>Switzerland</td>
<td>ICD-10</td>
<td>1990–97</td>
<td>No answer</td>
<td>7</td>
</tr>
</tbody>
</table>

DSM = diagnostic and statistical manual of mental disorders; ICD = international classification of diseases; Notified = suspicious cases, not approved; Acknowledged = approved cases; ± = yes; − = no; ± = a classification system is used, but not obligatory.

Results

SRCE AS AN OFFICIAL OCCUPATIONAL DISEASE

Table 1 contains the replies about the classification of SRCE and figures on notified and acknowledged cases as an occupational disease.

The criteria of the 9th and 10th revision of the international classification of diseases (ICD-9 or ICD-10) were mostly applied.

According to the current ICD-10, the disease can be classified in general as toxic encephalopathy (G 92). A specification is possible for intoxication or exposure to chemicals such as alcohols (X 45), solvents (X 46), and others (X 49).

In Finland SRCE has been acknowledged as an official occupational disease since 1948 and in Denmark, Norway, and Sweden since the 1970s.

In other European countries, recognition of SRCE as a legal occupational disease followed later or is awaiting regulation. In most countries a toxic encephalopathy could be related to a recognised occupational disease when caused by chemicals listed in the respective regulation. This is true for carbon disulfide, toluene, or trichloroethylene.

In France it seems that the introduction of SRCE as an occupational disease is under discussion. Cases can be acknowledged depending on the specific chemicals involved.

In Germany, SRCE was introduced into the list of occupational diseases at the end of 1997 in connection with a renewal of the Ordinance of Occupational Diseases. The official term is: “polyneuropathy and encephalopathy caused by organic solvents and solvent mixtures”.

Although SRCE is regarded as an occupational disease in The Netherlands, it is not formally recognised due to the lack of any system of recognition of occupational diseases since 1967.

In Spain and in the United Kingdom SRCE is not a legal occupational disease. In the United Kingdom there are even doubts about the entity of the disease.

In Spain it might be possible for SRCE to be recognised in the case of specific and regulated chemicals.

Table 2 gives an overview of the time course of the absolute number of acknowledged cases of SRCE since 1980. Most cases were reported...
from Denmark (about 5500), Sweden (about 4400), and Norway (about 1900). With the exception of Belgium, which reported few cases, the absolute number has decreased significantly since around 1990.

REPORTED INCIDENCES OF SRCE

In table 3 the total number of employed people and the calculated incidences are presented. Sufficient data were available from: Denmark, Finland, Germany, Italy, Norway, Sweden, and Switzerland.

The incidences describe the number of new cases during the period of 1 year/million employed people. Sources were the reports on statistical factors of the populations of Austria (1998) and Germany (1997).

The calculated incidences in 1997 were highest in Denmark (16.8/million) and Sweden followed by Norway and Finland.

By comparison, the incidences in Germany (0.5/million), Switzerland (0.3/million) and Italy (0.1/million) were clearly lower.

The number of workers exposed to solvents in Norway was estimated to be about 200 000. The Norwegian Labour Inspection Authority noted considerable underreporting.

Also, in Germany the exact number of workers exposed to solvents is unknown. The given numbers of employed painters, spray painters, printers, chemical workers, etc allow the reasonable conclusion that around 1 million people are regularly exposed to solvents at the workplace.

According to the Ministry of Social Affairs in The Netherlands the population at risk amounts to around 500 000 workers in The Netherlands and around 10 million workers in the EU.

HIGH RISK OCCUPATIONS AND NEUROTOXIC SOLVENTS

These questions were answered by only a few medical experts and authorities. Generally speaking, it is difficult to define and measure the health risk by occupations because of the widespread use of organic solvents in present and past workplaces. It is furthermore important to notice that it is not the job title that is relevant but the job activity. For instance, the profession of a painter may be associated with exposure to solvents, however, there are—at least in Germany—painters who performed specific activities without any contact with solvents.

Therefore the following summary of answers given should be understood as an orientation rather than an exact definition.

- High risk occupations:
  - Construction or house painter, laquerer or spray painter, printer, chemical worker, laminator, carpet layer, metal conservation or cleaning, dry cleaner, worker in the synthetic, plastics, automobiles, furniture, and leather industries.
- Exposure to solvents:
  - A single solvent cannot be identified as the main cause in most cases. SRCE is predominantly found in association with solvent mixtures.

DIAGNOSIS OF SRCE

Most diagnostic examinations are applied to confirm or exclude SRCE. To establish the diagnosis, a clinical examination of the patient is obligatory. This means a detailed anamnesis (general and occupational history) and extensive examination by an occupational physician, neurologist, and psychiatrist. Besides clinical examination a neuropsychological or neurobehavioural test is also obligatory in almost all countries. This is necessary to describe and measure psychological functions—such as memory, intellect, and emotion. According to symptoms and signs, additional specific diagnostic measures are applied in all countries. For neurophysiological examinations, an electroencephalogram (EEG) is often mentioned.
This can be supplemented by measuring evoked potential for instance, from visual or acoustic signals. Electromyography and electroneurography are applied to diagnose peripheral lesions of the nervous system. This is important for objective assessment of a polyneuropathy independent of its aetiology. Neuroimaging methods are also applied in all countries, most of them according to indication. They include radiotherapy, computed tomography (CCT/CAT), magnetic resonance imaging (MRI/MRT), and rarely single photon emission computed tomography (SPECT) and positron emission tomography (PET).

**CRITERIA OF CAUSALITY**

To show a causal relation between exposure and disease several criteria were mentioned.

An occupational history as well as adequate exposure to solvents are obligatory in almost all countries. For this exposure to solvents must be chronic and extensive. Chronic means a long lasting or permanent exposure to solvents for at least 10 years in Belgium, Switzerland, Germany, Sweden, and Finland and for less than 10 years in Denmark (6 years) and The Netherlands (5 years proposed).

Extensive exposure can be described as above current occupational exposure limits, and above threshold limit values (TLVs) in Belgium, Switzerland, Germany, Denmark, France, Norway, and Finland.

Although repeated acute prenarcotic symptoms are regularly found in most countries, their appearance is relevant only in Switzerland, Germany, and Denmark.

The medical experts agreed that primary neurological and psychiatric diseases—for example, dementia, Alzheimer’s disease, psychosis—and other well known causes of disorders of the CNS—for example, chronic hypertension, cerebral arteriosclerosis, disorders of metabolism, misuse of alcohol and drugs—must be ruled out or at least considered adequately.

There is also agreement that pathological neurobehavioural and psychological test results are obligatory to objectify the degree of impairment. Neurological signs are required in Belgium, Switzerland, Germany, and Italy.

The relevance of possible non-neurological solvent related diseases was judged differently. In several countries (Belgium, Switzerland, Germany, France, Italy, and Finland) liver damage or nephropathy is considered to be an indicator of intensive exposure to specific solvents such as chlorinated hydrocarbons.

The non-progressive course of the disease after the end of exposure to solvents is an important criteria. With the exception of Denmark and Sweden, all experts agree that a deterioration of the symptoms after removal from exposure makes a causal relation unlikely.

Thus a symptom free interval between the end of exposure and the onset of the disease is not acceptable in most countries.

An assessment was requested of the lowest level of probability which is necessary to establish a causal relation between exposure to solvents and psycho-organic syndrome—that is, to establish the diagnosis of SRCE.

In most countries (no information from Belgium, Netherlands, Spain, or United Kingdom) the probability a causal relation between exposure to solvents and psycho-organic syndromes was stated to be above 50%. This means, to our understanding, that for a causal relation more arguments must be for, and less against.

To illustrate this, the process of acknowledgement of an occupational disease in Germany is described briefly.

Each physician is obliged by law to notify the statutory accident insurance company of any suspicion of an occupational disease. Notification is also possible by the worker, the employer, or the legal insurance company responsible for treatment.

The statutory accident insurance institute must acquire all information about occupation and illness. An independent occupational physician is appointed to examine the patient and to give his opinion on causality.

Causality between exposure and disease must be confirmed with sufficient probability. This means that there can be no doubt about exposure and disease and there are more reasons for than against a causal association.

**COMPENSATION, REHABILITATION TREATMENT, AND PROGNOSIS**

Compensation or disability pension is granted in the case of a minimum grade of disability (loss of productivity) of about 20% in Austria, Belgium, and Germany; 50% in Denmark, 15% in Norway; and 10% in Finland. Sweden compensates an "economic loss".

Only a few countries (Belgium, Germany, Denmark, Norway) presented data on the assessment of the graduation of disability (%) according to the severity (type) of the disease (SRCE):

- **SRCE type 1**: Germany <20%, Denmark 0–50%, Belgium and Norway 0%
- **SRCE type 2 A**: Germany 20–40%, Denmark 50%, Norway 0–14%
- **SRCE type 2 B**: Germany 40–60%, Denmark 50–66%, Belgium 20%, Norway 15–29%
- **SRCE type 3**: Germany 60–100%, Denmark <66%, Norway 30–34%

The "observed average grade of disability" in Norway is 25% and in Finland 100%. In Germany an average range between 20% and 50% is registered. Around 80% of these patients have SRCE type I and about 20% have type II A and B.

A Finnish expert remarked that “almost exclusively our patients represent type III and are usually considered disabled for any kind of work (=100% disability)”. Eight countries (Austria, Belgium, Germany, Denmark, Norway, The Netherlands, Sweden, and Finland) offer a disability pension for loss of productivity. The disability pension is granted as well as the worker’s income in five countries (Austria, Belgium, Germany, Norway, Finland).

Rehabilitation in seven countries (Austria, Switzerland, Germany, Denmark, Norway,
Solvent related chronic encephalopathy as an occupational disease in Europe

The Netherlands, and Finland) consists of occupational retraining, and in seven countries (Belgium, Germany, Denmark, Norway, The Netherlands, Sweden, and Finland) the possibility of early retirement is offered. On the question of treatment, the answers can be summarised as follows. To end exposure is the only specific treatment for SRCE. Any further measures depend on the individual severity of the disease.

Treatment options are rehabilitation programmes for individual people as well as group training, mental training (memory, concentration, emotional control), and psychological or psychiatric treatment as well as psychopharmacological treatment. The success of any treatment as well as positive effects on the prognosis are unknown.

The answers about the prognosis of SRCE are similar in almost all countries. They relate to the recommendations of the international consensus reports of the Raleigh Conference and the World Health Organisation (WHO).

Several medical experts remarked on the prognosis, that:
- The complete reversibility of SRCE type I symptoms is doubtful (Denmark, Norway, and Finland)
- SRCE is almost non-reversible, because memory disturbance remain whereas secondary symptoms usually ease (Finland)
- The non-progression of type III is questionable (Denmark, The Netherlands, Sweden).

A progressive deterioration of symptoms after the end of exposure to solvents is not found in most countries with the exception in Denmark (type 3 after 5–10 years), The Netherlands, and Sweden.

The expenses of compensation and rehabilitation are paid individually by different institutions. The state—that is, by taxes—has to provide for the costs in Sweden, but in Denmark and Norway the costs are shared by the employer. A legal accident insurance is responsible for covering costs in Austria, Germany, and Switzerland. In Germany only the employer contributes to the legal accident insurance. In Switzerland an insurance related to occupation has to share the costs. An occupation or firm related insurance provides for the costs in Finland. The employer must pay into the Fund of Occupational Diseases (FOD) in Belgium, and in Italy to the Institute of Work Compensation (INAIL). There is no specific compensation of an occupational disease in The Netherlands. However pension is granted by the legal health insurance.

DEFICITS IN KNOWLEDGE AND FUTURE RESEARCH

SRCE AS AN OCCUPATIONAL DISEASE

As a consequence of scientific evidence, SRCE is an official occupational disease in most European countries. The number of acknowledged cases, however, differs considerably. In Denmark, Belgium, and Sweden, several thousand workers were diagnosed as having SRCE; in other European countries the figures are clearly smaller.

Health surveillance is regularly practiced in all countries with the exception of Denmark and Norway. This is also true for pre-employment examinations, which are usually performed to assess the suitability of the person to the specific work demands. However, there are no common guidelines for active health surveillance. Those examinations are mostly conducted once a year. They usually include medical history, physical examination, and additional measures according to need.

Regular worksite visits and risk assessment are obligatory in all countries. To control exposure, analyses of air samples are performed in most countries. Occupational exposure limits for solvents vary considerably in the individual nations.

PREVENTATIVE MEASURES, HEALTH SURVEILLANCE, AND OCCUPATIONAL EXPOSURE LIMITS

To our knowledge this is the first survey about the occurrence, diagnostic aspects, and prevention of chronic encephalopathy related to solvents in European countries. Important questions about the specific diagnosis, reversibility or irreversibility of effects, and the cumulative solvent dose necessary to induce this disease were raised in former studies. However, the aims were different and focused mainly on the national situation.

Our questionnaire method has several shortcomings—such as the selection of respondents and the use of their subjective views. To correct the potential bias we have selected medical experts in each country by literature review or by personal contact. Furthermore, the answers were compared and checked for discrepancies. In this case additional information was collected to obtain conclusive data.

Unknown mechanisms are the neurotoxic effects—for example, interactions with other chemicals (metals, pesticides) with the most susceptible structures of the CNS—and the impact of individual susceptibility.

Further activities are necessary to find suitable sensitive and specific methods to screen exposed workers for the early stages of SRCE, and to establish diagnostic procedures for SRCE. In this context several experts asked for a recommendation about a standardised protocol for diagnosis and proof of causality.

Discussion

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DEFICITS IN KNOWLEDGE AND FUTURE RESEARCH

Several experts have provided their views on lack of knowledge and need for further research about SRCE. An important question still unanswered concerns the real incidences of SRCE in Europe that depends on the classification of SRCE and the working populations at risk. Other questions are the time course and general prognosis of the disease, particularly for SRCE type 2 A and B after exposure has ended.
Mikkelsen\textsuperscript{33} analyzed the Danish situation and concluded that differences in exposure assessment, application of inadequate norms of performance, and insufficient adjustment for age and primary intelligence have resulted in many false positive diagnoses.

Another explanation of the differences could be the awareness of the disease as a possible consequence of workplace exposure in general medical practice. In Germany, for instance, the physician is obliged by law to inform the statutory accident insurance institution of the illness of a patient if there are suggestions of an occupational disease. This notification is compensated by the insurance. Employees, other insurance systems, lawyers, etc may also inform the statutory accident insurance institution. This system seems unique in Europe. By contrast, in Sweden, only notification by the patient can be considered.

The difficulties involved in ascertaining sound figures on occupational diseases in Europe are obvious. Butz\textsuperscript{36} described the efforts of Eurostat, which started a pilot study in 1992 about acknowledged occupational diseases in member states. There were several reasons for the failure of the pilot study to obtain results. Firstly, occupational disease was not defined, and the way in which possible occupational disease was notified was different in each nation. Secondly, the procedure of diagnosis of occupational disease depends and relies on the respective national legal system, which varies considerably from state to state.\textsuperscript{36}

A comparison of figures relating to the incidence of SRCE at a European level requires firstly a common approach about how to define a case of SRCE as an occupational disease. This demands common criteria for diagnosis and causality. Common criteria are currently not available and should be developed by a European scientific committee of experts in the near future.

The European list of occupational diseases—recommended in 1990—does not contain the disease toxic encephalopathy. However, several organic solvents are listed which are accepted as a cause of this disease. These are hydrocarbons petroether and fuels (No 116), halogenated aliphatic hydrocarbons (No 117), benzene and benzene homologues (No 126.0), and others.

INCIDENCE OF SRCE

Incidences were calculated on the basis of employed people. Therefore they do not allow firm conclusions. Incidences on the basis of people at risk—for example, workers exposed to solvents—would be more informative. However, appropriate figures were in general not available or not comparable because of specific national regulations in the classification of occupational groups.

It also has to be noted that incidences reflect more the procedure by which cases of SRCE are acknowledged as occupational disease than differences in the criteria for diagnosis and causality. It is assumed, that the real number of cases is higher, at least in those countries where SRCE is either not an official occupational disease or was recently introduced into the list of occupational diseases. Authorities in The Netherlands assumed 6000 to 60 000 new cases a year in the EU, which seems rather speculative.

It is of great interest that especially in Denmark, Italy, Norway, and Sweden the number of acknowledged cases of SRCE have declined considerably over the past 5 to 10 years. This trend can be explained by changes in legal requirements, by reduced exposure to solvents in the workplace, and by improved measures of prevention.

DIAGNOSIS AND CRITERIA OF CAUSALITY

Most criteria for diagnosis and causality are similar. Clinically the description and classification in documents by the Raleigh Conference\textsuperscript{24} or the WHO\textsuperscript{26} was applied. A chronic (10 years and more) and intensive exposure (solvent concentrations above exposure limits or prenarcotic symptoms at the workplace) to proved neurotoxic solvents was required to assume a causal relation.

PROGNOSIS OF SRCE

Most experts agree that the prognosis depends on the initial severity of the SRCE. This is also in accordance with the conclusion of former conferences.\textsuperscript{24–26} Reversibility is a common feature of type 1 of SRCE, however, the completeness is questioned by several experts. After the end of exposure it is unusual for SRCE to deteriorate. Positive aspects for the prognosis are an exposure period of only a few years, no acute prenarcotic symptoms, and no other diseases or risk factors causally linked with disorders of the CNS.

PREVENTION AND HEALTH SURVEILLANCE

With the exception of controlling and reducing exposure to solvents there is no common strategy for measures to protect workers from SRCE. This is particularly true of official guidelines as well as of recommendations in occupational medicine.

Conclusion

Experience in the recognition and acknowledgement of chronic encephalopathy related to solvents differs considerably in European countries, reflecting mostly differences in social law rather than in the criteria of diagnosis and causality.

To find out the real number of cases, a multicentre study in EU member states is required after consensus about a diagnostic procedure and criteria for causality has been reached with medical scientists.

Further research activities should focus on follow up studies to examine the prognosis and on randomised clinical trials on treatment. Additionally studies on treatment and studies on neurotoxic mechanisms as well as on interactions of solvent mixtures were highly recommended.

The conclusions of this study are in good agreement with the final discussion and recommendations of a recent EU conference on organic solvents and organic psychosyn-
The Netherlands, organised by the Finnish Institute of Occupational Health and the Dutch Ministry for Social Affairs and Employment.

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