

# Clinical Topics

## Solvent encephalopathy

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### Abstract

**Nineteen children aged 8-14 years were admitted over a six-year period with an acute encephalopathy due to toluene intoxication. Seven had a history of euphoria and hallucinations. The remainder presented with coma (4), ataxia (3), convulsions (3), and behaviour disturbance with diplopia (2). A history of glue sniffing was elicited in 14, but in the remainder toluene assay confirmed the diagnosis. Thirteen children recovered completely; five still had psychological impairment and personality change on discharge from hospital but were lost to follow-up, and one has a persistent cerebellar ataxia one year after the acute episode, despite absence of further exposure.**

**Toluene inhalation is an important cause of encephalopathy in children and may lead to permanent neurological damage. Diagnosis is most important if further damage due to continued abuse is to be prevented, and toluene assay is a valuable aid to diagnosis.**

### Introduction

Over the past decade glue sniffing has almost reached epidemic proportions among adolescents in some communities where there is extreme social or emotional deprivation. Although some earlier reports<sup>1</sup> concluded that the practice was free from serious side effects, evidence now suggests that this is not so. Glue sniffing has been directly responsible for over 60 deaths in the United Kingdom since 1970.

Toluene is the main solvent used in commercially available contact adhesives in Britain, and toxic effects on the central nervous system,<sup>2-5</sup> kidney,<sup>6</sup> liver,<sup>7</sup> and heart<sup>8</sup> have been described. Recently it has become apparent that toluene intoxication is an important cause of encephalopathy in children. We describe our experience and emphasise the value of a toluene assay as an aid to diagnosis.

### Patients and methods

During 1974-80 19 patients were admitted to the Royal Hospital for Sick Children, Yorkhill, Glasgow, with neurological symptoms and signs after sniffing glue. Ages ranged from 8 to 14 years and boys predominated with a male-female ratio of 2:1. All patients belonged to socioeconomic class V. Readily available proprietary brands of adhesives containing toluene were used in all cases. Toluene assay was performed by gas chromatography using a "Tenax GC" packed column.<sup>9</sup>

### Results

Only seven patients had a history of euphoria or hallucinations. The other 12 presented with coma (4), ataxia (3), convulsions (3), and behaviour disturbance with diplopia (2) (table I).

The diagnosis was made at presentation in 14 patients. In the remainder a history of sniffing glue was absent, and the diagnosis was established after toluene assay.

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TABLE I—Presenting features, toluene concentrations, and outcome in 19 children after glue sniffing

Case No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Age (years)	12	13	9	11	11	11	8	8	14	9	12	13	10	12	13	9	11	13	12
Euphoria (6)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Hallucination (3)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Suicidal (3)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Headache (3)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Vomiting (2)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Drowsiness (6)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Diplopia (2)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Convulsions (3)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Coma (5)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Dysarthria (5)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Ataxia (5)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Behaviour (2)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Ulceration (3)	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Toluene assay (ug/gm)	..	..	..	..	..	..	..	..	..	..	..	..	0.8	0.9	1.46	0.8	1.16	7.7	3.53
Outcome	L	N	L	N	L	L	N	L	L	N	N	N	L	N	L	L	P	N	N

N = Normal.

L = Lost to follow-up.

P = Persistent signs.

Blood concentrations ranged from 0.8 µg/g to 8 µg/g. Haematological and biochemical data were normal in all cases. Electroencephalograms (EEGs) were carried out on ten patients and were abnormal in three, showing diffuse slow wave activity in two and unilateral slowing in the other. Repeat EEGs three weeks later in these patients were normal. Recovery was complete in 13 cases. Five still showed psychological and personality changes on discharge from hospital, but the ultimate outcome is unknown as they were lost to follow-up. The remaining child (case 17) showed persistent signs, which are described in detail.

CASE REPORT

An 11-year-old boy presented with a one-week history of headache, vomiting, abnormal behaviour, slurred speech, and unsteady gait. The medical history, family history, and review of the systems were unremarkable. There was no recent contact with infectious disease, and exposure to drugs or toxins was denied. He was a thin apyrexial boy with superficial ulceration of the lips and nares. His mood was euphoric, speech was slurred, and he had coarse rotatory nystagmus in all directions of gaze. There was severe ataxia of gait with moderate limb inco-ordination and intention tremor. Cranial nerves, deep tendon reflexes, and sensory examination results were normal, and there was no muscle wasting or weakness.

Investigations

Examination of full blood count, urea and electrolyte concentrations, cerebrospinal fluid, skull radiograph, and computerised brain scan gave normal results. Initial EEG showed diffuse slow-wave activity with left-sided predominance.

There was no change in the clinical signs over 72 hours, and at this stage the possibility of a toxic encephalopathy due to sniffing glue was considered. Blood toluene concentration was 1.14 µg/g, and it was later confirmed that the patient had been sniffing glue for several months.

He improved slightly over the following three weeks. EEG at this stage was normal. On review one year later, however, despite confirmatory evidence of abstinence from glue sniffing, cerebellar signs persisted.

Discussion

Toluene is a hydrocarbon solvent that is insoluble in water. On inhalation it is absorbed by the lungs and bound to lipoproteins. Some 70-80% of toluene is metabolised in hepatic microsomes by oxidation to benzoic acid, which is conjugated with glycine to form hippuric acid, and is eliminated in this form through the kidneys.

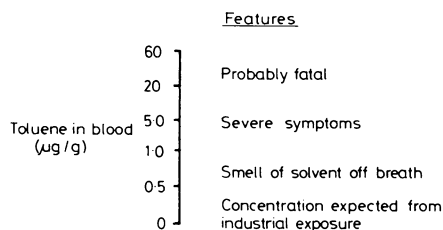
The mechanism of toluene toxicity is unknown, although it may be related to the lipid dissolving property, often used in vitro for extracting membrane lipids. The main toxic impact of toluene is on the central nervous system, probably explained by high cerebral perfusion and the affinity of toluene for lipid rich tissues, from which it is slowly released. Experiments in animals after toluene inhalation have shown toluene concentrations in fatty tissues 80 times higher than in blood.<sup>10</sup> We have assayed toluene concentrations in brain and blood in six fatal cases after glue sniffing (table II). All showed higher concentrations in brain tissue than in blood, supporting the experimental findings.

TABLE II—Toluene concentrations (µg/g) and clinical features in six fatal cases after glue sniffing

Case	Age (years)	Clinical features	Brain	Blood
1	15	Status epilepticus .. .. .	14.5	0.035
2	24	Coma .. .. .	22.5	5.9
3	16	Hallucinations: suicide (hanging) .. .. .	98.6	39.6
4	18	Hallucinations: suicide (drowning) .. .. .	15.3	13.0
5	16	Hallucinations: suicide (jumped off roof) .. .. .	55.9	54.0
6	18	Hallucinations: suicide (jumped from window) .. .. .	1.1	0.13

The effect on the central nervous system may be depressant or excitatory, with euphoria in the induction phase followed by disorientation, tremulousness, mood lability, tinnitus, diplopia, hallucinations, dysarthria, ataxia, convulsions,<sup>11</sup> and coma. The early features of euphoria, hallucinations, and behaviour change were absent in seven patients and should not therefore preclude consideration of the diagnosis. Irreversible neurological sequelae, such as encephalopathy,<sup>2-5 12 13</sup> optic atrophy,<sup>14</sup> and equilibrium disorders,<sup>15</sup> have been described in adult chronic abusers but not in children. One patient in this study had a persistent cerebellar ataxia, and another five patients, who were lost to follow-up, had neurological impairment when discharged from hospital. Permanent neurological damage may therefore be more common than recognised.<sup>1 16</sup>

In patients intoxicated by toluene, investigations may show impaired renal and hepatic function, cerebrospinal fluid pleocytosis,<sup>3</sup> or widening of cortical sulci on pneumoencephalogram or computerised brain scan.<sup>2 4 5</sup> EEG may show diffuse or focal slow or sharp wave complexes<sup>2 17</sup> and unilateral features may be misleading (see case report). Toluene assay, however, is the most sensitive indicator of exposure to toluene, and the correlation between blood concentrations and clinical features (based on 110 positive samples including 25 from industrial workers exposed to toluene) is shown in the figure.



Clinical features encountered at a range of blood toluene concentrations; based on analysis of 110 samples, including 25 from industrial workers exposed to toluene.

The interval between exposure to toluene and sampling is important when interpreting results. Blood concentrations of toluene may be biphasic; an initial peak is followed by a trough reflecting lipid binding by the central nervous system, and a subsequent peak may appear as toluene is slowly released into the blood. The assay may be positive up to several days after withdrawal from toluene (see case report). Measurement of urinary hippuric acid concentrations after exposure to toluene is not of diagnostic value, as hippuric acid is a normal urinary constituent that is influenced by diet. Reports of postmortem findings are few: diffuse cerebral and cerebellar cortical atrophy with giant axonopathy have recently been described.<sup>5</sup>

Toluene inhalation is an important cause of encephalopathy in children and in some patients may lead to permanent neurological damage. The wider social implications of glue sniffing are beyond the scope of this paper. Diagnosis is most important if further damage due to continued abuse is to be prevented. This demands an awareness of the possibility of glue sniffing in any child who presents with otherwise unexplained coma, convulsions, ataxia, or behaviour disturbance. Toluene assay is a valuable aid to diagnosis.

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## MATERIA NON MEDICA

### Armchair cricket

Television arrived in Western Australia in the late 1950s and for years I resisted the temptation to buy a set. I made a virtue out of my parsimony, implying that my children and I had far better things to do than mindlessly watch the flickerings of a cathode ray tube. I took refuge behind a spurious intellectualism, and loftily spoke of the Tolstoy, Rupert Brooke, and N-dimensional geometry with which my three were packing their receptive minds. Truth to tell, the little perishers were transfixed in front of my next-door neighbour's set much of the time. I know this because I had to go and fetch them in for tea, and I always knew where to find them.

They grew up, and eventually I put an end to the charade by buying a set when colour came in about 10 years ago. Even so, I continued to feel a certain righteousness when I spent an evening reading rather than watching. But then something happened on TV, the enormous technical expertise of which I initially used as an excuse for watching seven hours straight: a ball-by-ball live telecast of the England versus Australia test series was projected. As I rank cricket with Brooke and above N-dimensional geometry, and as play conveniently started at 6 00 pm local time, I felt TV had finally found a place in our culture. So now I finish my appointments to coincide with some Trevor Bailey prognosticating, or Brian Johnson flippancy. As the Australian Broadcasting Commission has been sensitive enough to reschedule their news readings to the lunch and tea intervals, we had undiluted pleasure from 6 00 pm to 1 00 am. True enough, *Robin's Nest* and *Yes Minister* have had to go, but you must be serious occasionally.

That all this is taking place 12 000 miles away and is seen with pristine clarity as it happens is something which never ceases to amaze me. Crowd ribaldry or a player's 5 o'clock shadow are faithfully transmitted. Further, as my now grown-up children, reversing the roles, collect me for the evening meal, it is obvious that everyone is unwrapping their luncheon sandwiches at Old Trafford, which is a plot even Tolstoy could not have imagined.—JAMES H LEAVESLEY (general practitioner, Perth, Western Australia).

### A vegetable gardener

My husband and I are both keen gardeners but differ in the direction of our enthusiasm. He likes to see a garden full of flowers and shrubs while I, more practical, like to grow vegetables for the kitchen. Initially in our small town garden the flowers battled with the vegetables for space. By adopting the rather underhand method of creeping colonisation during the vegetables' fallow season, the flowers gradually gained ascendancy, until the vegetables had their backs to the wall. Rescue came in the shape of a council allotment, and the vegetables emigrated.

Women allotment holders are not common around us, and my efforts as I battled with waist-high weeds were watched with interest by my neighbours. Later, when the planting season began, eyebrows were raised, and my artichokes and salsify nestled uneasily among the surrounding potatoes and cabbages. The senior gardeners were unable to resist giving advice: "You got them broccolis too close, mind," and, "You'll have to net your strawberries." My extravagance

was deplored: "You don't want to use slug pellets. Far too expensive. Get some soot from Bert. That'll do the trick." "Soot," I said with interest, "How does it work?" "They don't like it, do they?" said he, impatient with my stupidity. I was obliged to scatter my slug pellets late at night after everyone else had gone home.

But gardeners are generous people, and soon the elder statesman came over. "Don't waste money on cabbage. Here's some I brought on at home." I thanked him and took the magnificent specimens. "Do you like broccolis?" I asked timidly, "Why, yes, I'll have some of it," he said. And so I joined the fraternity.—ANN SAVAGE (Westbury-on-Trym, Bristol).

### We have put Sir Hadyn to bed . . .

The waiting-room has been swept out and is now still. We have checked that the lights are out and everything is locked up. We have put Sir Hadyn to bed; the old ladies were already quiet and still. Tired but satisfied we wend our way homewards after another day's work. No, this is no geriatric unit, but the Tallylyn Railway in Wales, and Sir Hadyn is one of the locomotives.

The line was built in 1865 to transport slate from the mountain quarries to the coastal town of Tywyn. Although the line's main traffic was slate, passengers were carried from the first. The railway and quarries were closely linked until the latter's closure in 1947. Even thereafter, the notable local landowner and once MP for Merioneth, Sir Henry Hadyn Jones, continued to operate an irregular passenger service until his death in 1950. By this time the railway was in a deplorable state for little had been done to the track for many years and the two locomotives and four coaches were still those which had been acquired for the opening of the line. The railway had been worked to death but a preservation society decided to try to revive it. Short of locomotives, one enthusiast bought an engine for £25 from the nearby Corris Railway though he could ill afford the expense. Wagons were five shillings each and he rashly purchased six. Thirty years later volunteers and a small salaried staff still spare no effort to make the line an example of all that is best on the narrow gauge.

What are my duties? Each guard is in charge of and is responsible for the safe working of his train (to quote the operating rule book). That also means that he is responsible for my safe working as his trainee. So together we shut doors, close windows during inclement weather, and keep a good lookout. Having learnt the procedures to be followed in event of derailment or a coupling breaking, I would not want to miss a rare opportunity of putting the theory lessons into practice. With what equipment are we issued for emergencies out in the hills? A whistle, watch, flags, and keys, of course. Also six detonators (to be kept dry and handled with care), a first-aid box, portable telephone, crowbar, and an axe. Our other routine duties include cleaning and polishing the train, issuing tickets at stations without a booking clerk, taking supplies up to the refreshment room at Abergynolwyn, and keeping a record of delays and mishaps for Control.

As an activity holiday, this has plenty to offer: fresh air, human contact, industrial archaeology, and scenery. We look forward to riding behind Sir Hadyn again tomorrow.—PETER BADCOCK (radio-therapist, Zwolle, The Netherlands).