Gasoline Sniffing and Lead Toxicity in Navajo Adolescents

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ABSTRACT. During a 6-year period, 23 Navajo adolescents were hospitalized 47 times for presumed lead intoxication secondary to gasoline sniffing. Most patients were male (87%) and sniffed gasoline as a social activity, more frequently in spring and summer. Sixty-five percent of the patients first presented with toxic encephalopathy. Of total episodes, 31% involved asymptomatic lead overload; 31% involved tremor, ataxia, and other neurologic signs; and 38% involved encephalopathy with disorientation and hallucinations. Free erythrocyte protoporphyrin levels were not consistently high, although blood lead levels were all elevated. One death occurred. Approximately 11% of 537 Navajo adolescents said they inhaled gasoline for enjoyment at least occasionally. Among 147 junior high school students, blood lead levels averaged 18 ± 6 μg/dL with no values >40 μg/dL. Three of these students had elevated zinc protoporphyrin levels and all three were anemic. No correlation was found between levels of blood lead or zinc protoporphyrin and whether or not the youth reported sniffing gasoline. However, sniffing gasoline was associated with poor school performance and delinquent behavior. Although apparently many Navajo adolescents experiment with gasoline inhalation, only a few engage in this activity frequently enough to develop either asymptomatic or symptomatic lead overload. Pediatrics 1983;71:113–117; lead toxicity, gasoline inhalation, North American Indians, trace metals, protoporphyrin.

Gasoline sniffing is the deliberate deep inhalation of gasoline vapors to achieve an altered mental state. Fifteen to 20 breaths may be sufficient to produce euphoria, ataxia, and disorientation, lasting five or six hours. More massive exposure to these volatile hydrocarbons can lead to acute CNS depression with loss of consciousness, coma, and death. Tetraethyl lead (TEL) is an antiknock compound used in some gasoline. Industrial workers exposed to high airborne concentrations of TEL can develop a toxic psychosis with hallucinations and disorientation. Although gasoline sniffing has been described frequently in the literature, only in recent years has a syndrome of ataxia, tremor, and toxic encephalopathy been observed in gasoline sniffers and attributed to TEL poisoning. Most reported cases have been in Canadian Indian adolescents.

Although a young Navajo girl with recurrent cerebellar dysfunction related to chronic gasoline sniffing was observed in 1974, it was not until 1979, when four adolescent Navajos with toxic encephalopathy were admitted to one hospital, that the investigation of gasoline sniffing toxicity described in this report was undertaken on the Navajo reservation.

METHODS

The Navajo Indian reservation occupies approximately 25,000 square miles of northern Arizona, northwestern New Mexico, and southern Utah. Approximately 150,000 Navajo people live on the reservation or in adjacent border areas, including several towns. The people traditionally live in scattered camps over the plateau and desert country, although a number of settlements with populations of 2,000 to 4,000 have developed in recent years. During the time covered by this survey (July 1974 through June 1980) five US Public Health Service hospitals and three other large outpatient clinics, all of which participated in a computerized data system, provided health care for Navajo people.
A list was obtained of all cases that had the following hospital-discharged diagnoses between July 1, 1974 and June 30, 1980: ICD-8 981.1 (toxic effects of petroleum products) and 984.0 (toxic effects of lead and its compounds). The charts of these patients were reviewed, and conditions unrelated to gasoline sniffing were excluded. Charts were abstracted for age, sex, home address, chief complaint, lead level, physical findings, treatment given, hospital course, psychiatric and social service evaluations of patients and home environment, hospital course, and discharge status.

In May 1981, all students (537) in Bureau of Indian Affairs junior and senior high schools at Tuba City were given a written questionnaire by their dormitory personnel. This was completed anonymously, identified only by a coded number. The questionnaire included 63 items relating to gasoline sniffing, other substance abuse, school performance, student beliefs, and family characteristics.

In addition to taking the questionnaire, all 147 junior high school students had venous blood samples taken. These were also coded. An observer, unassociated with the school, matched blood analysis data with questionnaire responses. Measurement of hematocrit was performed at Tuba City IHS Hospital and capillaries of whole blood were sent under ice to the Allegheny County (Pennsylvania) Health Department for determination of zinc protoporphyrin (ZPP) levels using the quantitative fluorometric micromethod described by Chiolsim and Brown. Analyses were completed within 72 hours of blood drawing. A second whole-blood sample for each student was sent in a lead-free glass container to the Arizona Department of Health Services Laboratory in Phoenix where lead content was determined by the atomic absorption technique.

RESULTS

Chart Survey

In the 6-year period, 23 patients (20 male and three female) were hospitalized 47 times for CNS toxicity or lead overload secondary to gasoline sniffing. Eight patients (35%) had three or more separate admissions, whereas 14 had only one. In 11/14 the diagnosis was made during the last year of the survey and one of these 14 died during hospitalization. Patients' age ranged from 10 to 20 years when diagnosis was first made (mean age 14.6 years); ten patients (43%) were in the 14- to 16-year age group. Forty (85%) of the admissions occurred during the latter 3 years of the period, and 38 (81%) occurred during the 6 months of March through August each year.

Clinical syndromes and blood lead levels seen in these Navajo adolescents are shown in Table 1. Sixty-five percent of the patients were first seen with definite encephalopathy, whereas only 22% had asymptomatic lead overload. "Encephalopathy" refers to nausea, vomiting, irritability, excitement, disorientation, hallucinations, and (in four patients) seizures. Three of the total episodes progressed to somnolence or coma. In 14 of the encephalopathic episodes, tremor, ataxia, and/or chorea were also present. There was one death, which was secondary to aspiration pneumonia in a comatose patient. One adolescent girl who was first seen with recurrent cerebellar dysfunction (three admissions) was first thought to have Sydenham's chorea, and her case has been reported elsewhere.

Anemia (hematocrit < 35%) was noted on admission in 14 patients, but only three had basophilic stippling of RBCs. Two patients, both aged 12 years, had radiographic "lead lines" observed in the metaphyses and epiphyses of radius and ulna. Only eight patients had free erythrocyte protoporphyrin (FEP) levels recorded on admission; 5/8 had elevated FEP levels, ranging from 98 to 300 μg/dL (normal <49 μg/dL). Three others had FEP levels of 42, 30, and 16 μg/dL. Ten patients on 14 separate occasions had urinary lead levels recorded at the time of hospital admission; all had elevated levels ranging from 233 to 3,226 μg/24 hr. Five of these were >2,000 μg/24 hr, and four others were between 500 and 1,999 μg/24 hr. Eleven patients had elevated SGOT (105 to 156 IU/L) and alkaline phosphatase (174 to 435 units/dL) levels on admission; none had

<table>
<thead>
<tr>
<th>Clinical Classification</th>
<th>1st Admission</th>
<th>Total Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>Blood Lead (μg/dL)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Range</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>5 (22%)</td>
<td>88</td>
</tr>
<tr>
<td>P focal CNS symptoms (eg, tremor, ataxia, chorea)</td>
<td>3 (13%)</td>
<td>88</td>
</tr>
<tr>
<td>Encephalopathy (eg, hallucinations, disorientation)</td>
<td>15 (65%)</td>
<td>95</td>
</tr>
<tr>
<td>Total</td>
<td>23 (100%)</td>
<td></td>
</tr>
</tbody>
</table>
hyperbilirubinemia. One patient had evidence of progressive liver cellular damage, with SGOT level rising from 123 to 935 IU/L by the fourth hospital day. This person subsequently died of aspiration pneumonia and adult respiratory distress syndrome. In all other cases, liver function abnormalities returned toward normal.

Clinical notes indicated that at least 15/23 patients belonged to four separate groups, each composed of siblings and friends who sniffed gasoline together. Psychiatric evaluations indicated that many had family problems that could have predisposed to this behavior. Ten were judged to have inadequate parental supervision, nine had older siblings who sniffed gasoline, and parental alcohol abuse was recorded in four instances.

Chelation therapy with calcium disodium edalate (EDTA) and dimercaprol (BAL) was begun in all episodes, except eight asymptomatic ones in which only EDTA was given. Four patients left the hospital six times (13%) against medical advice prior to completing therapy. Oral penicillamine was added, following EDTA and BAL, as a part of eight courses. Chelation was associated with reduction of blood lead in 33/34 cases in which pretreatment and posttreatment levels during the same hospitalization were recorded. In one case blood lead level was unchanged (61 μg/dL) after five days. The average decrease in lead level was 36 ± 23 μg/dL. With the exception of one death, all patients became asymptomatic during a 1- to 2-month follow-up period. However, nine patients had subsequent admissions, six for recurrent symptoms and three for lead overload only, because of continued gasoline sniffing.

School Survey

Among 537 junior and senior high school students at Tuba City boarding school, 61 (11.4%) answered positively to the question, "Have you tried sniffing gasoline for fun?", whereas 40 (7.5%) currently inhaled it with some regularity. Greater numbers drank alcohol (225 [42.8%]) or smoked marijuana (118 [22.4%]) and fewer inhaled other substances, such as glue or paint (17 [3.2%]). The average age at which gasoline sniffing began was 12.9 years, with a mode of 13.0 years. It was usually reported to be an infrequent activity ("a few times per year") in 37/56 students or 66.1%, and only 5.3% of the users (3/56) engaged in it weekly. Sniffing was primarily a group activity shared with friends (54.3%) or siblings (30.4%).

All junior high school students (147) also had blood lead and ZPP level measurements performed. Three had lead levels of 40 μg/dL, whereas nine different children had borderline or elevated ZPP values. The latter included six with levels between 40 and 50 μg/dL, and one each had values of 81, 94, and 126 μg/dL. For the whole group, mean blood lead level was 18.2 ± 5.9 μg/dL and ZPP was 20.0 ± 15.8 μg/dL. There was no significant difference in mean ZPP or lead values between those who said they sniffed gasoline and those who said they did not. Even within the normal range, variations in ZPP level could be associated either with iron deficiency anemia (inverse relationship) or with lead burden (direct relationship), and so we tested for these correlations. Children whose hematocrits were in the lowest quartile (30) had a significantly higher mean ZPP level than that of those in the highest quartile (31): 31 ± 27 μg/dL vs. 16 ± 7 μg/dL, t = 3.88, P < .001. Hematocrit was negatively correlated with ZPP in both sexes and over-all (Pearson r = -.452, P < .001), but lead level was not significantly correlated with ZPP. The difference in mean ZPP level between boys (21 ± 15 μg/dL) and girls (23 ± 16 μg/dL, t = 1.90, P < .05) was explained by the girls having lower hematocrits.

Adolescents who sniffed gasoline tended to have other behavioral problems as well. As indicated in Table 2, those who had failed courses, been suspended from school, been arrested, or used other drugs were all more likely than others to engage in gasoline sniffing.

### Table 2. Responses to Behavioral Questions and Percent Sniffing Gasoline by Positive or Negative Response in Tuba City High School Children, 1981

<table>
<thead>
<tr>
<th>Question</th>
<th>No. of Positive Responders</th>
<th>% Sniffing Gasoline</th>
<th>χ²</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you failed one or more subjects in school?</td>
<td>224 (42.6%)</td>
<td>15.2</td>
<td>9.9</td>
<td>4.29</td>
</tr>
<tr>
<td>Have you ever been suspended from school?</td>
<td>67 (12.7%)</td>
<td>22.4</td>
<td>10.0</td>
<td>7.64</td>
</tr>
<tr>
<td>Have you ever been arrested?</td>
<td>107 (19.3%)</td>
<td>21.6</td>
<td>9.2</td>
<td>11.22</td>
</tr>
<tr>
<td>Have you visited the school counselor for a problem?</td>
<td>150 (28.7%)</td>
<td>8.7</td>
<td>12.9</td>
<td>1.45</td>
</tr>
<tr>
<td>Do you drink alcohol?</td>
<td>221 (42.3%)</td>
<td>19.5</td>
<td>5.6</td>
<td>22.55</td>
</tr>
<tr>
<td>Do you smoke marijuana?</td>
<td>116 (22.1%)</td>
<td>25.0</td>
<td>7.6</td>
<td>25.40</td>
</tr>
<tr>
<td>Is there someone you can talk to and trust?</td>
<td>437 (83.1%)</td>
<td>19.1</td>
<td>9.8</td>
<td>5.39</td>
</tr>
</tbody>
</table>
DISCUSSION

Are these syndromes caused by TEL itself or are they effects of inhaling volatile hydrocarbons, with lead overload as simply a "fellow traveler"? The symptomatic episodes can be divided into two groups: those involving acute toxic encephalopathy (19) and those involving subacute neurologic symptoms, such as tremor and ataxia (14). Some patients who were seen initially with delirium and hallucinations, at the same time or later, on subsequent admissions, had focal CNS dysfunction. Both syndromes are consistent with previously reported cases of apparent TEL toxicity from gasoline sniffing.\(^5,7,9,10\) In 13 of our 14 episodes initial urinary lead concentrations were >300 \(\mu g/24\) hr, a level generally associated with TEL poisoning.\(^3\) Several patients had evidence of other adverse lead effects, such as basophilic stippling, radiographic lead lines, or acute hepatic dysfunction (as in cases described by Boeckx et al\(^1\) and Robinson\(^2\)). N-Hexane, a volatile component of gasoline, can cause a symmetrical polyneuropathy, clinically similar to inorganic lead poisoning.\(^14\) However, none of these patients had a polyneuropathy. The subacute CNS syndrome seen in our patients has not been reported in cases of gasoline inhalation, except in association with TEL.

Moreover, we searched hospital charts of all persons with discharge diagnoses indicating toxic effects of petroleum products (ICD-8 981.1), but found no cases with normal lead levels and acute CNS symptoms. Conversely, we observed no cases of lead intoxication (ICD-8 984.0) unassociated with gasoline sniffing. Thus, the preponderance of evidence suggests that TEL toxicity is paramount in these patients, although this does not rule out the possibility that aliphatic hydrocarbons contributed to the acute delirium and excitement.

Inasmuch as new cars and trucks designed since 1974 use only unleaded gasoline, this may, in fact, be a disease whose time has passed. However, gasoline sniffing has been most frequently reported among Indian or non-Indian rural adolescents\(^14,15,16-17\) from lower socioeconomic status backgrounds,\(^1,15\) who have multiple social stresses.\(^1,4\) Leaded gasoline might still be commonly used in vehicles to which these teenagers have access, because the vehicles are old and/or are fueled with less expensive leaded gasoline despite being designed to use only unleaded gasoline.

Three other questions deserve comment: (1) the efficacy of chelating agents in treating TEL poisoning; (2) the use of FEP as a diagnostic or screening test for TEL toxicity; and (3) the usefulness of screening for lead overload in high-risk groups. TEL is metabolized first to triethyl lead in the liver, probably within minutes; the triethyl lead has a biologic half-life of several days, being further metabolized to diethyl lead.\(^11\) Direct evidence for conversion to inorganic lead is lacking, but the increased lead excretion seen with chelation therapy in TEL poisoning supports such conversion, as neither TEL nor triethyl lead are chelated by EDTA or BAL.\(^9,18\) Authoritative sources state that chelation is ineffective in TEL poisoning,\(^2,3,11\) basing this conclusion on the inability of EDTA or BAL to chelate organolead compounds in rats.\(^18\) However, BAL does chelate diethyl lead,\(^18\) and numerous clinical cases have demonstrated both improvement of symptoms and markedly increased lead excretion associated with intravenous chelation therapy.\(^5,7,9,10,15\) The statement that "chelating agents are of doubtful value"\(^12\) appears to be incorrect.

TEL and its metabolite triethyl lead are more lipid soluble than inorganic lead. Beattie et al\(^19\) showed that 73% of blood lead resided in a lipid fraction of blood from four patients with TEL intoxication, whereas this lipid fraction contained only 24% of lead in two normal subjects and 20% in two persons poisoned by inorganic lead. Because of this lipid solubility, TEL and triethyl lead can accumulate rapidly in the CNS, causing early neurologic dysfunction and encephalopathy. When metabolized to its inorganic form, lead inhibits ferrochelatase, a heme biosynthetic enzyme required for insertion of iron into protoporphyrin. Because of their sensitivity and ease of performance, FEP or ZPP determinations, which measure protoporphyrin accumulation in the RBC, are widely used as screening tests for lead exposure.\(^20\) FEP levels >50 \(\mu g/dL\) in children are considered abnormally high and suggest either lead overload or iron deficiency anemia. However, Gutniak et al\(^21\) and Beattie and associates\(^10\) each reported that the level of FEP was only inconsistently elevated in workers with TEL poisoning. Only one of four patients in the series reported by Beattie et al\(^10\) had FEP >35 \(\mu g/dL\), whereas lead levels were all in excess of 60 \(\mu g/dL\).

In our series, 5/8 patients with paired lead and FEP determinations had elevated levels of FEP; the three who did not had lead levels of 71, 72, and 88 \(\mu g/dL\) at the time of admission. We were unable to determine duration of exposure in Navajo patients but, in the series reported by Beattie et al\(^19\), patients experienced industrial exposure 2 to 4 weeks before hospitalization. We believe that chronic gasoline sniffing would result in hemato logic changes, and that Navajo patients with normal FEP likely had recent onset of exposure.

Consequently, if acute TEL toxicity is under consideration, FEP is not a useful test in evaluating
neurologic syndromes. However, screening high-risk populations would more likely yield cases of repeated but smaller exposure to either TEL or inorganic lead. In this case, FEP, or the more convenient ZPP microdetermination,\textsuperscript{13} may well be adequate. We found no asymptomatic lead overload, even in those who said they sniffed gasoline. There was a correlation between lower hematocrit and higher ZPP levels in Navajo students, and all three children with abnormally high ZPP levels were anemic (hematocrits 32, 36, and 37 at 5,000 feet above sea level). These children had normal lead levels. In fact, all other children's paired ZPP and lead levels placed them in the CDC's low-risk categories (Class I or Ib).\textsuperscript{20}

These findings suggest that, at least in the 12- to 15-year age group, asymptomatic lead overload is not a frequent occurrence, despite the fact that lead toxicity is a significant clinical problem in a few adolescents. Approximately 11% of surveyed Navajo adolescents stated that they experimented with gasoline sniffing and, whereas two thirds continued to engage in it periodically, only 1/20 (0.5%) inhaled gasoline weekly. Among heavy users, some (23 in 6 years) develop CNS toxicity or come to medical attention because of their substance abuse. Frequent gasoline sniffing was associated with poor school performance and delinquency. Lead toxicity may be a consideration in Indian or other rural teenagers who have acute mental or neurologic symptoms. However, widespread screening for asymptomatic lead overload is unlikely to yield many new cases. Inasmuch as gasoline sniffing is a social activity, it might be useful to screen siblings and close friends of identified patients using the convenient ZPP micromethod. If there is a high index of suspicion, blood lead measurement should also be performed as TEL overload and toxicity may occur without erythrocyte protoporphyrin changes.

**ACKNOWLEDGMENT**

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