



Article scientifique

Article

1997

Published version

Open Access

This is the published version of the publication, made available in accordance with the publisher's policy.

---

## Needle length and injection technique for efficient intramuscular vaccine delivery in infants and children evaluated through an ultrasonographic determination of subcutaneous and muscle layer thickness

---

Groswasser, J; Kahn, A; Bouche, B; Hanquinet, Sylviane; Perlmutter, N; Hessel, L

### How to cite

GROSWASSER, J et al. Needle length and injection technique for efficient intramuscular vaccine delivery in infants and children evaluated through an ultrasonographic determination of subcutaneous and muscle layer thickness. In: Pediatrics, 1997, vol. 100, n° 3, p. 400–403.

This publication URL: <https://archive-ouverte.unige.ch/unige:88598>

exanthem subitum. Additional study is necessary to verify this interesting phenomenon.

SADAYOSHI TORIGOE, MD  
NOBUTADA TABATA, MD  
Department of Pediatrics  
Shingu Municipal Hospital  
Shingu, Wakayama 647, Japan

MASAO YAMADA, MD  
Department of Virology  
Okayama University School of Medicine  
Okayama 700, Japan

WAKA KOIDE, MD  
MASAHIRO ITO, MD  
Department of Pediatrics  
Mie University School of Medicine  
Mie 514, Japan

TOSHIAKI IHARA, MD  
HITOSHI KAMIYA, MD  
Department of Pediatrics  
Mie National Hospital  
Mie 514-01, Japan

## REFERENCES

1. Yamanishi K, Okuno T, Shiraki K, et al. Identification of human herpesvirus-6 as a causal agent for exanthem subitum. *Lancet*. 1988;1:1065-1067
2. Tanaka-Taya K, Kondo T, Torigoe S, Okada S, Mukai T, Yamanishi K. Human herpesvirus 7: another causal agent for roseola (exanthem subitum). *J Pediatr*. 1994;125:1-5
3. Asano Y, Yoshikawa T, Suga S, Yazaki T, Kondo K, Yamanishi K. Fatal fulminant hepatitis in an infant with human herpesvirus-6 infection. *Lancet*. 1990;335:862-863
4. Kondo K, Nagafuji H, Hata A, Tomomori C, Yamanishi K. Association of human herpesvirus 6 infection of the central nervous system with recurrence of febrile convulsions. *J Infect Dis*. 1993;167:1197-1200
5. Asano Y, Yoshikawa T, Suga S, et al. Fatal encephalitis/encephalopathy in primary human herpesvirus-6 infection. *Arch Dis Child*. 1992;67:1484-1485
6. Yanagihara K, Tanaka-Taya K, Itagaki Y, et al. Human herpesvirus 6 meningoencephalitis with sequelae. *Pediatr Infect Dis J*. 1995;14:240-242
7. Komura E, Hashida T, Otsuka T, et al. Human herpesvirus 6 and intussusception. *Pediatr Infect Dis J*. 1993;12:788-789
8. Huang LM, Lee CY, Lin KH, et al. Human herpesvirus-6 associated with fatal hemophagocytic syndrome. *Lancet*. 1990;336:60-61
9. Kitamura K, Ohta H, Ihara T, et al. Idiopathic thrombocytopenic purpura after human herpesvirus 6 infection. *Lancet*. 1994;344:830
10. Torigoe S, Koide W, Yamada M, Miyashiro E, Tanaka-Taya K, Yamanishi K. Human herpesvirus 7 infection associated with central nervous system manifestations. *J Pediatr*. 1996;129:301-305
11. Hashida T, Komura E, Yoshida M, et al. Hepatitis in association with human herpesvirus-7 infection. *Pediatrics*. 1995;96:783-785
12. Yakushijin Y, Yasukawa M, Kobayashi Y. T-cell immune response to human herpesvirus-6 in healthy adults. *Microbiol Immunol*. 1991;35:655-660
13. Porstmann T, Ternynck T, Avrameas S. Quantitation of 5-bromo-2-deoxyuridine incorporation into DNA: an enzyme immunoassay for the assessment of the lymphoid cell proliferative response. *J Immunol Methods*. 1985;82:169-179
14. Ito M, Nakano T, Kamiya T, et al. Activation of lymphocytes by varicella-zoster virus (VZV): expression of interleukin-2 receptors on lymphocytes cultured with VZV antigen. *J Infect Dis*. 1992;165:158-161
15. Nakano T, Ito M, Mizuno T, et al. Increase of interleukin 2 receptor and CD45RO antigen on lymphocytes cultured with human cytomegalovirus. *Cell Immunol*. 1993;147:73-80
16. Ito M, Watanabe M, Kamiya H, Sakurai M. Inhibition of natural killer (NK) cell activity against varicella-zoster virus (VZV)-infected fibroblasts and lymphocyte activation in response to VZV antigen by nitric oxide-releasing agents. *Clin Exp Immunol*. 1996;106:40-44
17. Torigoe S, Kumamoto T, Koide W, Taya K, Yamanishi K. Clinical manifestations associated with human herpesvirus 7 infection. *Arch Dis Child*. 1995;72:518-519

18. Yasukawa M, Yakushijin Y, Furukawa M, Fujita S. Specificity analysis of human CD4<sup>+</sup> T-cell clones directed against human herpesvirus 6 (HHV-6), HHV-7, and human cytomegalovirus. *J Virol*. 1993;67:6259-6264

## Needle Length and Injection Technique for Efficient Intramuscular Vaccine Delivery in Infants and Children Evaluated Through an Ultrasonographic Determination of Subcutaneous and Muscle Layer Thickness

ABBREVIATIONS. DTP-IPV, diphtheria, tetanus, pertussis, and inactivated poliovirus vaccine; WHO, World Health Organization; SCT, subcutaneous tissue; ML, muscle layer; SD, standard deviation.

The relationship between resulting reactogenicity and immunogenicity with route and site of vaccine injection is well documented.<sup>1-5</sup> Preference for intramuscular injection is given for aluminum-adsorbed vaccines (eg, diphtheria, tetanus, pertussis, and inactivated poliovirus [DTP-IPV], hepatitis A, and hepatitis B vaccines), because superficial administration leads to increased incidence of local reactions.<sup>6</sup> A better immune response for intramuscular compared with subcutaneous injection has been seen with several vaccines, such as the hepatitis B,<sup>1,5</sup> rabies,<sup>3</sup> and influenza<sup>2</sup> vaccines. Both the injection technique and the needle length are crucial for ensuring proper intramuscular delivery and thus are directly related to vaccine safety and immunogenicity.

Guidelines concerning the choice of the injection technique and needle length have been presented. Two injection techniques are currently recommended. The first, widely used in the United States, requires bunching the thigh muscle at the injection site to increase muscle mass and to minimize the chance of striking bone.<sup>6</sup> The second, recommended by the World Health Organization (WHO), suggests stretching the skin flat between the finger and thumb, and pushing the needle down at a 90° angle through the skin.<sup>7</sup> With respect to needle length, both the WHO and the Committee on Infectious Diseases of the American Academy of Pediatrics support the use of 7/8-inch (22-mm) or longer needles for intramuscular delivery.<sup>7,8</sup>

Some unidose vaccines are supplied in disposable syringes, equipped with 5/8-inch (16-mm) sealed needles that have been designed to provide an efficient, precise, and user-friendly tool for intramuscu-

Received for publication Jan 29, 1997; accepted Apr 28, 1997.

Reprint requests to (J.G.) Department of Pediatrics, Queen Fabiola Children's Hospital, 15 Av JJ CROCCQ, 1020 Brussels, Belgium.

PEDIATRICS (ISSN 0031 4005). Copyright © 1997 by the American Academy of Pediatrics.

**TABLE.** SCT and ML Thickness for the Thigh in Infants and Children and for the Deltoid in Children (in Millimeters)

	Right		Left	
	Infants	Toddlers	Infants	Toddlers
Thigh				
SCT				
Mean ( $\pm$ SD)	8.0 ( $\pm$ 0.3)	7.5 ( $\pm$ 0.4)	8.1 ( $\pm$ 0.3)	7.6 ( $\pm$ 0.4)
Median (range)	7.9 (4.8–12)	7.3 (5.1–11.6)	7.8 (5.1–11.7)	7.5 (4.8–11.2)
ML				
Mean ( $\pm$ SD)	9.2 ( $\pm$ 0.3)	9.5 ( $\pm$ 0.4)	9.3 ( $\pm$ 0.3)	9.3 ( $\pm$ 0.3)
Median (range)	8.7 (6.3–13.1)	9.3 (6.4–11.8)	8.9 (6.8–13.5)	9.3 (6.9–11.3)
Total SCT + ML				
Mean ( $\pm$ SD)	17.3 ( $\pm$ 0.5)	16.9 ( $\pm$ 0.6)	17.5 ( $\pm$ 2.7)	16.9 ( $\pm$ 0.6)
Median (range)	16.7 (13.2–23.9)	16.8 (14.0–22.6)	17.1 (13.1–24.5)	17.4 (13.0–21.0)
Deltoid				
SCT				
Mean ( $\pm$ SD)		4.9 ( $\pm$ 0.2)		4.9 ( $\pm$ 0.2)
Median (range)		4.8 (3.6–6.9)		5.0 (3.6–6.0)
ML				
Mean ( $\pm$ SD)		5.8 ( $\pm$ 0.3)		5.7 ( $\pm$ 0.3)
Median (range)		6.2 (3.4–7.5)		5.8 (3.7–7.5)
Total SC + ML				
Mean ( $\pm$ SD)		10.7 ( $\pm$ 0.4)		9.6 ( $\pm$ 0.8)
Median (range)		11.1 (7.0–14.2)		10.7 (8.0–13.2)

lar injection. Nevertheless, the adequacy of this shorter needle (compared with the 7/8-inch needle) has been questioned.<sup>6</sup> To determine the optimum needle size for intramuscular injection and eventually to make a correlation between needle length and appropriate injection technique, one must have accurate data on the morphometric characteristics of healthy people with respect to subcutaneous tissue (SCT) and muscular layer (ML) thickness. Relatively few such data have been published.<sup>8–10</sup> A recent study involving 40 adults showed that the mean SCT thickness in the deltoid region averaged 7 mm.<sup>11</sup> The aim of our study was to obtain SCT tissue and ML thickness values at the two sites recommended for vaccine injection, ie, the thigh and the deltoid,<sup>6</sup> in infants and children at the age of primary or subsequent booster immunizations.

## MATERIALS AND METHODS

A total of 58 patients from different departments of the Queen Fabiola University Children's Hospital (Brussels, Belgium) were included in this open study conducted during a 1-year period beginning in May 1995.

Tissue thickness was measured using a high-frequency, real-time ultrasonograph (ALOKA 2000 SSD) with a 6-cm-long, 7.5 Hz transducer. For the quadriceps, the anterolateral aspect of the thigh at the junction of the upper third and lower two thirds of the muscle was examined at a 45° angle to the horizontal plan. For the deltoid, the external aspect of the median part of the muscle (ie, between the acromial point and the deltoid tuberosity) was studied. The transducer was applied lightly to the skin to avoid tissue compression. Two concordant measurements were performed, at a 90° angle both to the skin and to the long axis of the leg or arm; an image taken at each point provided an automatic measurement in millimeters of the morphometric parameters. Two operators performed the experiments, each doing approximately half of all measurements.

The study protocol had been approved by the hospital ethics committee, and informed oral consent was obtained from all parents.

Descriptive analysis of the evaluation criteria, including mean, median, standard deviation (SD), and range, was performed using SPSS Software, version 5.01 (SPSS, Inc, Chicago, IL).

## RESULTS

Forty infants, median age 12 weeks (range, 9 to 27) and 18 toddlers, median age 79 weeks (range, 68 to

88) have been investigated. All were in apparent good health and without a history of upper or lower limb injury or any neurological or muscular disease.

Morphometric characteristics of infants and children included in the present study generally fell between the 10th and 50th percentiles, according to age and gender, of the Belgian normal growth curves. Among infants, these curves are similar to those currently in use in the United States<sup>12</sup> and France.<sup>13</sup> In 18-month-old children, the median weight corresponded to the 25th percentile of the US curve, and the median height corresponded to the 50th percentile of the US and French curves.

The tissue thickness values obtained in both groups are summarized in the Table. Over the anterolateral aspect of the thigh, the skin-to-bone depth was ~17 mm in both infants or toddlers, with the SCT thickness not >12 mm at the quadriceps. For infants, the SCT thickness was ~8 mm regardless of the side examined or the gender of the child, and SCT thickness ranged from 4.8 to 12.0 mm, which was noted in a 6-month-old girl weighing 7.95 kg (75th percentile). In toddlers, the skin-to-muscle depth had a mean value of 7.5 mm (range, 4.8 to 11 mm), quite similar to that observed in infants. In infants, the quadriceps thickness averaged  $9.3 \pm 0.3$  mm (mean  $\pm$  SD) and was similar on both sides (a median of 8.7 and 8.9 mm on the right and left sides, respectively). The quadriceps muscle was slightly thicker in toddlers, with a median value of 9.3 mm.

In the deltoid region, evaluated only in toddlers, the SCT thickness was ~5 mm and never >6.9 mm. The mean ML thickness of the deltoid was  $5.8 \pm 0.3$  mm (range, 3.4 to 7.5 mm) and was similar on the right and left sides. The average skin-to-bone depth was 10 mm and was never >14.2 mm.

## DISCUSSION

Several studies examined the SCT and ML. Our data are consistent with those obtained in an ultrasonographic evaluation conducted in Malmö, Swe-

den (C.-E. Flodmark, personal communication) of the subcutaneous adipose tissue in 3-, 6-, and 12-month-old children. The fat-fold thickness over the middle of the left thigh averaged  $5.4 \pm 1.7$ ,  $4.9 \pm 1.6$ , and  $5.0 \pm 1.7$  mm, respectively, in the three age groups. No child had a SCT thickness  $>10.4$  mm at 3 months or 9.0 mm at 13 months (C.-E. Flodmark, personal communication). However, Hick et al,<sup>9</sup> studying the depth of the fat layer over the thigh by ultrasonography with a transducer oriented at a 45° angle to the long axis of the leg in 24 infants aged 3½ to 4½ months, found the skin-to-muscle depth to be  $14.0 \pm 2.4$  mm in boys and  $13.0 \pm 2.8$  mm in girls. The skin-to-bone depth varied from  $32.0 \pm 4.5$  mm for boys to  $28.0 \pm 4.7$  mm for girls.<sup>9</sup> Lack of agreement with the results obtained in our study may be attributed, in part, to a difference in transducer orientation. If the transducer had been applied at a right angle to the leg, the skin-to-muscle depth obtained on extrapolation of the data would be 9.9 mm, close to the value obtained in the present study.

The difference in SCT thickness between infants and children is minimal. Only for infants did a significant correlation between weight and SCT thickness appear. This is consistent with the data obtained in a 1974 US Nutritional Survey that indicated that the arm circumference showed only a small change during childhood.<sup>10</sup> Nevertheless, because obesity is becoming common in a number of Western countries,<sup>14,15</sup> data from overweight children, beyond the 95th percentile, will be useful to complement our findings.

The ultrasonographic measurements demonstrate that the use of the technique recommended by WHO, ie, stretching the skin flat between the finger and thumb, followed by pushing the needle down at a 90° angle through the skin,<sup>7</sup> should allow perfect intramuscular vaccine delivery using 16-mm (5/8-inch) needles. Using 25-mm needles with this injection technique could present a real danger of damaging neurovascular structures or bone. On the other hand, 25-mm needles suit the injection technique widely used in the United States, ie, bunching of the tissue at the injection site. The use of 16-mm needles with the injection technique recommended in the US should be avoided, especially for adsorbed vaccines, to minimize the risk of subcutaneous delivery. The injection technique is as important as the needle length itself for ensuring proper intramuscular penetration. The effect of needle length on vaccine reactivity was examined by Ipp et al<sup>4</sup> in 18-month-old children receiving DTP-IPV vaccine by injection either into the deltoid muscle with a 16-mm needle or into the thigh muscle with a 16- or 25-mm needle. The use of a 16-mm needle causes more redness and swelling than use of a 25-mm needle, but the incidence of pain or systemic symptoms was independent of needle length. The implication of these results are difficult to analyze because, as in most vaccine trials,<sup>16</sup> the injection technique was not described.

We conclude that the injection technique is the

most important parameter in ensuring efficient intramuscular vaccine delivery. Consequently, the injection technique chosen determines the appropriate needle size. It should be stressed, however, that optimizing factors such as injection route, site, technique, and needle size will not eliminate reactions completely. As stressed by Bergeson and the American Academy of Pediatrics, practitioners should exercise clinical judgment about where and how to inject and adjust needle size appropriately.<sup>6,17</sup> If problems are encountered with a particular injection technique or needle size, a change of either should be considered.

## ACKNOWLEDGMENTS

We thank Dr. Carl-Erik Flodmark for helpful discussion and for providing unpublished data, and Inna Furman for editorial assistance during the preparation of this manuscript.

JOSÉ GROSWASSER, MD\*  
ANDRÉ KAHN, MD, PhD\*  
BEATRICE BOUCHE, MD‡  
SYLVIANE HANQUINET, MD‡  
NOÉMI PERLMUTER, MD‡  
Departments of \*Pediatrics and ‡Radiology  
Queen Fabiola Children's Hospital  
1020 Brussels, Belgium

LUC HESSEL, MD  
Pasteur Mérieux Connaught  
Department of Medical Affairs  
Lyon 69348, France

## REFERENCES

- Shaw FE, Guess HA, Roets JM. Effect of anatomic injection site, age and smoking on the immune response to hepatitis B vaccination. *Vaccine*. 1989;7:425-429
- Profeta ML, Pettenati C, Preglisco F. Administration of influenza virus vaccine in the gluteal area and in deltoid muscle in the elderly. *L'Igiene Moderna*. 1991;96:840-842
- Fishbein DB, Sawyer LA, Reid-Sanden FL, Weir EH. Administration of human diploid-cell rabies vaccine in the gluteal area. *N Engl J Med*. 1988;318:124-125
- Ipp MM, Gold R, Goldbach M, et al. Adverse reactions to diphtheria, tetanus, pertussis-polio vaccination at 18 months of age: effect of injection site and needle length. *Pediatrics*. 1989;83:679-682
- Fessard O, Riche O, Cohen JHM. Intramuscular versus subcutaneous injection for hepatitis B vaccine. *Vaccine*. 1988;6:469
- Bergeson PS, Singer SA, Kaplan AM. Intramuscular injections in children. *Pediatrics*. 1982;70:944-948
- World Health Organization. *Immunization in Practice (A Guide for Health Workers Who Give Vaccines)*. 3. *When and How to Give Vaccines*. EPI/PHW/84/3 Rev. 1. Geneva, Switzerland: World Health Organization, 1984
- American Academy of Pediatrics. *Report of the Committee on Infectious Diseases*. Elk Grove Village, IL: American Academy of Pediatrics, 1994; 11:19-21
- Hick JF, Charboneau JW, Brackke DM, Goergen B. Optimum needle length for diphtheria-tetanus-pertussis inoculation of infants. *Pediatrics*. 1989;84:136-137
- Friasancho AR. Triceps skinfold and upper arm muscle size norms for assessment of nutritional status. *Am J Clin Nutr*. 1974;27:1052-1058
- Study of the cutaneous thickness by biometrical methods and echography, Pasteur-Mérieux sérums et vaccins (internal report). 1996
- Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistic Percentiles. *Am J Clin Nutr*. 1979;32:609-610
- Ministère des Affaires Sociales de la Santé et de la Famille. M. SEMPE. Courbes de croissance. In *Carnet de Santé, mise à jour 1995*. CERFA. n° 65-0057, 1995:69-79
- Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults. *JAMA*. 1994;272:205-211
- Pi-Sunyer FX. The fattening of America. *JAMA*. 1994;272:238-239

16. Poirier MK, Poland GA, Jacobson M. Parameters potentially affecting interpretation of immunogenicity and efficacy data in vaccine trials: are they adequately reported? *Vaccine*. 1996;14:25-27.
17. Bergeson PS. Immunizations to the deltoid region. *Pediatrics*. 1990;85:134-135.

## Central Nervous System Infection Associated With *Bartonella quintana*: A Report of Two Cases

ABBREVIATIONS. CNS, central nervous system; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; PTA, prior to admission; GTC, generalized tonic clonic; IV, intravenous; bid, twice a day; WBC, white blood cell; CT, computed tomography; MRI, magnetic resonance imaging; PAS, periodic acid-Schiff stain; RBC, red blood cell; EEG, electroencephalography.

*Bartonella quintana* is a fastidious Gram-negative bacillus first identified as a cause of a febrile illness, trench fever, among troops engaged in World War I.<sup>1</sup> Infection with this agent in immunocompetent hosts, after an incubation period of 5 to 20 days, may result in one of four clinical patterns: 1) 4- to 5-day febrile illness, 2) periodic febrile illness with three to eight episodes lasting 4 to 5 days each, 3) prolonged febrile illness, or 4) afebrile bacteremia.<sup>2</sup> Associated symptoms are nonspecific and include headache, conjunctivitis, maculopapular rash, organomegaly, arthralgias, myalgias, and bone pain (shin bone fever). The infection is globally endemic, and outbreaks are associated with poor sanitation and hygiene. There is no known nonhuman reservoir, and the body louse *Pediculus humanus* is the only known vector.<sup>1</sup> Infection of immunocompromised hosts with *B quintana* or *B henselae* has been associated with angioproliferative disease of the skin and internal organs, including cutaneous bacillary angiomatosis<sup>3-6</sup> and bacillary peliosis of the spleen, liver, bone marrow, and central nervous system (CNS).<sup>7-10</sup> Endocarditis has also been reported in this population.<sup>11-13</sup>

We report two cases of CNS disease associated with *B quintana*. The patient in case 1 presented with a granulomatous process involving the right thalamus and surrounding tissues, and in case 2 with encephalopathy without evidence of focal involvement. *B quintana* was identified from the cerebrospinal fluid (CSF) by polymerase chain reaction (PCR), with nucleotide sequencing demonstrating >99% homology with a segment of the *B quintana* citrate synthase gene segment. These two cases represent distinctive CNS pathology and broaden the clinical spectrum of *B quintana* infection.

Received for publication Feb 7, 1997; accepted Apr 16, 1997.  
Reprint requests to (J.H.P.) 1600 7th Ave South, 516 ACC Building, Birmingham, AL 35233.  
PEDIATRICS (ISSN 0031 4005). Copyright © 1997 by the American Academy of Pediatrics.

## CASE REPORTS

### Case 1

A 19-year-old male presented to the emergency room with a complaint of frontal headache, left-side weakness, and slurred speech. Over a period of several weeks, the patient had developed clumsiness and weakness of his left upper and lower extremities without associated sensory complaints. The patient's mother reported that over a 2-month period, the patient's ability to attend to complex tasks had diminished, with associated decline in school performance. There was a personality change characterized by flattened affect and loss of initiative. Additional symptoms included incontinence of urine, vomiting after meals, intermittent blurring of vision without diplopia, and dysarthria. Several weeks of intermittent, subjective fever was noted. There was no history of head trauma, diarrhea, rash, weight loss, night sweats, cough, cat scratch, or insect bite.

The patient was diagnosed with epilepsy at 7 years of age, with his seizures well controlled with phenytoin. Over the 2 months prior to admission (PTA), the frequency and severity of seizures had escalated, and antiepileptic therapy had been augmented with Felbamate and Gabapentin without amelioration of seizures. The patient developed two prolonged (>30 minutes), generalized tonic-clonic (GTC) seizures 5 days before admission, with concomitant appearance of a dense left hemiparesis (inability to use the left upper and lower extremity).

Medical history was significant for chronic otitis media leading to significant conductive hearing loss. At five years' PTA, the patient had undergone surgical removal of a mass on the ulnar aspect of the left palm with a pathologic diagnosis of benign fibromatosis. He was hospitalized 3 years' PTA for incision and drainage of a perirectal abscess. Two years' PTA, he required hospitalization for tonsillitis and dehydration, treated with intravenous (IV) fluids and antibiotics. The patient was hospitalized 4 months' PTA with pneumonia and treated with IV antibiotic therapy. At that time, evaluation of a complaint of vomiting and gastric pain revealed gastritis with early evidence of ulceration at the pylorus. There was no history of drug or alcohol abuse.

Developmentally, the patient was mildly delayed for motor and language milestones. He was scheduled to graduate from high school in 1998, at 20 years of age.

Family history was noncontributory. The patient lived in a rural area of the southeastern United States with his parents. There was no history of recent travel, consumption of raw meat, or sexual contact. No illness was reported in family members or close personal contacts. There were multiple household pets including dogs, cats, rabbits, hamsters, and birds. The house had municipal water and sewage service.

Medications on admission included phenytoin, 200 mg twice a day (bid); Gabapentin, 1200 mg divided into four daily doses; Felbamate, 1200 mg bid; omeprazole, 20 mg bid; and Cisapride, 10 mg per day.

Physical examination on admission revealed a temperature of 98.2° F, pulse of 77/min, blood pressure of 136/66, respiratory rate of 16/min, height of 138 cm, and weight of 77 kg. General examination was unrevealing. There was no rash, lymphadenopathy, or hepatosplenomegaly. Auscultation of the heart was unremarkable. The patient was alert and active, but dysarthric with a paucity of spontaneous speech. Perseveration of speech was marked, and attention was poor throughout the examination. Pupils were equal, round, and reactive to light. The left disc margin was blurred, with a left homonymous hemianopsia to confrontation. There was a right ptosis. The left lower face was weak, with sparing of the forehead, consistent with a central seventh nerve palsy. Cranial nerves IX through XII were normal. Strength was 5/5 with normal tone on the right. On the left, there was 4/5 strength, hyperreflexia, increased tone, and extensor Babinski reflex. Cerebellar function was impaired on the left in proportion to weakness. Sensory examination was normal for light touch and vibration, with hyperesthesia to pin prick of the left. Gait was hemiparetic on the left.

Admission laboratories showed a phenytoin level of 9.1 µg/mL, sodium 122 mmol/L, potassium 4.0 mmol/L, chloride 80 mmol/L, HCO<sub>3</sub> 30 mmol/L, BUN 5 mg/dL, creatinine .7 mg/dL, glucose 121 mg/dL, and serum osmolality 262 mOsm/kg. Urine electrolytes were sodium 16 mmol/L, potassium 15 mmol/L, chloride 22 mmol/L, osmolality 266 mOsm/kg, and specific gravity 1.014. Complete blood count revealed 5800/mL white blood