

# An Outbreak of Aseptic Meningitis in the Area of Fort Smith, Arkansas, 1975, Due to Echovirus Type 4

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## INTRODUCTION

In 1975 a cooperative program was undertaken to provide clinical virology service in the state of Arkansas\*\*\*\*. The development of this program has facilitated laboratory and epidemiological investigations of illnesses associated with ~~viral~~ <sup>viral</sup> infections. In May, 1975 an outbreak of aseptic meningitis in Fort Smith was reported to the Arkansas Department of Health and the results of the investigation of this outbreak are reported in this paper.

## DESCRIPTION OF THE OUTBREAK

The reports of physicians to the Arkansas Department of Health were supplemented by review of records of all patients whose cerebrospinal fluid (CSF) was received for culture at the laboratories of the two major hospitals in Fort Smith — Sparks Regional Medical Center and St. Edwards Mercy Hospital. Descriptions of 99 cases were obtained from emergency room and in-patient hospital records and 41 of the patients also had personal or telephone interviews concerning epidemiologic features of the disease.

Most cases had mild prodromal symptoms, nausea and vomiting (50%), diarrhea (3%), sore throat (4%), and fever (100° to 102°, occasional of 104°) for one to several days, followed by the sudden onset of severe headache (98%). They usually came to the hospital during the first day of headache and were found to have mild or moderate nuchal rigidity (55%) and often photophobia (24%). Eleven percent had chills or sweats. Two patients had a rash.

Sixty-four patients had fever, headache and CSF pleocytosis (greater than 5 leukocytes per mm<sup>3</sup>).

CSF leukocyte counts ranged from less than 5 (in 8 patients) to 864 per mm<sup>3</sup>. Fifty-five percent had CSF protein levels of 45 mgm% (range 15 to 86) and all CSF glucose levels were above 58 mgm%. In the first two days of headache about three-fourths of the cells in the CSF were neutrophils; the few counts performed later showed 100% mononuclear cells. Thirty-three had severe headache and fever or stiff neck but did not have lumbar punctures. Most patients had a normal leukocyte count and liver function tests, when done, were normal. Typically hospitalized cases were afebrile on the second or third day and discharged by the fourth day.

Fifty-one of the cases lived in Fort Smith and the remainder over an area about 100 by 60 miles. Cases in May and early June were scattered among small towns outside of Fort Smith (Fig. 1). The outbreak peaked in Fort Smith the second week in June but was more gradual in the surrounding area (Fig. 2). By mid-August, no further cases were reported within the city. The last cases occurred outside of Fort Smith. The oldest case was

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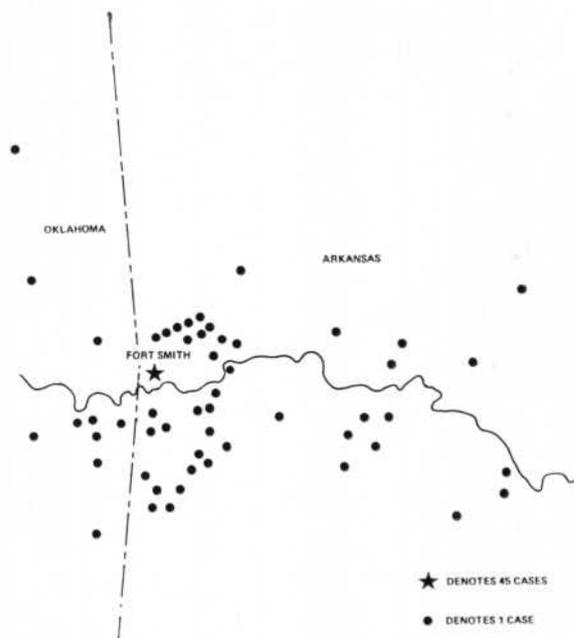


Figure 1. Distribution of cases, aseptic meningitis, Fort Smith Area, AR, May-Sept., 1975, (99 cases)

AN OUTBREAK OF ASEPTIC MENINGITIS IN THE AREA OF FORT SMITH, ARKANSAS, 1975, DUE TO ECHOVIRUS TYPE 4

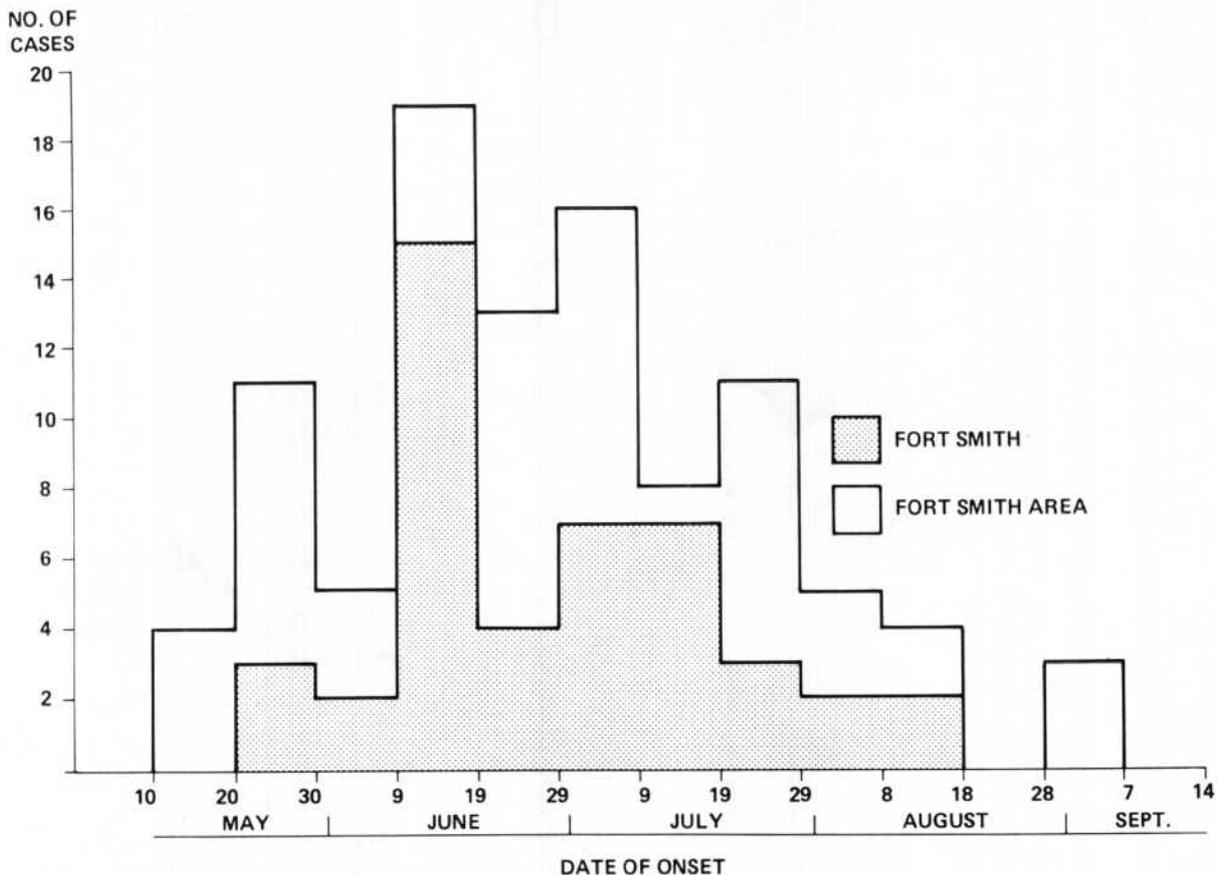


Figure 2.  
Dates of onset of cases of aseptic meningitis in the Fort Smith Area, May-Sept., 1975

48 years of age and the youngest was three years, with a peak from 15 to 29 years (Fig. 3). Only 13% were under 15 years of age. Females were affected slightly more frequently than males (55:45).

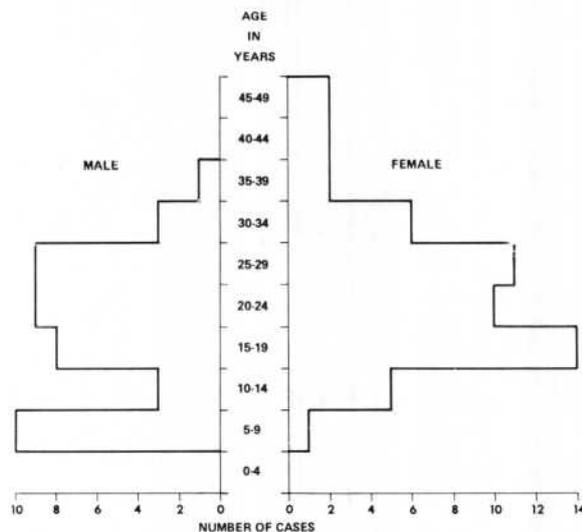


Figure 3.  
Age distribution, aseptic meningitis, Fort Smith Area, AR, May-Sept., 1975 (99 cases)

Two families had three cases each, and 51% of family members of other cases had had illnesses with headache within two weeks. Three patients of twenty-five questioned had received blows to the head respectively one day, one week and an unknown but short period before onset of meningeal symptoms. Two of these were described as severe enough to leave a visible contusion or laceration.

#### VIRAL ISOLATION & IDENTIFICATION DISCUSSION

Throat and rectal swabs collected from patients were placed in tubes containing transport medium. All specimens were frozen as soon as possible after collection and were transported to the laboratory in Little Rock on dry ice. Cerebrospinal fluids (CSF) submitted for bacterial culture at the two Fort Smith Hospitals were frozen at  $-20^{\circ}\text{C}$  and later shipped to Little Rock. In some instances transportation to the laboratory was delayed. Swabs and stool specimens were processed according to standard procedures.<sup>1</sup> Speci-

mens were inoculated into cell cultures of primary rhesus monkey kidney provided by Dr. Paul N. Morgan, Clinical Virology Laboratory, Veterans Administration Hospital, Little Rock. Cultures were maintained in Eagle Basal Medium (BME) containing 3% fetal calf serum and gentamicin 50  $\mu\text{g}/\text{ml}$  and amphotericin B 5  $\mu\text{g}/\text{ml}$  and observed regularly for viral cytopathic effect under the microscope. Specimens were considered negative if no cytopathic effect was detected within 13 days of incubation at 37° C. When cytopathology was observed, the material received a second passage. Identification of isolates was performed by the viral neutralization test employing procedures previously reported.<sup>2</sup> A standard dose of virus suspension was mixed with appropriate dilutions of intersecting reference antiserum pools (poliovirus types 1-3, coxsackievirus group B types 1-6, coxsackie group A types 7, 9, and 16, echovirus types 1-33, excluding type 8). All isolates identified by this procedure were verified by using monospecific echovirus type 4 antiserum prepared in a green monkey and provided by Dr. Thomas D. Flanagan, Erie County Virology Laboratory, Buffalo, New York. Simultaneously, specimens from eight cases were studied at the Center for Disease Control. Echovirus type 4 was isolated from seven of these cases. Other than contamination occurring in one specimen, there was complete agreement in the results obtained between the two laboratories.

Virus isolation was positive in 15 cases of 39 investigated in the laboratory (38%). In each case the virus isolated was identified as echovirus type 4. Echovirus type 4 was identified from six CSF specimens, four throat swabs, three rectal swabs and two stool specimens. From three patients an enterovirus was isolated from more than one specimen and the additional isolate was presumed to be echovirus type 4. The isolation rate from the specimens submitted was as follows: (No. pos./No. tested) CSF — 6/27 (22%), throat swab — 4/15 (27%), rectal swab (including two stool specimens) — 8/17 (47%).

In addition to the Fort Smith outbreak, a total of 20 cases of aseptic meningitis were studied in the Virus Laboratory at UAMS in 1975. Echovirus type 4 was isolated from the spinal fluid and throat swab collected from a 10-year-old girl hospitalized at the Arkansas Children's Hospital, Little Rock. In this case the onset date was approxi-

mately 11/24/75. Of interest is the fact that echovirus type 33 was isolated from the stool of a patient in Smackover, Arkansas, and a rectal swab from another patient in Ashdown. The onset of illness in these cases was approximately 9/18/75 and 9/17/76 respectively. From two additional patients, one in Newport and the other in Smackover, an adenovirus was recovered.

Enteroviruses were isolated from other individuals with illnesses other than aseptic meningitis. Echovirus type 9 was recovered from a patient with rash in Saline County and in two instances polioviruses were recovered from individuals with a history of recent polio vaccination. In one case, poliovirus type 3 was identified and in the other all three serotypes were recovered.

#### DISCUSSION

When eight cases of aseptic meningitis were first reported to the Arkansas Department of Health by a Fort Smith physician in early June, several possible diagnoses were considered. Enteroviruses are the most common cause of such outbreaks, but other possibilities were considered when it was learned that several of the patients had contact with hamsters, a possible source of lymphocytic choriomeningitis (LCM) virus. The presence of thousands of recent arrivals from Vietnam at Fort Chaffee in the center of the affected area raised the question of imported viruses such as dengue or Japanese B encephalitis. These questions were laid to rest within a week by the isolation of echovirus type 4 from seven of the first eight patients studied.

A number of human enteroviruses cause meningitis, including poliovirus and a variety of serotypes of echovirus and coxsackieviruses. The association of echovirus type 4 with outbreaks of aseptic meningitis has been well documented in this country as well as elsewhere in the world.<sup>3</sup> In the U.S. during 1975, echovirus type 4 was isolated from a single case of aseptic meningitis in Oregon.<sup>4</sup> In addition, echovirus type 4 was isolated from seven cases (Texas—3, North Dakota—2, New Hampshire—1, and Missouri—1) at the CDC laboratories. In the South, outbreaks have been reported in Kentucky, West Virginia, Georgia, and Texas.<sup>5</sup> In 1971, an epidemic of aseptic meningitis occurred in New Orleans and echovirus type 4 was recovered from 61 patients of 166 studied.<sup>6</sup> Of the 61 patients, the specimens giving the highest yield were throat (88%), stool (87%),

and CSF (75%) — the materials usually of most value in enterovirus epidemics.

Successful virus isolation in studies of such outbreaks depends on a number of critical factors, namely: time of collection of specimens, storage (refrigeration for short periods or freezing), transportation, and techniques used by the laboratory for viral isolation. In our study the number of positive cases, 15/39 (38%) was probably smaller than would be expected. This could be attributed, in part, to the time of collection of specimen after onset of illness but was probably more associated with delay in freezing of the specimens and transportation to Little Rock. Many of the CSF specimens collected in this epidemic had already been submitted for bacteriology and were not ideal specimens for virology after hours or days at room temperature. Despite this, virus was isolated from 6 of 27 CSF specimens.

The epidemic did not spread across the State, but remained localized to the Fort Smith area. This may have been due to differences in previous experience with this virus in different parts of the State, or to other factors. One case of echovirus type 4 associated with meningitis was identified in Little Rock in November, but no other cases involving echovirus type 4 were detected outside the Fort Smith area.

The prolonged time course, geographic distribution and high secondary attack rate within families in this epidemic all point to person-to-person transmission and this is the most likely mode of spread.

The primary control measures taken in the Fort Smith epidemic consisted of isolation of patients during hospitalization and the dissemination of information about the epidemic to the public and the medical community in Fort Smith. A rash accompanied the echovirus type 4 infections very rarely (2%), and this information facilitated recognition of two cases of Rocky Mountain Spotted Fever which occurred at the same time. A case of meningococcal meningitis was also recognized as being clinically more severe and was successfully treated after CSF examination. A check of culture and chlorination records and Fort Smith water supply revealed no cause for concern and cases did not center about any particular swimming area; indeed almost half had not been swimming recently. The investigation was therefore of immediate practical value, demonstrating that

combined epidemiologic and virologic investigation of community outbreaks is of more than academic import.

Most epidemics of meningitis due to echovirus type 4 have affected children more than adults and males frequently outnumber females.<sup>7</sup> In the epidemic reported here the reverse was true; females comprised the majority (55:45) and very few young children were involved. The average family size of cases was 3.6 compared with the 2.9 listed in the 1970 U.S. Census for Fort Smith, suggesting that individuals living with several children were more at risk than those living alone. If close contact with children was the main mode of transmission, this would also explain the higher attack rate in females of the childbearing age found in this epidemic.

Typically in enterovirus epidemics there are a number of asymptomatic infections and minor illnesses for every case of aseptic meningitis. The factors which determine the outcome of infection are largely unknown other than preexisting antibody and the age and sex of the patient. Minor trauma to an extremity such as from an intramuscular injection may predispose to paralysis of that extremity during an epidemic of poliomyelitis.<sup>8</sup> The history of head injury in three of twenty-five cases asked this question suggests that trauma to the meninges may tip the balance in favor of meningeal involvement during an infection with echovirus type 4.

The isolation of echovirus type 33 from two cases of aseptic meningitis occurring in Smackover and Ashdown, Arkansas, is worthy of comment. This serotype was originally isolated in Mexico from a normal individual<sup>1</sup> and its role in causing aseptic meningitis or other illnesses has not been established. There are no reports of isolation of this virus as the predominant serotype in outbreaks of aseptic meningitis. The fact that the virus was recovered in our study from stool specimens suggests but does not prove that echovirus type 33 caused the meningitis.

#### SUMMARY

At least 99 cases of aseptic meningitis occurred in the Fort Smith area of Arkansas between May 12 and September 1975. Echovirus type 4 was isolated from 15 cases of 39 studied virologically, and in six cases from cerebrospinal fluid. Approximately half of family contacts of cases had fever and headache. All available evidence pointed to

person-to-person spread of the illness. Viral isolation, epidemiologic studies and rapid dissemination of information to the medical community were the major public health measures applied.

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