# **Original Contributions**

## ASEPTIC MENINGITIS DUE TO ECHOVIRUS 4 IN PANAMA CITY, REPUBLIC OF PANAMA

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Between September 23 and November 30, 1981, 1,032 children from Panama City, Republic of Panamá were hospitalized with aseptic meningitis. Forty-four per cent of the cases were in the age group 5-9 years old; the disease was mild and self-limiting with an average hospital stay of five days. Echovirus 4 isolates were obtained from 48 of 160 patients. To identify risk factors associated with the epidemic, the authors randomly selected 10 per cent of hospitalized cases and conducted a family-based seroepidemiologic study. The closest neighboring house with at least one child younger than 15 years was similarly studied as a control. In total, 182 households and 1,083 of 1,177 residents were included. No risk factors ascertained by the study were associated with aseptic meningitis; however, several factors were related to recent echovirus 4 infection. Overall, 56 per cent of cases had echovirus 4 antibody, as did 29 per cent of their family members and 19 per cent of control family members. Children who attended kindergarten or primary school were more likely to have antibody than other household members and, within case families, individuals involved in child-care had an excess risk for infection.

echoviruses; enteroviruses; meningitis; virus diseases

Enteroviruses are common causes of acute febrile disease and may cause aseptic meningitis; echovirus type 4 has been frequently associated with aseptic meningitis epidemics (1, 2). Echovirus aseptic meningitis is usually a benign clinical entity but may present an acute public health emergency because during epidemics large numbers of patients inundate emergency rooms and those with meningeal signs are frequently admitted to the hospital awaiting results of laboratory tests. This type of public health emergency is particularly important in developing tropical countries

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since their limited health services resources are severely strained. Although much is known concerning classic tropical epidemics such as dengue, yellow fever, etc., aseptic meningitis epidemics have not been well documented in the American tropics. This may be because enteroviruses are highly endemic, so that the majority of the population becomes immune to the prevalent strains before reaching the 5–11 year age group, in which most disease occurs. However, as tropical public health improves (particularly in metropolitan areas), such epidemics will become more common.

The Republic of Panamá exemplifies a rapidly developing tropical Latin American country, and it has a Ministry of Health that is one of the best in the region. Between September 23 and November 30, 1981, 1,032 children with aseptic meningitis were admitted to Panamá City's two major public hospitals (3, 4). The unprecedented magnitude of the epidemic seriously disrupted hospital services. The study presented in this paper was conducted to define the epidemic. We first established daily hospital surveillance and a system to collect and process diagnostic specimens rapidly. Echovirus 4 was shown to be the causative agent, but since no obvious pattern of disease occurrence or risk factors emerged from the hospital surveillance data, we conducted a case-control seroepidemiologic study. This paper provides a detailed epidemiologic description of the Panamá City echovirus 4 aseptic meningitis outbreak. In addition, the Ministry of Health plan of action during the epidemic is an excellent example to be followed for such outbreaks in similar areas.

#### MATERIALS AND METHODS

Description of the area. The Republic of Panamá, located seven degrees north of the equator, links Central and South America both physically and culturally. The 1980 census (5) enumerated 1.8 million inhabitants; Panamá has a 77,082 sq km surface area and an overall population density of 25 persons per sq km. The country has experienced increasing migration from its rural provinces to its metropolitan capital, Panamá City, which in 1981 had 655,687 residents, or 36 per cent of the country's population. Population densities in Panamá City ranged from 185 to 3,062 people per sq km and approximately 40 per cent of the metropolitan population was younger than age 15 years. Two large hospitals account for the majority of pediatric care, Hospital del Niño, a Ministry of Health pediatric medical center with 356 beds, and the Social Security Metropolitan Medical Center, which has a 113 bed pediatric service. In addition, Panamá City has two private general hospitals with approximately 100 beds each, and Gorgas Army Hospital. in the former Canal Zone, serves US Department of Defense employees and dependents.

Hospital surveillance. The aseptic meningitis epidemic was recognized by Panamanian public health authorities in the first week of October 1981, or epidemiologic week 39, and by week 40 the Ministry of Health had implemented a hospital surveillance system. All hospitals in Panamá City and Colon, and in the remainder of the country, were asked to provide daily telephone reports concerning aseptic meningitis admissions; in addition, Ministry of Health Division of Epidemiology personnel made daily visits to each major hospital in Panamá City and reviewed the charts from all aseptic meningitis patients. Information concerning age, sex, race, address, school or day care center attendance, date of illness onset, symptoms, history of recent acute disease, and vaccination history were abstracted from the hospital chart or obtained from the parents and entered on standardized "self-coding" forms. At discharge, additional data on duration of hospitalization, cerebrospinal fluid findings, and virus isolation were recorded. Information was entered within 24 hours of acquisition into the Gorgas Memorial Laboratory Computer Center. Data processing utilized the CCSS data processing and statistics system (6).

Laboratory methods. Gorgas Memorial Laboratory staff instructed physicians at hospitals where active surveillance occurred as to proper collection of cerebrospinal fluid, throat swab, rectal swab, and acute blood specimens from patients with aseptic meningitis of less than 24 hours duration. Specimens were maintained at 4 C, picked up twice daily, and processed that day at the Gorgas Memorial Laboratory; virus isolation utilized Vero and fetal tonsil cells and standard methods (7). Cerebrospinal fluid specimens were also inoculated intracerebrally into one-day-old mice. Viral isolates were identified by microneutralization using anti-sera to echovirus 4 Pesascek strain obtained from the Centers for Disease Control, Atlanta, GA.

Patients from whom specimens were collected were requested to return to the Pediatric Emergency Room in two weeks to have a convalescent serum specimen collected. Paired sera as well as sera collected in the case-control study were serially diluted (beginning at 1:8) and tested in a microtiter neutralization assay; sera were incubated with 100 tissue culture infectious dose 50 of echovirus 4 and added to fetal tonsil cells. The prototype Pesascek strain of echovirus 4 provided by the Centers for Disease Control was used for all antibody determinations.

Case-control study. A case-control study was conducted during the two weekends of epidemiologic weeks 45 and 47. We worked on the weekends to optimize the possibility of finding most family members at home. The case-control study included case families (a selection of hospitalized cases and all their family members), neighbor control families, and distant control families; it involved interview and phlebotomy of entire households.

Case families were defined by a random 10 per cent selection from Panamá City residents younger than 15 years who were admitted with a clinical diagnosis of aseptic meningitis to Hospital del Niño or Social Security Hospital between August 22 and October 31, 1981. Nine teams, each composed of a Ministry of Health or Gorgas Memorial Laboratory epidemiologist and a public health nurse or epidemiology technician, conducted the field study. Each team had a list of case houses to visit; selected houses had been located by Ministry of Health personnel prior to the survev and their locations marked on maps, Teams contacted an adult head of household, explained the purpose of the study, and solicited the family's cooperation. If no one was home, word was left with neighbors, and up to three return visits were made. If a family could not be contacted or verbal informed consent was denied, the case was not replaced.

For each case household, a neighboring control home was selected; this was the closest residence to the case home with at least one child younger than 15 years of age and in which no resident had been diagnosed as having aseptic meningitis. The interview team ascertained the composition of neighboring homes until a suitable control family was located (virtually always within the first three homes). When a potential control family was located, the same procedures were utilized as with case families; if permission was refused, the next closest eligible neighboring family was substituted.

For every two case families in a "corregimiento", a distant control family was selected; Panamá City is comprised of 18 politically defined corregimientos, which are similar to boroughs. Interview teams selected a distant control family in the same general area within the corregimiento as the two case houses but not in the same block. Distant control homes were selected to be representative of the general area in which case families resided. Distant control families had to meet the same other criteria as neighboring controls. Similar interview and phlebotomy procedures were used as with cases and neighboring controls.

Data collection involved the same procedures for cases and controls. Upon obtaining permission, the study team inspected the house and filled out a standardized form describing the dwelling; this included address, type of house, number of rooms, total number of residents, number of people per sleeping room, water source, type of sanitary facilities, monthly household income, where food was normally purchased, and information on pets.

Standardized interviews were then conducted to collect the following information about each household resident; age, sex, race, occupation (for children, attendance at school, preschool, or day care centers), illness in the last month (mumps, measles, pharyngitis, flu. diarrhea. vomiting). whether or not a physician had diagnosed aseptic meningitis, attendance at specific large public gatherings in the last month, and contact with aseptic meningitis cases. If a family member was not home, information was obtained from a responsible adult informant.

Following interview, 10 ml of venous blood was obtained from all willing subjects older than one year of age. Blood specimens were held on wet ice until returned to the Gorgas Memorial Laboratory at the end of the day. Sera were separated the following morning, aliquoted, and stored frozen at -20 C until tested for echovirus 4 antibody.

Pre-epidemic serologic survey. In June 1980, the Ministry of Health and Gorgas Memorial Laboratory conducted a random serologic survey in Panamá City to assess immunity to vaccinable diseases. Briefly, the sample was picked by randomly selecting census tracts within each corregimiento and then randomly selecting households within the census tracts so that, by surveying all household members, approximately one per cent of the total population would be included (8). The survey obtained 2,704 sera, or 0.7 per cent of Panamá City's 1980 census population. Compliance varied from 36 to 80 per cent and was lowest in higher socioeconomic census tracts; adult males had the lowest compliance rates in all areas. In order to estimate pre-epidemic immunity to echovirus 4, we randomly selected 149 sera from children younger than age 15 years and 245 sera from adults older than age 15 years and screened them at a 1:8 dilution for antibody, as described above.

#### RESULTS

### Hospital surveillance

Course of the epidemic. Hospital records showed that the epidemic began in August 1981 and had peaked and started to decline by early November; however, an increased number of aseptic meningitis cases continued to occur until March 1982 (figure 1). Between August 16 and November 14, when the majority of cases occurred, 2.7 per 1,000 of Panamá City children younger than 15 years of age were hospitalized for aseptic meningitis. We reviewed 883 of 1,032 (86 per cent) of these childrens' hospital charts. All areas of the city were affected, corregimiento-specific attack rates varying from 0.4 to 6.8 per 1,000 children (figure 2). Attack rates were highest in lower socioeconomic areas, but no temporal or geographic pattern could be ascertained. Gorgas Army Hospital admitted several children with aseptic meningitis but no cases were documented among residents of the Canal Area.

Clinical characteristics. The disease had a sudden onset with fever between 38 C and 40 C (94 per cent of 883 patients with chart review), headache (85 per cent), vomiting (84 per cent), and meningeal signs (47 per cent). Rash was noted in fewer than 5 per cent of hospital charts. Other than lethargy, specific neurologic symptoms were not noted. The duration of illness was known for 379 of the 883 patients and varied from one to 12 days (two patients remained in the hospital for 20 days). The mean duration of hospitalization was 4.7 days. There were no deaths, and no major sequelae were noted.

Cerebrospinal fluid findings were reported in charts of 882 of the 883 chart review patients; 90 per cent of the cases had fewer than 100 cells per mm<sup>3</sup>, and, in 73 per cent of the cases, cells were classified as lymphocytes. Ninety-five per cent of cases had cerebrospinal fluid glucose levels between 40 mg/100 ml and 100 mg/100 ml,

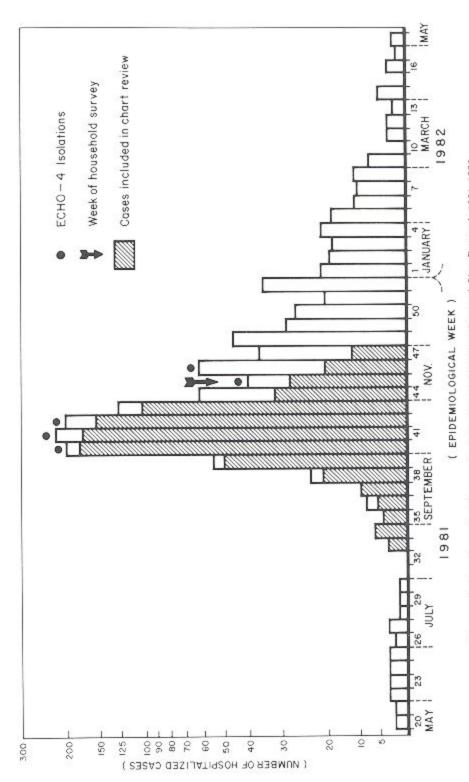


FIGURE 1. Aseptic meningitis cases by date of hospitalization, Panamá City, Panamá, 1981-1982.

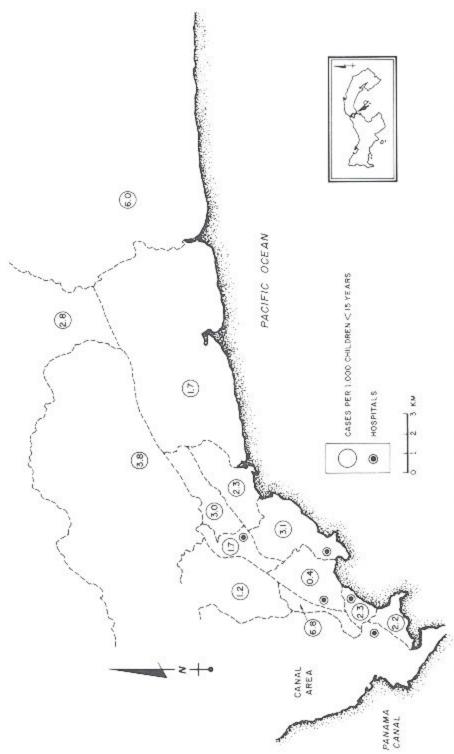


FIGURE 2. Corregimiento-specific aseptic meningitis attack rates per 1,000 children younger than age 5 years, Panama City, Panama, 1981.

and 88 per cent had protein concentrations less than 60 mg/100 ml.

Adequate specimens for viral isolation were submitted from 160 patients, and 48 (30 per cent) yielded echovirus type 4 isolates (table 1). The highest isolation rates were from throat swabs, and echovirus 4 was isolated throughout the course of the epidemic (figure 1). We also isolated five adenoviruses and one each of mumps, cytomegalovirus, and herpes simplex virus from throat swabs. Seven of 11 (64 per cent) acute/convalescent serum pairs showed seroconversion to echovirus 4 (at least fourfold titer rise).

Patient characteristics. Only six of the 883 patients with chart review were older than age 15 years, and the highest attack rates were in 5-9 year old children. Males predominated in all age groups (table 2). Age also correlated with severity of illness, the mean duration of hospitalization being 5.2 days for the 108 children less than 5 years old, 4.6 days for the 173 children 5-9

TABLE 1
Summary of echovirus 4 isolations\*, Panamá City,
Panamá, October 5-November 20, 1981

Specimen	No.	%
Cerebrospinal fluid	8/160†	5
Throat swab	36/134	27
Rectal swab	19/124	15
Total patients tested	48/160	30

Some patients had virus isolation from multiple specimens.

years old, 4.3 days for the 95 children 10-14 years old, and two days each for the two children 15 years old. Duration of specific signs and symptoms was not uniformly documented in hospital charts.

No other risk factors were apparent from hospital surveillance data. Patients' race was representative of the general Panamá City population. Information concerning day care appeared in the charts of 229 out of 281 children vounger than age 5 years; 178 (78 per cent) were cared for at home and did not attend public or private day care centers, preschool, or kindergarten. Information on recent vaccination was available for 482 of the 883 chart review patients, and only 22 (5 per cent) had been vaccinated in the past month. Vaccination status was known for 673, and 502 (75 per cent) had received complete vaccination coverage recommended for their age.

### Case-control study

Study population. We visited 182 living units, 71 case houses, 71 neighboring controls, and 40 distant controls. We detected ten additional previously hospitalized aseptic meningitis cases during interviews at case-households, so that a total of 81 physician-diagnosed aseptic meningitis cases are included in the study. Overall, 1,083 of the 1,177 known study household residents (92 per cent) were interviewed, and blood specimens were obtained from 973 of the 1,177 (83 per cent).

Disease risk factors. None of the house-

Table 2 Age-sex-specific aseptic meningitis attack rates\*, Panamá City, Panamá, 1981

Age† (years)	Male		Fe	Overall	
	No.	Attack rate	No.	Attack rate	attack rate
0-4	177	4.7	103	2.8	3.8
5-9	216	5.6	167	4.4	5.0
10-14	131	3.5	68	1.8	2.7
15-20	2	0.1	2	0.1	0.1
>20	2				

<sup>\*</sup> Attack rates are cases per 1,000.

<sup>†</sup> No. positive/no. tested.

<sup>†</sup> All 883 cases with chart review are included; for 11 cases, age was unknown, but all 11 cases were younger than age 15 years; four cases did not have sex recorded.

hold risk factors which we investigated correlated with the occurrence of aseptic meningitis (table 3). No aseptic meningitis cases were detected in potential control families at the time they were queried for recruitment into the study.

Echovirus 4 infection. Since the majority of echovirus 4 infections are asymptomatic, we analyzed overall infection rates, as determined by serology (table 4). Forty-one of 72 children with clinically diagnosed aseptic meningitis had echovirus 4 antibody (57 per cent), in contrast to 86 of 293 case family members who denied having aseptic meningitis (29 per cent). Ninety eight of 508 control family members had echovirus 4 antibody (19 per cent). Neighbor and distant control families were not different

Table 3

Association of household risk factors with occurrence of aseptic meningitis in the family, Panamá City, Panamá, 1981

	Type of household				
	200	Control			
	Case (n = 71)	Neighbor (n = 71)	Distant (n = 40)		
Type of dwelling					
Single-family	50*	54	69		
Multi-family	35	35	26		
Shanty	12	11	3		
Other	3	0	2		
Monthly household income					
<\$200	34	25	22		
\$200-500	26	36	30		
\$501-1,000	26	16	23		
>\$1,000	14	23	25		
No. of people per bedroom					
2	17	18	35		
3	21	24	25		
4	27	23	18		
5	20	14	5		
6+	15	21	17		
Sanitary facilities					
Private flush toilet	46	52	53		
Communal toilet	17	15	22		
Latrine	27	27	23		
None	10	6	2		
Water supply					
In the home	63	64	60		
Communal—indoors	20	25	23		
Communal—outdoors	17	11	17		
Open sewer near home					
No	67	73	75		
Yes	33	27	25		
Unusual event					
No	94	94	92		
Yes	6	6	8		

<sup>\*</sup> Per cent of families with risk factor in each category.

Table 4

Age-specific echovirus 4 antibody prevalence in different family groups, Panamá City, Panamá, 1981

Age	Case	Case		nily	Control family*		
(years)	No. %		No. %		No.	%	
0-4	11/24†	46	9/28	32	10/60	17	
5-9	17/31	55	21/59	36	13/92	14	
10-14	12/16	75	7/38	18	11/89	12	
15-19			6/33	18	14/57	25	
20-29			20/56	36	17/75	23	
30+			22/75	29	32/130	25	
Total±	41/72	57	86/293	29	98/508	19	
Noncompliance§	9/81	11	78/371	21	116/624	19	

\* Control family includes neighbor and distant control families combined.

† No. positive/no. tested.

‡ Denominators vary because of unknown age.

§ Noncompliance denotes number of people per category on whom blond was not obtained/total number of interviews in the category.

with respect to antibody prevalence or other risk factors, so they have been combined in this and subsequent analyses. Male and female antibody prevalence rates were similar within each age grouping of each category.

We analyzed a variety of other factors with respect to risk of infection. Analysis was limited to pediatric infection, because virtually all cases involved children younger than age 15 years, and echovirus 4 antibody in children was likely to reflect infection acquired in their current epidemiologic environment. Index cases were excluded from the comparisons in order to control for ascertainment bias. There was no apparent relation between attendance at day care centers or other school settings and echovirus 4 antibody prevalence in any of the specific population groups. Personal and environmental factors other than living in a case family were not related to risk of past echovirus 4 infection (table 5).

Echovirus 4 antibody prevalence in control families (19 per cent) was not significantly different from that in Panamá City during the 1980 serologic survey, in which 59 of 394 were seropositive (15 per cent). Corregimiento-specific echovirus 4 antibody prevalence rates differed in the 1980 survey (figure 3) but did not predict 1981 corregimiento-specific infection or attack rates (figures 2 and 3). Neighbor control families were rarely infected with echovirus 4, and, although there was a suggestion of increasing antibody prevalence with age, the effect was not dramatic. Within case families, children younger than age ten years and adults between ages 25 and 29 years had a twofold excess risk of being previously infected than comparable members of control families (table 6).

### DISCUSSION

The 1981 Panamá City echovirus 4 aseptic meningitis outbreak is one of the largest recorded in the epidemiologic literature, and we were fortunate that routine Ministry of Health surveillance recognized the epidemic almost at its inception. A detailed hospital surveillance program was implemented early in the course of the epidemic and Gorgas Memorial Laboratory provided rapid viral diagnosis. The clinical-epidemiologic aspects of hospitalized cases were similar to those documented in other echovirus aseptic meningitis epidemics in industrialized countries (1, 9-15); 5-9 year olds had the highest attack rates, the clinical course was generally mild, and the laboratory findings were typical.

We had hoped that the hospital surveillance and case-control studies would identify risk factors which could be manipulated to control the epidemic. The hospital surveillance study did not identify temporal, geographic, or socioeconomic risk factors. The case-control study did not identify risk factors for either aseptic meningitis or echovirus 4 infection, either between cases and controls or within either category. This is at variance with a household study conducted in Kentucky by Ray et al. (10), in which both infection and disease varied with race and number of household residents.

The case-control study showed that school-age children were important factors for intra-family transmission of echovirus

TABLE 5

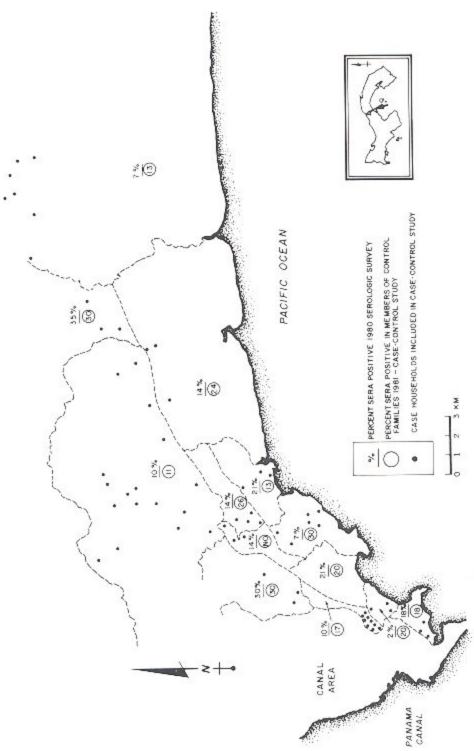
Association of echovirus 4 antibody in children younger than age 15 years in case and control families, according to specific rish factors, Panamá City, Panamá, 1981

	Case family $(n = 125)^*$		Control family $(n = 242)$	
	No.	%	No.	%
Type of dwelling	an factorism of	1740e	0.0000000000000000000000000000000000000	1,000
Single-family	14/52†	27	14/116	12
Multi-family	13/40	33	12/73	16
Shanty	3/14	21	3/21	14
Monthly household income				
<\$200	13/51	25	11/70	16
\$200-500	9/34	26	15/84	18
\$501-1,000	9/28	32	2/34	6
>\$1,000	6/12	50	5/50	10
No of people per hedroom				
	4/9	44	6/46	13
2 3	3/23	13	5/53	9
4	12/37	32	11/40	28
5	7/24	29	6/33	18
6+	11/32	34	6/70	9
Sanitary facilities				
Private flush toilet	21/55	38	13/126	10
Communa) toilet	6/19	32	15/52	29
Latrine	8/37	22	4/50	8
None	2/14	14	2/14	14
Water supply				
In the home	23/69	33	14/141	10
Communal—indoors	6/26	23	15/62	24
Communal—outdoors	8/30	27	5/39	13
Open sewer near home				
No	24/68	36	17/144	12
Yes	10/45	22	13/74	18
Unusual event				
No	36/123	29	32/225	14
Yes	1/1		1/11	9
Any recent illness				
No	23/71	32	19/132	14
Yes	14/54	26	14/109	13

<sup>\*</sup> The index case is excluded from each case family to control for ascertainment bias. Denominators may vary across cells because of unknowns.

<sup>†</sup> No. positive/no. tested.

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PIGURE 3. Corregimiento-specific echovirus 4 antibody prevalence before and after the aseptic meningitis epidemic, Panamá City, Panamá, 1981.

Table 6	
Age- and sex-specific echovirus 4 antibody prevalence rates in case and control families, Pe Panamá, 1981	<sup>P</sup> anamá City,

Age (years) Fema	Case family*			Control family				
	e Male		Female		Male			
	No. %	No.	%	No.	%	No.	%	
0-4	6/18†	33	3/10	30	5/30	17	5/30	17
5-9	12/34	36	9/25	36	9/54	17	4/38	11
10-14	6/27	22	1/11	9	6/40	15	5/49	10
15-19	5/22	23	1/11	9	6/27	22	8/30	27
20-24	2/12	17	3/12	25	7/32	22	3/14	21
25-29	11/25	44	4/7	57	6/22	27	1/7	14
30+	14/49	29	8/26	31	19/86	22	13/44	30

<sup>\*</sup> The index case is excluded from each case family to control for ascertainment bias.

4. Within case families, school-age children and adults between ages 25 and 29 years (largely the parents of such children) had inordinately high antibody prevalence rates compared to similar groups in the control families, and, within these two high-risk age groups, prevalence of antibody appeared to vary with household crowding, although the numbers were too small for adequate statistical analysis. Other studies have reached similar conclusions for echovirus 4 and other enteroviruses (1, 10, 16, 17).

Interpretation of our results must take into account limitations imposed by the study design. We defined case families on the basis of clinical diagnosis, rather than echovirus 4 infection. It is well known that most infections do not result in disease, and the determinants of aseptic meningitis are unknown. Also, not all aseptic meningitis cases identified in an epidemic are necessarily due to one agent; only 64 per cent of hospitalized patients seroconverted, and only 57 per cent of study cases had echovirus 4 antibody. We did not obtain paired sera from study cases, and seronegativity at the time of our study could have several explanations, one of which is another etiologic agent. However, failure to demonstrate neutralizing antibody is not proof of noninfection; the virus strain used in the neutralizing antibody test is important and the Pesascek strain may be less sensitive than other strains (10, 18). Other studies have documented seroconversion rates of 77 per cent (14) and 90 per cent (10, 13) during echovirus epidemics.

Control selection was another limitation. We used the closest neighboring family which met inclusion criteria, but did not keep specific count of neighboring families in which no one was home during the survey. We estimate that fewer than 15 per cent of neighboring dwellings could not be contacted, and thus that some bias operated in excluding these neighbors from consideration. Overmatching is also possible since cases and neighbor controls resided contiguously. The great disparity in antibody prevalence between case and neighbor control families would seem to obviate this. as would the findings that seroprevalence rates were the same in neighbor and distant controls and that antibody prevalence rates in both types of control families were the same as determined in the 1980 serologic survey.

That this epidemic occurred in the Republic of Panamá is particularly important since such epidemics have rarely been described in the tropics. An implicit assumption, classically exemplified by poliomyelitis virus (19) and hepatitis A virus (20), is that tropical populations are exposed early in life to a myriad of respiratory and fecalorally transmitted viruses and develop immunity prior to the age at which infection

<sup>†</sup> No. positive/no. tested.

produces characteristic symptoms (16, 21). Data from the previous serologic survey showed that exposure to echovirus 4, a classic enterovirus, was low in Panamá City before the epidemic. Only 15 per cent of persons sampled in 1980 had echovirus 4 antibody, and prevalence varied between 7–35 per cent, depending on corregimiento of residence. This is similar to rates reported in the United States (18, 22) but much lower than have been documented in other tropical areas (19, 23). Clearly, overall population immunity was low and environmental conditions were optimal to favor rapid transmission of the virus.

There is every reason to assume that similar epidemics will occur, perhaps with increasing frequency, in major Latin American cities, and infectious disease control strategies need to be maintained current. Vaccination programs against agents such as polio and measles need to be continuously evaluated and modified, and newer vaccines should be evaluated and deployed depending on local circumstances. However, many major epidemics such as the one in this report are not amenable to control by existing immunization methods, Echovirus 4 and many other enteroviruses are transmitted equally well by fecal-oral and respiratory routes (1, 10, 11, 13-15). Emergency control measures should aim to rapidly identify the etiologic agent and interrupt transmission but, as exemplified by the Panamá epidemic, this may be impossible. In spite of a well-organized, detailed study of virtually all hospitalized cases, no obvious risk factors could be detected. Nonspecific intervention methods such as closing swimming pools, schools, and day care centers are probably not sufficient to stem the outbreak, although common sense frequently dictates this sort of action (16).

The major public health impact of aseptic meningitis epidemics derives from their impact on hospital health services resources and high levels of public concern, and one form of control could attempt to lessen this impact. In Panamá, the Ministry of Health and Social Security Hospital systems, and particularly their pediatrics departments, have strict clinical standards. Children with a presumptive diagnosis of viral meningitis are usually hospitalized in order to rule out bacterial meningitis. During aseptic meningitis epidemics, virtually all children with minimal "classic" symptoms represent infections with the epidemic agent, and it has been suggested (12) that public health officials should implement specific outpatient procedures for mild and moderate "aseptic meningitis" cases in the midst of a documented enterovirus epidemic.

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