A COMPREHENSIVE SURVEY OF PEDIATRIC DIARRHEA AT A PRIVATE HOSPITAL IN METRO MANILA

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Abstract The epidemiology of diarrhea among Filipino pediatric patients, representing a cross-section of socioeconomic strata, was investigated over a one year period. Rotavirus was detected in 33.9% of the diarrhea stools examined and was the leading cause of diarrhea in the study population. Although proportionately more rotavirus was found during the cold season, most children became infected with rotavirus during the rainy season, when diarrheal disease was at its peak in Metropolitan Manila. Enteric adenovirus types 40 or 41 were associated with only 5.4% of the diarrhea cases. Overall, one or more etiologic agents of diarrhea were detected in 67.2% of the stools examined. Many of these positive stools (21.6%) contained multiple diarrheogenic agents. Bacterial enteric pathogens were isolated from 32.3% of the cases. Nearly 70% of these patients with bacterial gastroenteritis became ill during the rainy season. Etiology specific and general risk factors associated with diarrheal illness in the study population are discussed.

INTRODUCTION

Diarrhea is a major cause of morbidity and mortality among the pediatric populations of tropical developing countries (Snyder *et al,* 1982). In the Republic of the Philippines (RP) diarrhea has reportedly been associated with one third of all deaths in children under five and it has been estimated that Filipino children suffer an average of 2.8 episodes of diarrhea per year (Anonymous, 1985). With the notable exception of the community based study of Saniel *et al* (1985), diarrheal disease investigations in the RP have focused on the hospitalized patient (Adkins *et al,* 1987; Echeverria *et al,* 1978; Lucero *et al,* 1984). While hospitals present a convenient venue for identifying medically significant diarrheal cases, they can also bias studies in favor of the more seriously ill patient. Additional bias is introduced when public hospitals, serving as catchment centers for the critically ill, poor patient, are selected as the study site. The effect of study population on the observed etiology of diarrheal disease was evident in the studies of Saniel *et al* (1985, 1987), who detected rotavirus in 35% of hospitalized diarrhea patients but in only 7% of sporadic diarrhea cases in the community. The current study was undertaken to determine the etiology of diarrhea among pediatric patients representing a cross-section of socioeconomic strata and severity of illness. Additionally, we wished to relate etiology and clinical observations to personal and environmental attributes of the patients. In an attempt to circumvent the selective bias of the public hospital, but nonetheless ensure that diarrheas of actual or potential medical consequence were emphasized, we selected as our study site a private hospital which sees a significant number of pediatric diarrhea cases, from both urban and rural environments, on an out-patient basis. In addition to the comprehensive list of potential etiologic agents routinely sought in a survey of this nature, we also wished to determine if adenovirus types 40 and 41 are significant causes of

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pediatric diarrhea in the RP. Although these enteric adenovirus serotypes are reported to be important causes of gastroenteritis in children residing in countries with temperate climates (Madeley, 1986; Uhnoo *et al,* 1984), they were associated with very little diarrhea among children in Thailand (Hermann *et al,* 1988). The role of adenovirus as an etiologic agent of diarrhea among Filipino children has not previously been investigated.

MATERIALS AND METHODS

Study population and design: All pediatric diarrhea patients seen by the primary investigator (up to a maximum of 5 patients per day) during her normal clinic hours at Our Lady of Fatima Hospital, Valenzuela, Metro Manila were invited, via their parents or legal guardians, to participate in the study. Fatima is a 250-bed private hospital located just within the northern border of metropolitan Manila. The pediatric department sees approximately 25-50% of cases as out-patients depending on the season of the year. Diarrhea was defined as the passage of three or more loose or watery stools in a 24-hour period with or without any associated signs and symptoms. Clinical and demographic data in addition to feeding, water, and medical histories were systematically collected from all study volunteers. A stool sample was obtained from all volunteer patients and examined on site for consistency, visible blood and mucus, and occult blood. The pH of each stool sample was also determined and the stools examined microscopically for white blood cells (WBCs) and red blood cells (RBCs). A portion of each stool was mixed in 10% formalin and two stool saturated swabs were placed in modified Cary-Blair transport medium for microbiological examination at the US Naval Medical Research Unit No. 2 (NAMRU-2) laboratory. Swabs in the transport medium were kept refrigerated and cultured within 48 hours of collection. A portion of each stool was also frozen for subsequent viral antigen detection. Pediatric patients seen for reasons other than diarrhea, and who were not febrile, were invited to join the study as controls. Rectal swabs were obtained on control volunteers unable to provide a stool sample at the time of their hospital visit. Patients and controls were enrolled in the study from March 1989 through March 1990.

Laboratory examinations: Stool saturated swabs were cultured for *Salmonella* spp., *Shigella* spp., *Vibrio* spp., *Campylobacter* spp., *Plesiomonas* spp., and *Yersinia* spp., as described by Adkins *et al* (1987). Sheep blood agar plates containing 20% ampicillin were used for the selective isolation of *Aeromonas* spp. (Kelly *et al,* 1988). Five lactose positive *Escherichia coli* colonies recovered from each stool specimen were examined for enterotoxin gene sequences in a colony blot assay essentially as described by Seriwatana *et al* (1987), but using LT and ST $SNAP_R$ alkalinephosphatase-conjugated oligonucleotide probes (EI du Pont de Nemours NEN Products, Boston, MA). Sorbitol negative *E. coli* were reacted with *E. coli* 0157 antiserum in an attempt to identify entero-hemorrhagic strains. Additionally, a minimum of five lactose positive and all lactose negative *E. coli* from each stool were screened for lysine decarboxylase, motility, and high molecular weight plasmids (120-140 Mdal). Lysine negative, non-motile strains, possessing high molecular plasmids were forwarded to the Armed Forces Research Institute for Medical Sciences to be tested for invasion associated gene sequences by DNA probe assay. Stool specimens preserved in 10% formalin were subjected to ethylacetate concentration and examined microscopically for ova and/or parasites (O&P). Concentrated sediments were also examined for *Cryptosporidium* oocysts by acid fast stain. Frozen stool specimens were tested for rotavirus antigen using the Rotazyme II enzyme immunoassay (Abbott Laboratories, North Chicago, IL) and for adenovirus types 40 and 41 using Adenoclone-EIA (Cambridge Bioscience, Worcester, MA).

Data analysis: The Chi-square test of independence, employing Yate's correction for continuity, was used to analyze observed frequency counts of cross tabulated variables. Significant differences in the sample means of specific variables of interest were detected using two-tailed T-Tests with separate variance estimates. Multiple regression models were used to determine the combined and relative effects of multiple independent variables on selected dependent variables. Independent variables were entered into regression equations employing stepwise selection.

RESULTS

Clinical: A total of 186 diarrhea patients (52%

male) were enrolled in the study over a one year period. The patients ranged in age from 1 month to 13 years with mean and median ages of 15.7 and 8.5 months, respectively. The parents' educational level ranged from no schooling at all to 21 years of formal education. Patients resided in over 20 different barangays (local voting district) both within and outside metropolitan Manila. Additional signs and symptoms associated with diarrhea in these patients are presented in Table 1. While fever was the most commonly observed associated sign of illness, the majority of patients also suffered at least some degree of dehydration, abdominal pain, and nausea and/or vomiting. A surprisingly high number of patients (9%) were observed or reported to have seizures. Most seizures were associated with moderate to high grade fevers (axillary temp > 38°C). More than half of the patients experienced six or more diarrhea stools per day and the average duration of diarrhea was 4.5 days with a median of 4 days. No associated signs or symptoms of illness were related to the duration of diarrhea in the study patients. A regression model which included the personal attributes of age, sex, height percentile, and weight percentile accounted for very little of the variation in the duration of diarrhea, although age in months was found to be inversely related to the number of days that children continued to have loose or watery stools ($p < 0.01$). Eighty-seven percent of the diarrhea patients were hospitalized. The average hospital stay was 3.5 days. There were three fatalities among the diarrhea patients enrolled in the study, and over 16% of patients remained symptomatic for more than one week. The majority of diarrhea cases were seen in the rainy season (Table 2), which has historically been the season of highest diarrhea incidence in Manila (Adkins *et al,* 1987).

The results of visual and laboratory examination of the diarrhea stool specimens are presented in Table 3. Of the 83 stools which were positive for occult blood, 46% (20% of all diarrhea stools examined) also contained greater than 10 WBCs per high power microscopic field. Although highly indicative of invasive disease, fever was no more common in this group, and the duration of their illness was not significantly longer than that of patients with less pathologic stools.

A total of 58 non-diarrhea patients (64% male) were entered into the study as controls. Their mean and median ages were 39.1 months and 24 months respectively. As such, they were significantly older than the cases. When the population of interest is limited to children below the age of three, the cases and controls are comparable with mean ages of 10.4 months and 12.3 months respectively. In all case versus control analyses we either controlled for age or limited our comparisons to the less than three years old age group. In a multiple regression model using personal and environmental attributes as independent variables, the patient's age and weight percentile, and the mother's educational level were inversely associated with diarrhea cases, yielding Beta coefficients of -.25, -.19 and -.17, respectively. Procuring water from a community source (either municipal or

Table 1

Signs and symptoms associated with diarrhea in 186 pediatric patients seen at Fatima Hospital, March 1989 through March 1990.

Sign or symptom	No. of case (%)
Fever*	135 (73)
Nausea/vomiting	110 (59)
Abdominal pain	108 (58)
Tenesmus	29 (16)
Seizure	11 (6)
Chills	10 (5)
Dehydration	
None	32 (17)
Some	141 (76)
Severe	13 (7)

* Axillary temperature of 37.5°C or higher.

Table 2

Distribution of pediatric diarrhea cases at Fatima Hospital by season, March 1989 through March 1990.

Season	No. (%) of cases
Summer (Mar,Apr,May)	54 (29)
Rainy (Jun,Jul,Aug,Sep,Oct)	102 (55)
Cold (Nov,Dec,Jan,Feb)	30 (16)

Table 3

Laboratory examination of stool specimens from 186 diarrhea patients, Fatima Hospital, March 1989 through March 1990

Examination	No. (%) of stools positive
Mucus	120 (64.5)
Occult blood	83 (44.6)
Gross blood	22 (11.8)
WBCs/HPF*	
0	65 (34.9)
≤ 10	65 (34.9)
> 10	56 (30.1)

* White blood cells per high power microscopic field.

local well), as opposed to a personal residential source, was positively associated with diarrhea cases (Beta coefficient of .23). The adjusted R square for the regression equation was .27 indicating that, although statistically significant ($p < 0.001$), these risk factors were not strongly predictive of diarrhea. When the regression analysis was limited to children under the age of three, weight percentile score, mother's educational level, and community water source were still associated with diarrhea cases, however, the predictive value of the model was lessened. Variables found to be unrelated to diarrhea in the population studied included height percentile scores, educational level of the father, household size, travel outside the province of residence, occurrence of diarrhea in a family member, use of boiled drinking water, and reliance on local wells as a water source. Breastfeeding histories, which were recorded as exclusive, intermittent, or none, were obtained for all children below the age of two years. There were no significant differences in the breastfeeding histories of the cases and controls.

Microbiological: One or more etiologic agents of diarrhea were detected in 125 (67.2%) of diarrhea stools examined. Many of these positive stools (21.6%) contained multiple diarrheogenic agents. This does not include intestinal helminth ova, which were present in 18.4% of the stools positive for bacterial, viral, or protozoan enteric pathogens. An additional 13 stools (7.0%) contained helminth ova in the absence of any other infectious agents. Etiologic agents were detected in 66% of 68 diarrhea stools which were positive for both occult blood and WBCs. A summary of the etiologic agents of diarrhea detected in the 186 stool specimens examined is presented as Table 4. Rotavirus was found in 33.9% of the stools and was the most commonly identified etiologic agent of diarrhea. Although proportionately more rotavirus was found in the cold months than in the summer or rainy season ($p < .008$), the greatest number of rotavirus patients were seen in the rainy season when diarrhea incidence was at its peak. The mean age of patients infected with rotavirus was 11.2 as compacted to 17.9 months for patients with rotavirus negative stools ($p < 0.02$). Also, nausea and/or vomiting was reported in 76.3% of rotavirus patients but in only 51.2% of all other diarrhea patients ($p < 0.03$). Children who were breastfed intermittently had higher rotavirus infection rates (47.9%) than those who were breastfed exclusively or not at all (infection rates of 27.6% and 26.5% respectively; $p < 0.04$). Although nearly 20% of rotavirus patients were also infected with bacterial enteric pathogens, their presentation and clinical course were not appreciably different from patients suffering from rotavirus alone. Adenovirus types 40 or 41

Table 4

Etiologic agents of diarrhea among pediatric patients at Fatima Hospital, March 1989 through March 1990

Agent	No. (%) of stools positive
Rotavirus	63 (33.9)
ETEC	17 (9.1)
V. cholerae eltor	15 (8.1)
Aeromonas spp.	14 (7.5)
A. hydrophila	2 (1.1)
A. caviae	4 (2.1)
A. sobria	3 (1.6)
A. hydrophila group	5 (2.7)
Adenovirus type 40/41	10 (5.4)
Salmonella spp.	10 (5.4)
Shigella spp.	9 (4.8)
Cryptosporidium spp.	9 (4.8)
Non-O1 *V. cholerae*	7 (3.8)
G. lamblia	2 (1.1)
EIEC	1 (0.5)
V. fluvialis	1 (0.5)

were detected in 10 (5.4%) of diarrhea stools. The average age of patients infected with adenovirus was 11.0, nearly the same as for rotavirus patients. Both adenovirus and rotavirus were found in one patient.

Bacterial enteric pathogens were isolated from 32.3% of diarrhea cases. Nearly 70% of these patients with bacterial gastroenteritis became ill during the rainy season ($p < 0.02$). Although the majority of isolates (57.6%) were from children in their first year of life, bacterial agents of diarrhea were recovered from ten of 11 children over the age of three. Eighty-three percent of stools which yielded bacterial pathogens were microscopically positive for WBCs ($p < 0.001$) and enteric bacterial pathogens were isolated from 42.6% of 68 patients with stools that contained occult blood and WBCs. The mean pH of stools with bacterial agents of diarrhea was 7.1, compared to 6.2 for stools from which no bacterial pathogens were isolated ($p < 0.001$). ETEC was the most frequently encountered bacterial agent of diarrhea, infecting 9.1% of all patients. Four patients infected with ETEC also harbored additional diarrheogenic bacteria. *V. cholerae* eltor was isolated from 8.1% of the diarrhea stools examined and all but one of these cholera patients became ill during the rainy season. Although *Aeromonas* spp. were isolated from 7.5% of the diarrhea stools examined, they were also isolated from 12.8% of the control subjects cultured during the one year study period. *Vibrio* spp. other than cholera were present in only 4.3% of the diarrhea stools examined. Interestingly, two of the three patients who died during the study were infected with both Non-O1 *V. cholerae* and *A. hydrophila* group. Collectively, *Salmonella* and *Shigella* spp. were recovered from 10.2% of the diarrhea cases. *Salmonella* spp. were isolated from only one of the 58 study controls, and *Shigella* spp. from none. Like *Shigella,* EIEC were an infrequent cause of diarrhea in the study population. No *Campylobacter* spp., *Yersinia* spp., or *E. coli* type 0157:H7 were isolated from diarrhea patients or study controls. *P. shigelloides* was isolated from one control stool specimen. The majority of parents of diarrhea patients (76.2%) admitted to treating their children with antibiotics in the two week period prior to seeking medical help. Only 23.8% of the control group had received antibiotics ($p < .001$). In general, this antibiotic exposure consisted of ampicillin and amoxycillin in subtherapeutic dosages. When the isolation rates for specific bacterial enteric pathogens where examined with respect to antibiotic exposure, it was noted that only 21.4% of the *V. cholerae* isolations were from patients who had received antibiotics ($p < 0.01$).

Cryptosporidium was the most commonly detected parasitic agent of diarrhea, infecting 4.8% of the patients. Two *Giardia lamblia* infections and no *Entamoeba histolytica* were detected in the 186 diarrhea stools examined. A large number of diarrhea patients did harbor helminth ova (19.4%), predominantly *Ascaris lumbricoides.* Hookworm, and *Trichuris trichiura.* Helminth infections were more common in the rainy season ($p < 0.001$), and were also associated with children from households which procured their water from a community source ($p < 0.05$). Nearly 42% of the diarrhea patients aged one to three years were parasitized by intestinal helminths.

DISCUSSION

The range of residence barangays and educational levels of the patients' parents suggest that a variety of socioeconomic strata were represented in our diarrhea study population. Based on the Fatima Hospital Pediatric Department admissions rates as a whole, proportionately more diarrhea patients than anticipated were hospitalized. This indicates that parents served by the study hospital did not seek medical attention for their children's diarrhea unless, or until, such illness was complicated by additional signs and symptoms which frequently warranted hospitalization. As such, we appear to have achieved our goal of emphasizing disease of actual or potential medical consequence, however, since a parallel community based study was not conducted, we cannot dismiss diarrhea cases in the community, not coming to medical attention, as trivial. Our pediatric study population was appreciably different from the population seen at a large public hospital in Manila during the same time period. Over 35% of the pediatric diarrhea patients admitted to the public hospital suffered from cholera while only 13% were infected with rotavirus (data not shown).

It is apparent from the results of our investigation that rotavirus is the leading cause of medically significant diarrhea among infants and young children representing a range of socioeconomic

backgrounds in the around metropolitan Manila. While rotavirus causes proportionately more diarrhea during the cold season in the RP, an observation consistent with the epidemiology of rotavirus infections in children from temperate climates (Kapikian *et al,* 1976), most Filipino children become infected with rotavirus during the rainy season when diarrheal disease is at its peak. The observation that non-breastfed children were infected with rotavirus at about the same rate as those who were breastfed exclusively suggests that some unidentified attribute(s) or behavior of the non-breastfed children affords protection from rotavirus infections. While it seems reasonable to hypothesize that the non-breastfed children came from more affluent families, there was no significant difference between the educational levels (the only recorded socioeconomic status indicator) or the parents of breastfed and non-breastfed children. Although the rotavirus infection rate was predictably high, enteric adenoviruses caused very little diarrhea among infants and young children in the RP as compared to their counterparts from temperate climates. Only 5.4% of the diarrhea stool samples examined contained adenovirus types 40 or 41. This adenovirus infection rate is consistent with the finding of Herrmann *et al,* (1988), who detected enteric adenoviruses in only 2.0% of Thai children with diarrhea, and provides additional evidence that adenoviruses are not a major cause of diarrhea in infants and young children in Southeast Asia.

The predominance of bacterial enteric pathogens in the rainy season reflects the natural habitat and mode of transmission of many of the specific agents isolated. Over 50% of the bacterial species recovered from diarrhea patients during the study belonged to the family *Vibrionaceae.* Vibrios are most commonly associated with aquatic environments from whence they contaminate potable water and food items consumed by man. The flooding associated with the heavy rains which fall in Manila provides numerous opportunities for contamination of individual and local potable water sources. *V. cholerae* eltor infections were more common than previously reported (Adkins *et al,* 1987; Lucero *et al,* 1984) and reflect a relatively high level of cholera transmission in Manila during the 1989 rainy season as noted above for public hospital pediatric patients. Since in the current study, a history of antibiotic exposure resulted in significantly fewer *V. cholerae* isolations, it is possible that the actual cholera infection rate was even higher than the 8.1% that we observed. The isolation of ETEC from 9.1% of the diarrhea stools examined is consistent with previous reports for the RP (Adkins *et al,* 1987; Lucero *et al,* 1984).

Although *Aeromonas* spp. are being increasingly recognized as an enteric pathogens (Agger *et al,* 1985; Gracey *et al,* 1982), in the current study, *Aeromonas* spp. were more commonly recovered from control stools then they were from stools of diarrhea patients. Since we isolated *Aeromonas* spp. from relatively few individuals compared to other published reports, and did not test isolates for recognized virulence determinants, our findings with regard to this group of pathogens are largely anecdotal in nature. Nonetheless it is interesting that *A. hydrophila,* one of the two species widely considered to be virulent for the gastrointestinal tract (*A. sobria* being the other) was isolated from only one diarrhea patient but was recovered from four of 58 children without diarrhea admitted to the study as controls.

The detection of multiple diarrheogenic agents in stool specimens from diarrhea patients is a common finding in tropical developing countries as is infection with intestinal helminths. Since *Campylobacter* infections are common in children from many developing countries (Skirrow, 1982), our failure to isolate thermophilic *Campylobacter* spp. from any of the diarrhea stools examined is somewhat surprising, however, the low incidence of *Campylobacter* infections in Filipino children has been noted by others (Adkins *et al,* 1987; Lucero *et al,* 1984).

The etiology and severity of diarrheal disease seen in the current study were strongly influenced by the age of the patients. In Manila, rotavirus infections are most common in children six to 11 months old (Adkins *et al,* 1987; Lucero *et al,* 1984). Since the median age of the study diarrhea patients was 8.5 months, it is not surprising that rotavirus was the most commonly identified etiologic agent of diarrhea. *Shigella* spp., by comparison, which are reportedly more common older children (Taylor *et al,* 1988), were an infrequent cause of diarrhea in our study patients. Likewise, the relatively high proportion of children 18 months of age or younger (77%) no doubt contributed to the overall severity of disease and the high

hospitalization rates as evidenced by the inverse relationship between age and duration of diarrhea. Age differences also complicated case control comparisons. Controlling for age, however, we found that the weight percentile score of the patient and the educational level of the mother were inversely associated with diarrhea, and that obtaining water from a community source was reported more frequently for cases than controls. In Manila, what we refer to as community water is frequently obtained from a street vendor who dispenses either well or municipal water via a rubber hose connected to the water source. The association of diarrhea cases and community water is of particular interest because the Philippine Department of Health's Field Epidemiologic Training Program (FETP) has implicated the rubber dispensing hoses, which often lie submerged in floodwaters on the streets and sidewalks, as a potential source of cholera infections (Benabaye, FETP, personal communication). The case/control design of the study no doubt minimizes the importance of the noted risk factors in as much as children experiencing these potential risks would be asymptomatic for diarrhea most of the time, and therefore, could have been enrolled in the study as controls.

Despite the comprehensive laboratory protocol employed, we failed to detect an etiologic agent of diarrhea in nearly one-third of the diarrhea stools examined, and detection rates were no higher is stools containing occult blood and white cells than in less invasive appearing stools. Although examination of multiple stool samples from individual patients may have increased our detection somewhat, a significant number of diarrheas would still remain unexplained. Of the putative diarrheogenic *E. coli* groups, only enteropathogenic *E. coli* were not sought. It has been shown that *E. coli* which adhere to intestinal epithelial cells in a localized pattern are associated with diarrhea and also belong to recognized EPEC serotypes (Echeverria *et al,* 1987; Levine *et al,* 1985). While it is likely that these agents were responsible for diarrhea in some of our patients, the importance of adherent EPEC strains as a cause of diarrhea in the RP is yet to be determined.

The results of the current study complement the findings of previous investigators. The epidemiology of pediatric diarrhea in metropolitan Manila is complex and subject to annual, as well as seasonal variation. In addition, the age, nutritional status, feeding history, and socioeconomic background of the patient must also be considered when attempting to determine etiology in the absence of a comprehensive microbiological examination. While it is cost prohibitive to perform such comprehensive microbiological examinations on all diarrhea patients, temporal and local trends in the etiology of diarrhea could be identified by selective culturing of a sample of patients seen at representative hospitals. The results of such sampling, however, would have to be disseminated to the greater medical community in a timely manner in order to have a positive impact on patient management.

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REFERENCES

Adkins HJ, Escamilla J, Santiago LT, Ranoa C, Echeverria P, Cross JH. Two-year survey of etiologic agents of diarrheal disease at San Lazaro Hospital, Manila, Republic of the Philippines. *J Clin Microbiol* 1987; 25 : 1143.

Agger WA, McCormick JD, Gurwith MJ. Clinical and microbiological features of *Aeromonas hydrophila* associated diarrhea. *J Clin Microbiol* 1985; 21 : 909.

Anonymous. National Program on the Control of Diarrheal Diseases. Report of the joint MOH-UNICEF-USAID comprehensive program review, January-February 1985. Ministry of Health, Manila, 1985.

Echeverria P, Blacklow NR, Vollet JJ, *et al.* Reovirus-like agent and enterotoxigenic *Escherichia coli* infections in pediatric diarrhea in the Philippines. *J Infect Dis* 1978; 138 : 326.

Echeverria P, Taylor DN, Donohue-Rolfe A, *et al.* HeLa cell adherence and cytotoxin production by enteropathogenic *Escherichia coli* isolated from

infants with diarrhea in Thailand. *J Clin Microbiol* 1987; 25 : 1519.

Gracey M, Burke V, Robinson JR. Aeromonas associated gastroenteritis. *Lancet* 1982; 2 : 1304.

Herrman JE, Blacklow NR, Perron-Henry DM, Clements E, Taylor DN, Echeverria P. Incidence of enteric adenoviruses among children in Thailand and the significance of these viruses in gastroenteritis. *J Clin Microbiol* 1988; 26 : 1783.

Kapikian AZ, Kim HW, Wyatt RG, *et al.* Human reovirus-like agent as the major pathogen associated with "winter" gastroenteritis in hospitalized infants and young children. *N Engl J Med* 1976; 294 : 965.

Kelly MT, Dan Stroh EM, Jessop J. Comparison of blood agar, ampicillin blood agar, MacConkey-ampicillin-tween agar, and modified cefsulodin-irgasan-novobiocin agar for the isolation of *Aeromonas* spp. from stool specimens. *J Clin Microbiol* 1988; 26 : 1738.

Levine MM, Nataro JP, Karch H, *et al.* The diarrheal response of humans to some classic serotypes of enteropathogenic *Escherichia coli* is dependent on a plasmid encoding enteroadhesive factor, *J Infect Dis* 1985; 152 : 550.

Lucero MG, Saniel MC, Geronimo JG, *et al.* Etiology of diarrhea in hospitalized children. *Philippine J Microbiol Infect Dis* 1984; 13 : 17.

Maddeley CR. The emerging role of adenoviruses as inducers of gastroenteritis. *Pediatr Infect Dis J* 1986; 5 : S63.

Saniel MC, Sanvictores MA. A prospective study of diarrhea in infants and young children of a peri-urban community. Morbidity patterns and etiologies. In: Tzipori S. ed.Infectious Diarrhea in the Young: Strategies for Control in Humans and Animals. Elsevier, Netherlands, 1985.

Saniel MC, Moriles RR, Monzon OT, *et al.* The relative importance of various enteropathogens in the etiology of acute diarrhea: A hospital-based study in urban Philippines, 1987.

Seriwatana JP, Echeverria P, Taylor DN, Sakuldaipeara T, Changchawalit S, Chivoratanond O. Identification of enterotoxigenic *Escherichia coli* with synthetic alkaline phosphatase-conjugated oligonucleotide DNA probes. *J Clin Microbiol* 1987; 25 : 1438.

Skirrow MB. Campylobacter enteritis-the first five years. *J Hyg* 1982; 89 : 175.

Snyder JD, Merson MH. The magnitude of the global problem of acute diarrheal disease: A review of active surveillance data. *Bull WHO* 1982; 60 : 605.

Taylor DN, Echeverria P, Sethabutr O, *et al.* Clinical and microbiologic features of *Shigella* and entero-invasive *Escherichia coli* infections detected by DNA hybridization. *J Clin Microbiol* 1988; 26 : 1362.

Uhnoo I, Wadell G, Svensson L, Johansson ME. The importance of enteric adenoviruses 40 and 41 in acute gastroenteritis in infants and young children. *J Clin Microbiol* 1984; 20 : 365.