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Argentine Hemorrhagic Fever

Since the early 1950s Argentine hemorrhagic fever (AHF) has been recognized as a major public health problem in certain agricultural areas of Argentina.[1] Over 18,000 cases were reported in that country from 1958 to 1980, with a mortality rate of 10-15 per cent in untreated cases.

The disease occurs in an area of approximately 100,000 km^2, which includes parts of the Provinces of Buenos Aires, La Pampa, Santa Fe, and Córdoba and has over one million inhabitants.

Natural infections affect corn- and wheat-field workers almost exclusively. The etiologic agent is the Junín virus excreted by persistently infected rodents that live in the fields. It is believed that *Calomys musculinus* and *C. laucha* are the two principal species of rodent vectors of the Junín virus which transmit it to man. However, many serious laboratory-contracted infections have been reported. Asymptomatic cases also have been verified among field and laboratory workers.

AHF is reported through one system which covers the endemic area and uses more information than that reported for other infectious diseases. The National Campaign Against AHF uses the following standards for epidemiological surveillance:

- Instructions for reporting of cases with presumptive diagnosis of AHF.
- Instructions for reporting the development of the disease in patients.
- Instructions for obtaining, identifying, preserving, and sending serum samples for etiologic diagnosis of AHF.
- Weekly report form with the corresponding codes.
- Monthly report forms for reporting the development of the disease in patients with the pertinent instructions.

These standards were developed by the National In-

Table 1. Distribution of cases reported with presumptive diagnosis of AHF, by possible place of contagion, Argentina, 1977-1980.

Possible place of contagion (Province)	1977	1978	1979	1980
Buenos Aires	457	233	151	86
La Pampa	0	3	4	6
Santa Fe	169	137	62	53
Córdoba	363	31	112	9
Unknown	0	98	1	7
Total	989	502	330	161

[1] See: *PAHO Epidemiological Bulletin* 1:5, 1980.

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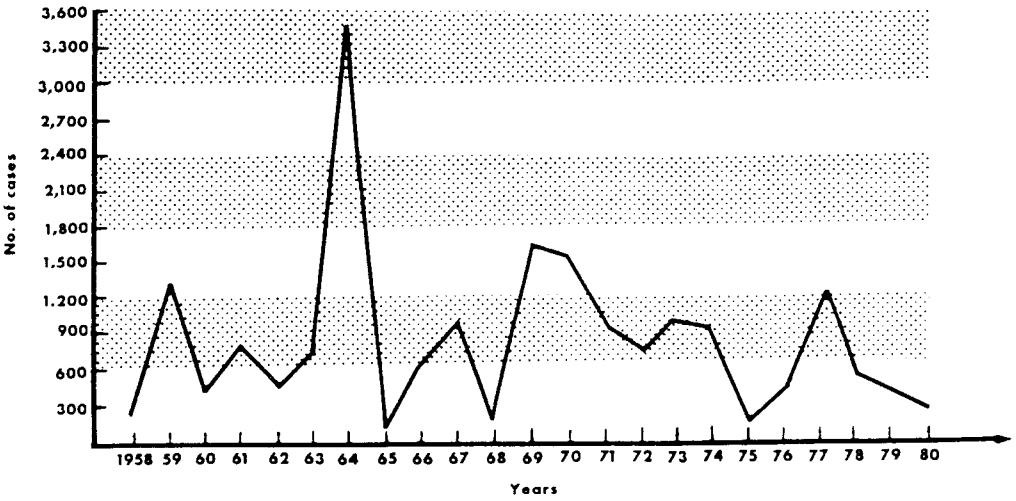
Figure 1. Annual distribution of total cases reported with clinical diagnosis of AHF, Argentina, 1958-1980.



stitute of Studies on Hemorrhagic Viral Diseases in conjunction with authorities from the provinces.

The Program staff meets annually to review the epidemiological status of the disease and other pertinent aspects. At the 1980 meeting—which was held at Villa Cañás, Province of Santa Fe on 16 December—cases occurring from 1958 to 1980, inclusive, were analyzed. Figure 1 shows the annual distribution of total cases with clinical diagnosis reported during that period. It can be noted that the disease reaches epidemic levels every two or three years, with the largest epidemic occurring in 1964. There is also some stability in the trend, which has declined during the last three years.

Table 1 shows the distribution of cases reported with presumptive diagnosis of AHF, by possible place of contagion (by province) for 1977-1980.

The monthly distribution of total cases reported in 1978, 1979, and 1980 (Figure 2), shows a definite seasonal variation, with the greatest concentration in April, May, and June.

As for the distribution of cases by sex (Table 2), there is a pronounced predominance of cases in males, possibly related to the type of rural work performed by them in those areas. This association is also evident in the distribution by age group.

In the diagnosis of AHF, the immunofluorescence technique (IF) permits earlier detection of Junín virus antibodies without the need to take serum samples at periods other than at convalescence from the disease, which must be done when the complement fixation (CF) method is used. Furthermore, when it is assumed that patients cannot come for a control check after 30 or 60 days (for example, harvest workers who return to their homes in distant places), the serologic diagnosis by IF can be made by prolonging their hospitalization up to 20 days after the onset of symptoms and obtaining a serum sample before their discharge.

As for treatment of AHF, the persistence of IF Junín virus antibodies after the disease is of practical importance because it permits the selection of donors whose plasma contains antibodies against the etiologic agent of the disease. Some treatment centers are now using plasma units from "convalescents" who lack these antibodies. This is because these units have been donated by persons

Table 2. Distribution of confirmed cases with diagnosis of AHF, by sex and age group, Argentina, 1978-1980.

Age group	1978			1979			1980			Grand total
	Male	Female	Total	Male	Female	Total	Male	Female	Total	
0 - 14	3	6	9	7	3	10	3	1	4	23
15 - 24	33	6	39	25	4	29	14	4	18	86
25 - 34	48	7	55	22	1	23	21	3	24	102
35 - 44	24	4	28	25	1	26	15	2	17	71
45 - 54	28	7	35	13	5	18	4	2	6	59
55 - 64	13	3	16	6	4	10	8	1	9	35
65 and over	8	1	9	7	0	7	2	0	2	18
Total	157	34	191	105	18	123	67	13	80	394

whose diagnosis of AHF was made solely on the basis of clinical criteria, when it should be kept in mind that the diagnosis of AHF is not confirmed in all reported cases (see Table 3). Studies carried out at Pergamino, Buenos Aires Province, from 1965 to 1979 show that the diagnosis of AHF was confirmed in about 70 per cent of the cases reported during that period; the remaining 30 per cent showed no CF Junín virus antibodies, nor was the virus isolated from the blood. It may be that these patients had infections of a different etiology but were clinically diagnosed as cases of AHF. A similar percentage of confirmation has been observed in the endemic area of AHF of the Province of Córdoba.

In view of the findings of the Pergamino studies, it can be inferred that about 5,500 of all cases reported in the country were not suffering from AHF, and consequently have no Junín virus antibodies. Therefore, they should not be accepted as plasma donors for the treatment of AHF patients. The persistence of IF antibodies long after the occurrence of the disease is of practical importance for the solution of this problem, since the use of the IF method will permit the identification and acceptance as plasma donors only those convalescents who have specific Junín virus antibodies.

(*Source: Boletín Epidemiológico Nacional,* National Office of Disease Prevention and Control, Ministry of Public Health and Environment, Argentina, Year 1981, No. 2.)

Figure 2. Monthly distribution of total reported cases of AHF, Argentina, 1978-1980.

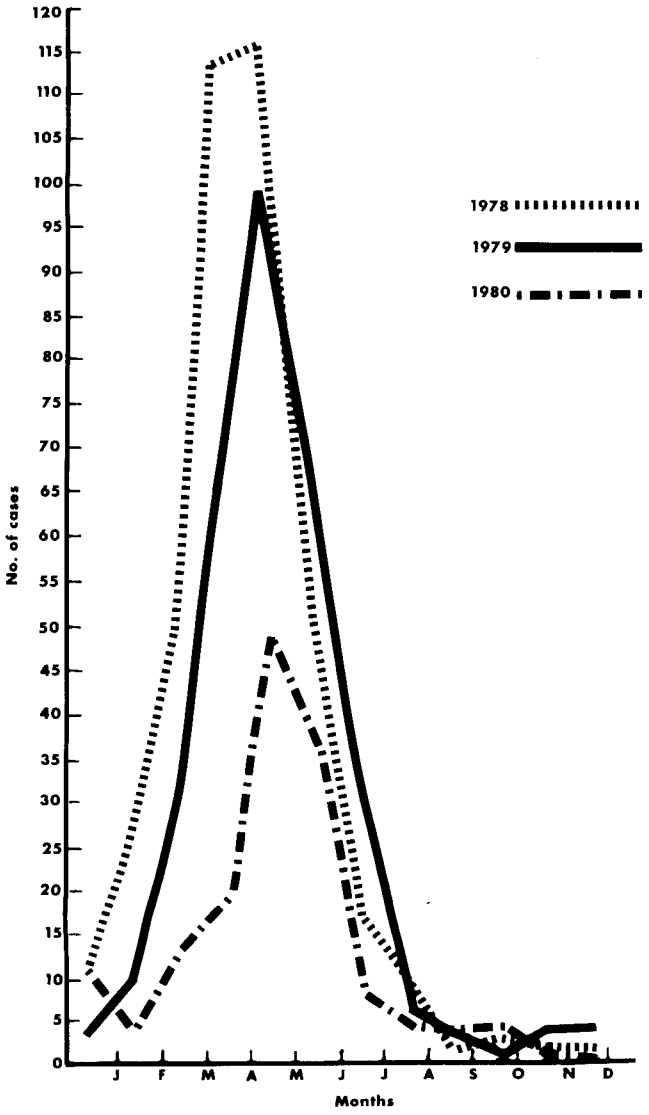


Table 3. Persistence of immunofluorescent Junín virus antibodies, distribution of cases studied and results obtained.

Years after AHF	No. of cases	Results		
		Positive	Negative	Percentage positive
1	48	46	2	96
2	35	33	2	94
3	32	29	3	91
4	26	25	1	96
5	21	20	1	95
6	17	16	1	94
7	22	20	2	91
8	25	23	2	92
9	17	16	1	94
10	18	18	–	100
11	20	19	1	95
12	10	10	–	100
13	7	6	1	86
14	2	2	–	100
Total	300	283	17	94

Diseases Subject to the International Health Regulations

Cholera, yellow fever, and plague cases and deaths reported in the Region of the Americas up to 31 March 1982.

Country and administrative subdivision	Cholera cases	Yellow fever		Plague cases
		Cases	Deaths	
BOLIVIA	–	*83*	*28*	–
Cochabamba	–	2	–	–
Santa Cruz	–	81	28	–
BRAZIL	–	*12*	*12*	*16*
Ceará	–	–	–	16
Matto Grosso do Sul	–	12	12	–
UNITED STATES	*1*	–	–	*2*
Arizona	–	–	–	1
California	1[a]	–	–	–
Texas	–	–	–	1

[a]Imported.
– None.

Tuberculosis in the United States and Canada, 1980[1]

In 1980, a total of 27,749 cases of tuberculosis were reported in the United States. This represents an increase of 80 cases (0.3 per cent) since 1979 and the second rise since 1953. The case rate in 1980 was 12.3 per 100,000 population, or 2.4 per cent lower than in 1979, representing a continuing leveling off of the downward trend of 5 per cent annually that has occurred over the last 26 years. This lessening in the case rate decrease has been observed for the past three years.

In Canada figures for 1980 show a total of 2,841 cases of tuberculosis reported, an overall increase of 44 cases over the 1979 figures. The case rate of 11.9 per 100,000 population revealed a lessening in the decline experienced since 1970 when compared with the 1979 rate of 11.8.

The factor slowing the downward trend of case rates per year in both countries is the high prevalence of tuberculosis in the large number of Indochinese immigrants admitted in recent years. This is an interesting phenomenon which illustrates the importance of a special population group—the immigrants—on the epidemiology of tuberculosis in the host country.

In Canada immigrant groups contributed to 38 per cent (1,085) of the cases reported in 1980. A total of 369 immigrants who arrived in Canada during 1979 and 1980 were diagnosed as having tuberculosis in 1980, representing 34 per cent of the case load for the year; 291 of these were of Asiatic origin.

State tuberculosis control programs in the United States have reported that 3,895 Indochinese refugees were treated for the disease in 1979 and 1980. The estimated prevalence of tuberculosis among this population was 1,138 cases per 100,000 refugees at time of entry, whereas the annual incidence after arrival for refugees with no evidence of disease when screened overseas was 407 per 100,000.

Based on these figures, it is estimated that of the Indochinese refugees who entered the United States in 1979 and 1980, approximately 1.5 per cent either had tuberculosis at the time of entry or developed it before the end of 1980. Considering only those cases included in the official morbidity count, the Indochinese refugees ac-

[1]For further information on the epidemiology and control of tuberculosis in the Americas, see PAHO *Epidemiological Bulletin* 2:5, 6, 1981.

counted for 2.8 per cent of the tuberculosis cases counted nationally in 1979 and 7.8 per cent in 1980 (5.3 per cent over the two-year period). The leveling off of the total number of reported tuberculosis cases observed in the United States over the past two and a half years is accounted for by refugee cases being added to the slowly declining number of indigenous cases.

Before entering the United States, Indochinese refugees are screened overseas for tuberculosis and categorized in one of three ways: active or suspected active disease (Class A-TB), disease not considered active (Class B-TB), and no evidence of tuberculous disease. Refugees with Class A-TB may travel only if their disease is noncontagious (i.e. two consecutive negative sputum smears taken on separate days). On arrival in the United States, all refugees with Class A-TB and Class B-TB are referred to a local health department for medical evaluation. Refugees certified as having Class A-TB accounted for about 2 per cent of all entering refugees and 57 per cent of the tuberculosis cases among refugees; refugees certified as having Class B-TB accounted for about 2 per cent of all entering refugees and 20 per cent of the cases among refugees; the remaining refugees accounted for 23 per cent of the reported cases.

The three-fold decrease in incidence from 1979 to 1980 for refugees who entered in 1979 probably reflects a combination of the natural decrease in risk of disease for those infected before arrival and successful efforts to reduce transmission of tuberculosis after arrival. Reduced transmission is the result of several factors: treatment of refugees with infectious tuberculosis (positive smear) is started in Asia; most refugees with Class A-TB have been evaluated promptly after arrival and, if necessary, are continued or started on treatment; over 46,000 refugees (about 18 per cent of the total) have been given preventive treatment; and, presumably, a high level of suspicion in the medical community has led to the prompt evaluation and treatment of refugees with symptoms compatible with tuberculosis. Because of the reduced transmission, tuberculosis case rates among refugees are expected to continue to fall. Nevertheless, they will remain higher than the rates of other persons in the United States for years to come because so many have been infected before arrival.

(*Source: Morbidity and Mortality Weekly Report* 30:26,48, 1981 and *Canada Diseases Weekly Report* 8:1, 1982.)

Drug Resistance in the Treatment of Leprosy

Leprosy control programs have used dapsone (diamino-diphenylsulfone), which probably acts as an antimetabolite, as a specific treatment because of its proven effectiveness, low cost, and reduced toxic effects. Rifampicin, clofazimine, ethionamide, and prothionamide also have a demonstrated bactericidal effect against *Mycobacterium leprae.* Other medications such as thiacetazone, sulfometoxipyridazine, and thiambutazine have only a bacteriostatic effect.

Outpatient monotherapy of leprosy, usually with dapsone (at a dose of 6-10 mg/kg of body weight per week), revolutionized the control of the disease from the operational standpoint. However, new knowledge of primary and secondary drug resistance in the treatment of leprosy indicates an urgent need to establish therapeutic regimens that combine two or three drugs. Large-scale application of this type of treatment requires sufficient resources and operational experience in order to select strategies that will permit more effective control of the disease.

Resistance to dapsone was first verified in 1964, by means of inoculations of mouse footpads. Table 1 summarizes some of the studies made subsequently, which have reinforced the findings of secondary dapsone resistance of *M. leprae.*

The finding of bacterial resistance to dapsone is based on the fact that until 1970 nearly all isolated strains of *M. leprae* (both in mice and in untreated patients) were inhibited when the drug was administered in the diet at a con-

centration of 0.0001 per cent. The following are the accepted definitions of levels of dapsone resistance of *M. leprae:*

Susceptible: strains inhibited by a concentration of 0.0001 per cent.

Resistant:

- Low-grade resistance: strains capable of multiplying with 0.0001 per cent, inhibited by concentrations of 0.001 per cent.
- Medium-grade resistance: strains capable of multiplying with 0.001 per cent, inhibited by concentrations of 0.01 per cent.
- Complete resistance: strains capable of multiplying with concentrations of 0.01 per cent in the diet of mice.

The concentration of 0.01 per cent produces dapsone levels in plasma of 1 mg/ml similar to that obtained by administering 100 mg of dapsone to humans.

From the bacteriological standpoint it is impossible to differentiate primary from secondary resistance, and it is clinically difficult to ensure that a patient has not been treated previously with sulfones. In theory, it is possible for a patient with lepromatous or dimorphous leprosy who shows secondary resistance, to infect a contact who in turn develops leprosy with primary resistance. Because the incubation period of tuberculoid forms is shorter than that of lepromatous forms, the prevalence of primary dapsone resistance is probably higher in the former. There has also been verification of secondary resistance to monotherapy with rifampicin and ethionamide, and in the latter cases, cross-resistance to prothionamide.

It is important to use the experience acquired in studies of drug resistance in the treatment of tuberculosis, which demonstrate the success of multiple drug regimens and the failure of monotherapy. The latter results in the survival and proliferation of drug-resistant mutant bacilli which are increasingly less sensitive. The bacilli remaining—in a state of metabolic quiescence—survive concentrations of bactericidal drugs in the blood even though they are sensitive to them. Personnel of leprosy control agencies should keep themselves informed about the problem of possible resistance to the monotherapy employed and, insofar as possible, should adopt combined treatment regimens.

In 1981 WHO formed a working group which studied

Table 1. Selected studies on resistance to dapsone in the chemotherapy of leprosy, 1966-1981.

Author	*Date*	*Drug*	*Place*	*No. of patients*	*Results*	*Remarks*
Pettit, J. H. S. *et al.*	1966	Dapsone	Malaysia	5,000	Prevalence of resistance: 1 x 1,000	Underestimation for large concentrations of dapsone in the diet of mice
Meade, T. W. *et al.*	1973	Dapsone	Malaysia	5,000	Prevalence of resistance: 25 x 1,000 Incidence of resistance: 0.3 x 100 per year	Same patients as study
Pearson, J. M. H. *et al.*	1975	Dapsone	Malaysia	100	Resistance verified in all	
Pearson, J. M. H. *et al.*	1976	Dapsone	Ethiopia	1,500	Prevalence of resistance: 190 x 1,000 Incidence of resistance: 3% per year	
Peters, J. H. *et al.*	1976	Dapsone	Costa Rica		Prevalence of resistance: 100 x 1,000	
Taylor, P. M. *et al.*	1976	Dapsone	India		Resistance verified	Patients with monotherapy since 1963
Levy, L. *et al.*	1977	Dapsone	Israel		Prevalence of resistance: 37 x 1,000	
Pearson, J. M. H.	1979	Dapsone	Ethiopia			
Balraj, V. *et al.*	1980	Dapsone	India		Prevalence of resistance: 50 x 1,000	
Balraj, V. *et al.*	1980	Dapsone	India	1,580	Prevalence of resistance: 2.3%	
Lim, K. J. *et al.*	1981	Dapsone	Malaysia	All cases detected	Prevalence of resistance: 10%	
Li Wenzhong *et al.*	1981	Dapsone	China	Small groups	Prevalence of resistance: 51 x 1,000	
Kyaw Lwin	1981	Dapsone	China	11	Prevalence of resistance: 34 x 1,000	

the problem of resistance, recommended combined treatment for multibacillary and paucibacillary cases, and defined areas for clinical and operational research on chemotherapy. The group's recommendations included the following:

- The purposes of the treatment program are to interrupt the chain of transmission and to cure the patient.
- Combined treatment prevents secondary bacterial resistance, and therefore the transmission of strains with primary resistance.
- *All* multibacillary patients (treated or not) should receive combined treatment. It is therefore not necessary to determine bacterial resistance in each patient.
- The basic drugs are rifampicin, dapsone, clofazimine, and ethionamide or prothionamide.
- The intermittent monthly administration of rifampicin (and probably of clofazimine) is effective and permits supervised treatment.
- In paucibacillary leprosy the appearance of resistant strains is very unlikely. Association with rifampicin solves the problem of possible primary resistance and permits a shortening of the treatment period, thereby lessening the workload of agencies and reducing abandonment by patients.

(*Source:* Leprosy Control Program, Division of Disease Prevention and Control, PAHO.)

Surveillance and Control of *Aedes aegypti* in Bolivia

In February 1980, *A. aegypti* was discovered in Bolivia after 32 years of absence. Findings were made at the Santa Cruz airport, at kilometer 15 of the Santa Cruz-Cochabamba highway, and in the communities of Cotoca, Warnes, and Montero near Santa Cruz.

The following control measures have been taken:

- *Antimalaria vaccination.* Between June 1980 and July 1981 there was 62.5 per cent coverage of the population of Santa Cruz Department.
- *Basic sanitation.* The health authorities, working with civic and development agencies, undertook the collection and disposal of solid wastes.
- *Treatment of positive localities.* The following treatments were applied: focal treatment with abate (1 ppm), perifocal treatment with malathion (50 per cent pH), intradomiciliary treatment using FONTAN packs, and malathion (96 per cent) from the street using ULV equipment.
- *Health education.* All possible means were employed to have the population of reinfested areas take part in health education activities.

From January to May 1981 entomological surveys were made, showing the following rates of infestation: 5.4 per cent in Santa Cruz, 0.0 per cent in Montero, 1.2 per cent in Cotoca, 0.0 per cent at kilometer 15, and 0.0 per cent in Warnes.

Entomological surveillance by regional teams confirmed the absence of *A. aegypti* in all other areas of the country. The inspection of airports and adjacent areas continues as does the spraying of international aircraft and trains.

(*Source: Boletín Epidemiológico,* No. 73, 1981, Ministry of Social Welfare and Public Health, Bolivia.)

Editorial comment:

A technical meeting on *A. aegypti,* dengue, and urban yellow fever will be held in Mexico City from 1-5 June 1982, in compliance with Resolution XXI of the XXVIII Meeting of the Directing Council of PAHO. Experts from several countries have been invited to present working papers which will guide the discussions on regional action aimed at controlling the *A. aegypti* problem.

An informal group met in Washington, D.C. in January to draw up the agenda for the meeting, which will cover five topics: the vector, the human host, the virus, the disease, and integrated programs for *A. aegypti* control.

Prevalence of Dental Caries in the United States

A national survey of schoolchildren in the United States has shown that the prevalence of dental caries has decreased substantially in the last decade. The survey was designed and funded by the National Caries Program of the National Institute of Dental Research, part of the National Institutes of Health, and involved children in the 5-17 year-old age group. The findings from the study were presented in a 1982 meeting of the American Academy for the Advancement of Science, in Washington, D.C.

Dental caries is the leading chronic childhood disease and costs the nation at least US$5 billion a year. Techniques utilized to prevent the disease include the fluoridation of water supplies, use of toothpastes with fluoride (which now comprise about 80 per cent of the current toothpaste market in the U.S.), topical applications of fluoride solutions, dentist-prescribed fluoride dietary supplements, school-based programs of daily fluoride tablets, and mouthrinsing with fluoride solutions. Furthermore, oral hygiene programs and publicity and educational campaigns have aimed at emphasizing reduced consumption of sugar and sugar products. The application of a plastic sealant to children's teeth, which provides added protection against the effect of cariogenic organisms, has also gained wider acceptance in recent years.

The nationwide survey was conducted on children enrolled in public or private schools in the contiguous United States. Clinical examinations were carried out on a sample of approximately 40,000 children drawn to represent the 48 million in that age group.

A total of 37 per cent of children aged 5-17 was found to be caries-free, that is, with no decayed, missing, or filled permanent teeth, as opposed to the 28 per cent found in the National Health Studies conducted from 1971-1973. The average number of decayed, missing, or filled permanent surfaces was found to have decreased from 7.1 to 4.8 in the present survey. A total of 36 per cent of all 5-9 year-olds had no decayed teeth.

Although the National Caries Program cannot point to a single causative factor in the decrease in prevalence of dental caries and the corresponding increase in caries-free children, it considers these to be the possible result of a combination of the techniques for the prevention of dental caries and their wide acceptance and use by the public, dentists, and the school system.

(*Source:* National Dental Caries Prevalence Survey, National Caries Program, National Institute of Dental Research, National Institutes of Health, Department of Health and Human Resources, United States Government, and Dental Health Program, Non-communicable Diseases, Division of Disease Prevention and Control, PAHO.)

Editorial Comment

Since 1967 the Pan American Health Organization, in compliance with recommendations of its Directing Council, has been carrying out a specific program aimed at introducing the use of fluorides for the prevention of dental caries in Latin America. At present it is estimated that nearly 50 million people are benefiting from fluoridized water supplies alone, and several million more children are participating in oral hygiene and fluoride mouthrinsing programs. Fluoride toothpastes are now available in many countries.

Despite the fact that survey results of the effects of water fluoridation have been comparable to those of the U.S., the introduction of the use of fluorides on a mass scale has been slow. The lack of treated water supplies and the rural nature of the population has indicated the need for additional universal and economical vehicles for fluoride ingestion, such as table salt.

The PAHO program has operated on the basis of collaboration with participating governments, promotional activities, technical cooperation, and training in the use and application of the techniques identified in the U.S. study. Over 1,500 professionals from all countries in Latin America (including water engineers, chemists, dentists, and government administrators), have been involved in the program.

It is hoped that the results of this survey will encourage the implementation of fluoride programs for children in areas where this preventive element against dental disease is still lacking.

Diarrheal Diseases

Microorganisms in Childhood Diarrhea[1]

The last decade has been an exciting one for clinicians and scientists interested in acute childhood diarrhea. In addition to well-known microbial causes of human diarrhea *(Vibrio cholerae, Salmonellae, Shigellae,* and certain strains of *Escherichia coli),* rotavirus, *Campylobacter,* and *Yersinia* are now recognized and our knowledge of the mechanisms involved in *E. coli* diarrhea has grown.

Epidemiological studies have highlighted the worldwide importance of rotavirus and *E. coli* diarrhea and this review will concentrate on these organisms.

Rotavirus

Rotavirus causes perhaps 50 per cent of childhood diarrhea increasing to 80 per cent in temperate climates during the winter. It was first identified in children in 1973, but had previously been found in other young mammals.

In young patients, watery diarrhea preceded by vomiting should suggest rotavirus infection. Dehydration occurs particularly rapidly because of vomiting and, although recovery is usually uneventful with proper rehydration treatment, deaths do sometimes occur. Though a proven cause of diarrhea, rotavirus has been found in the stools of healthy, newborn infants.

Loss of electrolytes and water. Rotavirus is thought to cause diarrhea by destruction of the cells lining the small intestine. The cells replacing those shed into the intestinal lumen are less able to absorb sugars. Unabsorbed sugar draws fluid from the rest of the body into the intestine by osmosis. At the same time, the process of sodium and water transfer, which depends on sugar absorption in the upper intestine, becomes less efficient. The overall effect is a huge loss of electrolytes and water from within the small intestine which the large intestine is then unable to reabsorb. The result is diarrhea and further dehydration.

Escherichia coli

Only certain strains of *E. coli* cause diarrhea in humans and these strains are classified in three groups:

- Enterotoxigenic *E. coli* (ETEC). These *E. coli* produce enterotoxins which stimulate the small intestine to secrete electrolytes and water. Two enterotoxins of *E. coli* are recognized: a high molecular weight protein readily destroyed by heating—heat-labile toxin (LT) and a low molecular weight heat-stable toxin (ST).
- Enteroinvasive *E. coli* (EIEC). EIEC invade the mucosa of the ileum and the colon, unlike ETEC, which remain on the mucosal surface.
- Enteropathogenic *E. coli* (EPEC). EPEC do not produce either LT or ST, nor do they invade the intestine; yet they certainly cause diarrhea. They have been implicated by epidemiological means in outbreaks of diarrhea in infants.

Serologic classification. E. coli can also be classified serologically on the basis of a bacterial cell wall antigen (O antigen). At present, 164 distinct O serogroups are recognized. ETEC, EIEC, and EPEC strains tend to have distinctive O serogroups (Table 1). However, *E. coli* possessing these O serogroups are not always pathogenic and *E. coli* which have not been serotyped may also cause diarrhea.

Nevertheless, the serotype of *E. coli* is a useful epidemiological tool since other means of identifying potentially pathogenic *E. coli* are difficult, expensive, and not widely available.

Infections. Infections with ETEC cause copious, watery diarrhea and are an important cause of warm season diarrhea in young children in developing countries.

EIEC produces fever, abdominal cramps, urgent and painful defecation (tenesmus) and watery diarrhea, followed by scanty discharges of blood and mucus (dysentery). Microscopic examination of methylene-blue stained fecal mucus shows pus and red cells.

EPEC can produce sudden cholera-like diarrhea in adults, whereas in infants the disease often tends to be more prolonged, with high mortality. It is possible that these organisms produce uncharacterized enterotoxins.

Another factor which may determine the ability of *E. coli* to cause diarrhea is whether they can produce hair-like structures called *fimbriae* or *pili.*[2] These *fimbriae* an-

Table 1. O Serogroups in which ETEC, EIEC, and EPEC strains commonly occur.

Escherichia coli strain	Serogroups
ETEC	O6, O8, O15, O20, O25, O78, O115, O148, O159
EIEC	O28, O112, O115, O124, O136, O143, O144, O147, O152
EPEC	O55, O86, O111, O127, O128, O142

[1]Rohde, J. E., and R. S. Northrup. Taking science where the diarrhoea is. Acute diarrhoea in childhood. *Ciba Found Symp* 42:339-366, 1975.

[2]Stickiness and sickness. *Diarrhoea Dialogue* Issue 2, 1980, page 3.

chor *E. coli* to the lining of the small intestine, overcoming the attempts of the intestine to expel them and allowing colonization.

Vibrio cholerae

The vibrio associated with cholera was probably confined to the area around Calcutta until 1813 when a series of pandemics occurred. Improved sanitation in industrialized countries now keeps cholera at bay, but it is still endemic in parts of Asia. Diarrhea caused by cholera looks like rice water and a liter or more of fluid can be lost every hour for several days. An enterotoxin almost identical to LT is the cause of this sympton.

Campylobacter

Campylobacter have been reported mainly from Europe, South Africa, and North America where as high as 15 per cent of infant diarrhea may be due to this organism. Abdominal pain, fever, diarrhea and, occasionally, dysentery are the usual features. Pet dogs, poultry, and milk are likely sources of infection.

Yersinia

Yersinia enterocolitica has been identified as a cause of gastroenteritis in children in Canada, Europe, Japan, and South Africa. It produces pain severe enough to suggest a surgical emergency. *Yersinia* are invasive and also produce ST. Special bacteriologic techniques are needed to grow *Yersinia* and *Campylobacter* from stools. During incubation, high temperatures favor *Campylobacter* and low temperatures encourage *Yersinia.*

Shigellae and Salmonellae

Shigellae are an important cause of diarrhea in infants aged six months to two years. Since shigellosis is spread by person-to-person contact, incidence is higher where environmental health and personal hygiene are poor.[3] As few as 10 swallowed bacteria are enough to cause the disease.

Salmonellae are foodborne and contamination of animal carcasses in slaughterhouses is the usual source. Symptoms resemble those produced by *Campylobacter.*

Salmonellae and *Shigellae* are invasive and probably release toxins from inside the intestinal cells. These cause secretion of fluid in the upper intestine and cell damage in the lower intestine.

Protozoal infections

Giardia lamblia and *Entamoeba histolytica* are single cell microorganisms (protozoa) which have been reported in most countries. *G. lamblia* grows in the small intestine and is thought to be a cause of both acute and chronic diarrhea, by unknown mechanisms. *E. histolytica* prefers tropical zones and causes ulceration of the large intestine.

Other causes

Diarrhea may be due to infections outside the intestine, such as pneumonia, and this possibility must be considered in any child with diarrhea.

Conclusions

At present, the main treatment for acute diarrhea is replacement of water and electrolyte losses. Even in rotavirus infections, when sugar absorption is impaired, the intestine has sufficient reserves to allow successful treatment of diarrhea by oral rehydration with sugar and salt solutions.

In the future, it may be possible to offer specific preventive measures or treatment for specific causes of diarrhea. Simple, low-cost methods for detecting the causative organisms will then be of great importance. Rotavirus can already be detected in stools by a test relying on antibodies against the virus (enzyme-linked immunosorbent assay—ELISA) which can be carried out without expensive equipment such as electron microscopes.

The use of simpler tests in the field will mean that specific therapy will be given only when necessary (Table 2) and that antibiotics will not be administered when contraindicated (e.g. rotavirus) or where such drugs may actually prolong the illness (e.g. *Salmonellae*). Accomplishing these goals will depend on the ability of health workers to recognize the causative organism in the early stages of the disease.

Oral Rehydration in Costa Rica

Since a trial oral rehydration therapy (ORT) project was begun in Costa Rica at the beginning of 1978, ORT has proved an effective life-saver in both bacterial and rotaviral infant diarrhea, including neonates.[4,5] Routine implementation of OR in the National Children's Hospital has resulted in more than an 80 per cent reduction in mortality. The technique is easily understood both by

[3]Kahn, M. U. Soap, water, and shigellosis. *Diarrhoea Dialogue,* Issue 2, 1980, page 3.

[4]Nalin, D. R., *et al.* Oral rehydration and maintenance of children with rotavirus and bacterial diarrhoeas. *Bull WHO* 57:453-459, 1979.

[5]Pizarro, D., *et al.* Evaluation of oral therapy for infant diarrhoea in an emergency room setting; the acute episode as an opportunity for instructing mothers in home treatment. *Bull WHO* 57:983-986, 1979.

Table 2. Clinician's guide to the etiology of diarrheal diseases.[a]

Complaint	Associated clinical features: Common	Associated clinical features: Others	Incubation period	Epidemiological features	Organisms	First line treatment
Acute watery diarrhea (The stool takes the shape of the container)	Vomiting Fever	Severe dehydration in some	24-72 hours	Infants and young children Common worldwide in all socioeconomic groups Peak in colder seasons in temperate climates	Rotavirus	Rehydration therapy
	Nausea Vomiting Abdominal pain	Fever Malaise Severe dehydration	6-72 hours	Infants and young children in developing countries Travelers diarrhea in adults	Enterotoxigenic *Escherichia coli* (ETEC)	Rehydration therapy
	Nausea Vomiting Fever Chills Abdominal pain	Malaise	8-36 hours	Children Common worldwide Foodborne outbreaks (animal products) Warmer seasons	Non-typhoid *Salmonellae*	Rehydration therapy
	Abdominal pain Fever Malaise	Chills Blood and pus in the stools	3-5 days	Worldwide distribution In developed countries may be foodborne (animal products) or transmitted by handling of animals	*Campylobacter*	Rehydration therapy Erythromycin in severe cases
	Vomiting Abdominal pain	Severe dehydration Circulatory collapse, "shock"	1-3 days	Children in endemic areas Adults in newly affected areas Not found in Latin America	*Vibrio cholerae*	Rehydration therapy Tetracycline
	Nausea Vomiting	Fever	6-72 hours	Nursery outbreaks in developed countries Uncertain in developing countries	Enteropathogenic *Escherichia coli* (EPEC)	Rehydration therapy
Dysentery (The stool is soft and watery with blood and/or pus)	Fever Abdominal pain	Malaise Vomiting Urgency to defecate Painful spasm on defecation	36-72 hours	Children Poor hygiene Malnutrition Institutions Warmer seasons	*Shigellae*	Rehydration therapy Ampicillin or Trimethoprim-Sulfamethoxazole
Prolonged diarrhea (or dysentery)	Abdominal discomfort		2-6 weeks	All age groups Worldwide distribution	*Entamoeba histolytica*[b]	Metronidazole
(For at least 7 days, stools have been more frequent or of softer consistency, with or without blood or pus)	Abdominal distension Flatulence	Anorexia Nausea Malabsorption Frothy stools	1-3 weeks	Young children Some travelers Poor hygiene Worldwide distribution	*Giardia lamblia*[b]	Metronidazole

[a]This table is greatly simplified. For example, some agents produce a variety of clinical features. Only agents of major worldwide importance have been included. In certain areas, at certain times, the picture may be quite different. Also, there are a number of other conditions associated with diarrhea such as infections outside the intestine (e.g. measles and malaria), malnutrition, food intolerance, etc.

[b]Can be identified on examination of the stools with a light microscope. Blood and pus from *Shigellae* and *Campylobacter* can also be identified.

Produced in collaboration with the Ross Institute of the London School of Hygiene and Tropical Medicine and The Save the Children Fund.

health personnel and mothers visiting the emergency unit at the hospital.[6] In addition, health centers in both urban and rural areas have also been able to introduce oral rehydration therapy.

Field Project

A field project to monitor oral rehydration therapy

[6]Pizarro, D., *et al.* Oral rehydration of neonates with dehydrating diarrhoeas. *Lancet* 2:1209-1210, 1979.

given by mothers to their children in rural areas was started by the Institute for Research in Health ("Instituto de Investigaciones en Salud," INISA) in 1980. Mothers soon learned the technique and treated children successfully. At the same time, comprehensive teaching material for health personnel was prepared by the state welfare system, while the Ministry of Health established a national program of diarrheal disease control with technical cooperation from PAHO.

Sharing Experiences

During the past three years, the Costa Rican experience has been shared with several Latin American countries. Health personnel from Bolivia, El Salvador, Guatemala, Honduras, Panama, Paraguay, and Venezuela visited Costa Rica for a first-hand view of the OR program. Visiting physicians spent a week in the emergency unit of the National Children's Hospital, INISA's rural program in Puriscal, the rural hospital in Grecia, and the Department of Maternal and Child Health of the Health Ministry.

Decrease in Mortality Rates

Since 1978, about 15,000 dehydrated children (including 160 neonates) have been rehydrated in the emergency unit of the National Children's Hospital. Mothers have been taught about the causes, transmission, and management of diarrhea as well as techniques to rehydrate and prevent dehydration among infants.

All these effort have had a considerable impact on both hospital mortality rates and overall diarrheal disease mortality in Costa Rica.[7]

(*Source: Diarrhoea Dialogue,* Issue 7, 1981.)

Editorial Comment

This article focuses on two aspects of diarrheal diseases which constitute a major cause of morbidity and mortality in children in Latin America and the Caribbean.[8]

The PAHO Diarrheal Disease Prevention and Control Program carries out the WHO expanded diarrheal disease program's commitment to reduce infant mortality and malnutrition related to diarrhea. It assumes a collaborative role with national diarrheal disease control programs, and emphasizes interdisciplinary strategies which are integrated into the existing primary health care infrastructure. These strategies include treatment through oral rehydration, maternal and child nutrition, adoption of measures aimed at improving water supplies, sewerage, and food hygiene facilities, intensification of health education efforts, and establishment of surveillance systems to detect and control epidemics and evaluate the program's impact. A final component of the PAHO program is support for research in all aspects of diarrheal diseases.

These diseases are critically important and developments in epidemiology, clinical aspects, research findings, and efforts aimed at their control should be emphasized. The PAHO *Epidemiological Bulletin* provides a forum whereby developments in the aforementioned areas are highlighted for all diseases; contributions in the specific area of diarrheal diseases are welcome.

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[7]Mata, L. J. Diarrhoeal diseases. How Costa Rica won. *World Health Forum* 2:141-142, 1981.

[8]See PAHO *Epidemiological Bulletin* 1: 2, 1980.

Reports of Meetings and Seminars

Meeting on Emergencies caused by Communicable Disease Epidemics

A group of specialists from several countries met from 9-13 November 1981 at WHO Headquarters in Geneva to discuss emergency situations caused by communicable disease epidemics. Participants included staff from the six WHO regions (America, Europe, Africa, Eastern Mediterranean, Southeastern Pacific, and Western Pacific).

The main objectives of the meeting were: to find more dynamic means of cooperation among countries and between these and WHO during emergencies caused by common disease epidemics, and to establish guidelines for surveillance, prevention, and control of certain communicable diseases.

As a framework for discussions, the characteristic elements of epidemics which threaten or cause emergency situations were defined to include the following (although

not all need be present and their importance must be interpreted judiciously):

- The disease is so severe that it leads to serious disability or death.
- A "large" increase in cases is observed or may reasonably be expected to occur (taking into account the disease and the circumstances).
- There is a risk of introduction or spread of the disease to other individuals or groups.
- There is a danger of international transmission.
- There is a risk of social or economic disruption from the introduction, continued presence, or spread of the disease.
- National authorities are unable to cope adequately with the situation for lack or insufficiency of technical or professional personnel, administrative experience, necessary supplies or equipment (drugs, vaccines, laboratory diagnostic materials, vector control materials, etc.).

Subjects discussed included: WHO's past experience in controlling epidemics which lead to emergencies (general aspects dealing with: cholera, plague, meningitis, viral diseases, diseases of unknown etiology, smallpox, and vector-transmitted diseases); management operations; epidemiological and disease control services; safety measures applicable in emergency situations; role of international teams and collaborating centers; dissemination of information; and, a review of guidelines set forth for the early detection and control of outbreaks caused by various bacterial and viral diseases.

The participants made the following recommendations to WHO:

1. The consultative process, begun during this informal consultation, should be continued and extended in all regions. Central, regional, and subregional consultations between national health authorities and WHO should result in the preparation of mutually compatible contingency plans, aimed at technical cooperation among developing countries and avoiding unjustified measures.

2. Realizing that anticipation and early identification of epidemics are the most essential elements for control, the development of efficient epidemiological surveillance should be given due attention by both national health authorities and WHO. There is a need to strengthen national institutions participating in surveillance activities and communicable disease control.

3. WHO should accelerate and extend its programs on training in epidemiological surveillance, application of technical, diagnostic, and preventive measures and on management of epidemics.

4. WHO should further develop syndrome-oriented modules for action in epidemic control, thereby providing practical guidelines against specific communicable diseases that may cause emergencies.

5. An inventory should be made of national resources, human and other physical, available to respond to epidemics; these should include laboratory resources. WHO should continue identifying experts in various fields, who could be called on to support Member States at times of emergencies. This panel, together with an inventory of collaborating centers for advisory, reference, and research services for emergency control, should be given the widest possible support.

6. Realizing the difficulties encountered because of delays in obtaining essential supplies and equipment from producers, WHO should investigate how to improve reserve stocks of supplies at regional and global levels.

7. WHO should disseminate information on safety measures in clinical and laboratory management to protect investigation teams, laboratory and hospital personnel, providing guidelines on these aspects to national authorities.

8. Future programming by WHO and Member States should consider the above-mentioned measures in preparedness for control of epidemics.

The technical cooperation Member States can expect from WHO when they face an outbreak of a communicable disease is a statutory commitment derived from the WHO Constitution, the International Health Regulations, and the resolution passed in 1969 by the Twenty-second World Health Assembly placing a group of diseases "under international surveillance." To provide for situations where other specific diseases without statutory ground cause epidemics of national and international concern, the Thirtieth World Health Assembly requested Member States to endorse the opinion of the Committee on International Surveillance of Communicable Diseases that "prompt reporting of significant outbreaks of communicable diseases is the best foundation for their international control, irrespective of whether or not they are on any particular list." This is intended to cover epidemics caused by other agents which do not lend themselves to such international specifications. In addition, virtually every outbreak has one particular aspect or more which cannot be envisaged in advance and covered by a regulation.

When a request is received from the competent national authorities, the criteria for WHO involvement are:

- that the situation is a genuine emergency;
- that the situation threatens to become an emergency if corrective measures are not taken;
- that national resources for meeting it are insufficient;
- that additional resources from other countries or agencies which can be foreseen at the time are also insufficient or impracticable.

WHO may give or offer governments technical cooperation and emergency assistance, even though no request has been received, provided that it is clear that WHO assistance would materially improve either the country's physical or administrative resources available to meet the situation and if the situation is so serious that it threatens the public health of that and adjoining countries.

International cooperation is generally available whenever an epidemic takes on disaster proportions. However, to be more efficient it should be organized in advance between epidemics. WHO can be efficiently instrumental

in this case if the modalities are defined. International cooperation will undoubtedly prove to be more efficient than international regulations.

II International Course in Malariology for Physicians

Held in Villavicencio, Meta, Colombia from 7 September to 27 November 1981, the course was financed by the National Malaria Eradication Service (SNEM) and PAHO/WHO. It was attended by medical officers of the SNEM and of the Sectional Health Services in the areas with the highest malaria incidence.

The course covered the following subjects: epidemiology, statistics, parasitology, entomology, vector control, malaria control and eradication, chemotherapy, organization and administration, thesis work, and *Aedes aegypti* control campaign.

The purpose of the course was to improve the health of the population in the malarious areas of Colombia through the technical training of high-level personnel who can help prevent malaria, reduce its morbidity, eliminate it as a cause of death and eradicate it in the long run, and, consequently, promote the economic and social development of the country. With this course, Colombia's Department of Direct Campaigns also intends to train personnel for programming, executing, and evaluating epidemiological surveillance and malaria and *A. aegypti* control activities.

The III International Course in Malariology for Physicians will be held in 1983.

International Seminar on Prevention and Control of Blindness in the Southern Cone Countries

This seminar was held in Montevideo, Uruguay from 17-19 September 1981. Its purposes were:

1. To determine the main characteristics of the problem of blindness in the participating countries.
2. To analyze the most important epidemiological and operational aspects of blindness, its prevention, and control.
3. To encourage and promote the development of integrated programs.
4. To prepare a plan of action for the next three years in each of the Southern Cone countries.

The information available at present does not give a full indication of the magnitude and severity of the problem of blindness in the Americas, or of the ophthalmologic resources available to combat it.

PAHO and WHO have proposed a program for prevention of blindness based on the following four components:

- Identification of communities with a high occurrence of preventable blindness and determination of its causes.
- Assignment of high priority to the most affected communities, and, as a first measure, attacking with therapeutic and preventive measures the leading causes of blindness in those communities, such as cataracts, trauma, diabetes, etc. Where a large number of patients are found to require surgery, the effectiveness of mobile surgical equipment has been demonstrated. Such intensive intervention has afforded a unique opportunity for mobilizing community participation and for selecting and training health workers in small towns to carry out preventive measures on a continuing basis.
- Inclusion in primary health care of the dissemination of simple, therapeutic, and preventive measures for the promotion of eye health. Any specific program for the prevention of blindness should involve primary health care.
- Strengthening of ophthalmologic services at the central and intermediate levels in order to establish an adequate system of referral and to facilitate supervision and training.

Blindness is thus seen as a public health problem that goes beyond the specialist.

One of the main difficulties is the multiplicity of definitions of blindness. Nonetheless, the data can be adjusted to give an initial idea of the magnitude of the problem, following the criteria proposed by WHO in 1972.

Programs for the prevention of blindness are aimed at reducing national indices of blindness to less than 0.5 per cent for the total population and 1.0 per cent or less in the most affected communities.

The final report of the meeting is available in Spanish through the Program for Prevention of Blindness, Division of Disease Prevention and Control, PAHO.

Courses

Workshop on the Teaching of Epidemiology in Courses on Health Administration

For the last three years PAHO has been providing support for training programs in health administration in Latin America and the Caribbean, as a basic programmatic component of the strategy for attaining the goal of health for all by the year 2000.

A joint project of PAHO and the W. K. Kellogg Foundation identified the programs underway in the Region in this field. Subsequently, subregional meetings held in Puerto Rico, Brazil, and Colombia led to the establishment of bases for a medium-term Program of Education in Health Administration (PROASA), to strengthen the institutions responsible for such training, and, in due course, to expand the capacity of the entire network of programs in this field.

A new programming phase began on 1 March 1980, with the following specific objectives:

1. To implement an effective information and communication system among programs.
2. To improve the education process and the content of instructional programs in health administration.
3. To carry out continuing education programs in accordance with the regional needs of health services.
4. To develop research in the area of medical care for the purpose of integrating education and health services.

The following workshops have been held to improve the education process and the course content of instructional programs in health administration in the various countries, with the assistance of consultants specializing in this field and the support of the Regional Library of Medicine and the Health Sciences (RLM):

- Teaching of Organizational Behavior Sciences (March 1981).
- Teaching of Economics, Finance, and Cost Control of Health Services (May 1981).
- Teaching of Evaluation and Planning of Health Services (November 1981).
- Teaching of Epidemiology in Courses on Health Administration. (This workshop will be held in Santiago, Chile, from 26-30 June 1982.)

One by-product of these workshops is the exchange of professors and the preparation of anthologies and instructional modules.

In order to develop an information and communication system among programs, the PAHO Office of Health and Biomedical Publications in Washington, D.C., is collaborating in this endeavor by publishing news about the various programs and their activities in the quarterly review *Educación médica y salud.*

The Directory of Regular Programs in Health Administration Education in Latin America and the Caribbean has been updated and distributed widely.

Course on Basic Methods for Epidemiological Research

The Division of Biological and Health Sciences of the Autonomous Metropolitan University-Xochimilco Unit, Mexico, will hold a course on basic methods for epidemiological research from 5-30 July 1982.

The course is intended for professionals in the fields of biological, health, and social sciences and management working in clinical research or public health in higher education institutions, health care agencies, and research centers.

The course is organized in modules designed for specific problems, and covers biostatistics and epidemiology. It will include the application of epidemiological methods in planning, and the epidemiology of infectious, chronic, occupational, and genetic diseases.

European Course in Tropical Epidemiology

This first course, to be held from 22 August to 3 September 1982 at the Bernhard-Nocht Institute, Hamburg, Germany, will provide practitioners with additional skills in the epidemiological determination of local health problems and service priorities, especially in the planning of local field studies. Emphasis will be placed on the adoption of standard epidemiological methods in the special conditions existing in most developing countries, on the interpretation of data obtainable in these countries, and on the reporting of field studies.

The course is open to qualified physicians with experience or interest in tropical medicine. Candidates should hold community health or hospital posts in developing countries or expect to do so in the near future. A good command of English is necessary since the course will be conducted in that language. For further information and an application contact: Dr. U. K. Brinkman, Bernhard-Nocht-Institut Für Schiffs-und Tropenkrankheiten, Bernhard Nocht Strasse 74, 2000, Hamburg 4, Federal Republic of Germany.

Publications[1]

Health Conditions in the Americas, 1977-1980. Washington, D.C., Pan American Health Organization, 1982 (in preparation).

This eighth compilation on health conditions in the Region is being prepared for presentation to the XXI Pan American Sanitary Conference (September 1982). It describes in statistical form the progress made by Member Countries of PAHO in controlling disease and extending life expectancy. It serves as a basis for the planning, development, and implementation of health services activities and as a crucial component of decision-making for the Organization in fulfilling its role of providing technical cooperation to governments; it also provides a statistical framework for the monitoring and evaluation of the Plan of Action for the implementation of the regional strategies designed to achieve the goal of health for all by the year 2000.

The publication contains data on population, vital statistics, communicable diseases, health services, health manpower, hospitals, and the environment. Major new sections include: (1) demographic and socioeconomic background which serves as a basis for the definition of the regional strategies; (2) health status of the population, with special analyses of high-risk populations as defined by the Plan of Action (children and youth, women and the aged); (3) health resources; (4) health services utilization; (5) development of the health infrastructure; (6) animal health; and (7) environmental health.

The main source of the information presented is the data obtained from the countries by means of the joint PAHO/WHO questionnaires on mortality and morbidity from communicable and reportable diseases, vaccinations, hospitals and other health entities, and human resources in the health sector. Additional sources include, but are not limited to, official government publications, scientific papers, and reports from the United Nations, WHO, and other U.N. specialized agencies.

Vaccination Certificate Requirements for International Travel and Health Advice to Travellers. Geneva, World Health Organization, 1982. (ISBN 92 4 158006 2). 70 pages. Price: Sw. fr. 12.-.

This 1982 edition, to be published in Spanish by PAHO in mid-1982 and distributed to its Member Countries, closely follows that of 1981, and has taken into account the comments and modifications proposed by national health administrations and other users.

In addition to providing the usual country-by-country list of vaccination certificate requirements, the book tabulates information on the malaria situation in each country where the disease occurs and lists appropriate drugs for its prevention. Guidance on some of the other main health risks to travelers in different parts of the world and advice on precautions that may be taken against them are provided. Country and subject indices are also included.

The publication is addressed to national health administrations and will assist them in fulfilling their responsibility of advising the health professions, travel and transportation organizations, and travelers themselves on the health risks that may be encountered in other countries and on measures to offset them.

[1]These publications are available at the quoted prices through the PAHO Office of Health and Biomedical Publications, Distribution and Sales Unit, 525 Twenty-third Street, N.W., Washington, D.C. 20037.

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