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Inside:

Incidence of Typhoid Fever, Dhaka 2001

Community-based surveillance for typhoid fever in Kamalapur during 2001 found that 49 (5.5%) blood cultures grew *Salmonella* Typhi. *S.* Typhi isolations represented 75% of all positive blood cultures; 53% were in children <5 years of age. The overall incidence of typhoid fever was 3.9 cases per 1,000 population per year; in children <5 years of age, the rate was 18.7 per 1,000 children per year. Children <5 years of age had an 8.9-fold increased likelihood of infection when compared with all others. Less than 50% of isolates were susceptible to ampicillin, cotrimoxazole or chloramphenicol. All isolates were susceptible to ciprofloxacin and 98% were susceptible to ceftriaxone. The findings of this report indicate a high burden of disease in this urban population. Age-specific infection rates suggest that vaccination would be most beneficial in the first year of life.

Typhoid fever is both a water-borne and food-borne gastrointestinal infection, with an estimated global prevalence between 16 million and 33 million cases per year, with 700,000 deaths (1,2). To determine disease incidence within a high-risk population, and to estimate age-specific incidence rates, a 10-month prospective community-based study among an urban poor population in Dhaka was conducted.

ICDDR,B operates a surveillance and intervention site in Kamalapur, an urban slum area in Dhaka. In August 2000, the Centre began surveillance for dengue and dengue haemorrhagic fever. Blood was collected to test for dengue and, from 6 December 2000 to 8 October 2001, blood was also cultured to rule out bacterial infection.

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Table: Organisms isolated from blood culture (n=65)

Organism	Number	Percent
Salmonella Typhi	49	75.4
Acinetobacter	4	6.2
S. paratyphi A	3	4.6
Group D *Salmonella*	2	3.1
S. viridans	2	3.1
S. epidermidis	2	3.1
S. pneumoniae	2	3.1
Enterobacter species	1	1.5

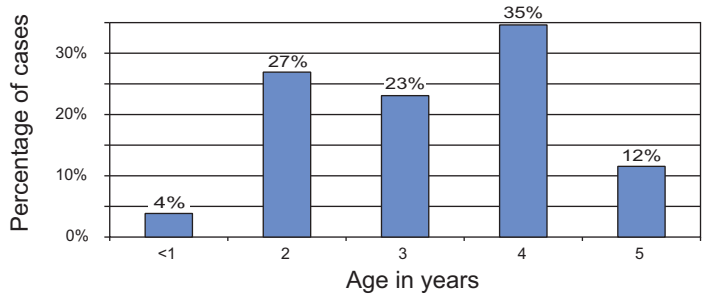
All cultures were sent to the Clinical Microbiology Laboratory at ICDDR,B and processed in blood agar, chocolate agar and MacConkey agar, and then incubated at 37˚C for 16–18 hours. Suspected colonies were identified by biochemical tests and confirmed by serological identification using commercial antisera (Denka Sieken, Japan). Antimicrobial susceptibility was determined by disk diffusion.

Cases of typhoid fever were defined as febrile patients with *Salmonella enterica* serovar Typhi (*S.* Typhi) isolated from blood. Control-patients were febrile patients whose blood cultures did not grow *S.* Typhi*, S. paratyphi* or other *Salmonella* species.

Among 888 blood cultures processed, 65 were culture positive (isolation rate 7.3%); S. Typhi was isolated in 49 (75.4%) (5.5% of all cultures). *Salmonella* species (*S. paratyph*i and Group D *Salmonella*) accounted for five of the other positive cultures (Table). Among the 49 cases of typhoid fever, 26 (53.1%) were in children < 5 years old.

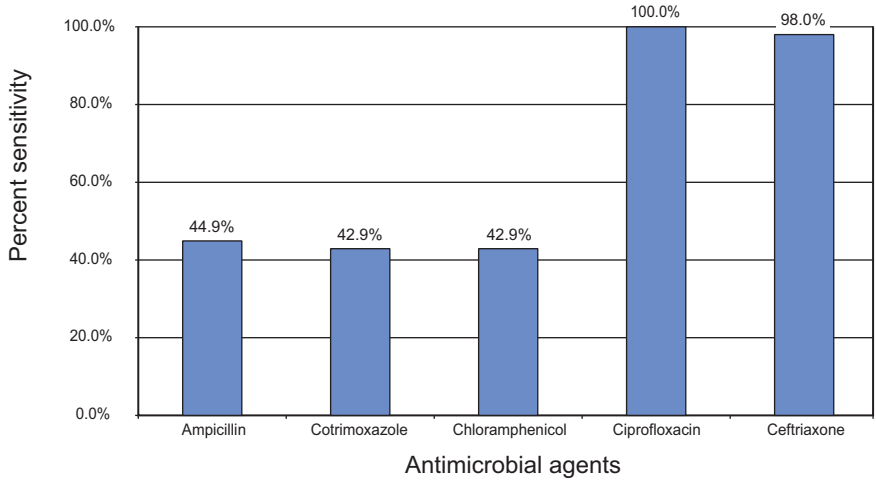
The overall incidence of typhoid fever for all age groups was 3.9 episodes per 1000 person-years. The incidence of typhoid fever among people >5 years of age was 2.1 episodes per 1000 person-years, and among children <5 years old was 18.7 episodes/1000 person-years. Children <5 years of age had an 8.9-fold increased risk of infection when compared with all others (95% confidence interval = 4.9-16.4). Among children <5 years of age, 85% of cases occurred between 2 and 4 years of age; 4.0% occurred during the first year of life (Figure 1).

Figure 1: Age distribution of typhoid cases for patients <5 years of age, Kamalapur 2001



No isolates were resistant to ciprofloxacin (based on currently defined breakpoints); 2% of isolates were resistant to ceftriaxone (i.e. one isolate was resistant), and a majority of isolates were resistant to cotrimoxazole (57%), chloramphenicol (57%), and ampicillin (55%) (Figure 2). Antimicrobial therapy was started before culture results were available. All patients made a complete recovery, despite 14 patients receiving full-course therapy with drugs (either cotrimoxazole or amoxicillin) to which the isolate was resistant.

Figure 2: Salmonella Typhi *antimicrobial susceptibility (n=49), Kamalapur 2001*



Reported by: Clinical Pathology Laboratory, Laboratory Sciences Division (LSD) and Infectious Diseases Unit, Health Systems and Infectious Diseases Division (HSID), ICDDR,B

Supported by: United States Agency for International Development (USAID)

Comment

These are the first community-based epidemiological data on typhoid disease burden from Bangladesh, and they indicate a high burden of disease in this urban population. The greatest incidence of infection was in children <5 years of age. The findings are similar to those of a recent community-based study of typhoid incidence from India (3). This is in contrast with hospital-based studies which have suggested peak incidence in children 5 to 15 years of

A laboratory-based study from Dhaka also showed that 54.5% of *S.* Typhi isolates were from children <5 years of age (6). Further study will be required to determine whether dissimilar clinical presentations, healthcare seeking behaviours, or clinical management are responsible for differences observed with hospital-based studies.

Age-specific infection rates suggest that vaccination would be most beneficial in the first year of life, before infection rates become high during the second and subsequent years of early childhood. For optimal impact in Bangladesh and in similar settings, new typhoid vaccines will need to be efficacious and practical for administration to infants and toddlers.

Surveillance also detected high rates of resistance of *S.* Typhi to commonly used antimicrobial drugs. It is an important finding that all patients fully recovered, despite some being treated with drugs to which there was *in vitro* resistance. Systematic evaluation of the impact of *in vitro* resistance on clinical outcome would be helpful to define the optimal treatment regimen for uncomplicated (non-hospitalized) typhoid fever in Bangladesh.

Surveillance for typhoid fever was re-initiated in Kamalapur in February 2003. In addition to more information on incidence of disease, information will be collected on risk factors, and on the utility of commercially-available rapid diagnostic tests.

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Screening for Syphilis in Routine Antenatal Care

Screening for syphilis was carried out among 1,103 women; 80% were screened in their late 2nd trimester or during the third trimester. The prevalence of syphilis was 1.5%. A comparison of results of testing done by paramedics with those from a reference laboratory, showed that the sensitivity of the test when carried out by paramedics was only 13%. Screening for syphilis as currently carried out by paramedics is unreliable. Simpler diagnostic tests that could more easily be carried out by paramedics are needed for ante-natal screening using paramedics to be effective.

In Bangladesh, the prevalence of syphilis in groups vulnerable to HIV infection is high (1), but insufficient information exists on the prevalence of syphilis infections in pregnant women in the general population. The effects of untreated syphilis on pregnancy include spontaneous abortion, stillbirth, prematurity and congenital syphilis (2). Congenital syphilis has a wide array of serious manifestations, including meningitis and meningovascular syphilis. To effectively prevent foetal wastage and congenital anomalies, appropriate treatment must be given by first or early second trimester of pregnancy.

In a study carried out in rural Bangladesh, the prevalence of syphilis was about 1% in women with symptoms related to the genital tract (3). In contrast, a study among Dhaka slum dwellers revealed that more than 11% of men and 5% of women had syphilis (4). Another recently-published study estimated the prevalence of syphilis among female clients attending a basic healthcare clinic to be about 3% (5).

Most women with syphilis neglect to seek medical care, probably because the primary lesions are often painless and not seen, since they are located inside the vagina or cervix. The secondary stage of syphilis is characterized by nonspecific signs and symptoms. Only serological tests for screening can assure detection of syphilis in women. Screening and treating pregnant women for syphilis was shown to be inexpensive and cost-effective, in a demonstration project in Lusaka, Zambia (6). Even in countries with seroreactivity rates lower than 1 per 1,000, syphilis screening in pregnant women is cost-effective (7).

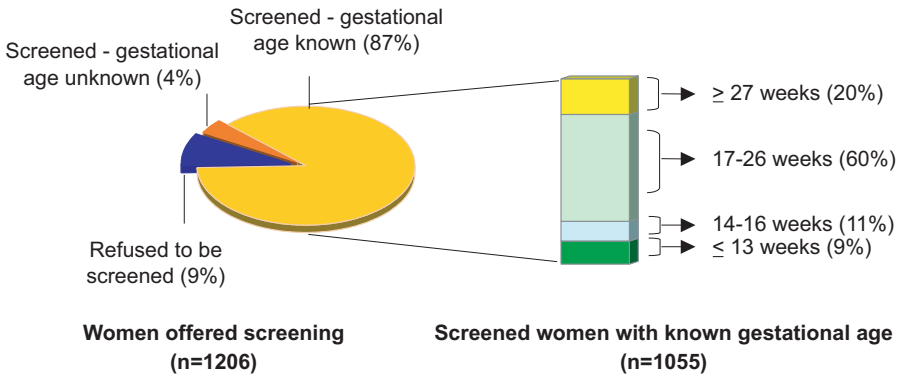
There is lack of information on the prevalence of syphilis among pregnant women in Bangladesh. Several operational questions have not been addressed, such as is antenatal care (ANC) screening for syphilis functional and valid in primary healthcare (PHC)-level clinics, using existing providers for ANC, and is routine screening acceptable to clients? This report presents findings of a cross-sectional, clinic-based study addressing these queries, conducted at two urban primary healthcare-level clinics: Sher-e-Bangla Nagar Government Dispensary (GoD) at Agargaon Pucca Market and the Mirpur PSKP clinic, between November 1999 and March 2001. It included 1,206 pregnant women who attended either of the clinics for ANC. Most were less than 25 years old, 36% had no education. About half of the pregnant women resided in slum dwellings. All were married.

In addition to routine antenatal care, each of these pregnant women was offered a blood test for screening for syphilis. Ninety-one percent (1,103 women) agreed to be screened. Of them, 96% knew their gestational age; eighty percent were screened in their late 2nd trimester or 3rd trimester (Fig 1). Almost all of these women were at their first antenatal visit with the current pregnancy.

The rapid plasma reagin (RPR) test for syphilis screening was done twice on each of the collected specimens. First, paramedics in the study clinics performed the test, and then the RPR was done at ICDDR,B RTI/STI Laboratory, where the TPHA was also done as a confirmatory test for syphilis. Reference laboratory testing of specimens was carried out to provide a gold standard against which to evaluate the reliability and validity of RPR test performed by paramedics.

Based on the results from the reference laboratory, the prevalence of syphilis was 1.5%. The reliability of the paramedics was measured by comparing the RPR test results from the paramedics with those of the reference laboratory, and calculating the degree of statistical agreement. The results of RPR from the reference laboratory agreed with those tests conducted by paramedics in only 13% of women. The sensitivity and specificity of paramedic testing was 13% and 96%, respectively. Based upon these results, it is estimated that if the clinics were to rely on the paramedic RPR testing, 87% of infected women would not be identified and 4 percent of non-infected women would be incorrectly labelled, and treated, as positive. By contrast, the findings from confirmatory TPHA testing showed that virtually all infected women were correctly identified in the reference laboratory by RPR, with 2% of non-infected women incorrectly found to be positive.

Figure 1: Women who were offered screening and screened for syphilis (n=1206)



Reported by: Sher-e-Bangla Nagar Government Dispensary, Agargaon, Dhaka; Progoti Samaj Kallyan Protisthan (PSKP) clinic, Mirpur, Dhaka; RTI/STI Laboratory, Laboratory Sciences Division (LSD) and Infectious Diseases Unit, Health Systems and Infectious Diseases Division (HSID), ICDDR,B

Supported by: US Agency for International Development (USAID)

Comment

The occurrence of syphilis in pregnant women, given the severity of its consequences, was found to be high (1.5%). Most started ANC at a point in their pregnancy too late to prevent congenital syphilis with conventional treatment. Treatment during the late second and in the third trimester greatly increases the risk of treatment failure (8). Alternative strategies that will result in earlier entry into ANC are needed and must be tested.

The majority of women accepted testing and appeared to understand what syphilis was. However, screening carried out by paramedics was found to be unreliable. Thus, the findings of this report suggest deficiencies in the antenatal syphilis-screening programme when carried out by paramedics at primary level healthcare clinics. Syphilis-screening is ongoing at 23 NSDP urban clinics. One potential solution would be to provide more extensive training for paramedics, and to monitor for quality assurance closely by periodically sending out a panel of sera to each of the clinics for assessment; such an approach would be expensive, unwieldy and difficult to carry out and sustain. Centralized testing at qualified reference laboratories would seem to be the preferred strategy.

It is essential to design strategies to implement improved syphilis screening. One option would be to use simpler treponemal specific-rapid diagnostic testing that would be more easily performed by paramedics. Over twenty companies now manufacture rapid simple treponema-specific tests that can be used on whole blood, serum, or plasma. The tests can be used in primary healthcare settings as they are stable at room temperature for months, require no equipment, and give visual readout in 8–15 minutes (9). Limited evaluation suggests that some have comparable performance to laboratory-based tests (10). Such a programme would also require counselling programmes and educational campaigns to promote earlier antenatal clinic attendance so that timely screening and management would be possible. Cost-benefit analyses through direct measurement of the effect of screening on the prevention of adverse pregnancy outcomes are needed.

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The Emergence of Severe Acute Respiratory Syndrome (SARS): Implications for Bangladesh

Severe acute respiratory syndrome (SARS) is a new disease, which has created health and economic concerns over the past several months, primarily in China and southeast Asia. While there is no evidence of SARS in Bangladesh, a variety of actions have been implemented, and additional steps may be needed for preparedness, because of its potentially severe impact in Bangladesh. Substantial progress has been made in characterizing clinical, virologic, epidemiologic aspects of SARS. Public health measures to control spread have been successful in several countries.

Severe acute respiratory syndrome (SARS) is a newly-emerged disease entity, caused by a previously unknown coronavirus. The disease first appeared in southern China in November 2002, and since late February 2003, spread rapidly around the world. Disease transmission is ongoing in most of China, Hong Kong, Taiwan, Singapore and Toronto, Canada. As of 28 May 2003, more than 8,000 cases and 745 deaths have occurred worldwide; none was documented in Bangladesh by this date.

The spectrum of illness is becoming clearer as more patients are being followed through the course of their disease (1,2). Illness is characterized by several days of fever, dry cough, mild sore throat, myalgias, and headache, followed by rapid respiratory compromise often with acute respiratory distress syndrome. Death occurs in 50% of patients >60 years of age, 15% of patients 45–59 years old, 6% of patients 25–44 years old, and 1% of patients <25 years old. Nearly 25% of patients may require mechanical ventilation with positive airway pressure. The incubation period for most cases appears to be 2 to 10 days. When infected, young children usually experience mild illness.

There is no highly effective specific therapy for SARS. Experienced clinicians disagree about the value of early treatment with ribavirin and high-dose corticosteroids. More data are needed urgently to help define the most effective treatment strategy, particularly for areas with limited resources, as in Bangladesh.

Disease is spread primarily via droplets and transmission appears to require close contact with an infected person. In China, nearly 30% of infected persons early in the epidemic were among healthcare workers with an additional 20% occurring in family members. Transmission has occurred in airplanes, hotels, and an apartment complex. In addition to respiratory secretions, the virus is shed within faeces. A role for faecal transmission has not yet been established. The causative virus also can survive on dry surfaces for several hours and possibly for days, so the potential for transmission of some cases via fomites also exists.

It is not clear how the virus has emerged in humans, but it is believed to have originated in an animal host, incidentally infecting at least one human.

Tests have been developed to detect SARS-associated coronavirus infection. These tests include polymerase chain reaction and antibody assays. None is available yet in Bangladesh.

The current international case definition for 'suspected SARS' is as follows: A person presenting after 1 November 2002 with history of high fever (more than 38ºC or 100.4ºF) AND cough or breathing difficulty AND one or more of the following exposures during the 10 days prior to onset of symptoms:

- close contact[1] with a person who is a suspect or probable case of SARS
- history of travel, to an area with recent local transmission of SARS, or
- residing in an area with recent local transmission of SARS

OR a person with an unexplained acute respiratory illness resulting in death after 1 November 2002, but on whom no autopsy has been performed AND one or more of the above exposures during the 10 days prior to onset of symptoms.

A 'probable' case is a suspect case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR); OR a suspect case of SARS that is positive for SARS coronavirus by one or more assays; OR a suspect case with autopsy findings consistent with the pathology of RDS without an identifiable cause.

Reported by: Disease Control Section, Directorate General for Health Services, Mohakhali, Dhaka; Health Systems and Infectious Diseases Division, ICDDR,B

Comment

SARS is a profound example of the potential for new infectious pathogens to emerge and to spread rapidly around the world. While SARS illness can be very severe, it appears to be relatively difficult to transmit outside of the healthcare setting. Had this disease been as easily transmittable as influenza, for example, the impact would have been much more catastrophic.

Substantial progress has been made in our understanding of this disease via strong international collaboration. Much is known about the clinical presentation (1,2), transmission patterns (3), and the causative agent (4). The entire genome of the SARS-associated coronavirus has been sequenced (5,6) which should help in the process of drug and vaccine discovery and diagnostic test development.

Given the frequency of travel of people between Bangladesh and countries where SARS transmission is ongoing, the potential exists for the introduction of SARS into Bangladesh. Because of dense population, suboptimal hygiene, crowded clinic and hospital settings, the potential for rapid spread of the causative agent would appear to be substantial, should introduction of the virus occur in Dhaka or elsewhere in Bangladesh. Introduction of SARS would likely be

[1]Close contact: having cared for, lived with, or had direct contact with respiratory secretions or body fluids of a suspect or probable case of SARS.

devastating, because of weak hospital infrastructure, which would be severely strained. Thus, it is critical to implement strategies to prevent introduction of SARS-associated coronavirus into Bangladesh and to prevent spread should the virus appear in the country.

The government of Bangladesh has implemented a number of steps in response to this global problem. These include screening of incoming travellers for respiratory illness with fever through a self-administered form, and by visual inspection and brief interview carried out by doctors and nurses at all international airports, seaports and landports. Quarantine centres have been established at international airports where arriving passengers suspected to have SARS will be retained until SARS can be ruled out. A hospital in Dhaka has been designated to care for patients suspected to have SARS.

All infectious disease hospitals in Chittagong, Sylhet, Khulna, Rajshahi, Barishal and Jessore have established separate isolation wards for managing SARS cases with barrier techniques. Three laboratories (at Bangabandhu Sheikh Mujib Medical University, the Armed Forces Institute of Pathology, and the Institute of Epidemiology, Disease Control and Research) have been designated as focal points for collection, preparation and storage of specimens, according to strict biosafety measures, and shipment to international SARS reference laboratories.

Hopefully, SARS will not be introduced in Bangladesh. However, it is important to be prepared for the possibility of an epidemic, because the effectiveness of screening at borders and airports is limited for a variety of reasons including the relatively long incubation period.

Preparedness for SARS should include training of clinicians nationwide on diagnosis and management of SARS, strategies for triaging patients at risk of SARS to decrease potential transmission to other patients and to healthcare workers, and implementation of stringent infection control when managing patients suspected to have SARS. Protective gear will need to be available, including masks that meet minimum standards, gowns and gloves. There will need to be a number of dedicated ventilators and staff who are experienced in using them. Surveillance and reporting mechanisms for SARS will be required. Surveillance should be linked to contact-tracing activities and should include a mechanism for quarantining of contacts of SARS patients.

Surveillance should also be established among healthcare workers. The occurrence of pneumonia among >1 healthcare workers at a clinic or hospital over a 14-day period, will signal the possibility that SARS has been introduced. While other communicable pathogens may cause clusters of pneumonia, identification of a cluster among healthcare workers should rapidly stimulate a system of diagnosis and prevention of spread until the diagnosis of SARS can be ruled out.

A mechanism for testing specimens needs to be established. Until a national laboratory for diagnosing coronavirus is fully functional, it will be necessary to arrange for specimens from clinically-confirmed cases of SARS to be sent to one of the existing international diagnostic laboratories in the region.

Public education campaigns will need to be carried out to make community residents aware of SARS, its clinical characteristics, the magnitude of disease, and its potential occurrence among people who have visited areas with known transmission of SARS, and what to do if they or someone they know has a condition consistent with the case definition for SARS. People will want to know what steps they can take to minimize their risks. Communication campaigns in clinic and hospital settings should also be carried out to increase awareness among healthcare workers for procedures that should be followed for reducing the risk of transmission in healthcare settings.

SARS has captured much attention because it is a new, sometimes fatal disease, and it has been transmitted rapidly globally. However, it is important to keep this disease in perspective. Among the 1.3 billion people living in China, only 5,000 cases have occurred over a 7-month period, indicating very limited transmissibility. In addition, evidence from Vietnam, Singapore and Toronto shows that with strong public-health measures, transmission can be controlled. After experiencing 63 cases of SARS, the disease has not occurred in Vietnam since 14 April following implementation of a variety of control strategies.

Excellent resources and detailed information on SARS are available on the websites of the World Health Organization and the US Centers for Disease Control and Prevention at www.who.int and www.cdc.gov.

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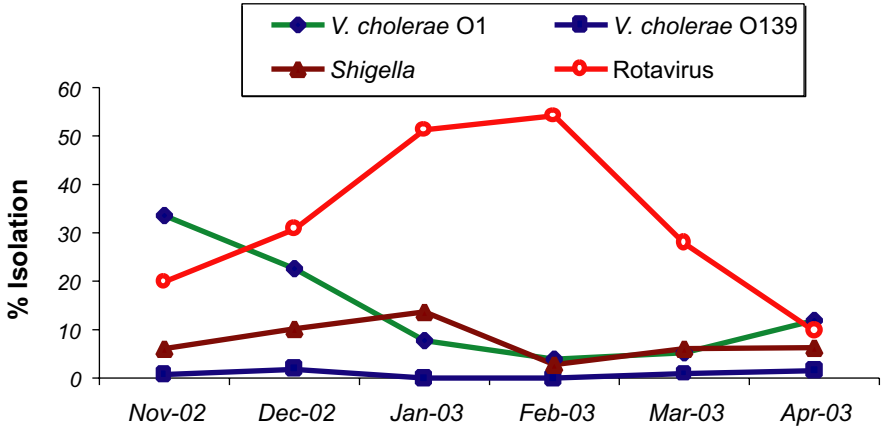
Surveillance Update

With each issue of the HSB, updates of surveillance data described in earlier issues will be provided. These updated tables and figures will represent the most recent observation period available at the time of publication. We hope these updates will be helpful to health professionals who are interested in current patterns of disease and drug resistance.

Susceptibility of diarrhoeal pathogens to antimicrobial drugs: November 2002-April 2003

Antimicrobial agent	*Shigella* (n=122)	*V. cholerae* O1 (n=242)	*V. cholerae* O139 (n=15)
Nalidixic acid	45.9	NT	NT
Mecillinam	99.2	NT	NT
Ampicillin	46.7	NT	NT
TMP-SMX	43.4	1.2	100
Ciprofloxacin	99.2	100	100
Tetracycline	NT	100	100
Erythromycin	NT	100	100
Furazolidine	NT	0.0	100

Monthly isolations of V. cholerae *O1,* V. cholerae *O139,* Shigella *and Rotavirus: November 2002–April 2003*



Antimicrobial resistance patterns of 158 M. tuberculosis *isolates: May 2002–January 2003*

Drugs	Resistance type		Total (n=158)
	Primary (n=133)	Acquired *(n=25)	
Streptomycin	66 (49.6)	12 (48.0)	78 (49.4)
Isoniazid (INH)	15 (11.3)	5 (20.0)	20 (12.7)
Ethambutol	7 (5.3)	4 (16.0)	11 (7.0)
Rifampicin	4 (3.0)	4 (16.0)	8 (5.1)
MDR (INH+Rifampicin)	3 (2.3)	3 (12.0)	6 (3.8)
Any drug	68 (51.1)	14 (56.0)	82 (51.9)

( ) column percentages

* Antituberculous drugs received for 1 month or more

Antimicrobial susceptibility of N. gonorrhoeae *isolated during January to April 2003 (N=122)*

Antimicrobial agent	Susceptible (%)	Reduced susceptible (%)	Resistant (%)
Azithromycin	84.4	15.6	0
Cefixime	100	0	0
Ceftriaxone	100	0	0
Ciprofloxacin	1.6	4.9	93.4
Penicillin	16.4	44.3	39.3
Spectinomycin	100	0	0
Tetracycline	0.8	10.7	88.5

44 (36%) of the isolates were resistant to three drugs

The ICDDR,B, Centre for Health and Population Research receives financial support from countries and agencies which share its concern for the health problems of developing countries. Current donors providing unrestricted support include: the aid agencies of the Governments of Australia, Bangladesh, Belgium, Canada, Japan, the Netherlands, Sweden, Sri Lanka, Switzerland, the United Kingdom and the United States of America; international organizations include the United Nations Childrenís Fund.

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Announcements

7-9 December 2003

10th Asian Conference on Diarrhoeal Diseases and Nutrition

The 10th Asian Conference on Diarrhoeal Diseases and Nutrition (ASCODD) will be held in Dhaka. The theme of this conference will be: Improving child health and nutrition. Further information is available on the web site at http://www.icddrb.org/enrollment/ ?type=Ascodd.

If you would like to contact the organisers or require any more information, please send an e-mail to ascodd@icddrb.org, or write to ASCODD 10, ICDDR,B, GPO Box 128, Dhaka 1000.