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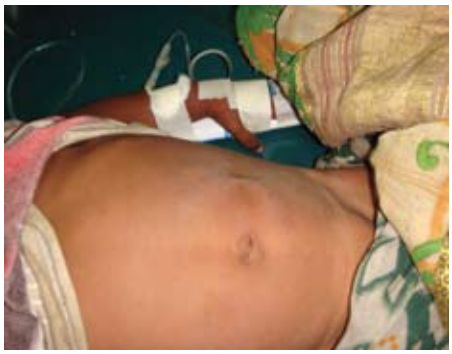


Cover photo: J Epstein

Fruit-bat *Pteropus giganteus* (photo: Muhammed Salah Uddin Khan)

Medicines offer hope for the treatment of Nipah encephalitis!

Scientists recently reported that common, low-cost drugs used in the treatment of hypertension and malaria may also be efficacious in the treatment of fatal encephalitis caused by Nipah virus. The group of scientists, led by Robin Buckland of INSERM in Lyons, France, announced this breaking news on 14 February 2009 at the International Meeting on Emerging Infectious Diseases and Surveillance, held in Vienna, Austria. Their findings on the biological aspects and transmission mechanism of the virus will lead to studies on these drugs with human subjects within a year, they said.

Nipah virus, belonging to the Paramyxoviridae family, was first reported to cause a serious febrile disease called encephalitis during an outbreak in Malaysia in 1998 and Singapore in 1999. During 2001-2005, four outbreaks of Nipah encephalitis occurred in rural Bangladesh, especially in Faridpur and Tangail. Simultaneous outbreaks were also reported from some parts of India. Immediately after the outbreaks, scientists from the Centre's Programme on Infectious Diseases and Vaccine Sciences (PIDVS) conducted surveys in the affected areas of Bangladesh, in collaboration with the Government of Bangladesh, Centers for Disease Control and Prevention (USA), and other partners. They confirmed that a fruit-bat species *Pteropus giganteus* is the natural reservoir of Nipah virus. The PIDVS team of scientists also found that people contracted the virus and associated encephalitis through drinking date-palm juice contaminated by these bats. It's very common in Bangladesh to collect date-palm juice in earthen pots by making a gouge in the tender part of a date palm-tree trunk near its top. Fruit-bats can contaminate the juice at night by sipping the juice that oozes through a semi-circular bamboo-tube or directly licking the trunk. The virus also contaminates juice through bat's urine and other excreta dropped on the pot. ICDDR,B scientists also investigated the epidemiology of Nipah encephalitis and various pathways of transmission, including person-to-person. The Centre's work on Nipah was disseminated through our publications, including Glimpse, Health and Science Bulletin, and annual reports.

In July 2008, a crew of cameramen and media personnel from the Discovery Channel filmed ICDDR,B's activities on Nipah encephalitis as part of their documentary on emerging diseases. The team visited the affected field sites in Faridpur district and interviewed survivors and relatives of the deceased victims. They also interviewed PIDVS Head Dr Steve Luby, IEDCR Director Professor Mahmudur Rahman, and Jonathan Epstein from the Consortium for Conservation Medicine, for the documentary.

Surveillance reports revealed that the disease caused by Nipah virus has a very high (almost 100%) case-fatality rate. Since no vaccines

or drugs are now available for the treatment of Nipah encephalitis, the news, published in the ScienceNOW, is of immense significance to medical scientists. Previously, scientists assumed that "the virus enters host cells through fusion between the cell's plasma membrane and the virus's envelope—a process that starts when a virus protein called G latches onto a host receptor ephrinB2". The INSERM team discovered that the virus rather "enters the cell through macropinocytosis, an ingestion process in which the cell membrane folds inward, engulfing the virus and its receptor in an intracellular vesicle."

Based on the above knowledge, the INSERM team tested three drugs: Amiloride used against hypertension and is known to block macropinocytosis; Chloroquine and Hydroxychloroquine—both known as anti-malarial drugs. In the near future the drugs will be tested against Nipah encephalitis in hamsters as part of the PhD work of Olivier Pernet who is included in the study group.

The ICDDR,B scientists are proud to have done important groundwork on the subject during the past few years. "We're very excited by these results," said Dr Steve Luby. Dr Luby and his colleagues are designing a study to try at least one of the drugs on human subjects the next time Nipah strikes Bangladesh. These drugs are being widely-used by humans in the treatment for hypertension and malaria and, therefore, there should be no ethical issues in using the drugs in trials with human subjects.

Dr Luby is planning a randomized trial in typical case-control design—half of the subjects will receive a drug and the other half a placebo. Comparison between recovery rate in the past and that after administration of the drug will help us determine the effectiveness of the drugs ■

Dhaka Hospital of ICDDR,B managed an early-summer peak of diarrhoea

The Dhaka Hospital of ICDDR,B has managed an overload of diarrhoeal patients during early summer this year. This was an unusual situation since the summer peak of patient-load is usually seen almost each year during flooding caused by the monsoon.

Make-shift treatment unit built at the parking area of ICDDR,B premises

This early-summer outbreak of diarrhoeal disease was characterized by another unusual feature: most patients were affected with rotavirus, as revealed in laboratory analyses, whereas past hospital-records showed higher numbers of patients to be affected with diarrhoeal pathogens other than rotavirus during this time of the year. Rotavirus infection in large numbers is usually seen in the winter peak of diarrhoeal disease.

Another trend which started to become apparent since mid-March is that the number of adult patients with various complications was

ICDDR,B's treatment unit established at the government-owned Unani and Ayurvedic Degree College and Hospital at Mirpur, Dhaka

gradually increasing, and this was attributed to a common factor—contamination of piped water in and around Dhaka city.

To avoid construction of make-shift treatment units to accommodate the increased patient-load during the monsoon peak each year, the Hospital was recently expanded with BRAC Bank funding. The new ward has a near-permanent look, with air-coolers and other facilities. However, with the outbreak, these wards were full requiring the patients to be accommodated in the corridors of the hospital building which led to the need for putting up tents in the parking area of the Centre.

In response to a request by Hon'ble Minister for Health and Family Welfare and Director General of the Directorate General of Health Services of the Government of Bangladesh, ICDDR,B established a new treatment unit at Mirpur in Dhaka city. This initiative was a move towards decentralization of ICDDR,B's clinical services and which substantially reduced the load of patients at the ICDDR,B's Dhaka Hospital. This 50-bed unit is housed inside the government-owned Unani and Ayurvedic Degree College and Hospital and became operational since 30 April 2009.

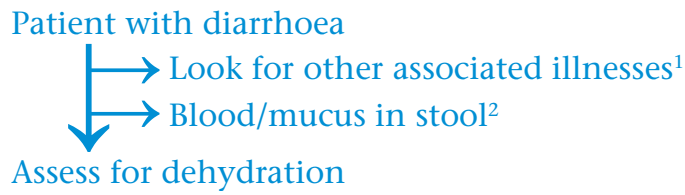
Adoption of new technologies, such as desktop computers with scanners, Personal Digital Assistant (PDA), and C5 Tablet Computer, has made the clinical services more efficient. However, there is a need to go further to make it a paperless hospital in the developing world, and to achieve this goal, a constant flow of financial assistance is required from donor agencies, large business houses, and philanthropic individuals from around the world.

For detailed information on how you can send your contributions to the Hospital Endowment Fund, please visit our website at: **http://www.icddrb.org/activity/donate** ■

Management of diarrhoea at ICDDR,B Hospital

[*The International Centre for Diarrheoal Disease Research, Bangladesh (ICDDR,B) is globally recognized as a unique institution for its health, population and nutrition-related research and clinical services to patients with diarrhoeal diseases, including cholera. A patient—just a heartbeat away from death due to diarrhoea—gets his/her life back once brought to the Centre's Dhaka Hospital at Mohakhali and the Matlab Hospital at Chandpur. Many at home and abroad are interested to know about the 'secrets of ICDDR,B's miracles'. With a hope that the adoption of ICDDR,B's treatment procedures will substantially reduce case-fatality rates in other diarrhoea treatment centres or make-shift units in the affected sites—both at home and abroad—Glimpse, through this coverage, wishes to share the diarrhoea management procedures of ICDDR,B among the instrumental readers so they can apply the same in their own setting. This plan for management of diarrhoea patients is contributed by the following at ICDDR,B: Tahmeed Ahmed, NH Alam, Azharul Islam, M Shahadat Hossain, Hasan Ashraf, M Iqbal Hossain, Munirul Islam, AM Shamsir Ahmed, Wasif A Khan, ASG Faruque, MA Salam, and Alejandro Cravioto*]

Plan for management of patients with diarrhoea

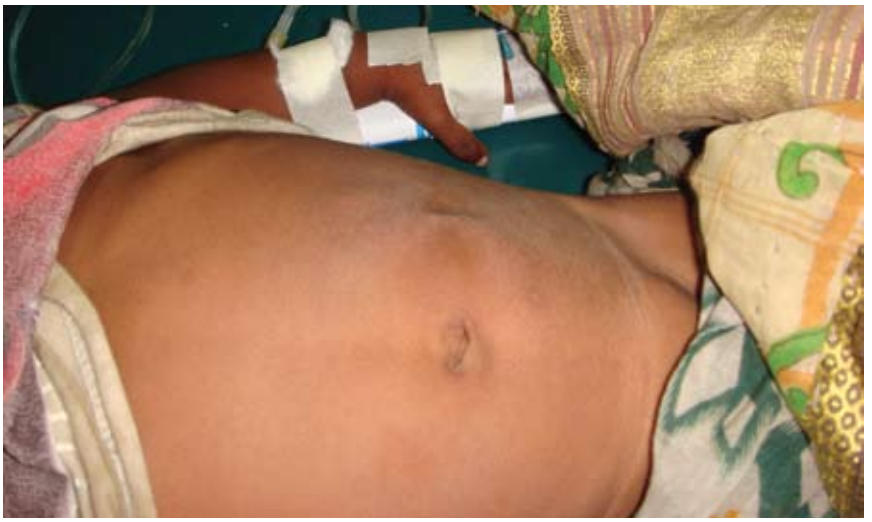


[1]Other associated illnesses include pneumonia, malnutrition, persistent diarrhoea, TB, septicaemia, meningitis, heart failure, jaundice, gross electrolyte imbalance, etc. These illnesses are identified and treated according to standard guidelines. National guidelines are followed where applicable, e.g. the national guidelines for management of severe malnutrition and for management of TB

[2]If shigellosis is likely, treat with an appropriate antibiotic

Assessment of dehydration (Dhaka Method)[3]				
Assess	Condition	Normal	Irritable/Less active*	Lethargic/ Comatose*
-	Eyes	Normal	Sunken	-
-	Tongue	Normal	Dry	-
-	Thirst	Normal	Thirsty (drinks eagerly)	Unable to drink*
-	Skin-pinch	Normal	Goes back slowly*	-
-	Radial pulse	Normal	Low volume*	Uncountable or absent*
Diagnosis	-	**No sign of dehydration**	If at least 2 signs, including one of the *-marked signs, are present, diagnose **Some Dehydration**	If some dehydration plus one of the *-marked signs are present, diagnose **Severe Dehydration**
Treatment	▪ Prevent dehydration ▪ Re-assess periodically		▪ Rehydrate with ORS ▪ Frequent re-assessment	▪ Rehydrate with IV fluids and ORS ▪ More frequent re-assessment

[3]Alam NH, *et al*. Modified WHO guidelines. Pediatric Drugs 2003



Delay in resettling skin after a pinch indicates the severity of dehydration of a diarrhoea patient

Management

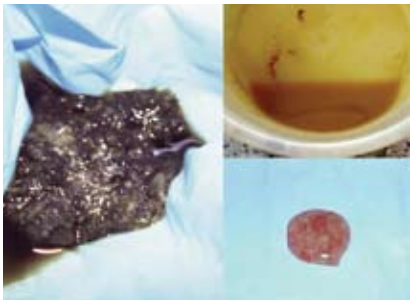
Rehydration

A. No sign of dehydration

Send patient home with packets of ORS after observation for 2-4 hours and counselling mothers on the use of ORS and continued feeding. Advise the mother on the volume of ORS to be given as per the following schedule:

- <2 years: 50-100 mL after each liquid stool
- 2-9 years: 100-200 mL after each liquid stool
- ≥10 years: as much as wanted
  - <4 months: 200-400 mL in 4 hours
  - 4-11 months: 400-600 mL in 4 hours
  - 11-23 months: 600-800 mL in 4 hours
  - 2-4 years: 800-1200 mL in 4 hours
  - 5-14 years: 1200-2200 mL in 4 hours
  - ≥15 years: 2200-4000 mL in 4 hours
- Re-assess dehydration status periodically
- Most cases can be managed by ORS only

Stool of cholera patient



Stool of shigellosis patient

B. Some dehydration

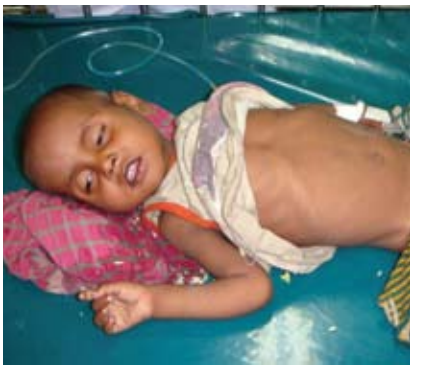
Treat with ORS, 75 mL/kg over ~4 hours. The patient should be kept under observation. The age-specific plan for giving ORS to patients is shown in the next column.

- In case of frequent vomiting (>3 times in 1 hour) with persisting dehydration, treatment with IV fluid may be considered
- If signs of severe dehydration appear, treat with IV fluids
- Continue normal feeding, including breastfeeding

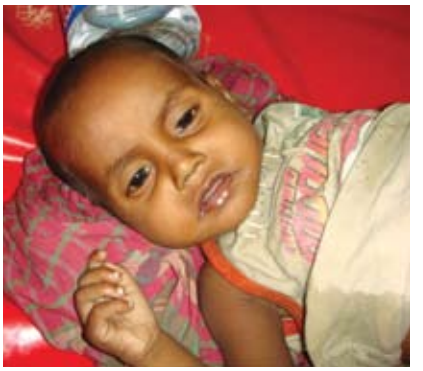
C. Severe dehydration

Start IV fluid immediately (100 mL/kg)

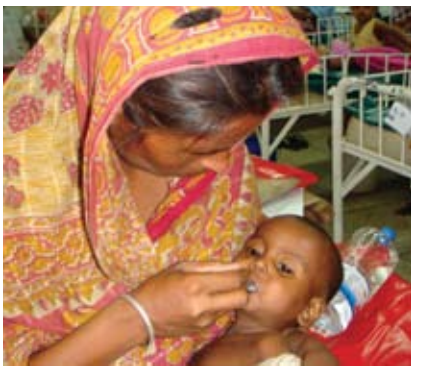
- Young children <1 year:
  - 30 mL/kg in first 1 hour
  - 70 mL/kg in next 5 hours
- Children (>1 year) and adults:
  - 30 mL/kg in first 30 minutes
  - 70 mL/kg in next 2½ hours



Condition of a young patient on arrival



One hour after administration of ORS



Almost in normal condition four hours after administration of ORS

Encourage the patient to take ORS as soon as he/she is able to drink. IV fluid of choice for management of severe dehydration is cholera saline.

Maintenance therapy

Should be done with ORS

Use the following volume of ORS after each liquid/watery stool:

- Children <2 years: 50-100 mL
- For older children: 100-200 mL
- For adults: Allow them to drink ORS as much as they want

Antibiotic therapy

For presumed cases of cholera (profuse watery stools, typically looking like 'rice-water', resulting in dehydration; many individuals affected in the same locality):

- Children: Azithromycin, 20 mg/kg body-weight, single dose orally
- Adults: Azithromycin, 1 g single dose orally

For presumed shigellosis (stools with blood and/or mucus, tenesmus or straining, and fever):

- Children: Ciprofloxacin, 10 mg/kg body-weight 12-hourly orally for 3 days
- Infants less than 6 months old: Azithromycin may be given at a dose of 10 mg/kg body-weight orally once daily for 5 days
- Adults: Ciprofloxacin, 500 mg 12-hourly orally for 3 days

For amoebiasis

Children: Metronidazole, 15 mg/kg 8-hourly orally for 7 days

Adults: Metronidazole, 400 mg 8-hourly orally for 7 days

Zinc treatment for episodes of diarrhoea

Children 6 months-5 years old:

Zinc 20 mg once daily for 10 days ■

ICDDR,B sends Emergency Response Team to Aila-affected area

ICDDR,B's emergency response team ready to leave for the Aila-affected areas

An emergency response team from ICDDR,B assisted in the management of diarrhoea in the outbreak following 'Aila', a cyclonic storm that recently hit the southwest region of Bangladesh. The badly-affected area was identified to be Koyra in Satkhira district. The ICDDR,B team comprising senior staff physicians and experts in the management of diarrhoea left for Koyra on 2 June 2009. The medical team was accompanied by a crew of audiovisual personnel to document and film the activities of the team.

The team was led by Dr Azharul Islam Khan, a senior clinician of the Centre's Dhaka Hospital. The team members worked closely with the personnel of the Directorate General of Health Services (DGHS) and distributed IV fluid, ORS, and other emergency medicines, including antibiotics, skin-ointments, and water-purification mixtures to those affected.

With decades of expertise, the emergency response team is geared to respond to large epidemic outbreaks both in Bangladesh and other countries. As requested by World Health Organization, ICDDR,B recently dispatched two teams of experts to help manage the cholera epidemic in Zimbabwe ■

June 2009 Meeting of the ICDDR,B Board of Trustees

June 2009 Meeting of BoT in full session

The first meeting of the Board of Trustees for 2009 was held on 19-20 June. The Board congratulated the Executive Director and the staff for the revised Strategic Plan 2020, and requested the Management to finalize the Plan paying particular attention to some issues raised as well as packaging of this important document.

While acknowledging the draft Implementation Plan, the Board requested the Centre Management to present a revised plan in November 2009 that can articulate the strategic actions for the implementation of the Strategic Plan, along with a proposal for the restructuring of the Centre with a clear indication of the function of the Board as the oversight body for the implementation of the Strategic Plan.

The Ethical Review Committee (ERC) of the Centre presented its annual report to the Board. The trustees expressed their satisfaction on the work conducted by the ERC and endorsed the modified ERC Guidelines.

The Board bade farewell to Dr Haruo Watanabe (Japan) and extended its gratitude for his outstanding contribution to the Centre as a member of the Board from January 2007 to June 2009. Dr Norma Binsztein from Argentina was selected to serve on the Board in substitution of Dr. Watanabe for a period of three years. The tenures of Dr Nicolaus Lorenz of Switzerland and Dr Thomas Cheasty of the United Kingdom were extended for a second term of three years from 1 January 2010. Dr Jalal Abbasi-Shavazi was elected Chair of the Human Resources Committee, and Dr Ann Larson was elected Deputy Chair of the Programme Committee.

The Board also reviewed the audited financial statements and approved the 2009 forecast, noting that the Centre has been able to generate an annual operating surplus over the past ten years.

The meeting concluded with a decision to hold its next session on 22-23 November 2009 ■