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Managing disease in Bangladesh

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Bangladesh and infectious disease

In the Bay of Bengal, Bangladesh lies in the river rich area of the Ganges delta, almost entirely surrounded by India. Since its independence it has been one of the poorest countries in the world, struggling with political turmoil, famines and a high burden of disease. The combination of being one of the most densely populated and poorest areas in the world is a challenge in the battle of the spreading of disease in the country. This journal covers surveillance, monitoring and control of infectious disease in Bangladesh with a focus on the work done by icddr,b.

Initially a part of Pakistan, what today is known as Bangladesh was formed as East Pakistan upon the departure of the British from the Indian and Bengal region. 24 years later, in 1971, Bangladesh became an independent state after a bloody liberation war. Since the beginning, the country has suffered from severe poverty, political turmoil and several environmental catastrophes, which have contributed to keeping the country among the poorest in the world. During the last decade Bangladesh have made tremendous achievements in economical development and public health. Despite this, 30% of the country's inhabitants are still living below the poverty line.

Close to 160 million people live on the flat river-covered region, making Bangladesh one of the most densely populated countries on earth. The flatness, tropical location and density of rivers put the country at risk of floodings, cyclones and droughts. Bangladesh is thus a country dominated by water; either by the lack of high quality water in times of drought or the threat of floods during rain periods. The access to clean water is very often limited and not surprisingly, waterborne pathogens are among the major killers in the country.

Alongside the economical situation, literacy has improved greatly in the last decades, but 40% of the population can still not read or

write. This inability for people to obtain information aggravates a situation where knowledge about proper hygiene is crucial to avoid propagation of infectious diseases in the population. The malnutrition that often follows poverty leads to an impaired immune system making people more susceptible to infections. Infections then often contribute to a more severe state of malnourishment in the individual, which gives rise to a downward spiral.

Taken together, poverty, dense population, lack of education and limited access to clean water make Bangladesh a hotspot for infections spread by water and food as well as directly between people. The country faces large challenges but also opportunities for development of solutions that can change the lives of millions.

The Centre for Diarrheal Disease Research, Bangladesh (icddr,b) was formed as the Cholera Laboratory in Dhaka 1960. Since the beginning the mission has been to save lives, both directly in the hospital facilities and indirectly by the research conducted. Counted among its many achievements is the invention of the oral rehydration solution (ORS), estimated to have saved 40 million lives, the identification of the El Tor cholera strain, as well as the contribution to several WHO guidelines.

Today the hospital facilities treat patients with diseases such as diarrhea, HIV, pneumonia and malnutrition, and the research conducted spans over a broad field of diseases of the poor. Despite the location in a developing country, icddr,b have a modern approach to health care and research stressing the importance of evidence-based, cost-efficient solutions for the poorest. In line with this the centre has been paperless since 2008.

Together with the large central facilities in Dhaka, icddr,b has several rural field sites.

Since 1962 disease surveillance has been conducted in these areas generating one of the largest databases of diarrheal disease in the world, consisting of data of approximately 30 000 patients.

This journal will focus on the surveillance, monitoring and prevention of different infectious diseases in Bangladesh with the work of icddr,b as a starting point.

By Elsa Willebrand

Cholera - a disease of the poor

Climate change, rapid urbanization and increased population size all together lead to a less secure water supply for the people of a developing country. The number of cholera cases is increasing worldwide and due to the many urban slum areas and badly planned water pipelines, Bangladesh is a country suffering from frequently recurring cholera outbreaks.

All over the world, diarrheal diseases are a great burden for humans, especially in developing countries. One major cause of diarrhea is cholera, caused by the bacterium *Vibrio cholerae*. It affects as many as three to five million people annually, with approximately 100 000 death each year according to the World Health Organization (WHO). One third of these infections occur in Bangladesh, compared to only a few cases in Sweden.

Cholera is spread via contaminated food and water. Due to the mode of transmission it affects people of all ages in Bangladesh, but generally more adults than children and more women than men. Upon infection, it can take from a couple of hours up to a few days before symptoms occur depending on the prior health status of the infected individual and how many bacteria were ingested. The majority of those who are infected do not develop any symptoms, although they still spread the bacteria. Of those who develop symptoms, only a fraction ends up in the hospital with acute watery diarrhea and vomiting. The watery diarrhea resembles rice water to such an extent that it has become a descriptive feature of the disease. Severe dehydration develops as a result of the

Quick facts about cholera

- Cholera is caused by *V. cholerae*, a motile bacterium that excretes cholera toxin and causes infection in the intestine.
- More than 200 types of *V. cholerae* exist, but fortunately only two of them cause disease in humans, *V. cholerae* O1 and O139.
- Symptoms are usually mild, but sometimes the infection can be severe and cause acute watery diarrhea. The majority of cases can be cured with oral rehydration solution.
- A cholera patient can loose up to 20 liters of fluid in a day.

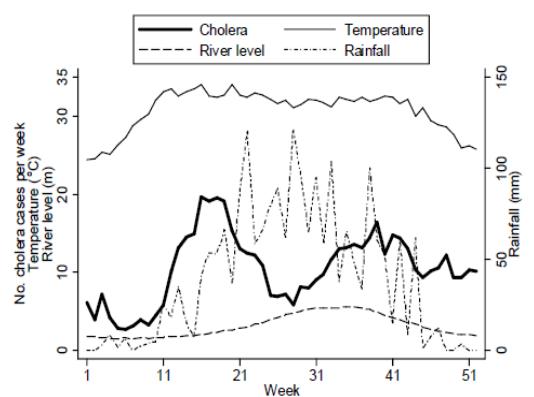
extreme water loss and can lead to organ failure, coma or death if not treated in time.

Cholera hits Bangladesh twice a year

In Bangladesh, cholera outbreaks usually follow a seasonal pattern with large outbreaks around April to May and September to October.

The bacterium, *V. cholerae*, is a marine organism that can survive in fresh water for up to a couple of weeks according to Dr A. Faruque at icddr,b. In its aquatic environment the cholera bacterium is part of the algae community and can attach to plankton. In spring time, bloom of the plankton following warm weather allows *V. cholerae* to multiply within the vegetation. This increase in bacterial quantity can surpass the amount required for infection in humans. Extreme draught leads to evaporation of water in rivers and ponds and the bacteria multiply to even higher concentration favored by the increased salt concentration. Drought force people to find water else were, in sources they would not normally use. Outbreaks start at coastal villages in the Bay of

Bengal and spread upstream towards the inland. As Bangladesh is situated in a lowland delta, tidal changes and annual monsoon rain, around late summer, may contribute to flooding and bring coastal water as far as Dhaka. When cholera-infected plankton are brought inland with sea water they can contaminate human water sources. The massive water load also causes flooding of sewage water into normally safe water sources which allows a continuous spread. These are factors that give rise to the correlation between warm weather as well as rain season and cholera outbreaks.



Seasonal variation of cholera outbreaks in Bangladesh¹.

Treatment, simpler than you think

The main step when handling a cholera patient is to replace the water loss, and survival depends upon aggressive and rapid treatment. Mild cases are treated with oral rehydration solution (ORS), and in severe cases, intravenous saline solution is administered to more quickly replace the water that has been lost.

ORS is a solution of salt, water and sugar. It can easily be purchased at the local pharmacy and during outbreaks mass media in Bangladesh provide the ORS recipe. Icddr,b distributes ORS for free to people in and around Dhaka during these outbreaks. In 2004 icddr,b found that supplementation of ORS with zinc was very effective in reducing both the dura-

tion of current diarrheal episodes and the severity of secondary infections. Although the disease is self-limiting, antibiotics are given to cholera patients to reduce duration time even further, hence reducing further spread of bacteria. All together, saline solution, ORS, zinc, and antibiotics contribute to a shorter hospital stay for the patient, a lower risk of reinfection and less water needed during treatment. This is because an untreated patient requires more water than a patient treated with antibiotics, which is important in a country like Bangladesh with limited clean water.

Monitoring the disease

Since 2009, cholera has been notifiable in Bangladesh, meaning that detected cases are to be reported to the WHO. Bangladesh does not have any extensive surveillance system. The poor surveillance does not give a good overview of the whole country, and is in need of improvement, according to Dr. Farhana Haque, research investigator at the facilities of icddr,b in Dhaka. Icddr,b, with its facilities in Dhaka and Matlab, has always had a main focus on decreasing the number of cholera cases. A program is currently running where diarrheal patients are randomly tested for cholera and other diseases. Collected data is stored in an online database. On a daily basis, icddr,b also collects information on cholera cases that have been reported in the last 24 hours in newspapers and by other hospitals. If there is a high incidence of cases, an investigation is started. However, due to financial issues only the most severe outbreaks are investigated. Since cholera became notifiable in 2009, the government of Bangladesh has only managed to identify five outbreaks.

Dr. F. Haque is part of a new surveillance platform which is under development. The plan is to include nine strategic sites around Bangladesh where the cholera frequency is high. Samples will be taken weekly from these

sites and sent to a lab for detection of *V. cholerae*. This may allow for an earlier warning system.

How to control and prevent cholera

During cholera outbreaks informative campaigns encouraging people to wash their hands, take care of their personal hygiene and boil their water is issued by the media. Although boiling the water before usage is one of the most effective ways to reduce cholera, Dr. F. Haque mentions that even though parts of the population is aware of the risks of drinking unclean water, there is some resistance to taking this precaution. This may be due to several factors, such as superstition, laziness, or lack of time and resources. Another way of getting rid of cholera in drinking water is to add chlorine. This precaution has been met with resistance, since people tend to dislike the smell and taste of chlorine treated water, but also due to the increasing cost. For women in the rural areas using surface water, reducing the cholera by filtering the water with a sari has proven to be effective.

There are two cholera vaccines available, Dukoral and ShanCol. Dukoral is licensed in over 60 countries. ShanCol is only licensed in India. There are certain criteria that must be fulfilled for a vaccine to work optimally in a developing country. The vaccine must be easily distributable, affordable, safe, and only require a few doses to give full protection. Dukoral is not considered to be an optimal vaccine for a poor country since it is hard to distribute, expensive, needs to be dissolved in buffer prior to administration and an intact cold chain. ShanCol, on the other hand, is a good vaccine candidate in a developing country like Bangladesh since it can be purchased for only a tenth of the cost of Dukoral. It does not need a buffer and is as safe as Dukoral, although equally hard to distribute.

Both vaccines require additional re-vaccination, Dukoral after two years and ShanCol after five years. Currently ShanCol is being tested in the slum areas of Bangladesh and will hopefully soon be made available for the general population.

What about the future?

Bangladesh is still a country of many cultural differences. Unfortunately religion allows a class separation between men and women where the male gender has higher priority. Since men are family providers, they are of main concern when the economy only allows one family member to go to the hospital. This easily leads to a misconception that the disease affects men more than woman.

Since the majority of the Bangladeshi people live below the poverty line and can rarely afford the luxury of clean water, exposure to the cholera bacteria can occur at any time. The most basic chores like cooking, doing dishes and washing clothes without practicing proper hand hygiene and lack of proper toilettes are strong causes for transmission of cholera. Women are mainly responsible for such chores and are also the caretakers of the family, thus they are more prone to get cholera.



Beds for diarrheal patients in Dhaka hospital, Bangladesh.

Many women of Bangladesh are malnourished due to poverty and a lower social status. Malnourished women often have problems producing enough breast milk and therefore are forced to bottle feed their children. Due to extreme poverty, the milk replacement formula may be diluted with (even low quality water) to last longer. Subsequently, the malnourished children have an increased risk of cholera.

Since cholera is mainly considered a disease of the poor, the problem with cholera reaches considerable heights in a developing country like Bangladesh. Although extremely easy to treat, cholera is one of the leading causes of death in patients with diarrheal disease. Icddr,b has done a magnificent work to reduce the number of people dying of cholera at the Dhaka hospital. Research is currently conducted by icddr,b in rural areas, slums and urban areas. Even though death rates have gone down at the hospital, climate change and a rapid growth of the population will increase the number of cholera cases in Bangladesh

with about ten percent per degree Celsius. Therefore, a good surveillance system is needed.

Contrary to many other diseases, vaccination does not seem to be the solution to the problem with cholera. Although vaccination is a good way to reduce the number of people spreading the bacteria, the protection only last for a few years and other preventative measures have to be applied.

Improved water sanitation and sewage systems require financial support which in turn requires political engagement. Before this can be implemented the problems with cholera have to be recognized and prioritized - because cholera is mainly not an issue of infection, but an issue of poverty.

By Ellinor Andersson, Irma De La Cruz, Tove Hoflund and Frida Wennerholm

***Mycobacterium tuberculosis*, the poor man's nightmare**

Bangladesh is ranked number six on the list of countries with high-burden of tuberculosis¹. According to Dr. Shaikh A Shahed Hossain “the prevalence of tuberculosis is difficult to estimate.” This fact is due to numerous factors, for instance poverty, health access and variations in health care seeking behavior.

The bacterium of slow death

Mycobacterium tuberculosis is the bacterium that causes the disease tuberculosis. Dr. Shaikh A Shahed Hossain says: “Not all infected persons actually develop disease. Half of the population carries the bacterium.” Healthy persons most often will not develop disease. The bacteria will get encapsulated in the lungs until something compromises the immune system, such as malnutrition or smoking.

Active tuberculosis, meaning when the infected person has developed symptoms, affects mainly the lungs, but can also spread to other organs. The bacterium is transmitted between individuals when the diseased person coughs, sneezes, laughs or talks. In pulmonary tuberculosis the affected person often has coughs with bloody streaks. When detected, the disease can usually be treated with antibiotics, which need to be taken daily for at least 6 months. The preferred choices of antibiotics are rifampicin and isoniazid. However, the mass use of these drugs creates a new problem: the bacteria may get resistant and need to be treated with more aggressive or less efficient drugs, IF they can be treated at all.

These bacteria do not only pose a threat to the health of the patients but also to that of

the people who surround them, such as family members.

Persons with active tuberculosis, who are not or cannot be treated, will eventually succumb to the disease due to scar tissue-formation in the lungs, disabling breathing.

Tuberculosis in numbers^{1,2}

| | |
|----------------|-----------------|
| TB prevalence: | 434 per 100.000 |
| Detection: | 49% |
| Mortality: | 45 per 100.000 |

Does the country care?

Bangladesh has the highest population density in the world, which facilitates spread of infectious diseases, including tuberculosis. To worsen the situation, approximately one-fourth of the inhabitants live below the national poverty line².

Even though the government tries to find all people that are affected by tuberculosis, it is a difficult task since not all have easy access to public health care. Another problem is that not all affected people are diagnosed with the disease and therefore are sent back home, which enables further spread. Children are most likely to go undetected partly due to their inability to produce sufficient amount of mucus that can be taken from the lungs for testing.

What is actually done?

Almost all infants in Bangladesh are vaccinated with a vaccine called BCG. The vaccine is based on a different type of mycobacterium and although it gives some protection against the pulmonary variant of the disease, it is not sufficiently effective to completely prevent infection in all exposed individuals³. Conse-

quently, there is still a desperate need for a more effective vaccine.

Since 1993, as a part of DOTS (Directly Observed Treatment Short course), the World Health Organization-recommended tuberculosis control strategy, free anti-tuberculosis drugs have been given to the Bangladeshi people.¹



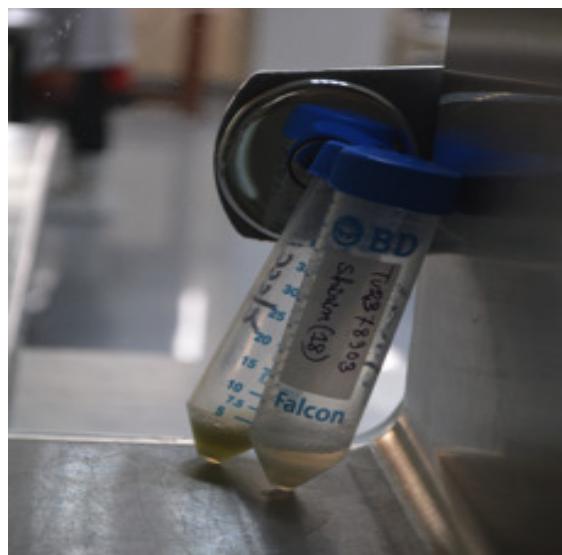
Slums in Dhaka city, the capital of Bangladesh.

In an attempt to defeat tuberculosis in the country, BRAC, a non-governmental organization, with the support from the National Tuberculosis Program started an education on how to recognize people possibly having TB and refer them to a hospital⁴. This initiative has increased the detected number of people with the disease. The limitation of the program is that there are not enough trained people to cover all levels of society in Bangladesh.

The most vulnerable are those living in the slums. The slums are known to be the home of the poorest amongst the poorest, which live in overcrowded housings, without safe water, sanitary conditions, education and access to healthcare. All these factors contribute to spread and maintenance of the disease burden.

Is there any hope for Bangladesh?

At present there are many different projects aiming to establish the prevalence of tuberculosis. To get a better hold of the burden, two screening programs are conducted: (1) an urban mass screening of about 100,000 people living in the slums, where people are asked to answer a simple questionnaire about symptoms like low grade fever and cough, and (2) a screening amongst prison inmates at entry and during their stay.⁵



Suspected TB-samples awaiting analysis.

Since it is so difficult to diagnose tuberculosis in children, new diagnostic techniques are desperately needed. A team of highly trained scientists at icddr,b is working on an alternative method, where they analyze feces. This method has proven to be effective when testing adult faeces, although further trials are still needed to show that it is applicable to children.⁵

By Fredrika Rajer, Daniël Leenheer and
Borbála Katona

Parasites in Bangladesh: Prevalence and surveillance of *Entamoeba histolytica*

The parasitic burden in Bangladesh has been very high but the situation has greatly improved, much due to better hygiene and education among the people in combination with good and available drugs. The focus of this article will be on the single cell pathogen, *Entamoeba histolytica*. This parasite is a major cause of diarrhea and an important research topic at icddr,b.

Parasitic infections are common worldwide and range from harmless asymptomatic cases to severe infections giving rise to both morbidity and mortality. As in most developing countries situated in tropical areas, the people of Bangladesh are at risk of intestinal worms, cyst forming intestinal pathogens and malaria. These infections can be deadly, as during cases of untreated malaria or give rise to diarrheal disease, as in the case of amoebiases. Like during infection with the common worms *Ascaris lumbricoides* and *Trichuris trichiura*, parasites can also go unnoticed and chronically contribute to a malnourished state of the individual by stealing the nutrients consumed¹. Thus all parasitic infections will in different ways impair the health of the individual and add to the morbidity.

According to Dr. Rashidul Haque, Scientist and Head of Parasitology Laboratory at icddr,b, Bangladesh carried a high burden of parasitic infections two decades back¹. Malaria and the parasitic infection of the internal organs, which is known as kala azar, was a big problem and 80-90% of the population had some type of worm infection. Every day three to four patients would arrive to the icddr,b

with diarrhea caused by the unicellular parasite *Entamoeba histolytica*. At least one of these cases was diagnosed as dysentery, i.e. when the parasite invades the intestinal wall giving rise to bloody diarrhea.

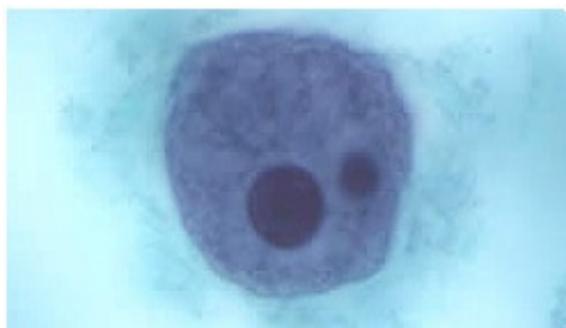
Entamoeba histolytica is one of the leading parasitic causes of death in the world with an estimated 50 million people infected. Approximately 1% develop liver abscess and 100 000 yearly succumb to the disease. It is morphological indistinguishable from the harmless organism *Entamoeba dispar*. Before molecular techniques enabled diagnostic differentiation between the two species, several of *E. dispar* infected people were misdiagnosed as asymptomatic cases of *E. histolytica*^{2,3,4}.

***Entamoeba histolytica*: route of infection**

Infections with *Entamoeba histolytica* is however still common in Bangladesh, especially in the slum areas, due to the poor conditions and bad hygiene. It transmits through ingestion of food and water infected by parasitic cysts. The forming of the hard shell of the cysts enable the parasite to survive both passage through stomach acid and staying in the outside environment for weeks. It escapes the protection of the cyst when reaching the small intestine and then continues to the large intestine, where it multiplies by dividing. Some parasites are directly secreted in the stool, but only the ones forming cysts before exit survive and can infect new humans⁵.

Symptoms of infection with *Entamoeba histolytica* can differ widely, from asymptomatic infections to severe symptoms. During invasive infections the parasite invades

through the intestinal wall, clinically manifested as dysentery. In some cases it can travel with the blood stream and end up in organs like liver, brain, and lungs, where it forms cysts and cause severe morbidity⁵. The most common organ infected is the liver, giving rise to amoebic liver abscess.



Entamoeba histolytica viewed by microscopy. When the parasite is invasive it can ingest red blood cells as seen in this picture⁵.

Icddr,b research and surveillance

Regardless of diagnosis, patients with diarrhea or malnourishment are routinely de-wormed when coming into the icddr,b. *Entamoeba histolytica* is one of the pathogens that are routinely searched for in 2% of all stool samples from patients coming to the icddr,b hospital. The prevalence of this pathogen in Bangladesh has thus been monitored since 1971. However in contrast to diseases such as malaria or kala azar information about infected patients are not communicated between different hospitals^{1,6}. Beyond this, the icddr,b is conducting active surveillance of infection and research in the field areas. The studies cover factors such as genetic diversity of the parasites, immunity and clinical symptoms^{7,8}. Icddr,b has also been in the forefront of developing different diagnostics of *Entamoeba histolytica*.

Currently there is an ongoing cohort field study in the Mirpur slum area of Dhaka city, examining the prevalence of *Entamoeba histolytica* in children. The study, which includes 500 children, has been going on for two

years and is planned to continue for two more. The children are tested once a month by sampling their stools, which are then analyzed by molecular methods. When cases are found they are treated by the antibiotic drug metronidazole, which until now has not been subjected to any development of resistance. The researchers have seen that the children have less immunity and hence more severe infections and symptoms if they are malnourished. This is a problem since a parasitic infection and diarrhea contribute to a malnourished state and the malnourished state increases the susceptibility to infections making it a vicious cycle¹.



Water resource in Mirpur, Dhaka slum area.

A country in progress

Even though parasitic infections still are present among the people in Bangladesh the current situation is improved and is now more under control, according to Dr. Rashidul Haque. Bangladesh is a developing country, making good progress in the last years. People are more aware of their personal hygiene and there is an ongoing process of further improvements. Treatment against intestinal parasites, like worms and amoebas, are cheap and effective and there is currently no or low antibiotic resistance. The more expensive drugs required for treatment of malaria and kala azar are now provided for free at governmental facilities.

The improved knowledge among the people and better access to clean water together with the availability of treatments has contributed to a reduced burden in parasitic infections.

By Elsa Willebrand, Sara Willumsen Fransson,
Linda Åkesson

Hepatitis E virus infection in Bangladesh: a significant but under-recognized problem

Hepatitis E (HEV) infections are a great burden in Bangladesh especially in public health. More than a quarter of the population is affected by this devastating disease. Establishing a national surveillance system for early detection, water management and using safe injections as well as disposable instruments are important measures to control transmission of HEV.

Know more about HEV

Hepatitis E Virus (HEV) is a naked, positive-sense, single-strand RNA virus that can cause acute liver infections. The virus has one serotype and four genotypes. Genotype 1 and 2 only infect humans and are responsible for large outbreaks and frequently sporadic cases in developing countries where sanitation conditions are poor. Genotype 3 and 4 infect both humans and animals and are responsible for the sporadic cases in developing and developed countries¹. HEV is the common cause of acute hepatitis outbreaks in south Asia, such as Bangladesh and is recognized as the main cause of enterically transmitted non-A, non-B hepatitis². Outbreaks usually follow flooding, which leads to sewage contamination of piped water through nearby sewage lines or from contaminated surface-water.

HEV is transmitted through the fecal-oral route, mainly through contaminated drinking water. The virus can also be transmitted via eating contaminated or undercooked meat. There are also a few cases reported in developed countries showing that HEV can infect by transfusion of infected blood product and

through vertical transmission from mother to child.

HEV infections are self-limiting and cause acute illness, but there are a few reported cases in developed countries, indicating a potential for becoming chronic in solid organ transplant patients¹. The incubation period is usually between 15 to 60 days, with an average of 40 days. The symptoms are mostly undistinguishable with other acute liver illnesses, which include fever, nausea, jaundice, anorexia, hepatomegaly, etc. The symptoms might get even worse if patients take acetaminophen for fever.



Sewage contaminated water is the main source for HEV transmission in Bangladesh.

Most HEV infections can be diagnosed based on the detection of specific antibodies to HEV or HEV-RNA in the blood. Confirmation of the diagnosis using an IgM antibody test costs about \$10. The high cost is one of the factors contributing to an underestimation of the HEV disease burden. RT-PCR to detect HEV-RNA and immune electron microscopy to detect the virus are only used in research studies. There is no specific treatment for HEV, and hospitalization is mainly required only for the

severe cases such as pregnant women in the third trimester.

Who gets infected? National surveillance program is needed

There are approximately 20 million HEV infections globally each year, of which 3.4 million develop symptomatic illnesses and 70,000 succumb to the infection³. More than half of the global burden, roughly 12 million of HEV infections occur in the Southeast Asia region. Since the first report of non-A, non-B hepatitis in 1980, several seroprevalence studies have been conducted and these have for example shown that 23-56% of Bangladeshi have anti-HEV antibodies, mostly genotype 1. On the contrary to HAV infection, HEV affects mostly young adults aged 15-40 years and there is a slightly male preponderance. Children infected by HEV are usually undiagnosed due to absent or mild symptoms without jaundice. An 18-month (from 2003 to 2005) cohort study (following 1,172 person-years) was conducted in Matlab⁴, where the population baseline prevalence was 22.5%, showing an incidence rate of 64 per 1,000 person-years. Thus, HEV infections are the huge burdens of disease in Bangladesh and account for up to 50-65% of fulminant hepatitis cases as well as caused devastating infection in pregnant women. Pregnant women, particularly those in second and third trimesters, infected by HEV usually have a poor outcome regarding maternal and fetal health, including membrane rupture, spontaneous abortion, stillbirth, fulminant hepatitis, and even death⁵. Approximately 20% of all maternal deaths and 10% of all neonatal deaths in Bangladesh are associated with jaundice and around 60% of deaths in pregnant women with acute liver disease in hospital were associated with HEV⁶. Annual outbreaks hit Bangladesh during monsoon season especially in urban areas. Geographical features as the river delta, climate, flooding and the way of living in the rural areas are ideal for

water-borne contamination. For instance, the large outbreak due to water contamination from ineffectively maintained distribution system in urban slum of Tongi, adjacent to Dhaka, during Aug 2008 - Jan 2009 affected more than 4000 patients (attack rate of 3%) and caused 20 deaths⁷.

- HEV infects 20 million people worldwide and Bangladesh is one of the endemic areas.
- 23 to 56% of Bangladeshi have antibody against HEV.
- Fatality during pregnancy might be as high as 20%.
- China produced the first licensed vaccine in 2012, but it is not yet available globally.

Despite being considered as hyperendemic area with at least one outbreak happening every year, there is still no national surveillance program for HEV infection. "We are now preparing the proposal of national surveillance- the community-based program as well as surveillance in pigs for potential zoonosis problem", said Dr. Hossain M. S. Sazzad, icddr,b's infection epidemiologist who is responsible for outbreak investigations in Bangladesh. "Surveillance will provide true prevalence of disease and identifying high-risk groups could guide how to design the strategies of prevention and control in our country", he says. For example, a study from a 22-month household surveillance recently published in PLoS ONE⁸ was conducted in Matlab and raised the novel possibility of person-to-person transmission as well as parenteral transmission in non-epidemic, sporadic disease setting.

How to handle HEV?

HEV is one of the most epidemic hepatitis viruses in the Indian peninsula. Therefore, preventing and controlling this disease are crucial for public health. Despite the im-

portance of HEV, health professionals in Bangladesh are more concerned about other infectious diseases and not a lot of effort is put on HEV. Having said that, some studies have been published within this topic as well as some studies being in progress.

Water-borne control

It is essential to provide safe drinking water in order to avoid water-borne infections. Water distribution systems are compromised in urban and rural areas of Bangladesh and the availability of safe water is not enough to cover the needs⁷. Another challenge is sewage water that causes a lot of infections when contaminating drinking water. However, improving water and sanitary infrastructure is difficult to achieve in the near future in a resource poor setting. Bangladeshi government tries to find good solutions that fit their resources and abilities.



Safe water by using chlorine provided by icddr,b.

The best method to improve water supply and sanitary infrastructure is separating sewage from drinking water and keep it under control⁷. Another method is boiling all drinking water, but with an average of 12 households (like in slum area) with more than 60 people sharing a single stove and kitchen, it's impossible to find sufficient time for boiling all drinking water⁷. Treating water with chlorine when it is used is another way for decontam-

inating the water. To accept the good taste of water, health professionals ask people to keep treated water with chlorine over night then use it⁷. A proper dose of chlorine is important for inactivation of HEV; an outbreak occurring within a Sudanese refugee camp was due to insufficient dose and infrequent use of chlorine. Finally, low cost, practical and acceptable approaches as well as more research are needed to improve drinking water quality⁷.

Blood-borne control

Different rules and policies have been adopted to prevent infection through contaminated blood, organ donation, contaminated needles, hemodialysis and any other procedures that can transmit HEV. These policies include safe injections and also, for example, using disposable blades at the barber's. Altogether this may reduce the risk of sporadic HEV infections in Bangladesh⁹.



Exposure to sharp instruments, including therapeutic injection and being shaved by a shared razor blade in a barber shop in Dhaka⁹.

Finally, health education about personal and environmental hygiene in communities at high risk is a preferable way to reduce the probability of HEV outbreaks. It is also important to identify outbreaks early and recommend prophylactic measures. This can be achieved by establishing surveillance systems for HEV. For example, dealing with any pregnant woman who comes to hospitals with acute hepatitis as an indicator of a potential HEV outbreak².

By Zixuan Liu, Rongpong Plongla,
and Nader Kameli

The HIV situation is under control – for now

Bangladesh is situated in a high-prevalence area, but still maintains a low HIV prevalence. HIV is restricted to certain risk groups, but prevention programs need to be constantly up-scaled to prevent an epidemic. The HIV community is constantly battling stigma and ignorance, and the HIV related organizations are highly dependent on external funding.

A low prevalence country

Bangladesh is considered a low prevalence country with less than 1% of the general population being infected by HIV^{1, 2}. However, there is an ongoing concentrated epidemic among injection drug users (IDUs). The first case of HIV in Bangladesh was detected in 1989 and it was estimated that at least 7500 people were living with HIV in the country in 2011². In this year, the number of new cases of HIV was 445² and it is possible that the prevalence of HIV will increase in the near future. Since Bangladesh is closely located to high-prevalence countries such as India, many HIV infections arise due to migration^{1,2,3}. Other reasons may be severe poverty, prostitution, over-population, lack of education about STIs and the low social status of women^{1,4}. It is possible, and likely, that the prevalence of HIV in Bangladesh is greater than believed since there is a low awareness of the disease³ and the condom use is generally low¹.

IDUs and sex workers are at risk

High-risk groups for HIV worldwide are generally sex-workers and injecting drug users (IDUs) and this is also the case in Bangladesh. The number of IDUs in the country is estimated to be 20 000-40 000, and the sharing of equipment for injection is a widespread phe-

nomenon. As a result of this, one out of ten HIV infections is associated with injecting drug use. Thus, sharing needles and syringes is the main issue and the prevalence in these groups reached 7% a few years ago⁵. Migrant workers returning from abroad are also common sources of the infection³. Hijra, transgender individuals who often sell sex are particularly vulnerable to HIV since they have poor knowledge about HIV, rarely use condoms and have a high rate of new sexual partners⁶.



"Use a condom!" - poster at the male clinic at subcenter B. Matlab.

The prevalence of HIV among male IDUs is especially high and homeless drug users have shown to be at least five times as likely to test positive for HIV compared to other drug users. It has been reported (2006/2007) in Dhaka that two out of three male IDUs visited prostitutes and not even half of these used a condom. Only one out of four used condoms on regular basis³.

Combating ignorance

The stigma associated with HIV in Bangladesh is extensive, especially in the poor areas. There have been numerous campaigns in the media to make people aware of HIV and its transmission routes, in order to reduce the stigma surrounding the disease. The campaigns also aim to eliminate the misperception that HIV can be transmitted by sneezing, coughing or sharing meals.

In Bangladesh the stigma is not limited to the general population – even health care workers have prejudices against HIV positive patients. The fear of the disease and of being infected is so widespread in Bangladesh that HIV patients are discriminated in hospitals and often denied proper care, even in life-threatening situations. The awareness and knowledge of HIV seems to increase with education and therefore teachers have a great impact on their students⁷. It has been shown that barely half of the uneducated women have heard of HIV, while nine out of ten women with secondary education and all of those with higher education have heard of it. Living in an urban or a rural area also appears to matter – women living in urban areas generally have better education and thus better knowledge about HIV⁴.

Surveillance is aimed at risk groups

Due to the estimated low prevalence of HIV in Bangladesh there has not been any nationwide active surveillance in the general population – it has rather been concentrated to the people most likely to get infected, as well as the people who might be the link to the general population. The Government of Bangladesh acted quickly in the 1980s when HIV was discovered and in 1985, before a case

even was detected in the country, when they formed the National AIDS Committee and the National AIDS/STD program, NASP. NASP is responsible for monitoring and coordination of measures for control and prevention of AIDS and HIV.

Two parts of the surveillance system

- Serological surveillance

Non-random sampling in specific population groups of intervention programs. The first 400 to visit a clinic to donate their blood will constitute the sample group. In the ninth round of surveillance a total of 12 894 individuals from 36 different locations in the country were sampled^{8,9}.

- Behavior surveillance

Random sampling, where a fixed number of people located on a specific place at a specific time is chosen to be interviewed⁸.

There are also several hundreds of non-governmental organizations that have started programs for HIV prevention⁸. Since 1998, nine rounds of surveillance, conducted by icddr,b, in high risk groups have been performed². The surveillance system is executed according to the guidelines of UNAIDS and WHO⁹ and is based on two components. One is serological testing and monitoring of the HIV prevalence in specific risk groups at certain sites across the country. The second is behavior surveillance, where high risk individuals are interviewed^{8,9}. The surveillance is built to monitor the infection and risk behavior, and to function as a warning before an epidemic emerges⁹.

Prevention keeps HIV under control

One prevention strategy, which is currently used, is the needle and syringe program (NSP). 59% of IDUs needing the NSP are estimated to have access to it. Another strategy, which has not yet been started, is opioid substitution treatment (OST) to avoid the use of needles in drug addiction. The OST is however not enough as a sole prevention strategy, and needs to be accompanied by an up-scaling of the existing NSP⁹.

In 2002, icddr,b opened Jagori. This was the first center for voluntary counseling and testing, but in only five years the number of centers in the country had risen to over fifty in total. Access is still limited though, and more efforts need to be done to enhance availability. Due to the low prevalence of HIV in Bangladesh, prevention is the main focus, rather than treatment. At Jagori, people can therefore come to receive counseling on how to reduce their risk behavior, such as increasing their condom use or learning safer injection routines. They are also offered HIV testing, and in the case of testing positive, visitors are offered several types of supportive services. These include knowledge on how to prevent transmission to others and management of diseases related to their HIV infection⁹. Only a few health facilities can provide treatment⁸.

The general population is informed in various ways, e.g. in radio, television and secondary schools. There are collaborations with opinion leaders, such as imams in mosques. Condom use is also promoted and distributed by the government as well as by non-governmental organizations.



Informational poster on ways of transmitting – and not transmitting – HIV, placed at Jagori clinic, Icddr,b.

Preventive measures appear to have had some effect on the risk behavior of IDUs, as can be seen in decreasing number of cases of HCV and syphilis⁸.

Maintaining control

Data indicates that behavior that increases the risk of getting HIV is high in Bangladesh and if intervention and prevention do not proceed, the country might suffer from an HIV epidemic, with the IDUs as the source population¹⁰. However, the situation is under control and as long as the government and non-governmental organizations are supported by funding from external sources the country will be able to maintain the low prevalence.

By Mikaela Glader, Joanna Gradin
and Malin Thoudal

The successful story of vector control in Bangladesh

One of the first things noticed upon our arrival at the hotel-room is a sign next to our beds with this message: "Please do not open the window's glass. Keep your room free from mosquitoes".

The country of Bangladesh has throughout the years proved an excellent example of the tremendous public health improvements that can be obtained with simple measures to control and prevent spread of the so called vector-borne diseases.

According to Dr. Dinesh Mondal, scientist at icddr,b, the main vector-borne diseases in Bangladesh are malaria, filaria, dengue and kala-azar. In 1960, the first Malaria eradication program in Bangladesh was initiated. The whole country was sprayed with the insecticide DDT two times per year, and the country got rid of all vector-borne disease - but only temporarily. In 1971 the program was stopped and later on the import of DDT was banned¹. As a consequence, Dr Dinesh Mondal tells us, the diseases started to re-emerge in Bangladesh. This called for new interventions and has led to the current control programs and successful health improvements described in this article.

What is a vector?

- A vector is an organism that transmits infectious pathogens to their hosts.
- Important vectors in Bangladesh are mosquitoes and sandflies.

Malaria

The word malaria comes from "*mala aria*" that means bad air in Italian, this because people thought that the disease was spread by bad air. Nowadays we know that malaria is

caused by the protozoan parasite plasmodium. Species present in Bangladesh are *P. falciparum* and *P. vivax* and the first mentioned is the most common². The vectors for the malaria parasite are the mosquitoes *Anopheles dirus*, *Anopheles minimus* and *Anopheles philippensis*. Malaria manifests as cycles of fever, headache and vomiting and if not treated it can lead to anemia and be life threatening³.

In Bangladesh malaria is endemic in 13 eastern and northern districts and the prevalence measured 2007 was around 3.1%². The most vulnerable groups for malaria are children under five years old and pregnant women. Bangladesh has been very successful in utilizing strategies for controlling malaria and has managed to reduce the number of cases and deaths. From 2011 to 2012 there has been a 42% and 70% reduction of cases and deaths respectively, which is a huge improvement².

Government-operated non-governmental organization (GO-NGO) and the global fund to fight AIDS, Tuberculosis and Malaria (GFATM) have implemented early diagnosis and prompt treatment. This has shown to be very effective⁵. Informing and providing people with insecticide treated bed nets and changing the treatment to combination therapy, using several drugs, have given good results. Also information and education campaigns are very important to make people aware and understand the importance of vector control.

Filariasis

Lymphatic filariasis (LF) is a disease that is caused by the nematode *Wuchereria bancrofti* and in Bangladesh the main vectors belong to the *Culex* mosquitoes. When the worm gets



Several vectors spreading diseases in Bangladesh. From left to right: *Anopheles minimus* spreading malaria, *Culex quinquefasciatus* vector for filariasis, *Aedes aegypti* spreading Dengue and *Phlebotomus papatasii*, a sandfly spreading Kala-azar. Credits to: CDC/ James Gathany

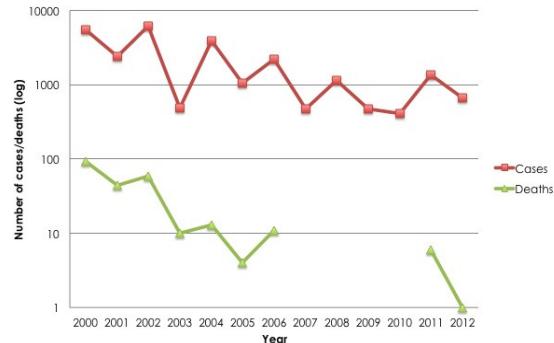
into the blood by a mosquito bite it goes to the lymphatic vessels and manifests as swelling, also called elephantiasis³. Filariasis is endemic in approximately half of the districts in Bangladesh and most of them are located in the northern parts of the country. In November 2001 Mass Drug Administration (MDA) was launched for the risk population and has gradually been implemented in many of the districts with filariasis. From 2001 until 2011, with help of the MDA, five districts reduced the microfilaria (larva stage of the nematode) prevalence down to less than 1%. The remaining districts are now getting treated with MDA and the goal is to eradicate the disease by 2015².



Elephantiasis. Credits to: CDC

Dengue fever

Aedes aegypti is a black and white striped mosquito spreading the dengue virus. The dengue virus causes dengue fever which is a severe flu-like disease. In the last 50 years dengue incidence has increased 30 times globally³. Bangladesh on the other hand has



Dengue cases and deaths per year 2000-2012. The numbers are decreasing tremendously².

managed to decrease the numbers with almost 90% in the last 10 years⁴.

Dengue is found in the whole country, but is most prevalent in urban areas, such as Dhaka and Chittagong. These cities are under continuous urbanization, more houses are needed and building sites throughout the whole city are created. These building sites create many possible breeding places for the mosquito. Other places for breeding are storage of water in jars or drums during dry season or car tires collecting stagnant water^{2,4}. All these different breeding possibilities make it hard to controlling the disease by controlling the vector.

So how has Bangladesh managed to reduce the cases of dengue fever, while the rest of the world has an increasing number of cases? In 2000 Bangladesh experienced the first outbreak of dengue since the 1960s. Since then the disease has re-emerged and caused great morbidity and mortality up to 20%⁴.

Because eradication of the disease is difficult, the government of Bangladesh has focused on decreasing the morbidity and mortality from dengue. This is done by spreading awareness to the population about usage of bed nets and recognition of the symptoms. In the hospitals and under the care providers there has been improved education and better diagnosis². These implications have helped to reduce the number of dengue cases as said earlier. Also the mortality has gone down to only sporadic cases.

It will not be possible to free Bangladesh from dengue fever, but in 2016, the government wants dengue to not be a major public health problem².

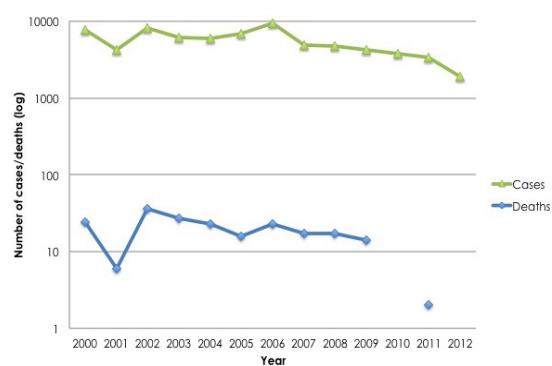
Support of vector control

Apart from vector control, continuous surveillance together with early diagnosis and treatment of the diseases are also essential strategies used to control and reduce disease. It pinpoints the endemic areas and lowers morbidity, mortality and transmission. This requires qualitative education of health care workers, into which the health authorities of Bangladesh has put a great effort. One of the most important actions is to raise the awareness of these diseases among the people. Knowledge within the population facilitates compliance of vector control as well as early diagnosis. It can be difficult to inform the illiterate part of the population by written announcements, but this issue is met by educational sessions in affected areas along with explanatory theatres and songs that hopefully spread this life-saving

Kala-azar

Kala-azar, “black fever” or visceral leishmaniasis is a fatal disease caused by the parasite *Leishmania donovani*, which uses

female *Phlebotomine argentipes* sandflies as vectors to infect humans². The disease displays with symptoms of fever, weight loss, anemia, enlargement of the spleen and liver as well as skin lesions³. Infection mainly occurs in rural areas, putting an estimate of 147 million people at risk in Bangladesh, India and Nepal together². Since human is the only parasitic host and *Phlebotomine* is the only vector, elimination should be possible. Because of this, these three countries declared to eliminate kala-azar by 2015.



Kala-azar cases and deaths per year 2000-2012. The numbers are decreasing tremendously².

The elimination program was initiated in 2005 and mainly focuses on in- and outdoor residual spraying (IRS) within endemic areas all over the country, using pyrethroid-deltamethrin as insecticide. Apart from IRS, insecticide treated bed nets are distributed free of charge to households in endemic regions, especially in areas with a high annual parasite incidence.

This initiative follows three stages: make sure that everyone gets a net; that people actually use the nets; and to replace old nets. Another control measure is microenvironment management that involves elimination of vector breeding sites around households. This can be done by plastering cracks in walls; keeping indoor rooms clean and cover any kind of containers. The program also promotes commu-

nity participation to increase compliance of these measures.

Using this program Bangladesh has successfully decreased the number of deaths from Kala-azar to zero in 2012. Between 2006 and 2012 the number of diseased cases declined with 80%, suggesting that the goal of elimination in 2015 is far from being a mere fantasy.

The bright side

Considering the results so far, Bangladesh demonstrates that vector control interven-

tions are highly effective tools to reduce the impact of vector-borne diseases, even within as little as 10 years. This requires a tremendous amount of work as well as dedication to inform and aid the affected. However, as is seen in the case of malaria, filariasis, dengue and kala-azar, it evidently pays off in the numbers of lives saved.

By Jonas Andersson, Linnéa Garoff and
Ymke de Jong

From pregnancy to childhood – surviving in a developing country

“Every pregnancy is risky” says Dr. Abdul Quaiyum, a researcher on maternal health at the icddr,b. There are many aspects threatening the health of expecting mothers and children in Bangladesh. Everything from traditional believes to infections needs to be taken into account.

When a Bangladeshi woman is expecting her first child, she is on average 19 years old and has been married for some time¹. As any expecting mother, she is probably happy and excited, but ahead of her and her baby is the troublesome journey associated with giving birth and being born in a developing country.

Being pregnant

During her pregnancy the chance that our pregnant woman will seek any prenatal care is about 50% and the two main reasons for not doing so are the feeling that it is “not needed” and that it is too expensive². Poverty is widespread in Bangladesh and contributes to the low number of women seeking health care during pregnancy. Also associated with poverty is malnutrition; this can be harmful to the pregnant woman and her unborn child in several ways, there among increased susceptibility to infections, low birth weight and premature labor.

Another risk during pregnancy is toxoplasmosis, a zoonotic disease transmitted from mainly cats to humans. If our pregnant woman becomes infected during her pregnancy the parasite can be transmitted to her fetus and cause congenital toxoplasmosis. This can lead to severe neurological diseases in the child such as mental retardation as well as

speech and hearing defects. The infection may even be fatal to the unborn child, contributing to an increased abortion rate among young mothers. Toxoplasmosis is endemic in Bangladesh but no study has examined the disease’s impact on pregnant women and their children³.

Parameters associated with child and maternal health^{4,7,8}.

| | 1990 | 2012 |
|---------------------------------|--------------|--------------|
| Children per woman | 4,6 | 2,2 |
| Skilled attended births | <10% | 31% |
| Maternal mortality | 593 /100'000 | 194 /100'000 |
| Neonatal mortality | n/a | 32/1000 |
| Infant mortality | 100/1000 | 43/1000 |
| Under 5 child mortality | 144/1000 | 53/1000 |
| Malnutrition in children | 64% | 41% |

A good thing is that our expecting mother probably is vaccinated against tetanus due to the very high coverage of this vaccination of women in childbearing age. By making sure that she is vaccinated she protects herself and also, to a degree, her baby from neonatal tetanus, which can be a huge problem when deliveries are not carried out in a safe manner⁴.

Facility deliveries are uncommon

A delivery is considered safe when it is supervised by some kind of skilled health personnel, but as more than 85% of deliveries in Bangladesh occur at home the chance that our pregnant woman will receive any skilled help is slim. When delivering the baby at home, the woman is often supported by an untrained “dai”, a type of traditional birth attendant,

and female relatives. Among the very poor, such as urban slum dwellers, home deliveries are often the only option as they can't pay for any other alternative. Respect for traditions passed down through the generations may be another reason for choosing to deliver at home.



A sterile delivery kit with Q-mat for safe home deliveries.

To protect this vulnerable group of women Abdul Quaiyum, together with other researchers at the icddr,b invented the "Q-mat". This simple tool is used to measure the blood loss after delivery; it is placed under the woman directly after delivery of the child. If the mat gets fully soaked with blood, the loss is too big and she should be sent to a health care facility to recover. The advantage of this mat is that the measurement is easy to carry out; it is cheap and can be handled without a lot of medical knowledge⁵.

If our pregnant woman is lucky she might be enrolled in one of the programs trying to increase the maternal and child health in Bangladesh. In 2007 BRAC, a Bangladeshi NGO, initiated the Manoshi program which has been applied among the disadvantaged populations in urban slums. In this program each pregnant woman is motivated to trust and follow the program, and the staff health workers educate the women and their supportive helpers about safe delivery practices and childcare. The women are also encour-

aged to deliver at community facilities, but are given sterile delivery packages in case they won't or can't do that⁶.

In the rural area of Matlab, icddr,b operates a very successful child and maternal health program. By implementing an extensive prenatal care schedule with prenatal check-ups, home visits by health workers before and after delivery and education in home-based life saving skills of newborns they have achieved a much lower maternal and neonatal mortality than Bangladesh as a whole.

Threats in early childhood

When the long awaited child is finally born his/her first month of life is the most crucial. More than half of all deaths of children under five years of age in Bangladesh occur during the first month of life. Most often it is due to problems during the delivery, such as asphyxia or birth traumas associated with unsupervised deliveries. The other major cause of death among children is infectious diseases with respiratory infections and diarrhea as the main problems.

Childhood diarrhea is very prevalent. Our newborn might suffer from as many as two to eight episodes of diarrhea per year in his/her first years of life and this is the second most deadly infection among children. The leading causes are rotavirus, enterotoxigenic *E. coli* and cholera. The main problem with diarrhea in children is that dehydration can quickly become life-threatening if appropriate care is not initiated immediately. Luckily the knowledge and use of ORS is widespread and many lives are saved due to the use of this ingenious invention. However, more knowledge is needed since it is not uncommon that the ORS is prepared with water from unsafe sources, which is from the same source that made the child sick in the first place.

Since many diarrheal deaths are prevented through the use of ORS, pneumonia is nowadays the most deadly disease among children. One fourth of the deaths of children under five and half of the deaths in children less than one year old are due to pneumonia. Preventing these deaths has shown to be a bigger issue than decreasing the diarrheal deaths since pneumonia requires more extensive health care and a “quick-fix” like ORS is not available. Icddr,b is conducting both hospital- and community-based surveillances of pneumonia in children living in the Dhaka area, including studies on antibiotic resistance in the infectious agents⁵.



A child receiving an oral vaccine in Matlab.

It is likely that our child will receive at least some of the recommended childhood vaccinations. The coverage has increased but still varies over the country; rural areas are the major problem with immunization coverage of 40 to 60%. Numbers for Bangladesh as a whole range between 80 and 90% for most of the vaccines^{4,5}. Icddr,b has established a mobile technology based surveillance and

control system that also aims to increase the vaccination coverage in children. Women are registered during pregnancy and communication is done through text messages to their mobile phones. When the time is due, the mothers receive reminders to where and when their children should be vaccinated. The system is especially developed for families in rural areas that are otherwise hard to reach⁵.

The child vaccination program in Bangladesh

Children in Bangladesh are vaccinated against tuberculosis, diphtheria, tetanus, pertussis, *Hemophilus influenzae* type B, hepatitis B, polio, measles and rubella. Women of childbearing age receive additional shots of tetanus and rubella vaccines as a maternal and child health improvement.

The biggest health problem our child will face is malnutrition and this can have many underlying causes. Poverty is a major contributor since the family often can't afford to buy the necessary amount of supplementary food for their children when breast-feeding does not provide enough calories. Lack of knowledge on the appropriate diet for children and on how to prepare the food can also be a problem⁷. The abundant infections in young children contribute to malnutrition by decreasing the child's appetite and absorption of the food in the gut. This can subsequently lead to weight loss, which then in turn weakens the child's immune system so that he/she is even more prone to develop further diseases. This is a vicious cycle where infections and malnutrition feed each other in a pattern that is hard to break.



Mothers getting educated in how to interact with their child and feed them properly at the nutritional rehabilitation unit for malnourished children at the icddr,b hospital in Dhaka

Today there are several programs that work to help and prevent malnutrition in children. The icddr,b hospital in Dhaka has a program that targets malnourished children which have been hospitalized for other reasons, mainly infections. The children get medication and proper food while their mothers are educated on what food their children need and how to cook it. Similar education is done by community health workers that visit mothers all over the country⁷.

If they are lucky our mother and child have now navigated through the difficult childhood years without too much trouble. Health programs are spreading throughout Bangladesh and the chance that families receive health care is increasing. But Bangladesh still has a long way to go to provide every mother and child in the country with the appropriate health care they need.

By Stina Lundberg, Raheleh Masoumi and Theresa Schmidt

Antibiotic resistance in Bangladesh

Despite the improvements of the health-care system in Bangladesh, the growing problem with antibiotic resistance has been neglected. National surveillance and prevention programs are currently not present in the country. This constitutes a threat not only to Bangladesh, but can also cause problems when treating infectious diseases worldwide.

Since Alexander Fleming discovered the penicillin in 1928, bacterial infections in both humans and animals have successfully been treated with antibiotics. In 1967 the Surgeon General of the United States of America, William Stewart, declared: "The time has come to close the book on infectious diseases. We have basically wiped out infections in the United States."

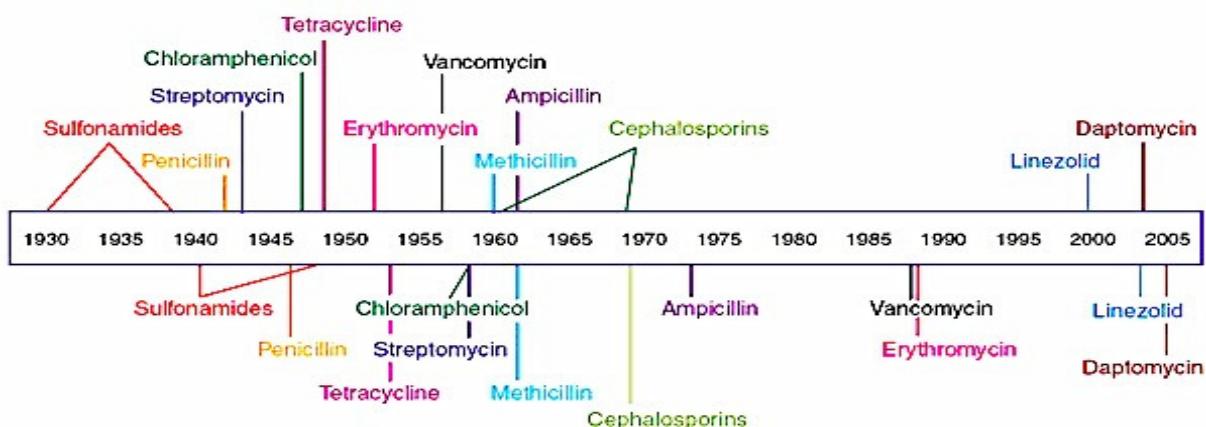
The naïve statement demonstrates the ignorance towards the emerging problem of antibiotic resistance (AR) among bacteria. In the late 1940's resistance against penicillin had been reported – a scenario also facing each of the antibiotics developed thereafter. Due to

WHO guidelines for fighting antibiotic resistance

- Develop and promote guidelines to minimize and contain antimicrobial resistance (AMR) arising from use of antimicrobials in food producing animals.
- Develop a list of Critically Important Antimicrobials (CIA) for human health in order to guide risk management strategies for use of similar agents in food animal production and agriculture.
- Provide technical support and capacity building in monitoring AMR through research projects, training activities and reference services of the WHO Global Foodborne Infections Network (GFN).
- Establish pilot studies to address lack of data from developing countries for risk assessment.

Stewart's declaration, development and production of new antibiotics declined. Meanwhile the usage of antibiotics and consequently antibiotic resistance increased, making way for the huge problems with antibiotic resistant bacteria that the world is facing today.

Antibiotic deployment



Antibiotic resistance observed

Timeline showing the introduction of new antibiotics and the first reporting of resistant bacteria.
Credits to: Anne E Clatworthy, et. al. Nature Chemical Biology, 2007.

The World Health Organisation (WHO) provides guidelines to restrict the use of antibiotics and to fight the upcoming resistance problems. Informing the public, preventing the spread of antibiotic resistant bacteria and reducing the level of resistance in Critical Important Antimicrobials (CIA) are regarded essential actions for human health.

Antibiotics are substances that target specific bacterial structures or functions leading to disturbance in the growth or killing of the microbe. Having rapid lifecycles, high mutation rates and the ability to acquire new genetic material from other bacteria or the environment, bacteria can easily establish large populations with enormous diversity providing great chances for surviving new threats.



Dr. Dilaruba Ahmed, MBBS; PhD, working with antibiotic resistance in bacteria at icddr,b in Dhaka.

Human use of antibiotics has lead to a selective pressure in the bacterial environment. New and fast developing ways to escape the antibiotic killing is constantly occurring in the bacterial population. As long as antibiotics are used, there will always be antibiotic resistance. There will be a constant race between devel-

opment of new antibiotics and bacterial resistance.

In Bangladesh no prevention or surveillance programs for antibiotic resistance have been established. Dr. Dilaruba Ahmed, associate scientist and head of the clinical microbiology laboratory and the diagnostics laboratory services at the icddr,b in Dhaka, is worried about the situation and emphasises on the restriction the political climate has on developing such programs. "There is a lack of discussion concerning antibiotic resistance. There is needs for defining the problem with antibiotic resistance in Bangladesh and to develop guidelines for the usage of antibiotics", she says.

The use of antibiotic in Bangladesh is extensive but since no registration of antibiotics sold or prescribed is required it is hard to estimate the extent of the flow on the market. Walking down the streets of Dhaka you find drug stores in almost every corner, selling all types of antibiotics - no prescription required. The accessibility of the drugs and the lack of knowledge among the population concerning what, when and how long to treat causes over usage of antibiotics. This consequently puts high pressure on the bacteria to continuously develop or acquire resistance mechanisms. "There is a problem with uneducated physicians having their own clinics and prescribing antibiotics without any knowledge of antibiotic resistance. Instead of using first-alternative antibiotics they usually prescribe second- or third-alternative antibiotics for minor infections", says Dr. Dilaruba Ahmed at icddr,b.

In addition to the high usage in the human population the load of antibiotics is also increased by a wide spread use in animal production. Antibiotics are very stable compounds and are not easily degraded in the environment, nor metabolized in the body, enabling

them to persist and accumulate in water and soil.

Bangladesh is vulnerable to infectious diseases, making the problem with antibiotic resistance an even greater problem. The population density is very high in Bangladesh, which increase the risk of transmission of any type of infectious agent, including antibiotic resistant bacteria. Also, malnutrition is a large problem among the population and the individuals suffering from the condition are more susceptible to infections.



Pharmacy selling non-prescription antibiotics in central Dhaka, Bangladesh.

The failure to treat antibiotic resistant bacteria cause severe problems for the individual person and may cause minor infections, which previously were easy to treat, to become very severe. Detecting the resistance profile and

designing new treatment scheme however can take time and is not generally performed. The extended antibiotic resistance and multi-resistant bacteria will eventually cause physicians to run out of treatment options. High prevalence of antibiotic resistant bacteria may finally restrict surgery, transplantation, and other invasive methods when the risk of acquiring untreatable infections becomes too high.

Antibiotic resistance is a major threat for public health and should be a national priority in Bangladesh. The rising problem with antibiotic resistant bacteria in the country should also be a concern for the rest of the world due to the high risk of such bacteria to spread. Financial support and putting pressure on political leaders in Bangladesh are possible ways for other countries to contribute to a solution.

When asked to describe a dream scenario for how Bangladesh should deal with the problems of antibiotic resistance, Dr. Dilaruba Ahmed replies: “National-wide surveillance and a centre that focuses on and discusses the problems with antibiotic resistance. Public hospital could lead the surveillance and match the findings of antibiotic resistance to private practices and develop national guidelines for the usage of antibiotics.”

We can only hope this does not remain just a dream scenario.

By Malin Berggrund, Linnea Ek Blom
and Stina Hedblom

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