Infectio

A quarterly Magazine

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1st Issue, November 2013

Current News

Crimean-Congo haemorrhagic fever (CCHF) in Pakistan, 14 June 2013

Community-acquired CCHF happens through transmission of virus by direct contact with blood or other infected tissue of livestock or from an infected tick bite.

Symptoms

Fever, myalgia (muscle ache), dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light), nausea, vomiting, diarrhoea, abdominal pain and sore throat, sharp mood swings and confusion.

Signs

Tachycardia, lymphadenopathy, petechial ecchymoses, and other haemorrhagic phenomena.

Suspected cases of CCHF reported in Pakistan, 2000–2012

Year	Cases	Deaths	Case–fatality rate (%)
2000-2002	191	59	30.89
2003-2006	328	42	12.8
2010	29	3	10.34
2012	61	17	27.8

http://www.who.int/mediacentre/factsheets/fs208/en/

Message of the Chairman / Head of Project

It gives me great pleasure to welcome an infectious disease magazine specifically devoted to doctors. Infectious diseases are still a major burden of diseases in Pakistan. Expanded immunization has contributed significantly for control of infectious disease but recent measles epidemic has exposed some short comings in the program.

The polio is still with us and efforts to eradicate requires comprehensive struggle against social stigma, religious bigotry and organizational problems.

There is need to disseminate information on control and management of infectious diseases. Current issue contains articles by leading experts on Cholera, *Naegleria fowleri,* adult immunization programs which is a reflection on old problems and new emerging diseases.

Pediatric immunization is well established with universal coverage with Bacillus Calmette-Guerin (BCG), Polio, Diphtheria, Pertussis and Tetanus (DPT), Hepatitis-B, Haemophilus Influenzae Type B (Hib), Measles, Mumps and Rubella (MMR) and recently conjugate Pneumococcal vaccine has been added.
Adult immunization is not well established in routine practice. There is need to disseminate information on Adult vaccination program.

I wish this magazine a great success in achieving its aim.

Prof. Dr. Ejaz Ahmed Vohra
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Acknowledgement

As the Managing Editor of the Infectio magazine I would like to express my appreciation and gratitude to all those who have contributed to construction of this quarterly magazine. I also deeply thank the strong involvement and efforts of all members of editorial board whose scientific support and suggestions have been helpful in compiling this magazine.

My special thanks to Prof. Ejaz Ahmed Vohra who thoroughly guided & supported us in every step of this project.

The main contributors are as under:

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Dr. Farhana Zafar

Dr. Faisal Iqbal Afridi

We have tried to make it informative but there is space for improvement in this magazine and it will be revised as per need or suggestions.

Finally I would like to thank **M/s SAMI Pharmaceuticals (Pvt) Limited** for their generous efforts and helpful contribution for publication of this magazine.

Prof. Badar Jahan Farooqi
Professor and Head of Microbiology
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Cholera…
Still a Devastating Disease

Professor Badar Jahan Farooqi
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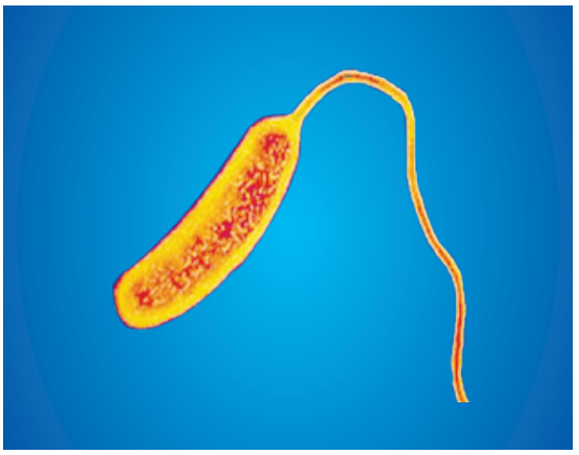

Introduction

Cholera is an acute intestinal infection. It is caused by ingestion of food or water contaminated with the bacterium *Vibrio cholerae (V. cholerae)*. It has a short incubation period, from less than one day to five days, and produces an enterotoxin that causes a copious, painless, watery diarrhea that can quickly lead to severe dehydration and death if treatment is not promptly given. Vomiting also occurs in most patients.

Epidemiology

Cholera is an endemic disease in many parts of developing world including India, Bangladesh and other Asian countries.[1-4] The International Center for Control of Diarrhoeal Disease Research Bangladesh (ICDDRB) treats 10000 to 12000 cases of diarrhea each year. Imported cases of cholera occur in developed countries sporadically. In 1988, 14 cases of cholera were reported from European countries.[1] In addition to endemic cholera, epidemics and pandemics also occur periodically leading to high morbidity and mortality. Epidemics of cholera occurred in 1991 and 1992 in Latin America including Peru, Brazil and Equador.[5, 6] The causative organism for the disease is *V. cholerae* which was first isolated in 1883. In 1905, another biotype called El-Tor was isolated which was responsible for the major epidemic of 1961-62 in South East Asia. The El-Tor variety is equally pathogenic and the disease caused by it is also as severe as by classical *V. cholerae*.[7, 8] The El-Tor variety entered India in 1964 and appeared in Chittagong in 1963 and in Dhaka in 1964 where it completely replaced classical type in 1973.[9] Serologically, two types of *V. cholerae* are common i.e., Ogawa and Inaba. However, in 1991 a new serological variety was isolated in Bangladesh which was not typeable with O1 sera and was called as *V. cholerae* Non O1 sera and was named as *V. cholerae* Non O1, 0139, Bengal.[2, 10] Clinically, this variety is also similar to Ogawa and Inaba in its severity.[11] Later it was reported from India[12] and Thailand.[13] *V. cholerae* 0139 was also isolated in Pakistan in 1994 in Aga Khan Hospital.[14] In Pakistan cholera has been suspected as one of the major causes of outbreaks of gastroenteritis each year during the monsoon season but never confirmed bacteriologically. In 1988 only two cases of cholera were reported in adults from Mansehra.[15] Since 1988, cases of cholera are encountered each year during and after the monsoon season and have been reported mostly in adults. Cholera has been encountered not only in children but also in newborns and infants, which is rather uncommon.

Cholera outbreaks: (Prevention and control)[16]

Clinical features of cholera are sudden onset of acute watery diarrhea that can lead to death by severe dehydration. The extremely short incubation period (two hours to five days) enhances the potentially explosive pattern of outbreaks, as the number of cases can rise very quickly. About 75% of people infected with cholera do not develop any symptoms. However, the pathogens stay in their feces for 7 to 14 days and are shed back into the environment, possibly infecting other individuals. Cholera is an extremely virulent disease that affects both children and adults. Unlike other diarrheal diseases, it can kill healthy adults within hours. Individuals with lower immunity, such as malnourished children or people living with Human Immunodeficiency Virus (HIV), are at greater risk of death if infected by cholera.

Important messages

- Cholera is transmitted through contaminated water or food.
- Cholera can rapidly lead to severe dehydration and death if left untreated.
- Prevention and preparedness of cholera require a coordinated multidisciplinary approach.

World Health Organization (WHO) recommendations for Cholera outbreaks Control[16]

Among people developing symptoms, 80% of episodes are of mild or moderate severity. The remaining 10-20% of cases develop severe watery diarrhea with signs of dehydration. Once an outbreak is detected, the usual intervention strategy aims to reduce mortality by ensuring access to treatment and controlling the spread of disease.

WHO recommends the following tools for cholera control[16]

- Proper and timely case management in cholera treatment centres.
- Specific training for proper case management, including avoidance of nosocomial infections.
- Sufficient pre-positioned medical supplies for case management (e.g. diarrheal disease kits).
- Improved access to water, effective sanitation, proper waste management and vector control.
- Enhanced hygiene and food safety practices.
- Improved communication and public information.

Case management

WHO recommends prompt rehydration through the administration of Oral Rehydration Salts (ORS) or intravenous fluids, depending on the severity of cases. Up to 80% of patients can be treated adequately through the administration of ORS (WHO/UNICEF ORS standard sachet). Very severely dehydrated patients are treated through the administration of intravenous fluids, preferably Ringer lactate. Appropriate antibiotics can be given to severe cases to diminish the duration of diarrhea, reduce the volume of rehydration fluids needed and shorten the duration of *V. cholerae* excretion. Cholera treatment centres should be set up among the affected populations whenever feasible.

Important messages

- ORS can successfully treat 80% of cholera cases.
- Appropriate antibiotics can reduce the duration of purging.

Cholera vaccines[16]

The use of the parenteral cholera vaccine has never been recommended by WHO due to its low protective efficacy and the high occurrence of severe adverse reactions. An internationally licensed Oral Cholera Vaccine (OCV) is currently available on the market and is suitable for travelers. This vaccine is proven safe and effective. Individuals aged two years and above can take it safely. It is administered in two doses 10-15 days apart and given in 150 ml of safe water. WHO official recommendations for its use in complex emergencies have been issued, and state that:

- OCV should always be used as an additional public health tool and should not replace usually recommended control measures such as improved water supplies, adequate sanitation and health education. It needs also to be linked to strengthened surveillance and early warning.
- The current internationally available prequalified vaccine is not recommended once a cholera outbreak has started due to its 2-dose regimen and the time required to reach protective efficacy, high cost and the heavy logistics associated with its use.

Travel and trade[16]

Today, no country requires proof of cholera vaccination as a condition for entry and the International Certificate of Vaccination no longer provides a specific space for recording cholera vaccinations. In 1973, the World Health Assembly deleted from the International Health Regulations the requirement for presentation of a cholera vaccination certificate.

Past experience clearly showed that quarantine measures and embargoes on movements of people and goods especially food products are unnecessary. At present, WHO has no information that food commercially imported from affected countries has been implicated in outbreaks of cholera in importing countries. The isolated cases of cholera that have been related to imported food have been associated with food which had been in the possession of individual travelers. Therefore, it may be concluded that food produced under good manufacturing practices poses only a negligible risk for cholera transmission.

Consequently, WHO believes that food import restrictions, based on the sole fact that cholera is epidemic or endemic in a country, are not justified.

Important messages

- Imposing travel and trade restrictions have proven inefficient.
- WHO has no information that food commercially imported from affected countries.

WHO recommendations to unaffected neighboring countries[16]

Countries neighboring an area affected by cholera should implement the following measures:

- Improve preparedness to rapidly respond to an outbreak, should cholera spread across borders, and limit its consequences.
- Improve surveillance to obtain better data for risk assessment and early detection of outbreaks, including establishing an active surveillance system.

Following measures should be avoided, as they have been proven ineffective, costly and counter-productive:

- Routine treatment of a community with antibiotics, or mass chemoprophylaxis, has no effect on the spread of cholera. It can have adverse effects by increasing antimicrobial resistance and provides a false sense of security.
- Restrictions in travel and trade between countries or between different regions of a country.
- Set up a cordon sanitaire at borders, a measure that diverts resources, hampers good cooperation spirit between institutions and countries instead of uniting efforts.

Cholera – a waterborne disease – is closely linked to poor environmental conditions. The absence or shortage of safe water and of proper sanitation, as well as poor waste management, are the main causes of spread of the disease. These factors conducive to epidemics concur in many places in the developing world, and even more acutely in overcrowded settings, where cholera is either endemic or a recurrent problem. Typical at-risk areas are peri-urban slums, with precarious basic infrastructures, as well as internally displaced or refugee camps, where minimum requirements of clean water and sanitation are not met. However, inhabitants of rural areas, particularly along rivers and lake shores, are not spared. Populations most affected are the ones living in insalubrious conditions, where environmental safety is not ensured.

Oral cholera vaccines[16]

Global efforts to control resurgence of cholera worldwide are now entering a new phase following the development of safe and effective OCV. These new tools have opened up the possibility of preventing outbreaks among the most vulnerable populations living in high risk areas, where usually recommended control measures are not sufficient.

WHO recommended that immunization should be used with other prevention and control strategies in areas where the disease is endemic and in areas at risk for outbreaks. The use of OCVs should also be considered reactively to reduce mortality in areas where other interventions cannot be delivered effectively. As such OCV use is part of a multidisciplinary approach and should be considered within the wider scope of public health priorities.

Experience gained from different mass vaccination campaigns in Mozambique, Indonesia, Sudan, and Zanzibar clearly indicates that mass vaccination campaigns cannot be improvised at the last moment – they need careful advance planning and preparation, while major challenges remain, including improving the assessment of risk, identification of target populations and logistics.

Currently WHO is facilitating a multi-partner initiative aimed at establishing an OCV stockpile along with criteria for its use and monitoring. This should allow access to sufficient vaccines for outbreak response as an adjunct to established prevention and control measures, particularly in complex emergency settings.

International Health Regulations (IHR) of WHO[16]

The IHR is an international legal instrument that is binding on 194 countries across the globe, including all the Member States of WHO. Their aim is to help the international community to prevent and respond to acute public health risks that have the potential to cross borders and threaten people worldwide.

Building on the unique experience of WHO in global disease surveillance, alert and response, the IHR define the rights and obligations of countries to report public health events, and establish a number of procedures that WHO must follow in its work to uphold global public health security.

The Global Task Force on Cholera Control[16]

WHO Global Task Force on Cholera Control was launched in 1992 following the adoption of resolution WHA44.6 on cholera by the Forty-fourth World Health Assembly. The aim was to reduce mortality and morbidity associated with the disease and to address the social and economic consequences of cholera.

This partnership brings together governmental and non-governmental organizations, United Nation (UN) agencies, and scientific institutions to coordinate activities against epidemic enteric diseases and develop technical

guidelines and training materials for cholera control. Currently, priority activities are aimed at:

To date, the Task Force has provided technical advice and support for cholera control and prevention at country level; training of health professionals at national, regional and international levels in prevention, preparedness and response of diarrheal disease outbreaks; and the dissemination of information on cholera and other epidemic prone enteric diseases to health professionals and the general public.

Currently, priority activities are aimed at:

- Encouraging improved surveillance and using data to identify high risk areas and guide intervention.
- Providing evidence based support to countries for preparedness and response.
- Gaining evidence on the use of OCV as an additional public health tool to diminish incidence of cholera in high risk areas and vulnerable groups.
- Linking health and management of the environment in order to improve access to safe water for vulnerable populations and diminish incidence of waterborne diseases.

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Naegleria fowleri... Lethal BUT Avertable

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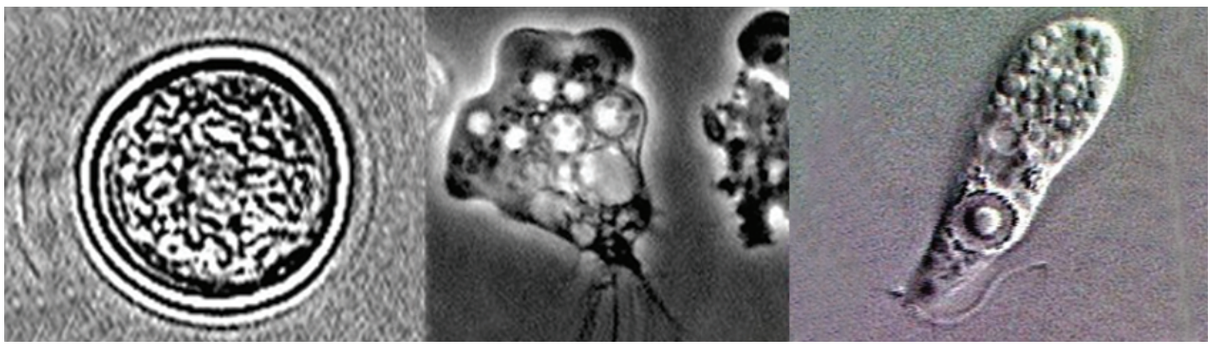

Background

Naegleria fowleri (N. fowleri) commonly referred to as the "brain-eating amoeba" is a thermophilic, free-living amoeba, typically found in warm bodies of fresh water, such as lakes, rivers, and hot springs.[1] It can also be found in soil, near warm-water discharges of industrial plants, and unchlorinated swimming pools in an amoeboid or temporary flagellate stage. *N. fowleri* is not found in salt water, like the ocean.[2] Of the approximately 30 species in the genus, *N. fowleri* is the only known pathogen of humans.[3] *Naegleria species* have three life cycle stages: trophozoites, flagellates, and cysts (Figure 1).[3] The trophozoites are the reproductive stage of the parasite and cause invasive human disease. On transfer to distilled water or a non-nutrient medium, trophozoites can transform rapidly to a transitory flagellate form, which does not divide or feed. When trophozoites encyst, they produce a cyst, which is resistant to environmental stresses. Although this occurs rarely, *N. fowleri* can invade and attack the human nervous system by entering the nose during water-related activities. Once in the nose, the amoeba travels to the brain and causes a severe brain infection called Primary Amoebic Meningoencephalitis (PAM), which nearly always results in the death of the patient.[4] The case fatality rate is predicted up to 98%.[5]

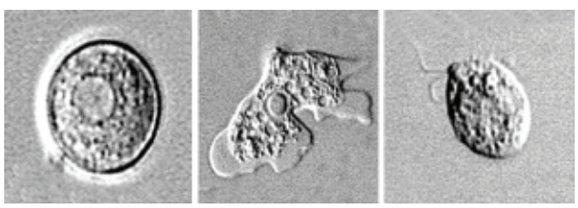

Figure 1: Left: *Naegleria fowleri* in its cyst stage. Center: *Naegleria fowleri* in its amoeboid trophozoite stage. Right: *Naegleria fowleri* in its flagellated stage. Credit: DPDx and GS Visvesvara.

History

N. Fowleri was named after Malcolm Fowler of Adelaide Children's Hospital of Australia, who with R.F. Carter described the initial cases of PAM in 1965.[3] A retrospective study determined that the first documented case of PAM possibly occurred in Britain in 1909.[6] The initial cases of PAM in the United States (US) were reported in 1962 in Florida.[1] Subsequent investigations in Virginia using archived autopsy tissue samples identified PAM infections that had occurred in Virginia as early as 1937.[1] Since 1965, more than 144 cases have been confirmed in a variety of countries.[2]

Epidemiology

As stated earlier that *N. fowleri* has been found worldwide in soil, river, and lake water samples. Pathogenic *N. fowleri* are thermophilic and proliferate at temperatures up to 45°C.[3] The trophozoites and cysts can survive from minutes to hours at 50-65°C with the cysts being more resistant at these temperatures.[1] *N. fowleri* is naturally found in warm freshwater environments such as lakes and rivers, naturally hot (geothermal) water such as hot springs, warm water discharge from industrial or power plants, geothermal well water, poorly maintained or minimally chlorinated swimming pools, water heaters, and soil, where it lives by feeding on bacteria and other microbes in the environment.[1] N. fowleri has been frequently isolated from thermally polluted waters in temperate climates.[3] As water temperatures drop in winter, *Naegleria* is typically isolated from lake-bottom sediments; *Naegleria* cyst are stable for up to 8 months at 4°C.[7]

PAM due to *N. fowleri* has been reported in the central and southern US, southern Australia, New Zealand, Europe, Africa, Asia, and Latin America.[8] Hundreds of cases of PAM have been reported worldwide. Most patients have a history of recreational freshwater exposure.[3] Although there have probably been billions of exposures of people to *Naegleria-*

contaminated fresh water, very few develop PAM.[9] The factors that protect most individuals from invasive *Naegleria* infection are not understood. In the United States there have been 128 PAM cases from 1962 through 2012, with only 1 survivor.[10] Most infections occurred in southern-tier states, with more than half in Texas and Florida. PAM also disproportionately affects males and children (more in under 18 years of age), maybe because of the types of water activities (such as diving or water sports) that might be more common among young boys. Infections linked to freshwater swimming mostly occur during the heat of summer in July and August when water temperatures peak and water levels are low. Although swimming in warm freshwater remains the predominant risk factor for infection, in 2011, 2 cases of PAM in Louisiana, in people who did not have a recent history of swimming in warm freshwater, were found to be regular users of neti pots for sinus irrigation and apparently made their irrigation solutions with *N. fowleri*-contaminated household tap water.[11] In other countries, PAM has occurred in patients who perform ritual nasal rinsing, which is practiced to prepare for prayer.[12] Clusters of cases of PAM with common environmental exposure have occurred, including 16 deaths over a three year period that were retrospectively traced to a swimming pool in Czechoslovakia with a low chlorine concentration.[13] In Pakistan, more than 10 cases were documented from 2010 until 2012 from the southern part of Pakistan.[2] Two more cases of PAM were reported in Karachi in the year 2013 until date.

Infection and Illness (Signs and Symptoms)

Humans become infected when water containing *N. fowleri* enters the nose, usually while swimming. People do not get infected by drinking contaminated water. *N. fowleri* can invade the central nervous system via the nose specifically through the olfactory mucosa and cribriform plate of the nasal tissues. From there, the amoeba climbs along nerve fibers through the floor of the cranium via the cribriform plate and into the brain. The organism begins to consume cells of the brain piecemeal by means of a unique sucking apparatus extended from its cell surface.[2] It then becomes pathogenic, causing PAM. *N. fowleri* has never been shown to have spread from one person to another.

Clinically, a patient with PAM presents much like a patient with bacterial meningitis. Symptoms start 1 to 14 days after exposure. Signs and symptoms include:

Stage 1

- Severe frontal headache
- Fever
- Nausea
- Vomiting

Stage 2

- Stiff neck
- Seizures
- Altered mental status
- Hallucinations
- Coma

After the start of symptoms, the disease progresses rapidly over 3 to 7 days, with death occurring from 7 to 14 days after exposure.[2] PAM is nearly always fatal.

Diagnosis

Cerebrospinal fluid (CSF) studies of PAM patients typically demonstrate a pattern similar to bacterial meningitis with an elevated opening pressure, a polymorphonuclear pleocytosis, normal or low glucose, and elevated protein. However the observations of blood in the CSF and/or motile amoeba serve as clues for potential diagnosis of PAM.[14] Because of the rarity of the infection and difficulty in initial detection, about 75% of diagnoses are made after the death of the patient.[15]

Direct Visualization in CSF[14]

The diagnosis can be made most quickly by microscopic examination of fresh, unfrozen, unrefrigerated CSF. Frozen or refrigerated samples are not appropriate because cold temperatures kill the amoebae. A wet mount of freshly-centrifuged CSF can demonstrate actively moving trophozoites in a generally linear forward direction (Figure 2).

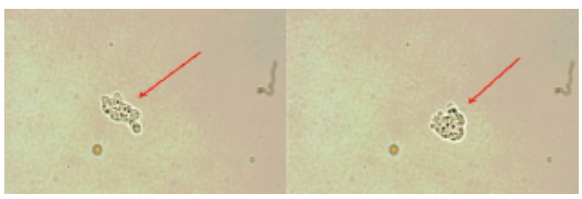

Figure 2: Wet mount of CSF showing Trophozoite (Amoeboid form) of N. fowleri.

Additionally, *Naegleria* can be identified in CSF smears or cultures using hematoxylin and eosin (H&E), periodic acid-Schiff (PAS), trichrome, Giemsa, or Wright-Giemsa stains. A stained smear will show amoeboid trophozoites with morphology typical of *Naegleria* i.e. nucleus with a centrally located, densely staining large nucleolus.

Immunohistochemistry (IHC)[15]

A specific antibody to *N. fowleri* can be used in conjunction with another antibody that deposits a chemical or glows under specific types of light (Indirect fluorescent antibody [IFA]) to directly stain the amoebae in tissue.

Polymerase Chain Reaction (PCR)[15]

Specific molecular tools can amplify Deoxyribonucleic acid (DNA) from the amoebae in CSF or tissue to specifically identify if the amoebae are present.

Amoeba culture[15]

The sample is added to a growth plate covered in bacteria that can serve as a food source for *N. fowleri*. Incubating at higher temperatures selects for *N. fowleri* growth, which can be seen as tracks made by the amoeba as it moves across the plate eating the bacteria. Growing *N. fowleri* in mammalian cell culture and looking for toxic cell effects is also possible.

Environmental Detection[15]

Water samples can be collected, concentrated, and put into culture to grow and select for *N. fowleri*. Samples can be tested using the serologic or molecular methods described above.

Treatment

Optimum treatment for PAM has not been well defined. There have been two well-documented survivors in North America: one in California and one in Mexico.[16] It has been suggested that the survivor's strain of *N. fowleri* was less virulent, which contributed to the patient's recovery. Usually a combination of high dose amphotericin B (Intravenous and intrathecal both) plus rifampicin along with steroids is used.[3] Other options may include systemic and intrathecal miconazole, fluconazole, and sulfisoxazole. The role of newer drugs such as azithromycin, miltefosine, voriconazole as part of combination regimens in the treatment of PAM remains to be determined.[3]

Prevention and Control

The only certain way to prevent PAM due to swimming is to refrain from water-related activities in warm freshwater. Personal actions to reduce the risk of *N. fowleri* infection should focus on limiting the amount of water going up the nose and lowering the chances that *N. fowleri* may be in the water. These actions could include:

Swimming-related risk[17]

1. Hold the nose shut, use nose clips, or keep the head above water when taking part in water-related activities in bodies of warm freshwater.
2. Avoid putting the head under the water in hot springs and other untreated thermal waters.
3. Avoid water-related activities in warm freshwater during periods of high water temperature and low water levels.
4. Avoid digging in, or stirring up, the sediment while taking part in water-related activities in shallow, warm freshwater areas.

Non-swimming-related risk[17]

Even more rarely, infections have been reported when people submerge their heads, cleanse during religious practices, or irrigate their sinuses (nose) using heated and contaminated tap water. If making a solution for irrigating, flushing, or rinsing the sinuses use water that has been:

1. Previously boiled for 1 minute (at elevations above 6,500 feet, boil for 3 minutes) and left to cool.

   OR
2. Filtered, using a filter with an absolute pore size of 1 micron or smaller.

   OR
3. Purchased with a label specifying that it contains distilled or sterile water.

Rinse the irrigation device after each use with water that has been previously boiled, filtered, distilled, or sterilized and leave the device open to air dry completely.

Adequate Chlorination

N. fowleri is susceptible to chlorine and can be controlled in swimming pools by adequate chlorination. Tiewchaloren *et al* reported that the trophozoites of *N. fowleri* were destroyed in chlorine concentration greater than 0.75 ppm[18] (1 ppm = 1 mg/L). Monitoring and maintaining adequate

levels of chlorine in the tap water at the consumer's end is also of prime importance to control this fatal disease.

Lastly, enhanced education of the public in advance of the summer swim season might be helpful. Education should put *N. fowleri* infection in the context of other risks associated with recreational water use to help raise awareness and assist swimmers in making informed choices about their recreational activities.

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Recommended Adult Immunization Schedule - 2013

Infectio

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

VACCINE ▼ / AGE GROUP ▶	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza [2]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap) [3]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					
Varicella [4]	2 doses					
Human papillomavirus (HPV) Female [5]	3 doses					
Human papillomavirus (HPV) Male [5]	3 doses					
Zoster [6]					1 dose	
Measles, mumps, rubella (MMR) [7]	1 or 2 doses					
Pneumococcal polysaccharide (PPSV23) [8,9]	1 or 2 doses					1 dose
Pneumococcal 13-valent conjugate (PCV13) [10]	1 dose					
Meningococcal [11]	1 or more doses					
Hepatitis A [12]	2 doses					
Hepatitis B [13]	3 doses					

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indication)

No recommendation

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), American College of Obstetricians and Gynecologists (ACOG) and American College of Nurse-Midwives (ACNM).

VACCINE ▼ / INDICATION ▶	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) [4,6,7,10,15]	HIV infection CD4+ T lymphocyte count [4,6,7,10,14,15]: < 200 cells/μL	HIV infection CD4+ T lymphocyte count [4,6,7,10,14,15]: ≥ 200 cells/μL	Men who have sex with men (MSM)	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) [10,14]	Chronic liver disease	Kidney failure, end-stage renal disease, receipt of hemodialysis	Diabetes	Healthcare personnel
Influenza [2]	1 dose IIV annually				1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap) [3]	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella [4]	Contraindicated			2 doses							
Human papillomavirus (HPV) Female [5]		3 doses through age 26 yrs				3 doses through age 26 yrs					
Human papillomavirus (HPV) Male [5]		3 doses through age 26 yrs				3 doses through age 21 yrs					
Zoster [6]	Contraindicated				1 dose						
Measles, mumps, rubella (MMR) [7]	Contraindicated			1 or 2 doses							
Pneumococcal polysaccharide (PPSV23) [8,9]	1 or 2 doses										
Pneumococcal 13-valent conjugate (PCV13) [10]	1 dose										
Meningococcal [11]	1 or more doses										
Hepatitis A [12]	2 doses										
Hepatitis B [13]	3 doses										

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Recommended Adult Immunization Schedule - 2013

Footnotes — Recommended Immunization-2013 Schedule for Adults Aged 19 Years and Older

1. Additional information

- Additional guidance for the use of the vaccines described in this supplement is available at http://www.cdc.gov/vaccines/pubs/acip-list.htm.
- Information on vaccination recommendations when vaccination status is unknown and other general immunization information can be found in the General Recommendations on Immunization at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm.
- Information on travel vaccine requirements and recommendations (e.g., for hepatitis A and B, meningococcal, and other vaccines) are available at http://wwwnc.cdc.gov/travel/page/vaccinations.htm.

2. Influenza vaccination

- Annual vaccination against influenza is recommended for all persons aged 6 months and older.
- Persons aged 6 months and older, including pregnant women, can receive the inactivated influenza vaccine (IIV).
- Healthy, nonpregnant persons aged 2–49 years without high-risk medical conditions can receive either intranasally administered live, attenuated influenza vaccine (LAIV) (FluMist), or IIV. Health-care personnel who care for severely immunocompromised persons (i.e., those who require care in a protected environment) should receive IIV rather than LAIV.
- The intramuscularly or intradermally administered IIV are options for adults aged 18–64 years.
- Adults aged 65 years and older can receive the standard dose IIV or the high-dose IIV (Fluzone High-Dose).

3. Tetanus, diphtheria, and acellular pertussis (Td/Tdap) vaccination

- Administer one dose of Tdap vaccine to pregnant women during each pregnancy (preferred during 27–36 weeks' gestation), regardless of number of years since prior Td or Tdap vaccination.
- Administer Tdap to all other adults who have not previously received Tdap or for whom vaccine status is unknown. Tdap can be administered regardless of interval since the most recent tetanus or diphtheria-toxoid containing vaccine.
- Adults with an unknown or incomplete history of completing a 3-dose primary vaccination series with Td-containing vaccines should begin or complete a primary vaccination series including a Tdap dose.
- For unvaccinated adults, administer the first 2 doses at least 4 weeks apart and the third dose 6–12 months after the second.
- For incompletely vaccinated (i.e., less than 3 doses) adults, administer remaining doses.
- Refer to the Advisory Committee on Immunization Practices (ACIP) statement for recommendations for administering Td/Tdap as prophylaxis in wound management (see footnote #1).

4. Varicella vaccination

- All adults without evidence of immunity to varicella (as defined below) should receive 2 doses of single-antigen varicella vaccine or a second dose if they have received only 1 dose.
- Special consideration for vaccination should be given to those who have close contact with persons at high risk for severe disease (e.g., health-care personnel and family contacts of persons with immunocompromising conditions) or are at high risk for exposure or transmission (e.g., teachers; child care employees; residents and staff members of institutional settings, including correctional institutions; college students; military personnel; adolescents and adults living in households with children; nonpregnant women of childbearing age; and international travelers).
- Pregnant women should be assessed for evidence of varicella immunity. Women who do not have evidence of immunity should receive the first dose of varicella vaccine upon completion or termination of pregnancy and before discharge from the health-care facility. The second dose should be administered 4–8 weeks after the first dose.
- Evidence of immunity to varicella in adults includes any of the following:
  - documentation of 2 doses of varicella vaccine at least 4 weeks apart;
  - U.S. born before 1980 except health-care personnel and pregnant women;
  - history of varicella based on diagnosis or verification of varicella disease by a health-care provider;
  - history of herpes zoster based on diagnosis or verification of herpes zoster disease by a health-care provider; or
  - laboratory evidence of immunity or laboratory confirmation of disease.

5. Human papillomavirus (HPV) vaccination

- Two vaccines are licensed for use in females, bivalent HPV vaccine (HPV2) and quadrivalent HPV vaccine (HPV4), and one HPV vaccine for use in males (HPV4).
- For females, either HPV4 or HPV2 is recommended in a 3-dose series for routine vaccination at age 11 or 12 years, and for those aged 13 through 26 years, if not previously vaccinated.
- For males, HPV4 is recommended in a 3-dose series for routine vaccination at age 11 or 12 years, and for those aged 13 through 21 years, if not previously vaccinated. Males aged 22 through 26 years may be vaccinated.
- HPV4 is recommended for men who have sex with men (MSM) through age 26 years for those who did not get any or all doses when they were younger.
- Vaccination is recommended for immunocompromised persons (including those with HIV infection) through age 26 years for those who did not get any or all doses when they were younger.
- A complete series for either HPV4 or HPV2 consists of 3 doses. The second dose should be administered 1–2 months after the first dose; the third dose should be administered 6 months after the first dose (at least 24 weeks after the first dose).
- HPV vaccines are not recommended for use in pregnant women. However, pregnancy testing is not needed before vaccination. If a woman is found to be pregnant after initiating the vaccination series, no intervention is needed; the remainder of the 3-dose series should be delayed until completion of pregnancy.
- Although HPV vaccination is not specifically recommended for health-care personnel (HCP) based on their occupation, HCP should receive the HPV vaccine as recommended (see above).

6. Zoster vaccination

- A single dose of zoster vaccine is recommended for adults aged 60 years and older regardless of whether they report a prior episode of herpes zoster. Although the vaccine is licensed by the Food and Drug Administration (FDA) for use among and can be administered to persons aged 50 years and older, ACIP recommends that vaccination begins at age 60 years.
- Persons aged 60 years and older with chronic medical conditions may be vaccinated unless their condition constitutes a contraindication, such as pregnancy or severe immunodeficiency.

  Although zoster vaccination is not specifically recommended for HCP, they should receive the vaccine if they are in the recommended age group.

7. Measles, mumps, rubella (MMR) vaccination

- Adults born before 1957 generally are considered immune to measles and mumps. All adults born in 1957 or later should have documentation of 1 or more doses of MMR vaccine unless they have a medical contraindication to the vaccine, or laboratory evidence of immunity to each of the three diseases. Documentation of provider-diagnosed disease is not considered acceptable evidence of immunity for measles, mumps, or rubella.

  Measles component:
- A routine second dose of MMR vaccine, administered a minimum of 28 days after the first dose, is recommended for adults who
  - are students in postsecondary educational institutions;
  - work in a health-care facility; or
  - plan to travel internationally.
- Persons who received inactivated (killed) measles vaccine or measles vaccine of unknown type during 1963–1967 should be revaccinated with 2 doses of MMR vaccine.

  Mumps component:
- A routine second dose of MMR vaccine, administered a minimum of 28 days after the first dose, is recommended for adults who
  - are students in a postsecondary educational institution;
  - work in a health-care facility; or
  - plan to travel internationally.
- Persons vaccinated before 1979 with either killed mumps vaccine or mumps vaccine of unknown type who are at high risk for mumps infection (e.g., persons who are working in a health-care facility) should be considered for revaccination with 2 doses of MMR vaccine.

  Rubella component:
- For women of childbearing age, regardless of birth year, rubella immunity should be determined. If there is no evidence of immunity, women who are not pregnant should be vaccinated. Pregnant women who do not have evidence of immunity should receive MMR vaccine upon completion or termination of pregnancy and before discharge from the health-care facility.

  HCP born before 1957:
- For unvaccinated health-care personnel born before 1957 who lack laboratory evidence of measles, mumps, and/or rubella immunity or laboratory confirmation of disease, health-care facilities should consider vaccinating personnel with 2 doses of MMR vaccine at the appropriate interval for measles and mumps or 1 dose of MMR vaccine for rubella.

8. Pneumococcal polysaccharide (PPSV23) vaccination

- Vaccinate all persons with the following indications:
  - all adults aged 65 years and older;
  - adults younger than age 65 years with chronic lung disease (including chronic obstructive pulmonary disease, emphysema, and asthma); chronic cardiovascular diseases; diabetes mellitus; chronic renal failure; nephrotic syndrome; chronic liver disease (including cirrhosis); alcoholism; cochlear implants; cerebrospinal fluid leaks; immunocompromising conditions; and functional or anatomic asplenia (e.g., sickle cell disease and other hemoglobinopathies, congenital or acquired asplenia, splenic dysfunction, or splenectomy [if elective splenectomy is planned, vaccinate at least 2 weeks before surgery]);
  - residents of nursing homes or long-term care facilities; and
  - adults who smoke cigarettes.
- Persons with immunocompromising conditions and other selected conditions are recommended to receive PCV13 and PPSV23 vaccines. See footnote #10 for information on timing of PCV13 and PPSV23 vaccinations.
- Persons with asymptomatic or symptomatic HIV infection should be vaccinated as soon as possible after their diagnosis.
- When cancer chemotherapy or other immunosuppressive therapy is being considered, the interval between vaccination and initiation of immunosuppressive therapy should be at least 2 weeks. Vaccination during chemotherapy or radiation therapy should be avoided.
- Routine use of PPSV23 is not recommended for American Indians/Alaska Natives or other persons younger than age 65 years unless they have underlying medical conditions that are PPSV23 indications. However, public health authorities may consider recommending PPSV23 for American Indians/Alaska Natives who are living in areas where the risk for invasive pneumococcal disease is increased.
- When indicated, PPSV23 should be administered to patients who are uncertain of their vaccination status and there is no record of previous vaccination. When PCV13 is also indicated, a dose of PCV13 should be given first (see footnote #10).

9. Revaccination with PPSV23

- One-time revaccination 5 years after the first dose is recommended for persons aged 19 through 64 years with chronic renal failure or nephrotic syndrome; functional or anatomic asplenia (e.g., sickle cell disease or splenectomy); and for persons with immunocompromising conditions.
- Persons who received 1 or 2 doses of PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years or later if at least 5 years have passed since their previous dose.
- No further doses are needed for persons vaccinated with PPSV23 at or after age 65 years.

10. Pneumococcal conjugate 13-valent vaccination (PCV13)

- Adults aged 19 years or older with immunocompromising conditions (including chronic renal failure and nephrotic syndrome), functional or anatomic asplenia, CSF leaks or cochlear implants, and who have not previously received PCV13 or PPSV23 should receive a single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later.
- Adults aged 19 years or older with the aforementioned conditions who have previously received one or more doses of PPSV23 should receive a dose of PCV13 one or more years after the last PPSV23 dose was received. For those that require additional doses of PPSV23, the first such dose should be given no sooner than 8 weeks after PCV13 and at least 5 years since the most recent dose of PPSV23.
- When indicated, PCV13 should be administered to patients who are uncertain of their vaccination status history and there is no record of previous vaccination.
- Although PCV13 is licensed by the Food and Drug Administration (FDA) for use among and can be administered to persons aged 50 years and older, ACIP recommends PCV13 for adults aged 19 years and older with the specific medical conditions noted above.

11. Meningococcal vaccination

- Administer 2 doses of meningococcal conjugate vaccine quadrivalent (MCV4) at least 2 months apart to adults with functional asplenia or persistent complement component deficiencies.
- HIV-infected persons who are vaccinated also should receive 2 doses.
- Administer a single dose of meningococcal vaccine to microbiologists routinely exposed to isolates of Neisseria meningitidis, military recruits, and persons who travel to or live in countries in which meningococcal disease is hyperendemic or epidemic.
- First-year college students up through age 21 years who are living in residence halls should be vaccinated if they have not received a dose on or after their 16th birthday.
- MCV4 is preferred for adults with any of the preceding indications who are aged 55 years and younger; meningococcal polysaccharide vaccine (MPSV4) is preferred for adults aged 56 years and older.
- Revaccination with MCV4 every 5 years is recommended for

adults previously vaccinated with MCV4 or MPSV4 who remain at increased risk for infection (e.g., adults with anatomic or functional asplenia or persistent complement component deficiencies).

12. Hepatitis A vaccination

- Vaccinate any person seeking protection from hepatitis A virus (HAV) infection and persons with any of the following indications:
  - men who have sex with men and persons who use injection or noninjection illicit drugs;
  - persons working with HAV-infected primates or with HAV in a research laboratory setting;
  - persons with chronic liver disease and persons who receive clotting factor concentrates;
  - persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A; and
  - unvaccinated persons who anticipate close personal contact (e.g., household or regular babysitting) with an international adoptee during the first 60 days after arrival in the United States from a country with high or intermediate endemicity. (See footnote #1 for more information on travel recommendations). The first dose of the 2-dose hepatitis A vaccine series should be administered as soon as adoption is planned, ideally 2 or more weeks before the arrival of the adoptee.
- Single-antigen vaccine formulations should be administered in a 2-dose schedule at either 0 and 6–12 months (Havrix), or 0 and 6–18 months (Vaqta). If the combined hepatitis A and hepatitis B vaccine (Twinrix) is used, administer 3 doses at 0, 1, and 6 months; alternatively, a 4-dose schedule may be used, administered on days 0, 7, and 21–30, followed by a booster dose at month 12.

13. Hepatitis B vaccination

- Vaccinate persons with any of the following indications and any person seeking protection from hepatitis B virus (HBV) infection:
  - sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., persons with more than one sex partner during the previous 6 months); persons seeking evaluation or treatment for a sexually transmitted disease (STD); current or recent injection-drug users; and men who have sex with men;
  - health-care personnel and public-safety workers who are potentially exposed to blood or other infectious body fluids;
  - persons with diabetes younger than age 60 years as soon as feasible after diagnosis; persons with diabetes who are age 60 years or older at the discretion of the treating clinician based on increased need for assisted blood glucose monitoring in long-term care facilities, likelihood of acquiring hepatitis B infection, its complications or chronic sequelae, and likelihood of immune response to vaccination;
  - persons with end-stage renal disease, including patients receiving hemodialysis; persons with HIV infection; and persons with chronic liver disease;
  - household contacts and sex partners of hepatitis B surface antigen-positive persons; clients and staff members of institutions for persons with developmental disabilities; and international travelers to countries with high or intermediate prevalence of chronic HBV infection; and
  - all adults in the following settings: STD treatment facilities; HIV testing and treatment facilities; facilities providing drug-abuse treatment and prevention services; health-care settings targeting services to injection-drug users or men who have sex with men; correctional facilities; end-stage renal disease programs and facilities for chronic hemodialysis patients; and institutions and nonresidential daycare facilities for persons with developmental disabilities.
- Administer missing doses to complete a 3-dose series of hepatitis B vaccine to those persons not vaccinated or not completely vaccinated. The second dose should be administered 1 month after the first dose; the third dose should be given at least 2 months after the second dose (and at least 4 months after the first dose). If the combined hepatitis A and hepatitis B vaccine (Twinrix) is used, give 3 doses at 0, 1, and 6 months; alternatively, a 4-dose Twinrix schedule, administered on days 0, 7, and 21–30 followed by a booster dose at month 12 may be used.
- Adult patients receiving hemodialysis or with other immunocompromising conditions should receive 1 dose of 40 µg/mL (Recombivax HB) administered on a 3-dose schedule at 0, 1, and 6 months or 2 doses of 20 µg/mL (Engerix-B) administered simultaneously on a 4-dose schedule at 0, 1, 2, and 6 months.

14. Selected conditions for which Haemophilus influenzae type b (Hib) vaccine may be used

- 1 dose of Hib vaccine should be considered for persons who have sickle cell disease, leukemia, or HIV infection, or who have anatomic or functional asplenia if they have not previously received Hib vaccine.

15. Immunocompromising conditions

- Inactivated vaccines generally are acceptable (e.g., pneumococcal, meningococcal, and influenza [inactivated influenza vaccine]), and live vaccines generally are avoided in persons with immune deficiencies or immunocompromising conditions. Information on specific conditions is available at http://www.cdc.gov/vaccines/pubs/acip-list.htm.

Courtesy: Centers for Disease Control and Prevention

Face to face with Prof. Dr. Naseem Salahuddin

Diplomat, American Board of Internal Medicine
Aga Khan University/ Indus Hospital Karachi
Interviewed by: Dr. Muhammad Salman

A noble profession – Medicine is not just a job or a profession, it is a lot more than that. For some, medicine is a noble calling that captures heart and soul

It is a passion that fuels the desire of a person to help others, do good!

Dr. Naseem Salahuddin, a well known and respected figure among medical professionals of Pakistan and abroad is known for her hard work and devotion for the betterment of common people of Pakistan. Her services in the field of medicine and particularly 'Infectious diseases' has been acknowledged world wide and a source of inspiration for many.

Q. No.1- Please tell us about yourself?

I am presently Professor and Head, Dept of Infectious Diseases, and Director TB Clinics at The Indus Hospital, Karachi, and non-full time faculty at the Aga Khan University Hospital (AKUH).

Q. No.2- Your professional experience: Tell us about your background as a doctor: education and experience. What are your specialties/ expertise?

I did MBBS from FJ College, Lahore, and then left for USA to do my internship and residency in Internal Medicine from Henry Ford Hospital, Detroit, Michigan. I qualified for American Board of Internal Medicine, and Fellowship in Infectious Diseases (ID). Thereafter I returned to Karachi to join Liaquat National Hospital (LNH) as full time Consultant in Internal Medicine and non-full time Consultant at AKUH. At LNH, I established and directed a structured Medical Residency Training Program and the section of ID. In 2007, I left LNH to join Indus Hospital where I am working presently.

My special interests in ID are AIDS, Rabies prevention, TB and Multi Drug Resistant TB (MDR). MDR TB is an extremely serious condition that threatens society, and is clearly the outcome of poor diagnosis and treatment of TB.

I believe I have made some contribution to the improvement in management of dog bites and Rabies in Pakistan. I am Member, Expert Panel for Rabies for WHO, and President of Rabies in Asia (Pakistan Chapter).

I am the founder of the Infectious Diseases Society of Pakistan (IDSP), which is now into its fifteenth year and continues to flourish. I also started the Infectious Diseases Journal of Pakistan (IDJP). Competent and enthusiastic members are now running both IDSP and IDJP.

Q. No.3- Why did you choose this career?

It was to fulfill a childhood desire. There was no parental or societal pressure but I received great support from my family.

Q. No.4- Why did you choose this specialty?

ID is one of the most exciting, dynamic and progressive fields in medicine. It incorporates a vast expanse of knowledge and is intellectually stimulating. Unlike surgical specialties there are no physical tasks or procedures involved. One only needs a listening ear, a stethoscope and a brain to sort out the enigmas of a complex disease. ID requires a great deal of reading, studying and computing in one's brain.

In fact, ID is not an isolated subject: it is an integration of clinical medicine, microbiology, pharmacology, public health and epidemiology. As a stand-alone ID stretches across all body viscera, tropical and travel medicine. No other specialty can match this diversity!

Q. No.5- What are the key challenges of this (field of medicine)? What are your personal challenges?

As a developing, poverty stricken country, Pakistan is faced with enormous challenges of IDs. Sadly, IDs are being managed by physicians who have not kept pace with changing patterns of diseases, diagnostic tests and management. Drug resistance is threatening to make once easy-to treat infections now untreatable. Common infections like typhoid, malaria, TB are no longer treatable with antimicrobials as they once were. As the population continues to proliferate, civic facilities decline. Environmental filth, unclean water supply, crowded, poorly ventilated homes and economic pressures cause a proportionate increase in IDs in children and adults in urban and rural societies. In a rush to see large number of patients, physicians spend little time with patients, misdiagnose and mistreat them. Viral infections are not recognized and antibiotics are prescribed randomly. As a result the patient's misery is prolonged, and drug resistance amplified.

Ironically, there are very few trained ID specialists in the country. I would like to see the specialty of ID expand. Family physicians, surgeons, pediatricians, diabetologists, in fact all clinicians should practice evidence based ID so that they can take better care of their patients.

Q. No.6- What is the greatest achievement of being a doctor?

Watching a fever resolve, see a wound heal, and a smile on the face of a recovered patient.

Q. No.7- What advice can you give to people who want to follow your path?

I would like to get more clinicians into the fold. A 2-year ID fellowship, approved by CPSP is open to any FCPS graduate in Internal Medicine. There are four designated centers, which give excellent comprehensive training under highly qualified and motivated supervisors to prepare them for a second FCPS. We look forward to having more and more ID fellows so that we can expand this much-needed discipline.

Quiz

Infectio

1. What percentage of Cholera can be successfully treated with ORS?

a. 100%
b. 80%
c. 65%
d. 40%

2. Regarding Cholera vaccine?

a. Parenteral vaccine is recommended by WHO
b. Oral vaccine has high occurrence of adverse effects
c. Individual 2 years & above can take it safely
d. Oral cholera vaccine is only effective tool for prevention

3. Naegleria infects brain through?

a. Skin
b. Mouth
c. Nose
d. Ear

4. One of the following is not associated with Naegleria risk?

a. Swimming in hot spring
b. Ablution with contaminated tap water
c. Drinking tap water
d. Using Neti pots for irrigating nasal cavity

5. PPSV23 pneumococcal polysaccharide is not recommended for?

a. Adult < 65years & younger with no comorbidity
b. Adult > 65 and older
c. Residents of nursing home
d. Immuno compromised patients