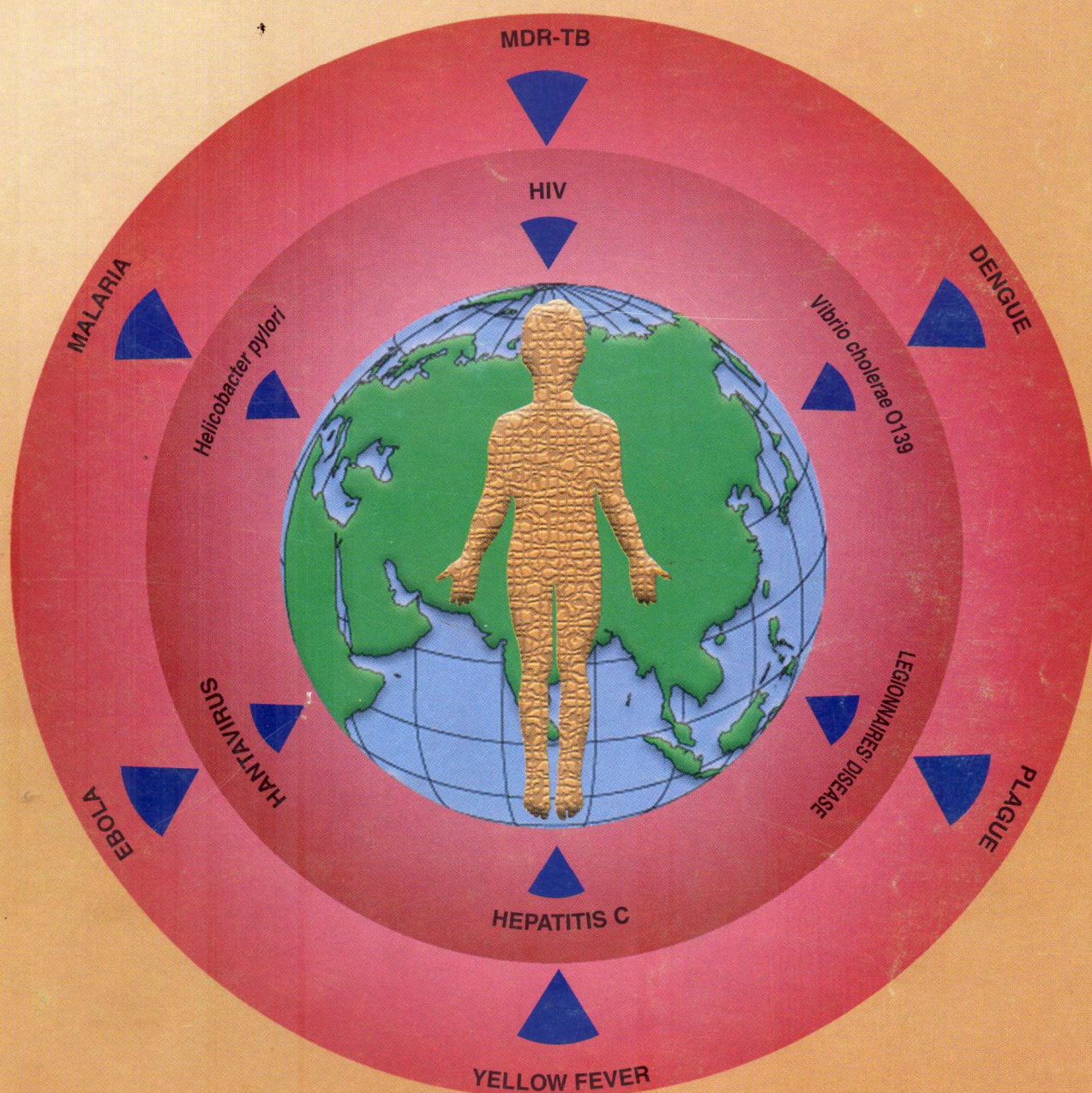


# The **ORION**

Medical Journal

**ERID**

Vol 3 May 1999



## The World Faces Emerging and Reemerging Infectious Diseases



ORION LABORATORIES LIMITED

MEDIQUIZ



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*Cover Illustration:* A pictorial depiction of the threat of ERID to mankind and the world.

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# Editorial

Inspired by the continued support and appreciation from our valued readers, we are presenting our third issue of "The ORION". We hope that our previous issue on *Gene Therapy* was a subject of great interest among doctors community and we expect that it soon becomes a clinical reality for us so that we can better alleviate the sufferings of mankind.

In this issue, we have chosen *Emerging and Reemerging Infectious Diseases* (ERID) as the main theme considering the threat and challenge of ERID to the whole world.

The spectrum of infectious diseases is changing rapidly in our society and environment. Worldwide explosive population growth coupled with expanding poverty and urban migration, increased international travel and rapid changes in technology – all these factors affect our risk of exposure to the infectious agents with which we share our environment. Contrary to past optimism we remain vulnerable to a wide variety of new and resurgent infectious diseases. Our vulnerability to ERID has been demonstrated time and again in recent outbreaks of AIDS, MDR-TB, malaria, plague, O139 cholera, hantavirus pulmonary syndrome etc. in different geographic locations. In many parts of the world, ERID has reversed the achievements gained in health sector with broader socioeconomic implications for the regions. To combat the scourge of ERID, an international multidisciplinary collaborative effort is urgently needed.

In this issue in view of the suggestion by our esteemed readers, we have changed the format of MediQuiz to MCQ style. We hope that this will be appreciated by you.

Wishing you all the best

Dr ATM Azizur Rahman

Manager

Medical Services Department



## MSD News

IN THE FIRST QUARTER OF 1999, THE MEDICAL SERVICES DEPARTMENT (MSD) OF ORION LABORATORIES LTD. HAS ARRANGED PROGRAMMES IN DIFFERENT HOSPITALS AND INSTITUTIONS TO SERVE THE INTEREST OF MEDICAL PROFESSIONALS BY PROVIDING RELEVANT INFORMATION.

### CLINICAL MEETING: IMPORTANCE OF ZINC FOR MATERNAL AND CHILD HEALTH

One of ORION'S most recent products **FERROLIN TR** has the unique property of having *Zinc sulphate* in addition to *Ferrous sulphate* and *Folic acid*. Accordingly, MSD arranged a number of clinical meetings in the following venues to bring into focus the significance of Zinc for Maternal and Child Health:

Bangladesh Medical College Hospital (BMCH) on 15-02-99 chaired by Prof. Syed Ershad Ali (Head, G&O Dept.), BIRDEM on 27-02-99 chaired by Prof. TA Chowdhury (Sr. Consultant, G&O Dept.), Dhaka National Medical College Hospital (DNMCH) on 4-03-99 chaired by Dr. MR Azad (Director), Bangabandhu Sheikh Mujib Medical University (BSMMU) on 7-03-99 chaired by Prof. Shahla Khatun (Chairperson, G&O Dept.), Holy Family Red Crescent Hospital (HFRCH) on 11-03-99 chaired by Col. Labibuddin Khan (Director), Dhaka Medical College Hospital (DMCH) on 15-03-99 chaired by Prof. Atika Begum (Head, MAT-IV), Training Institute of Maternal and Child Health, Dhaka on 23-03-99 chaired by Dr. Rahima Ali (Superintendent), DMCH on 24-03-99 chaired by Prof. Mahmuda Khatun (Head, MAT-II), Mohammadpur Fertility Service and Training Centre on 25-03-99 chaired by Dr Sabera Rahman (Director), DMCH on 11-04-99 chaired by Prof. Anowara Begum (Head, MAT-I),

Unit-I, II & III, G&O Dept. of Sir Salimullah Medical College Hospital (SSMCH) on 12-04-99 chaired by Prof. Rehana Begum (Head, G&O Dept.), DMCH on 15-04-99 chaired by Prof. Sayeba Akhter (Head, MAT-III) and Unit - I & II, G&O Dept., MMCH, Mymensingh on 19-04-99 chaired by Prof. Jinatun Noor (Head, G&O Dept.). Moreover, a meeting focusing on the ongoing clinical trial in MU-I, DMCH on triple therapy against *Helicobacter pylori* was held on 14-03-99 chaired by Prof. Firdous Ara J. Janan, Head of the Department of Medicine, DMCH.

### LAUNCHING OF NEW PRODUCTS

ORION has immense pleasure in announcing that it has launched a new product named Capsule **ORIXYL 500** (Amoxycillin 500mg) first ever of its kind in Bangladesh from March, 1999. This product will not only provide effective clinical application but also ensure better patient's compliance and become real cost effective. Another two products Capsule **ORFENAC TR** (Diclofenac sodium Timed Release) and Tablet **EC** (combined Vitamin E & C) - also for the first time in Bangladesh - have been introduced by ORION with a view to offering better clinical benefit and treatment.





# The World Faces Emerging and Reemerging Infectious Diseases

Dr Mahbubur Rahman, Dr ATM Azizur Rahman

Infectious disease accounts for almost half of mortality in developing countries in contrast to less than 10% in the developed world as a primary cause of death. Changes in society, environment and technology with diminished effectiveness of certain approaches to infectious disease control has propelled the world into a new era, the spectrum of infectious diseases is expanding and many infectious diseases are reemerging. "Emerging infectious diseases are diseases of infectious origin whose incidence in humans has increased within the past two decades or threatens to increase in the near future."<sup>1</sup>

Reemergence of infectious diseases may occur because of the development of antimicrobial resistance in existing agents (e.g., gonorrhea, malaria, pneumococcal disease) or breakdowns in public health measures for previously controlled infections (e.g., cholera, tuberculosis, pertussis).

With the significant public health successes against infectious diseases in the 20th century due to modern scientific advances such as safe handling of food and water, improvement in environmental sanitation, development of vaccines and the

integration of childhood immunisations in the national health programmes of all countries, and the discovery, development and popularisation of antimicrobial agents/drugs, it was expected that infectious diseases were no more threat to human beings, particularly in the industrialised nations.<sup>2</sup> The incidence of childhood diseases such as polio, diphtheria and whooping cough was declining due to vaccines. Fast-acting, effective antimicrobial agents were used to combat fatal bacterial diseases such as pneumonia and meningitis.

Chemical pesticides like DDT were lowering the incidence of malaria by controlling the population of mosquitoes. In spite of initial achievements, as it turned out, our euphoria regarding the reduction of the threat and burden of infectious diseases was premature. Today most health pro-

professionals realise that new microbial threats are appearing in significant numbers while old diseases thought to be under control are reemerging. Whether due to diseases previously unknown to medical science, such as acquired immunodeficiency syndrome (AIDS), O139 cholera, Hantavirus pulmonary syndrome or the morbillivirus pneumonia or the return of known scourges like plague, cholera and tuberculosis, infectious diseases are in a state of flux globally raising serious concern. Many people are aware

## CATEGORIES OF EMERGING AND REEMERGING INFECTIOUS DISEASES:

E  
M  
E  
R  
G  
I  
N  
G

### Newly identified pathogens and syndromes:

HIV/AIDS, Hepatitis C, *Vibrio cholerae* O139 cholera, Cryptosporidiosis, *Helicobacter pylori* associated peptic ulcer diseases, Hantavirus pulmonary syndrome, Lyme disease, Legionnaires' disease

Evolution in existing organisms or new techniques identified existing organism or transmission to humans from other hosts

R  
E  
M  
E  
R  
G  
I  
N  
G

### Reemergence of old diseases:

Cholera, dengue, yellow fever, plague, Ebola haemorrhagic fever

Spread of old disease to new area or population, ecological changes, environmental resources that harbour pathogens and breakdown of public health measures

### Emergence of organisms resistant to antimicrobial agents:

Tuberculosis, malaria, streptococcal infections, gonorrhoea, shigellosis, *Salmonella* infections, staphylococcal and enterococcal infections

Overuse or inappropriate use of antimicrobial agents  
Use of antimicrobial agents in animals  
Crowding and increased population  
Poor sanitation  
Immunocompromised or malnourished population

Dr Mahbubur Rahman, MBBS, MSc, PhD  
Dr ATM Azizur Rahman, MBBS, Manager, MSD



of the epidemic of AIDS and related increase in many infectious diseases throughout the world. Emerging infectious diseases are not however restricted to dramatic epidemics of new or resurgent diseases; the irrational use of antibiotics and other chemotherapy can cause common bacterial pathogens to develop resistance to antimicrobial agents, thereby creating new challenges to their treatment and control. Many strains of *Shigella dysenteriae* type 1 and gonococci are resistant to multiple drugs as are the strains of *Staphylococcus* and *Streptococcus pneumoniae*. Emergence and spread of multidrug resistant tuberculosis in India, Nepal and Thailand is a matter of concern.

### Changes contributing to the Emergence & Reemergence of Infectious Diseases

The contributing factors to the emergence of new or emerging infectious disease include genomic changes of existing pathogens, ecological alteration

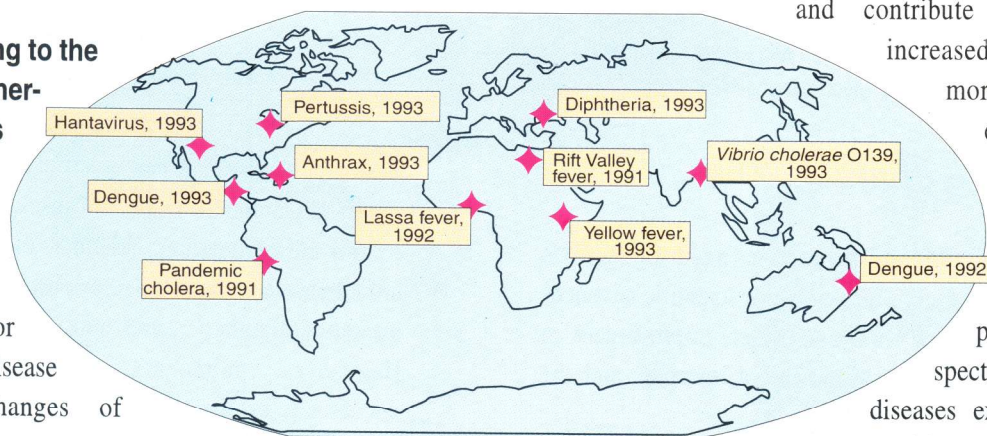
**Table 1. CHANGES CONTRIBUTING TO THE EMERGENCE & REEMERGENCE INFECTIOUS DISEASES**

| Changes                                                                    | Contributing factors                                                                   | Diseases                                                        |
|----------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-----------------------------------------------------------------|
| 1. Migration of people from rural to urban areas                           | Overcrowding, poor hygiene, inadequate sanitation<br>Unclean water                     | Cholera, Shigellosis<br>Cryptosporidiosis                       |
| 2. Changes in technology                                                   | Better detection                                                                       | <i>Helicobacter pylori</i> infections                           |
| 3. Ecological changes<br>i) Earthquake<br>ii) Dams and irrigation channels | Migration of <i>Y. pestis</i> infected rats to human dwellings<br>Growth of mosquitoes | Plague (India, 1993)<br>Malaria and Japanese encephalitis (SEA) |
| 4. Changes in human behaviour                                              | Multiple sexual partners<br>Intravenous drug users                                     | HIV/AIDS, Syphilis                                              |
| 5. Industry of mass food production and distribution                       | Contamination during handling                                                          | <i>E. coli</i> O157H7 diseases<br>Salmonellosis                 |
| 6. Reforestation                                                           | Increased host (deer) for vector (deer ticks)                                          | Lyme's disease (USA)                                            |
| 7. Adaptive change in pathogens                                            | Antibiotic resistant organisms                                                         | Drug resistant Malaria and Tuberculosis, Nosocomial Infections  |
| 8. Break down in public health services                                    | Increase in pathogens/vectors/hosts                                                    | Malaria<br>Meliodosis                                           |

(natural or man-made), advances in industry and technology, changes in human demography and behaviour, economic development and land use, international travel and commerce, changes and breakdown of public health measures, increased population and lack of safe water and food supplies. (Table 1)

### The Threat of Emerging and Reemerging Infectious Diseases

Infectious diseases increasingly threaten public health and contribute significantly to increased morbidity, mortality and escalating health care cost throughout the world. The number of pathogens and spectrum of infectious diseases expand every year with the changes in environment, technology,



**Fig 2.** Emerging and Reemerging Infectious diseases in the 1990s



society, pattern of lifestyle, increased population and public health measures.

Worldwide people are at risk to develop acquired immunodeficiency syndrome (AIDS), tuberculosis, hepatitis C, cholera infections caused by multiresistant pathogens and other infecting agents. Nobel laureate Dr. Joshua Lederberg has stated, "The microbe that felled one child in a distant continent yesterday can reach yours today and seed a global pandemic tomorrow." Old persons, children attending day care centres, persons living in institutional settings (hospitals, nursing homes) and patients with lower immunity (patients with cancer, HIV/AIDS, organ transplantation) are at increased risk for emerging infections. Intake of contaminated foods and water markedly increases the risk for enteric infections, such as cholera, hepatitis A, cryptosporidiosis, shigella and *E coli* O157:H7 diseases. Travel and exposure to certain animals/insects may increase risk for travel-associated illness and zoonotic diseases (hantavirus pulmonary syndrome, plague, Chaga's disease, kala-azar etc.) respectively.

### The Burden of Emerging and Reemerging Infectious Diseases

Infectious diseases remain the leading cause of death worldwide. Emerging and reemerging infections contribute significantly to the ongoing burden of infectious diseases by increasing the health care cost and days of disability. For

example, the estimated cost of common infectious diseases in the United States exceeds US\$ 120 million per year.

The higher prevalence of emerging and reemerging infectious diseases in Southeast Asia (SEA) raises concern among health professionals. For example, the region accounts for 50% of 8.7 million cases of tuberculosis worldwide and 70% of the registered leprosy cases of the world. New infections such as HIV/AIDS and cholera caused by *Vibrio cholerae* O139 raise serious concern. In this region, more than 2 million adults have been infected with HIV according to WHO. As of 1995,

more than 20 000 HIV infected cases have been reported. By the end of century, 8-10 million men, women and children are likely to be infected with HIV infection within the region accounting for more than 25% of cumulative HIV infections in the world. The new strain *Vibrio cholerae* O139 emerged first in October 1992 during a large outbreak in Madras, India. Since then it has spread rapidly within India and Bangladesh infecting large number of people with significant mortality. Cases of O139 cholera have been reported also from Myanmar, Nepal, Pakistan, Sri Lanka, Thailand and other neighbouring countries. Malaria, kala-azar and plague

have reemerged in SEA. More than 3 million malaria cases are reported in the region each year. The proportion of *Plasmodium falciparum* malaria increased up to 40%. Drug resistant malaria is responsible for large number of case fatalities, particularly in forest and forest fringe areas of the region. Since 1987, kala-azar has become an important health problem in rural areas of Bangladesh, India and Nepal. In

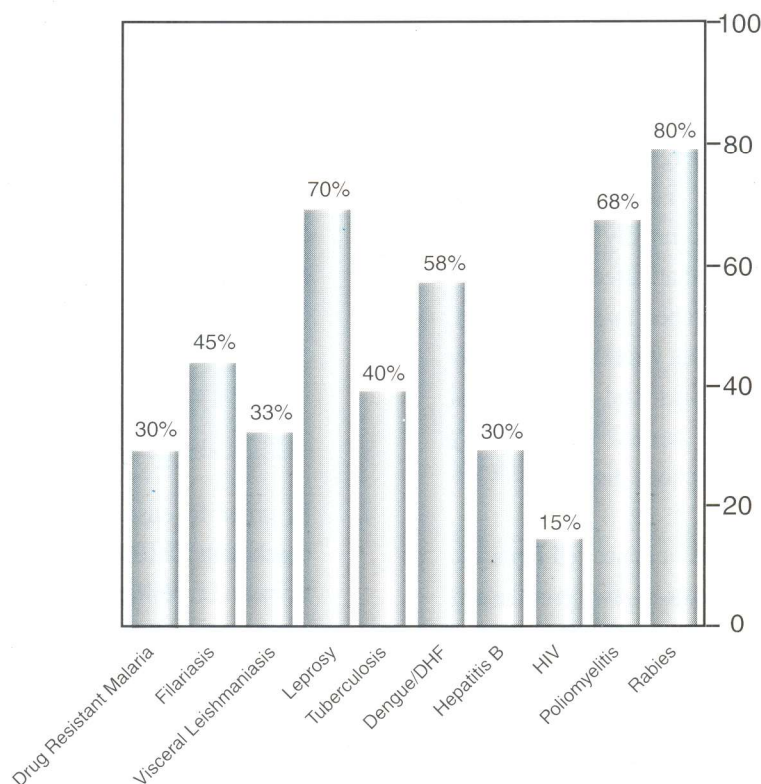


Figure 2. Communicable Disease Burden in Southeast Asia (SEA) vis-a-vis Globally, 1995



Bangladesh 30 million people live in kala-azar affected area. In 1994, the outbreak of plague occurred in Maharashtra and Gujarat of India and raised a global concern. Natural foci of plague in SEA also exists in Myanmar, Indonesia and possibly in Nepal. There was no report of plague in the recent past in Bangladesh. The other emerging diseases in SEA include dengue/dengue hemorrhage fever, Japanese encephalitis, viral hepatitis (A, B and E), acute respiratory infections, hantavirus haemorrhagic fever, drug-resistant bacterial infections (nosocomial infections, *Salmonella* infections, Shigellosis) and some vaccine-preventable diseases (diphtheria, whooping cough).

### Control and prevention of emerging and reemerging infections diseases

For the prevention and control of emerging and reemerging infectious diseases, a combination of normal, regional and global approach is urgently required to rapidly build a strong defense against infectious diseases that affect or threaten public health. We should also remember that in principle, many infectious diseases are manageable with the old standby of vaccines, passive immunoglobulins and antimicrobial agents. However, programmes are needed to effectively address emerging and reemerging infectious diseases:

- Surveillance of infectious diseases: a concerted domestic and global surveillance and diagnosis of disease outbreaks and endemic infections.
- Strengthening laboratory capacities and services in each country, particularly in developing countries
- Enforcement of safe water and food supplies
- Vector management and monitoring
- Epidemic preparedness and responses
- Public and professional education
- Scientific research on causes of diseases, pathogenic

mechanisms, defence mechanism, vaccines and antimicrobial agents

- Adequate financial support and training of health professionals
- A global network monitored by World Health Organisation or similar organisations

In conclusion ERID not only have worldwide health implications but is also capable of disrupting commerce and industry. The appearance of the ERID has set back the significant progress achieved in health development during the recent years in SEA. The spread of these diseases also has significant social and political implications.

Thus it needs effective surveillance from epidemiological investigations and building up of adequate laboratory capabilities and it also emphasises the need for maintaining an ecological and environmental integrity in various developmental activities. It is very important to formulate country-specific strategies and action plans to anticipate, recognise quickly and respond rapidly to the threat of these diseases.

In order to ensure sustainability in development strategies combating ERID should form an integral part of the existing infrastructure, particularly infectious disease control programmes and should build on capacities that already exists. ■

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# The Challenge of MDR-TB

Dr ABM Abdullah

Tuberculosis (TB) is a disease that is present in the world for a long time. It was present before, is present now and probably will persist in future for a few decades; though there is a hope for its total eradication from many countries of the world.

It is a reemerging disease with a great threat for both developing and developed countries especially after detection of Multi-drug Resistance Tuberculosis (MDR-TB).

TB was a great killer before the advent of chemotherapy. After 1950, it was no more considered as a threat as it was easily treatable but again it has reemerged as a great killer with the emergence of MDR-TB which is difficult to treat because of lack of available drugs, cost, toxicity and prolonged duration of therapy etc.

## HIV and MDR-TB

MDR-TB is a burning problem in HIV persons. Dramatic outbreak of MDR-TB infected patients in the USA and Western world focused international attention on the emergence of MDR-TB.

When MDR-TB occurs in AIDS patients, life expectancy shortens to 1-3 months only.

## Definition

**Multi-Drug Resistant Tuberculosis (MDR-TB):** Unlike other multi-drug resistant diseases the definition of MDR-TB is a bit different. MDR-TB means "mycobacterium organism is resistant to at least isoniazid (INH) and rifampicin".

**Strain W:** It is the strain of *Mycobacterium tuberculosis* resistant to all of the 7 anti-TB drugs namely INH, rifampicin, streptomycin, kanamycin, ethionamide and rifabutin.

## Types

MDR-TB is of two types:

- **Primary resistant :** When a patient is infected with a drug resistant TB from the beginning of the disease. It is acquired from other infected person with MDR-TB and reflects the status of TB bacilli in the community.

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- **Secondary/Acquired resistant:** It is developed in a patient previously treated with anti-tuberculosis drugs. It is almost entirely man-made phenomenon because of inappropriate drugs or insufficient dose, lack of compliance, irregular drug supply etc. and reflects effectiveness of TB control programme.

## Epidemiology

One-third of the world population is now infected with tuberculosis bacillus. Each year an estimated 8 million cases of TB occurs, leading to 3 million death.

After several outburst of MDR-TB in different countries, WHO, CDC and IUATLD took a global project of TB-drug resistance surveillance in 35 countries from 5 continents covering 20% of world population. The main findings are summarised below:

| Type of Resistance | Total Resistance | Range of Resistance | MDR-TB average | Resistance to all 4 drugs (average) |
|--------------------|------------------|---------------------|----------------|-------------------------------------|
| Primary            | 10.4%            | 2-41%               | 1.4%           | 0.2%                                |
| Secondary          | 36%              | 5.3-100%            | 13%            | 4.4%                                |

Among the drugs, resistance to INH was found to be the highest.

Various studies were done to find out the drug resistance pattern in Bangladesh. They are summarized below:

| Place of Study    | No. of Patient | Total Resistance | Highest Resistance | 2nd highest Resistance | MDR   |
|-------------------|----------------|------------------|--------------------|------------------------|-------|
| IDCH              | 116            | 49.13%           | H - 32.75%         | R - 20.685             | 9.9%  |
| IDCH              | 131            | 43.5%            | H - 16.4%          | R - 16.4%              | 9.9%  |
| Shamoli TB clinic | 91             | 19.8%            | R - 19.8%          | H - 2.2%               | 2.2%  |
| Damien Foundation |                |                  |                    |                        |       |
| Total             | 645            | 18.60%           | H - 12.25%         | R - 2.74%              | 2.02% |
| Primary           |                | 10.96%           | H - 5.36%          | R - 0.47%              | 0.23% |
| Acquired          |                | 33.80%           | H - 25.93%         | R - 7.4%               | 5.56% |



## Aetiology

The aetiology of MDR-TB is multifactorial and may be conveniently divided into following groups:

- **Iatrogenic:** It is one of the most important factor and is due to incomplete prescription, insufficient dose, incorrect duration, lack of counselling/motivation and improper follow-up.
- **Patient-made:** Patient's poor compliance is a very important factor. It is due to lack of proper understanding, ignorance, poverty etc. Many patients stop treatment in a short time after feeling a sense of wellbeing. Some also discontinue treatment due to side effects of the anti-TB drugs without consulting the physician.
- **Administrative problems:** These includes irregular and insufficient supply of drug, lack of attention, irregular tracing of defaulters, manpower shortage etc.

## Mechanism of Resistance

Mycobacteria becomes drug resistant by spontaneous genetic mutation which is not related to drug exposure. Rate of development of resistance to different drugs is estimated to be  $10^{-6}$  for INH,  $10^{-8}$  for Rifampicin,  $10^{-6}$  for Ethambutol and  $10^{-5}$  for Streptomycin. Probability of developing resistance to more than one drug is the product of individual rate e.g. for Rifampicin and INH it is  $10^{-8} \times 10^{-6} = 10^{-14}$ . Now a patient with cavitary TB usually has a bacterial load of  $10^{8-9}$ . Therefore the development of drug resistance to a single drug is highly probable in this patient and this forms the rationale for combination chemotherapy. The bacterial load is enormous in patients with bilateral extensive pulmonary TB, disseminated TB and tuberculous abscess. When bacteria is resistant to one drug e.g. INH which is not suspected and is treated with two drugs e.g. Rifampicin and INH (as in continuation phase of TB therapy), only one further mutation results in MDR-TB bacilli. Inappropriate use of anti-TB drugs results into killing of sensitive bacteria with selection of resistant bacteria which ultimately leads to MDR-TB emergence.

## How to Diagnosis MDR-TB?

A high index of initial suspicion is the crucial factor. For the diagnosis: a) If a patient with TB with persistent symptoms (fever, weight loss, chronic cough & haemoptysis) does not respond to standard therapy for 2 months or more, b) Patient previously treated with anti-TB drugs, c) Patient with a history of contact with drug-resistant patient or d) There are worsening of

symptoms following therapy should arouse a high degree of suspicion.

## Diagnostic Criteria:

- Culture of AFB: Resistant
- Culture remaining +ve after 3 months of treatment
- Smear remaining +ve after 5 months of treatment

## How to Manage a Patient with MDR-TB:

Management of MDR-TB is difficult, expensive and lengthy because of lack of available drugs, cost, toxicity etc.

### General Management:

For management of MDR-TB the following general points should be considered:

- ◆ Detailed history of previous drug usage including dose, duration, compliance, response, side-effects, cause of discontinuation (if any)
- ◆ Patient's age, body weight, economic status, presence of primary disease like Diabetes mellitus, HIV infection etc.
- ◆ Availability of drugs, efficacy, cost, side-effects etc.
- ◆ Result of culture sensitivity, motivation and counselling

### Specific Treatment:

## First line anti-TB drugs

| Drug             | Action                | Min. dose<br>mg/kg/day | Min. & Max.<br>for MDR-TB |
|------------------|-----------------------|------------------------|---------------------------|
| INH (H)          | Bactericidal          | 5                      |                           |
| Rifampicin (R)   | Bactericidal          | 10                     |                           |
| Pyrazinamide (Z) | Bactericidal          | 15                     | 1200-1600                 |
| Ethambutol (E)   | Bacteriostatic        | 15                     | 1000-1200                 |
| Streptomycin (S) | Bactericidal          | 15                     | 750-1000                  |
| Thiacetazone (T) | Weakly Bacteriostatic | 2.5                    | Not in use                |



## Second line anti-TB drugs

| Drug                         | Action                               | Dose<br>mg/kg/day                                               |
|------------------------------|--------------------------------------|-----------------------------------------------------------------|
| Aminoglycosides              | Kanamycin<br>Amikacin<br>Capreomycin | Bactericidal<br>750-1000                                        |
| Ethionamide<br>Prothionamide | Bactericidal                         | 500-750                                                         |
| PAS                          | Bacteriostatic                       | 10,000-12,000                                                   |
| Quinolones                   | Ciprofloxacin                        | Weakly bactericidal<br>1000-1500<br>(80-90%<br>bioavailability) |
|                              | Ofloxacin                            | 600-800<br>(90-98%<br>bioavailability)                          |
| Cycloserine<br>Terizidone    | Bacteriostatic                       | 500-750                                                         |
| Macrolides                   | Azithromycin<br>Clarithromycin       | Active against atypical<br>mycobacteria                         |
| Clofazimine                  | Not recommended<br>by WHO for MDR-TB |                                                                 |
| Amoxiclav                    | Investigational                      |                                                                 |
| Rifabutin<br>Rifapentine     | Bactericidal                         | Long acting<br>weekly dose                                      |

### Principles of Management

- The general principle is to add at least 2 or preferably 3 drugs which are sensitive or not used previously.
- Before starting treatment it is preferable to sent sputum for culture sensitivity test.
- First line drugs are preferred
- Resistant drugs should be excluded
- Treatment should be started in a hospital to observe the side-effects
- 4 to 7 drugs may be started together

### How long the therapy should be continued?

- *Intensive (Bactericidal) phase:* For at least 3 months or till culture sensitivity becomes negative. Aminoglycosides for 3 months or till side-effects develops.

- *Continuation (Sterilizing) phase:* Should be at least 18 months after sputum becomes negative

Total duration of treatment may be upto 24 months or even 36 months.

### Follow up

Follow up is very important to ensure patient's compliance, response to treatment and appearance of side effects. Usually follow up is done after first week of treatment and subsequently on a monthly basis till completion of the therapy. Even in the USA, one fourth of patients with TB do not complete the course of therapy.

Investigations done during follow up are: sputum for AFB smear, ESR, and body weight recorded at each visit, culture done at 2 months or monthly until culture is negative, then at the end of treatment; chest X-ray is done at the beginning of 2 months and at the end of treatment.

### Preventive Measures to Combat MDR-TB

There is no alternative to the age old saying: "Prevention is better than cure." Proper prescription and strict compliance of the patient is extremely essential which is the best way to achieve the prevention of MDR-TB. Identification and isolation of patient, quick treatment with standard drugs in proper dose is the mainstay of disease control. According to WHO, DOTS (Directly Observed Treatment of Short Course Chemotherapy) are usually advocated. Once MDR-TB is diagnosed or isolated the patient must get proper attention and vigorous treatment should be started. Availability of drugs specially the second line of anti-TB drugs must be ensured which may be necessary for MDR-TB.

### Points to remember during treatment of TB

- Before starting the drug therapy, proper counselling is essential. The patient should be explained thoroughly regarding the disease, future problems to the patient himself, to the family as well as to the community
- Patient compliance is very important which should be emphasised to the patient strictly
- Standard drugs, proper dose and appropriate duration should be maintained
- Probable side effects should be explained to the patient and the patient should be advised not to discontinue the drugs without consulting the physician
- Regular follow up is an essential part of treatment of TB

### Conclusion

TB is a great threat to every nation. Now-a-days reemergence of MDR-TB is a new burden. High prevalence of MDR-TB is the result of therapeutic anarchy which threatens our future. We should check it before it goes out of control.



# Reemergence of Malaria

Dr James Jacob Ribero

Contrary to previous expectations, malaria is far from being eradicated. Indeed, the incidence of malaria is greater than that was 40 years ago. Malaria has become a clear example of a reemerging disease.

## Failure of Eradication Programme

WHO and other international organisations committed themselves to eradicate malaria through the use of antimalarial drugs e.g. chloroquine and residual insecticides e.g. DDT. This later proved to be impossible because of emergence of chloroquine resistance in *Plasmodium* and insecticides resistance in *Anopheles* mosquitoes. Additionally there were problems with logistics, planning, resource allocation and lack of operational research. For example, malaria eradication programme was mainly confined to Southeast Asia and South America instead of sub-Saharan Africa where transmission as well as morbidity and mortality of malaria is highest. It was not also appreciated at that time that malaria is not an ideal candidate for eradication like smallpox (see below).

**Criteria favouring eradication of a disease: Comparison between Smallpox & Malaria**

| Criteria                                         | Smallpox   | Malaria                   |
|--------------------------------------------------|------------|---------------------------|
| Distinct clinical signs/symptoms                 | Yes (rash) | No (fever, malaise)       |
| Subclinical human illness                        | No         | Yes                       |
| Seasonal variation (periods of low transmission) | Yes        | Yes                       |
| Effective vaccines                               | Yes        | No                        |
| Life-long immunity after infection               | Yes        | No (frequent reinfection) |
| Non-human vector                                 | No         | Yes                       |
| Non-human reservoir                              | No         | No                        |

## Antimalarial Drug Resistance (Table 1)

The factors responsible for antimalarial drug resistance are not fully understood. Single drug based treatment and suboptimal dose usage in malaria eradication campaign are thought to be the main factors. Chloroquine was the only antimalarial drug used by most national malaria programmes and was mass distributed to the entire populations. In fact, chloroquine was actually added to table salt in many programmes. Also many programmes used suboptimal dose schedule to economise and patients often shared their pills with

other family members especially children. Thus there was a tremendous *selection pressure* on malarial parasite for the last 50 years which ultimately resulted into emergence of drug resistance. Similar scenario occurred with pyrimethamine and other antimalarial drugs.

## Insecticide Resistance

Insecticides such as DDT spraying was one of the central strategy used in malaria eradication programme which initially gave rise to much success. However, subsequent development of vector resistance to DDT was one of the most important reasons of the failure of the eradication programme. To make the matter worse, DDT was later shown to have disastrous environmental and ecological effects which led to virtual abandonment of its use. Alternatives to DDT for vector control includes pyrethroid insecticides (permethrin, deltamethrin) but resistance to them is emerging because of their extensive use in agriculture and cross-resistance to DDT.

## Vaccines against Malaria (Table 2)

Unavailability of an effective vaccine is one of the stumbling block in eradication of malaria. Development of vaccine is being considered now as an alternative strategy after failure of anti-malarials and vector control. Several types of vaccines against different phases of the life-cycle of malarial parasite are under active research. These include: *Sporozoite vaccines* for prevention of infection, *Merozoite vaccines* for prevention of disease development and *Gametocyte vaccines* for prevention of transmission of parasite. However at the present time, there is no vaccine which has achieved 80% or more success rate which is necessary for the eradication of malaria.

## Conclusion

There is clearly a conflict between strategies for malaria eradication. One group of investigators advocate that the use of bednet and curtains will be more effective in control and eradication of malaria. Other investigators consider this to be inadequate and want greater investment in antimalarial drugs. A third strategy is the development of effective vaccines against malaria. It is hoped that a combination of all the strategies especially effective vaccines, non-toxic antimalarial drugs effective against drug-resistance parasites as well as improvement in economic status of the people affected will enable us to curb the reemergence of malaria and to eradicate it eventually.

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TABLE 1. ANTIMALARIAL DRUG RESISTANCE

| DRUG                                                   | MECHANISM                                                                                                        | REMARKS                                                                                                                                                                                                                                                 |
|--------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Chloroquine                                            | Efflux pump in <i>P. falciparum</i> which is inhibited by verapamil.<br>Mechanism yet unclear in <i>P. vivax</i> | In <i>P. falciparum</i> , drug resistance first appeared in 1960s in South America and Southeast Asia and spread to neighbouring regions. In Africa it appeared two decade later in 1978.<br>In <i>P. vivax</i> , it is relatively a recent phenomenon. |
| Pyrimethamine                                          | One or more mutations in dihydrofolate reductase (DHFR) enzyme which is the molecular target of pyrimethamine    | Appeared in South America and Africa                                                                                                                                                                                                                    |
| Combination of pyrimethamine and sulfadoxin (FANSIDAR) | Point mutations in DHFR and in dihydropteroate synthase (DHPS)                                                   | Common in Southeast Asia and South America but rare in sub-Saharan Africa                                                                                                                                                                               |
| Mefloquine                                             | Amplification of <i>pfmdr1</i> gene inhibited by penfluridol                                                     | Southeast Asia (Thailand-Myanmar border)<br>Rare in Africa                                                                                                                                                                                              |
| Halofantrine                                           | Amplification of <i>pfmdr1</i> gene                                                                              | Southeast Asia                                                                                                                                                                                                                                          |
| Multidrug resistance and partial resistance to quinine | Multiple mechanism                                                                                               | Southeast Asia (Thailand)                                                                                                                                                                                                                               |

Table 2. Vaccine Candidates for Malaria

| Category   | Vaccine Name                                                                                                          | Status                                                                 |
|------------|-----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Sporozoite | NANP (asparagine (N), alanine (A), proline (P) peptides)<br>Sfp66 (Synthetic peptide)                                 | 30% population protection rate                                         |
| Merozoite  | MSP-1 (Merozoite surface protein-1)<br>EBA-175 (Erythrocyte binding antigen-175)<br>AMA-1 (Apical membrane antigen-1) | May prevent cerebral malaria<br>Effectiveness in human yet to be shown |
| Gametocyte | Pfs25 ( <i>P. falciparum</i> sexual stage antigens)<br>Pfs230                                                         | Experimental                                                           |



# Complications/Side Effects and Satisfaction of the Interval and post MR tubectomy clients : A comparative study

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## Abstract

*One hundred clients each from selected post MR and Interval tubectomy cases done at Mohammadpur Fertility Services and Training Centre was followed up for six months to assess the differences of complications and side effects between the two groups.*

*The complications observed during three follow up visits (in six months after operation) were very few and of minor nature. No complication was observed during operation. Resuturing of wound was done for two cases of Interval and one case of post MR clients. Menstrual irregularities were same for both the groups and these decrease rapidly in post MR clients than Interval clients. Heavy bleeding in last follow up visit was more in post MR clients (8.2%) than Interval clients (5.5%) and irregular bleeding was more in Interval clients (4.4%) than post MR clients (3.0%). Complications related to general health and psychological status of the clients was more or less similar. The differences observed were very few and these were not significant. Post MR tubectomy should be provided to MR clients when they are highly motivated to get this. The tubectomy operation after MR is easy and safe. It also saves additional expenditure and botheration of the willing clients.*

## INTRODUCTION

Female sterilisation (tubectomy) is a popular method of birth control in the Family Planning Programme of the Government of Bangladesh. It stands second to the use of oral pill in the country. About one lac forty thousand<sup>1</sup> tubectomies are performed in Bangladesh every year. Almost all the tubectomy clients are Interval cases. A large number of MR cases want to undergo tubectomy operation immediately after MR but because of the restriction by the Family Planning Directorate they do not receive this service. The Government is concerned about the complications of post MR tubectomy which may cause adverse effect on MR and tubectomy programme.

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It has been observed that motivation of clients for contraception is high during post-partum period and with passage of time this motivation declines. This is more true for surgical procedure. Motivation of clients after MR is very positive for tubectomy operation. If tubectomy service is not provided at the prime stage of motivation (after MR) these clients are likely to be victims of unwanted pregnancy and also repeat MR.

MR is a popular method of averting unwanted pregnancy. About 4,97,000 MR<sup>2</sup> is performed in Bangladesh every year. Mohammadpur Fertility Services and Training Centre is located at Dhaka Metropolitan area and perform about 700 MR<sup>3</sup> procedures every month. On the average 300 MR<sup>4</sup> procedures are performed in every Medical College Hospitals of Bangladesh. About 20% of MR clients are aged 28 years and more and have 3 or more living children. A fair number of these MR clients desire permanent stoppage of birth and are willing to undergo tubectomy operation. About 4% of all MR<sup>5</sup> clients of Mohammadpur Centre have gone tubectomy operation. This number is about 40% of all tubectomy operation done in the centre. So far no untoward effect has been reported in this clinic. In 1988, 678 tubectomy operations were performed in Mohammadpur Clinic : of these 259 were post MR cases. Complications so far are most negligible.

Mohammadpur Fertility Services and Training Centre did not have any built in procedure to follow defaulter clients at home. It was not known what happens to those clients who did not visit the Centre for follow up. Further those who came to the Centre mostly came within 7-10 days for stitch removal. Long term follow up was not done for these clients. This lack of long term follow up system and no follow up to defaulters posed question about delayed complications that might occur to clients. Further there were no way to assess the level of satisfaction of the clients with the procedure. The Centre did not have any information about complications and satisfaction between a post MR and Interval tubectomy clients. This study was conducted to assess differences of complications/side effects between Interval tubectomy & post MR tubectomy that was done within the study period at Mohammadpur Clinic.



## METHODOLOGY

The study was conducted in Mohammadpur Fertility Services and Training Centre. This Centre is known as the Model Clinic for comprehensive Family Planning services in the country. This clinic is also known in many parts of world for the introduction of Pomeroy method of tubectomy operation and introduction of different types of IUDs, oral pills, and injectable contraceptives in the Family Planning Programme of the country.

All the MR clients and Interval tubectomy clients who came to Mohammadpur Fertility Services and Training Centre during July 1991 to February 1992 were included in the study. MR clients for this study was selected on consideration of duration of pregnancy (6-10 weeks), parity, voluntary willingness to undergo tubectomy and agreeing to visit the centre for follow up. Out of 4748 MR clients during the study period, 100 clients were selected on the basis of criteria noted above.

Sample of Interval tubectomy clients was taken on the basis of laid down criteria of the Government of Bangladesh for tubectomy operation, voluntary participation in the study and agreeing to come to the Centre for follow up visits.

Total number of tubectomies performed during the study period was 296: of them 100 were post MR clients and 196 Interval clients. All the 100 clients of post MR tubectomy and 100 case of selected Interval tubectomy clients were included in the study.

On admission in the study every client was interviewed by a trained counsellor and relevant socio-demographic information were recorded in a specially developed form. A detailed physical and clinical examinations was done for every client by investigators and co-investigators. Laboratory examination was also done for every client. MR was performed in a separate room adjacent to the operation theatre. Tubectomy operation was performed immediately after MR procedure in the adjacent operation theatre.

Technique for tubectomy operation was same for clients of both the groups. It was performed by minilaparotomy process. A transverse incision of 2-5 cm was given at about 2 finger (2cm) above the symphysis pubes. Abdomen was opened routinely and 2 cm knuckle of tube approximately midway between the ampulla and the isthmus was held in a pair of Babcock forceps and the waist was tied with chromic no. 1 catgut. The knuckle to the distal end of the ligature was excised. Abdomen was then closed routinely. Skin was closed with chromic catgut. This is the Pomeroy's method of operation and is the accepted technique in the Family Planning Programme.

All clients on admission and at the time of discharge from the ward were motivated to attend the centre on 7th day, one month and six months after operation for follow up visits. They were informed about the purpose of this follow up visit. These clients were supplied with specially designed follow up card.

At the time of discharge all clients were given thirty combined iron and folic acid tablets and 20 antibiotic capsules (ampicillin). They were given proper direction for the use of the medicine and for follow up visits.

The clients who did not turn up to the Centre for follow up visit were visited at their homes by trained field workers.

## RESULTS

### Age

Mean age of the Interval tubectomy clients was 31.3 years and 20% of the clients were aged 35 years or more. Similarly mean age of the post MR tubectomy clients was 31.7 years and 27% of the clients were aged 35 years or more. There was not a single client under the age 25 years in either of the groups.

### Parity

Mean parity for Interval and post MR tubectomy clients were 4.2 and 4.3 respectively. There was no client with parity of two or less in the Interval group while six percent of the post MR clients had two parity. Parity of six and more were reported by 13% of the Interval clients compared to 19% of the post MR clients.

**Table I.** Distribution of post MR & Interval tubectomy clients by Age & Parity

| Tubectomy clients | Mean Age in years ( $\pm$ SD) | Mean Parity ( $\pm$ SD) |
|-------------------|-------------------------------|-------------------------|
| Post MR n = 100   | 31.7 ( $\pm$ 4.8)             | 4.2 ( $\pm$ 1.4)        |
| Interval n = 100  | 31.3 ( $\pm$ 4.4)             | 4.3 ( $\pm$ 1.3)        |

## EDUCATION

The post MR tubectomy clients were better educated than the Interval clients. Illiteracy was reported by 53% of the post MR clients compared to 79% by the Interval clients. Education with high school graduation and above was reported by 2% of post MR clients and 1% by the Interval clients.

## HUSBAND'S EDUCATION

The husbands of post MR clients were better educated (77%) than the husbands of the Interval client (51%). Husbands with education



of high school graduation and above were reported by 18% of the post MR clients and 7% by Interval clients.

**Table II.** Percentage Distribution of post MR & Interval tubectomy clients & their husbands by Education.

| Education in years | Post MR n = 100 |         | Interval n = 100 |         |
|--------------------|-----------------|---------|------------------|---------|
|                    | Wife            | Husband | Wife             | Husband |
| 0                  | 53              | 23      | 79               | 48      |
| 1 - 5              | 30              | 26      | 14               | 30      |
| 6 - 8              | 12              | 16      | 6                | 10      |
| 9 - 10             | 3               | 17      | 0                | 5       |
| 11 - 13            | 2               | 14      | 1                | 5       |
| 14+                | 0               | 4       | 0                | 2       |

### Complication during follow-up

At the first follow up visit discharge from wound and non-healed wound was reported by 7.7% and 3.3% of Interval clients and 15.4% and 10.3% by post MR tubectomy clients respectively. Resuturing of wound was done for 2.2% (2 cases) of the Interval clients and 1% (1 case) for post MR tubectomy client. These complications became reduced gradually and on third follow up visits complications related to wound was nil for both the group of clients.

**Table III.** Percentage Distribution of post MR & Interval tubectomy clients by complications of Wounds at different follow up visits.

| Complication of wound | Interval n = 90* |        |        | Post MR n = 97** |        |        |
|-----------------------|------------------|--------|--------|------------------|--------|--------|
|                       | 1s FU            | 2nd FU | 3rd FU | 1s FU            | 2nd FU | 3rd FU |
| Not healed            | 3.3              | 3.3    | 0      | 10.3             | 6.1    | 0      |
| Discharge             | 7.7              | 6.6    | 0      | 15.4             | 5.1    | 0      |
| Resuturing needed     | 2.2              | 0      | 0      | 1.03             | 0      | 0      |
| None                  | 86.6             | 90.0   | 0      | 73.19            | 88.65  | 0      |

\* 10 cases lost to FU \*\* 3 cases lost to FU

### General Complications/Side effects

Complications/Side effects for both the groups were of simple nature and general type. Complications for Interval tubectomy clients in first follow up visit were weakness (50 %), pain in lower abdomen (28.8 %), fever (8.8 %), itching of whole body (5.5%) and

vertigo (2.2%). While for post MR tubectomy clients these complications/side effects were weakness (41.2%), pain in lower abdomen (18.5 %), fever (14.4 %), vertigo (9.2 %), and pain in operation site (4.1 %). These complications/side effects found to be decreased in subsequent follow up visits. In the third follow up visit the complications/side effects were weakness (10 %), pain in lower abdomen (11.1%), vertigo (4.4%), pain at the operation site (3.3%) and itching of whole body (1.11%) for Interval client and for post MR tubectomy clients these were weakness (19.5%), pain in lower abdomen (14.4%), vertigo (7.2%), pain in operation site (2.6%), and fever (1.03%). In the first follow up visits almost all the general complaints were reported more by Interval clients than the post MR clients. In the third follow up visit though the complaints were reduced to a great extent in both the groups but these persisted more in MR tubectomy clients than Interval tubectomy clients. The difference was not significant by  $\chi^2$  test.

**Table IV.** Percentage Distribution of Interval & post MR tubectomy clients by General Complications at different follow up visits

| General Health            | Interval n= 90 |        |        | Post MR n= 97 |        |        |
|---------------------------|----------------|--------|--------|---------------|--------|--------|
|                           | 1st FU         | 2nd FU | 3rd FU | 1st FU        | 2nd FU | 3rd FU |
| Weakness                  | 50.0           | 33.3   | 10.0   | 41.2          | 18.6   | 19.5   |
| Pain in L/A               | 28.8           | 20.0   | 11.1   | 18.5          | 20.6   | 14.4   |
| Fever                     | 8.8            | 5.5    | 0      | 14.4          | 3.09   | 1.03   |
| Vertigo/<br>Headache      | 2.2            | 2.2    | 4.4    | 9.2           | 12.3   | 7.2    |
| Itching of<br>whole Body  | 5.5            | 0      | 1.1    | 0             | 2.06   | 0      |
| Pain at<br>Operation site | 0              | 0      | 3.3    | 4.1           | 2.06   | 2.06   |
| No Complaints             | 4.4            | 38.8   | 70.0   | 12.3          | 41.2   | 55.6   |

### Menstrual Problem

Menstrual problems reported were irregular bleeding and heavy bleeding. On first follow up visit 8.9% and 2.2% of the Interval clients and 10.3% and 5.1% of the post MR tubectomy clients reported of irregular and heavy bleeding respectively. Irregularity of menstrual bleeding increased at the second follow up visits in both the groups and then reduced to a minimum level at the third follow up visits. At the second follow up visit irregular and heavy bleeding was 9.2% for post MR tubectomy clients. At third follow up visit irregular and heavy bleeding for interval clients were 20.0% and 6.7% compared to 19.6% and 9.2% for post MR tubectomy clients.



At third follow up visit irregular and heavy bleeding for interval clients was 4.4% and 5.6% and 9.2% for post MR tubectomy clients. Heavy bleeding after tubectomy increased in both the group in same proportion i.e. from 2.2% in first follow up to 5.6% in third follow up for Interval clients and 5.1% from first follow up to 8.2% in third follow up for post MR tubectomy clients. The difference was not significant by  $\chi^2$  test. The change in menstrual pattern is the effect of tubectomy operation and does not reflect the effect of MR.

**Table V.** Percentage Distribution of Interval & post MR tubectomy clients by Menstrual change at different follow up visits

| Menstrual change          | Interval n= 90 |        |        | Post MR n= 97 |        |        |
|---------------------------|----------------|--------|--------|---------------|--------|--------|
|                           | 1st FU         | 2nd FU | 3rd FU | 1st FU        | 2nd FU | 3rd FU |
| Irregular P/V bleeding    | 8.9            | 20.0   | 4.4    | 10.3          | 19.6   | 3.0    |
| Menstrual not established | 85.6           | 30.0   | 10.0   | 84.5          | 39.1   | 10.3   |
| Heavy P/V bleeding        | 2.2            | 6.7    | 5.6    | 5.1           | 9.2    | 8.2    |
| Regular                   | 3.3            | 43.3   | 80.0   | 0             | 32.0   | 76.3   |

#### Psychological status of post MR & Interval clients after operation

Important psychological changes observed in different follow up visits were irritability, lack of interest in life and surrounding and recommendation to others to undergo tubectomy. For Interval clients irritability was reported by 4.4% in first follow up and 5.5% in third follow up visit. For post MR clients irritability was reported by 9.2% in first follow up and 6.1% in third follow up visits.

No interest in life and surrounding was reported by 5.5% of the Interval groups in first follow up and 3.3% in third follow up visits. While for post MR tubectomy clients these were 11.3% in first follow up visits and 4.1% in third follow up visits. Recommendation for tubectomy was reported by 3.3% of the Interval and 6.1% by post MR tubectomy clients. Minor psychological changes were regret for the operation and lack of interest in child. These were about 1% in both the groups of the cases in first follow up visits. In third follow up visits there was no change in post MR clients while for Interval clients it came down to nil. The differences observed were no regret for tubectomy operation was mentioned by 1.1%. Interval clients in first visit regretted in first visit and none in the third visit while no post MR tubectomy clients regretted in first visit while 1.03% mentioned regret in third follow up visit.

**Table VI.** Percentage Distribution of Interval & post MR tubectomy clients by Psychological Status at different follow up visits

| Psychological status             | Interval n = 90 |        |        | Post MR n = 97 |        |        |
|----------------------------------|-----------------|--------|--------|----------------|--------|--------|
|                                  | 1st FU          | 2nd FU | 3rd FU | 1st FU         | 2nd FU | 3rd FU |
| Irritable                        | 4.4             | 3.3    | 5.5    | 9.2            | 7.2    | 6.1    |
| No interest in life/surrounding  | 5.5             | 4.4    | 3.3    | 11.3           | 8.2    | 4      |
| Not interested in children       | 1.1             | 0      | 1.1    | 5.1            | 2.06   | 1.03   |
| Regret for tubectomy             | 1.1             | 0      | 0      | 0              | 0      | 1.03   |
| Recommended the method to others | 5.5             | 2.2    | 3.3    | 5.1            | 7.2    | 6.1    |
| Normal reaction towards husband  | 0               | 0      | 2.2    | 2.06           | 1.03   | 6.1    |
| Other                            | 0               | 0      | 0      | 2.06           | 3.09   | 6.1    |
| Normal                           | 82.2            | 90.0   | 84.4   | 64.9           | 71.1   | 71.1   |

#### Blood Pressure

The systolic and diastolic blood pressure of both the groups of clients at different follow up visits were more or less similar with a little lower tendency for diastolic BP in post MR tubectomy clients. Systolic BP for both the groups in all the follow up visits was between 101-110 mmHg, while diastolic BP for Interval group was 76-80 mmHg and for MR group it was 66-70 mmHg.

#### Change in Haemoglobin level

Change in Haemoglobin level was more or less same for both groups of study population.

**Table VII.** Percentage Distribution of Interval & post MR tubectomy clients by change of Hb% at different follow up visits

| Hb%       | Interval n = 90 |        |        | Post MR n = 97 |        |        |
|-----------|-----------------|--------|--------|----------------|--------|--------|
|           | 1st FU          | 2nd FU | 3rd FU | 1st FU         | 2nd FU | 3rd FU |
| Increased | 5.6             | 4.4    | 18.1   | 4.1            | 6.1    | 22.7   |
| Decreased | 4.4             | 11.1   | 16.7   | 6.1            | 11.3   | 17.6   |
| No change | 90.0            | 84.4   | 75.6   | 89.7           | 81.4   | 59.8   |

#### Change in Weight

Decrease in weight was noticed from first follow up visit to third follow up visits in both the groups of tubectomy clients. However percentage of decrease in weight was higher for MR group. In third



follow up visit, decrease in weight for Interval group was 8.9% compared to 12.3% in post MR group. The difference observed was not significant.

**Table VIII.** Percentage Distribution of Interval & post MR tubectomy clients by change in weight at different follow up visits

| Weight    | Interval n = 90 |        |        | Post MR n = 97 |        |        |
|-----------|-----------------|--------|--------|----------------|--------|--------|
|           | 1st FU          | 2nd FU | 3rd FU | 1st FU         | 2nd FU | 3rd FU |
| Increased | 2.82            | 23.3   | 33.3   | 4.1            | 26.9   | 28.9   |
| Decreased | 4.4             | 8.9    | 8.9    | 6.1            | 14.4   | 12.3   |
| No change | 93.3            | 67.8   | 57.8   | 89.7           | 69.7   | 58.8   |

## DISCUSSION

The study was conducted in a well known clinic of the country, known for its quality care in the field of comprehensive family planning services, both in the country and abroad. On the average 7000-8000 MR procedures and 400 tubectomy operations are performed in this clinic every year.

The study sample of 100 cases of post MR tubectomy and 100 cases of Interval tubectomy was selected from MR and tubectomy clients who visited this centre from July, 1991 to February, 1992 on laid down criteria. The clients were meticulously examined by expert surgeons for contra-indications, if any, through clinical, physical and laboratory procedures. All the clients before operation had proper counselling by trained counsellor and medical doctors. The operation was performed under local anaesthesia and through Minilap technique.

Age and parity of the clients in both the groups were more or less same. Post MR clients were better educated than the Interval clients. In general the MR clients were young, better educated and had lower parity. Dr. Rahman<sup>6</sup> reports that MR clients of Mohammadpur Fertility Services and Training Centre were young, better educated and had less parity than the women using IUD, tubectomy or other semipermanent contraceptive method.

No problem during operation was experienced in either group of the clients except few cases (3.3%) of vomiting among Interval clients. Vital signs for both groups were more or less similar. Wound at the operation site healed for all the clients at third month follow up visit. Resuturing of wound was done in two cases of Interval group and one cases of post MR group.

General complication/side effects were mostly weakness, pain in lower abdomen and vertigo. These complications were more or less same in both the groups. Mostly the symptoms could be related to

nutrition of the clients than the operation, Menstrual problems observed in the first follow up visit decreased rapidly among post MR cases than Interval cases. However heavy bleeding was seen more in post MR clients (8.2%) than the Interval clients (5.6%) and irregular bleeding was more prominent in the Interval clients (4.4%) than significant. Change in blood pressure and haemoglobin level was more or less same in both the groups. No significant difference in psychological status was reported between post MR and Interval clients at any follow up visit.

The study results show that post MR tubectomy is as safe as Interval tubectomy. There is no valid scientific reason for not conducting tubectomy operation, just after MR procedure for those clients who voluntarily desire to accept the procedure. In Bangladesh women generally are not very free to visit the static centre for services at their own free will. They need permission from a number of family members, need a companion to go to the centre and there is a question of financial expenditure involved. So once the women go back to their homes without necessary services (tubectomy) it becomes difficult for them to come back for the service next time even if they want tubectomy. Further there are lots of factors which influence change in the decision of the clients once they leave the centre.

Thus it is recommended that tubectomy being a safe method after MR, it should be provided to all such cases who voluntarily desires to undergo the operation. This will save many unwanted pregnancies. Further this will prevent repeat MR operation or clandestine abortion which causes danger to health of the women and even death.

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# Prevention of Ischaemic Heart Disease

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## Introduction

Ischaemic heart disease (IHD) is a major health problem, both for the developed and developing societies. It is the most fatal form of cardiovascular disease and is responsible for 80% of all cardiac mortality and 35% of all deaths in the United States.

The developing countries like developed nations face an epidemic of ischaemic heart disease, which is signalled by a slogan of the World Health Organisation in 1988, "Heart attacks are developing in developing countries. Prevent them now". This disease is also very common in Bangladesh.

Although very limited works are being done in this field, one study shows the prevalence rate of this disease is 3.3 per thousand population in Bangladesh and another study shows the rise of incidence rate of myocardial infarction is 0.5 per thousand population per year over a period of 1978-81.

A big mountainous work has already been done in different societies to mark the risk factors associated with this disease and their prevention.

Coronary heart disease mortality has declined in a number of European countries including Belgium with a better application of prevention in addition to pharmacological and interventional approach.

"Prevention is better than cure" runs the proverb. This particularly holds good in ischaemic heart disease, because failure of prevention may leads to sudden premature death.

## PRIMARY PREVENTION OF ISCHAEMIC HEART DISEASE:

Primary prevention means "Prevention of death and non fatal events in a healthy population." Ischaemic heart disease is a health problem where many amenable risk factors are identified which can be controlled either by education or modification of life style and early treatment of related risk factors.

Primary prevention includes early identification of risk factors and their prevention e.g.:

- Cessation of smoking
- Correction of dyslipidaemia
- Control of hypertension
- Maintenance of physically active life
- Avoidance of obesity
- Control of diabetes mellitus
- Low to moderate daily consumption of alcohol
- Low dose aspirin

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- Intake of anti-oxidant vitamins e.g. vitamin E & C, ( $\alpha$ -tocopherol and betacarotene)
- Postmenopausal oestrogen replacement therapy
- Reduction of clotting factors (e.g. fibrinogen, factor VII) by physical exercise, low to moderate alcohol consumption, Post-menopausal oestrogen therapy, intake of polyunsaturated fatty acid in diet

## Our observation:

Efforts of primary prevention are lacking in our country because of the lack of adequate primary health care, health education and coordinated efforts of family physician and concerned personnel. Primary preventive measures should be the main object in this regard particularly in developing countries like ours, where poor socio-economic conditions fail to bear the huge cost of treatment of the disease during attacks and of secondary measures. Children or adolescents who are obese, inactive, have hypertension or diabetes, who smoke with family history of coronary heart disease or peripheral vascular disease are the suitable candidates for primary prevention.

Primary prevention can be accomplished by early detection of risk factors and their prevention by increasing public awareness through health education. Family physician, social workers & mass media must play positive role in this regard. Introduction of at least physical exercise & healthy diet in developing countries may contribute significantly in this connection.

## SECONDARY PREVENTION OF ISCHAEMIC HEART DISEASE:

Secondary prevention of coronary heart disease may be defined as action taken to prevent recurrence of IHD, sudden death or fatal arrhythmia in a patient who experienced at least one event of coronary episode.

The concept of secondary prevention of reinfarction and death after recovery of AMI is gaining importance day by day. Patients, who survive the initial attack of MI, are at an increased risk of developing further serious attacks. Therefore it is obligatory to take adequate measures to control the amenable risk factors in a rational way, although ideally primary prevention should have been the ultimate goal in a conscious society. If this is not accomplished, it is a must to have at least secondary prevention to reduce morbidity and mortality in patients who have clinically apparent IHD. Secondary prevention following acute myocardial infarction begins at the very start of hospitalisation. An aggressive approach should focus on appropriate life style change as well as pharmacotherapy.

## STRATEGIES FOR SECONDARY PREVENTION OF IHD:

The strategy of secondary prevention of IHD will depend upon individual patient, nature of the disease, its complications, previous attacks, age of the patient and other serious associated disease. However the following strategies may be followed as a guideline:

- Life style modification
- Control of risk factors
- Drug therapy -



- Drugs which prevent sudden death and reinfarction:
  - (i)  $\beta$ -adrenoceptor blocking agents
  - (ii) Anti-platelet agents and anticoagulants
  - (iii) Calcium channel blockers
- Drugs which prevent ventricular remodeling
  - (i) Angiotensin converting enzyme (ACE) inhibitors
  - (ii) Anti-arrhythmic agents
- Revascularisation
  - (i) Coronary artery bypass grafting
  - (ii) Coronary angioplasty

### Life Style Modification:

Modification of life style after an ischaemic attack is very important and proved to be very beneficial for long term survival. Cessation of smoking, increased physical activity and lipid lowering are key to life style modification objective.

In many studies, patients with coronary artery disease, it has been shown that intake of polyunsaturated fatty acids, fibre containing diet, exercise, weight reduction, cessation of smoking and modification favourably altered the rate of luminal narrowing of coronary arteries.

### Physical exercise:

It is recommended that exercise training should be instituted as soon as possible after an AMI in order to prevent deconditioning. Exercise improves oxygen transport, evident as an increase in cardiac output, a reduction in heart rate, systolic blood pressure and thereby myocardial oxygen consumption at rest and at submaximal work levels. Other effects of exercise includes weight reduction, control of diabetes mellitus, improvement of lipid profile, psychological benefits including greater confidence of performing activities of daily life and overall improvement of functional status.

Exercise prescription needs prior assessment by ETT. Physical exercise after MI establishes natural bypass and increases left ventricular ejection fraction and correction of risk factors. The reduction of risk factor of coronary heart disease after ischaemic event is very important in prevention of reinfarction and sudden death.

### CONTROL OF ALL RISK FACTORS<sup>9</sup>

Early detection & reduction of risk factors after an attack of ischaemic heart disease is of prime importance in the prevention of reinfarction and sudden death. The most important steps in the area are the cessation of smoking, control of hypertension & diabetes mellitus, reduction of LDL, cholesterol & body weight and increase in blood HDL level.

### Cigarette Smoking:

It is an established risk factor for development of angina, myocardial infarction and increases the risk of reinfarction and death. Many studies proved that who remained abstinent from smoking for more than 3 years showed significant decline of second cardiac event similar to survivor who never smoked.<sup>8,21</sup>

Cessation of smoking is facilitated by explaining physiological and psychological aspects of the habit and its strong association of cardiac

disease. Gradual nicotine withdrawal may be done by tapering cigarette smoking, gradually changing to lower nicotine cigarettes and substituting chewing nicotine gum, if there is withdrawal symptoms.

### Control of high Blood Pressure<sup>11</sup>

The higher the blood pressure, whether systolic or diastolic, the greater is the risk of developing ischaemic heart disease. Evidence from clinical trials suggests that antihypertensive agents lower coronary mortality only moderately - less than one might have anticipated.

### Cholesterol:

Elevated cholesterol is found in the genesis of atherosclerosis and ischaemic heart disease, which is an established fact. Numerous trials proved that reduction of cholesterol lead to a reduction in morbidity and mortality from cardiovascular disease.

### TREATMENT OF HYPERLIPIDAEMIA<sup>11</sup>

It should start with dietary measures. Weight reduction and alcohol restriction substantially reduce hypertriglyceridaemia. Total fat should be reduced to 25-30% of food energy having polyunsaturated fatty acids, especially linoleic acid should be 7-10%, substitution of vegetable oils, fish and carbohydrates, soluble fibre, garlic and soy protein & skimmed milk in the diet.

### Drugs used to correct hyperlipidaemia include:

- Bile acid sequestrants (Cholestyramine) are effective in hypercholesterolaemia.
- Nicotinic acid reduces triglycerides and to lesser extent cholesterol.
- Fibrates reduces triglycerides and to lesser extent cholesterol.
- HMGCoA reductase inhibitor reduces plasma cholesterol by 25% or more and its use is recommended if cholesterol level is in excess of 7.8 mmol/L which is unresponsive to other therapy.
- Secondary causes like diabetes mellitus, myxoedema, biliary obstruction, nephrotic syndrome etc. should be treated. Severe form may need gastrointestinal bypass surgery.

### Bile acid sequestrants:

Adverse effect: GIT upset and interfere with absorption of certain drugs. Niacin causes flushing of skin, GIT upset. Common side effects are myopathy, neutropenia, impotency and abnormal liver function test.

### $\beta$ -adrenoceptive blocking agents:<sup>12</sup>

A number of placebo control secondary prevention trials involving >35000 patients indicate that chronic  $\beta$ -blockade began in the early phase of infarction improves survival, decrease the incidence of reinfarction and sudden death for at least the first several month after AMI. The Beta Blocker Heart Attack Trial (BHAT),<sup>13</sup> first International Study of Infarct Survival (ISIS-I),<sup>14</sup> the Norwegian Multicentre Study Group,<sup>15</sup> Multicentre International Study<sup>16</sup> showed almost similar results.

Selection of patients for empirical long term blocker for prophylaxis:

- Patients at high risk (complicated MI) appears to be most benefited, provided there is no contraindication.
- In Q wave infarction, if one of the following is present:
  - i) In hospital, electrical complication (e.g. VT or cardiac arrest)
  - ii) Asymptomatic non-sustained VT
  - iii) Frequent ventricular premature beats



iv) Objective evidence of ischaemia

v) Recurrent myocardial infarction

— Silent myocardial infarction:

Patient with non-Q wave infarction have no proven benefit from  $\beta$  blocker. Dose and administration of  $\beta$  blocker for acute  $\beta$  blockade, drugs are used intravenously in a dose of atenolol 5-10 mg, metoprolol 5-15 mg. Over 5 minutes it relieves pain, reduces arrhythmia and improves short-term mortality provided there is no contraindication.

For long term oral administration it is preferable that the dose is adjusted as such to keep pulse rate between 50-75/minutes and systolic blood pressure does not go below 100-90mm of Hg.

#### Contraindication of $\beta$ blockers:<sup>12</sup>

- Heart rate <60 beats/min
- Systolic blood pressure <100 mm of Hg
- Moderate to severe left ventricular failure
- Sign of peripheral hypoperfusion
- AV conduction abnormalities
- Chronic obstructive pulmonary disease

Relative contraindications are:

- History of asthma
- Severe peripheral vascular disease
- Difficult to control IDDM

Adverse effects of  $\beta$  blockers: Fatigue, Depression, Sexual dysfunction, Nightmares, Bradycardia and Heart block.

#### Thrombolytic agents, Anticoagulants & Antiplatelet agents:

The goals of antithrombotic therapy during and early after myocardial infarction includes

- i) Prevention of deep vein thrombosis and pulmonary embolism
- ii) Prevention of arterial embolism
- iii) Reduction of early recurrence, extension of myocardial infarction and death
- iv) Reduction of early re-occlusion and death
- v) Secondary prevention of late recurrence of myocardial infarction and death. ISIS-2 study<sup>17</sup> showed that 5 weeks vascular mortality rate was reduced by 23% with aspirin alone and was reduced a further 19% when aspirin and streptokinase were both used.

#### Aspirin as an antiplatelet agent:

In patients with stable angina aspirin decreases the risk of first myocardial infarction. Aspirin should be used in patients with unstable angina and in most severe cases in conjunction with heparin. It is also beneficial in the prevention of re-occlusion following coronary angioplasty, but does not prevent the late restenosis.

#### Mechanism of action of aspirin:

Aspirin irreversibly inhibit cyclooxygenase by acetylating the serine residue at the active site of the enzyme and this inhibition lasts for the lifetime of the cell. As a result the synthesis of thromboxane  $A_2$  is inhibited and the preaggregatory & vasoconstrictive action of thromboxane  $A_2$  is prevented.

#### Dose of aspirin:

The present recommendation is a single loading dose of 200-300 mg of aspirin followed by a daily dose of 75 to 100 mg. This dose is clinically efficacious and is safer than higher doses

#### Adverse effect:

Gastrointestinal disturbances e.g. heart burn, erosive gastritis, peptic ulcer, GI bleeding etc.

#### Dipyridamole:

It is a vasodilator and has different anti-platelet effects from aspirin. No convincing study report is yet available.

#### Sulphapyrazine:

Anturan Reinfarction Trial claimed that sulphapyrazine prolongs survival after MI.

#### Ticlopidin:

It is another anti-platelet agent as found effective in reducing the occurrence of death and myocardial infarction in patients with unstable angina. The dose of this drug is 250 mg twice daily.

#### Anticoagulants:

Many studies are carried out for the rationality to use anticoagulant as secondary cardioprotective agent, but results are not uniform. Anyway, use of anticoagulant where there is an increased risk of thromboembolism are definitely helpful to reduce death, reinfarction and incidence of systemic or cerebral embolism. It to be noted that warfarin and aspirin cannot safely be taken together.

#### Calcium channel blocker:

The joint task force of the American Heart Association & American College of Cardiology recommended that the patient with non-Q wave infarction should be given Diltiazem in the 1st 24 hours routinely and that therapy is to be continued at least for 1 year.

Verapamil may be used instead of propranolol where there is contraindication ( $\beta$ -blockers) but nifedipine is not safe as it cause reflex tachycardia and potentiate the anginal attacks.

Common adverse effects are Headache, Flushing, Palpitation, Hypotension, Ankle oedema, Bradyarrhythmia and Constipation. Limitation of using calcium channel blocker is negative inotropic action & conduction defect.

#### Angiotensin converting enzyme (ACE) inhibitors:

Several major independent studies of clinical outcome involving almost 100,000 patients have reported results that demonstrate the prolongation of survival<sup>18</sup>, particularly in patients with MI with heart failure, impending heart failure, massive anterior infarction with reduced ejection fraction.

#### Cardioprotection by ACE inhibitors<sup>20</sup>:

- Reduces preload and afterload & reduces ventricular remodelling
- Increases coronary blood flow
- Decreases infarct size
- Scavenging of oxygen free radicals
- Antiarrhythmic effect
- Modulation of neurohormonal response
- Prevention of inappropriate growth & hypertrophy



### Selection of patients<sup>20</sup>:

- Patients with acute Anterior MI.
- Maximum benefit patients having LV ejection fraction of 28%-32%
- Systolic blood pressure more than 100mm of Hg.

ACE inhibitor is to be started soon after myocardial infarction without unnecessary delay.

ACE inhibitors are to be continued for at least one year or even longer.

### Adverse effects:

Persistent dry cough, angioneurotic oedema, skin rash, stomatitis, neutropenia, deterioration of renal failure, proteinuria and blood disorders.

### Antiarrhythmic drugs:

Arrhythmia accounts for a large number of mortality after AMI. So use of antiarrhythmic drugs as secondary preventive agents are studied by many trials. These drugs have got proarrhythmic activity and negative inotropic effect. So it is recommended that treatment of symptomatic arrhythmias are justified and asymptomatic patient detected by ECG only should be left untreated. Amiodarone is found as one of the promising drug but with wider spectrum of side effects. Final recommendation for its use is to be decided according to the result of large trials. So its effectiveness as secondary prevention cannot be predicted.

### Interventional & Surgical techniques:

Surgical treatment in comparison to medical therapy in patient with unstable angina and after acute MI either by angioplasty or by bypass grafting was found superior in relieving symptoms regardless of severity of coronary disease and reducing the need for antianginal medications. There is no definite proof whether bypass grafting did really reduce the further attacks or not and same is applicable for LV function.

### Our experience:

CCU was started in Dhaka National Medical Institute Hospital in the year 1987, since then we have been treating patients with acute myocardial infarction and unstable angina. In order to have secondary preventive action, we used to prescribe Tab. Aspirin in a dose of 300mg initially followed by 75mg to 100mg daily after meals & continued indefinitely, if there was no contraindication. Inj. Streptokinase was being used in selected cases if the patient comes within 12 hours of AMI and patients were economically solvent.  $\beta$  blockers were used orally if there was tachycardia and hypertension particularly in Q-wave infarction provided there was no contraindication. Maximum dose requirements were usually less in our patients compared to other study groups. Inj. Heparin was used in very selected cases of unstable angina and where there was strong suspicion of thromboembolism and Aspirin was discontinued during that period. Dipyridamole was chosen if Aspirin was contraindicated.

Diltiazem (calcium channel blocker) was preferred in non-Q wave infarction. ACE inhibitors were selected when AMI was complicated by heart failure and dry cough was the commonly encountered side effect.

With all limitations only 10-15% patients got admission in our center with re-infarction as per hospital record. This low figure could reflect the success of secondary prevention although our patients had no fixed choice of coming to our centre with re-infarction and the second attack may be more fatal which did not allow them to come for medicare.

### CONCLUSION:

Coronary heart disease mortality remains the leading cause of mortality in man over 45 years and women over 56 years although there have been a significant improvement in the management of acute attacks.

That is why emphasis should be given to ensure primary and secondary preventive measure for the control of ischaemic heart disease. This can be easily done by health education to increase people awareness. Active participation of family physicians, prompt and better medicare in CCU, better follow up system and finally patient-physician relationship must play a significant role in this regard. For developing countries more attention are to be given in the field of primary prevention of ischaemic heart disease at least by introducing physical exercise and appropriate nutrition for the vulnerable group.

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## Self Assessment

- 1) Villous adenoma most often occurs in
  - a. Appendix
  - b. Caecum
  - c. Transverse colon
  - d. Rectum & sigmoid colon
  - e. Anal canal
- 2) The most common cause of right subhepatic (Morrison's pouch) abscess is
  - a. Gastric surgery
  - b. Biliary surgery
  - c. Appendicitis
  - d. Pancreatitis
  - e. Colon surgery
- 3) Metabolic consequences of partial gastrectomy include all except
  - a. Megaloblastic anaemia
  - b. Iron deficiency anaemia
  - c. Metabolic alkalosis
  - d. Calcium deficiency
  - e. Steatorrhoea
- 4) Prognosis of colonic carcinoma is worst when it is located at
  - a. Caecum
  - b. Transverse colon
  - c. Hepatic flexor of colon
  - d. Splenic flexor of colon
  - e. Ascending colon
- 5) Carcinoma of pancreas is commoner in diabetis than in general population by
  - a. Three times
  - b. Four times
  - c. Five times
  - d. Ten times
  - e. Twelve times
- 6) Creeping of fat from mesentery into bowel wall is the feature of
  - a. Crohn's disease
  - b. Ulcerative colitis
  - c. Ischaemic colitis
  - d. Amoebic colitis
  - e. Bacterial enteritis
- 7) Malignant ascitis is frequently due to
  - a. Carcinoma of pancreas
  - b. Carcinoma of ovary
  - c. Malignant hepatoma
  - d. Carcinoma of colon
  - e. Carcinoma of bladder
- 8) The most useful immunosuppressant drug used in organ transplantation is
  - a. Azithioprine
  - b. Cyclophosphamide
  - c. Nitrogen mustard
  - d. Mitomycin
  - e. Actinomycin
- 9) Prognosis following resection of carcinoma of stomach is specifically determined by
  - a. Extent of stomach removed
  - b. Short clinical history
  - c. Age of the patient
  - d. Histology of the growth
  - e. Sex of the patient
- 10) Serum carcino-embryonic antigen (CAE) level is elevated in
  - a. Colon carcinoma
  - b. Colon and pancreatic carcinoma
  - c. Carcinoma of rectum and anal canal
  - d. Gastric carcinoma
  - e. Testicular and ovarian carcinoma

**Answers:**  
 1. D 2. A 3. C 4. D 5. D  
 6. A 7. C 8. D 9. D 10. B



# Resident Round

## Round Worm in the Middle Ear

Although round worm (*Ascaris lumbricoides*) infestation is quite common globally, it is more so in the developing countries especially in children from lower socio-economic strata. Round worm infestation usually causes abdominal discomfort or colic. A heavy infestation can cause nutritional deprivation and at times intestinal obstruction. It can also produce symptoms because of abnormal migration of adult round worm. Two cases are being reported of abnormal migration of the round worm into the middle ear.

**Case - 1:** A two and half year old child was brought to the emergency with the complaint of severe pain in the right ear. On clinical examination the only positive finding was an intense congestion of the tympanic membrane. A diagnosis of acute otitis media was made and the child was put on amoxicillin and ibuprofen. Next day the child was again brought to the ENT out-patient department as there was no relief of pain. Ear was again examined and this time a whitish worm-like organism was seen wriggling in the external auditory canal. On pulling out of the ear it was found to be an adult *Ascaris*. After removal of the worm the tympanic membrane was seen to be having central perforation. Child was given deworming agent and the antibiotic was continued. Pain subsided and the tympanic membrane healed in about 10 days.

**Case - 2:** A 12 year old male child was admitted to the ENT ward with the history of discharge from the left ear associated with otalgia and hearing loss for the last 6 months. Examination of the left ear revealed the external auditory canal to be full of polypoidal granulation tissue; mastoid tenderness was also present. Patient was taken to the operation theatre for removal of the polypoidal mass from the ear canal to facilitate the drainage. While removing the polyp, a whitish worm was caught in

the suction and pulled out. It was confirmed to be an *Ascaris*. Patient was dewormed and put on antibiotic and was later taken up for mastoid exploration. During surgery mastoid segment was found to be full of granulation tissue. A cortical mastoidectomy was done, clearing out all the diseased tissue. Middle ear mucosa was found to be oedematous. Tympanic membrane perforation was repaired using a temporalis fascia graft.

### Discussion

*Ascaris* infestation is quite common in this subcontinent. It causes numerous infrequent complications because of abnormal migration of the adult worm such as blockage of the pancreatic duct and obstruction of the appendix. Adult worm can also be vomited out or at times it comes out through the nose causing great discomfort and distress to the patient. Migration of the adult round worm up the Eustachian tube into the middle ear is very rare but it has been documented. In children the Eustachian tube is shorter, wider and horizontal. So it may be possible for a migrating round worm to enter it. *Ascaris* in the middle ear can also cause mastoiditis, facial paralysis, suppurative labyrinthitis and even intracranial suppuration.

In the first case, migration of the round worm through the Eustachian tube into the middle ear caused acute middle ear suppuration and ultimately causing breakdown of the tympanic membrane and movement of the worm into the external auditory canal. In the second case, there might have been preexisting chronic suppurative otitis media. But the possibility of the round worm entering the middle ear cleft and causing suppuration leading to mastoiditis and exuberant granulation tissue formation cannot be ruled out.

### MediImage



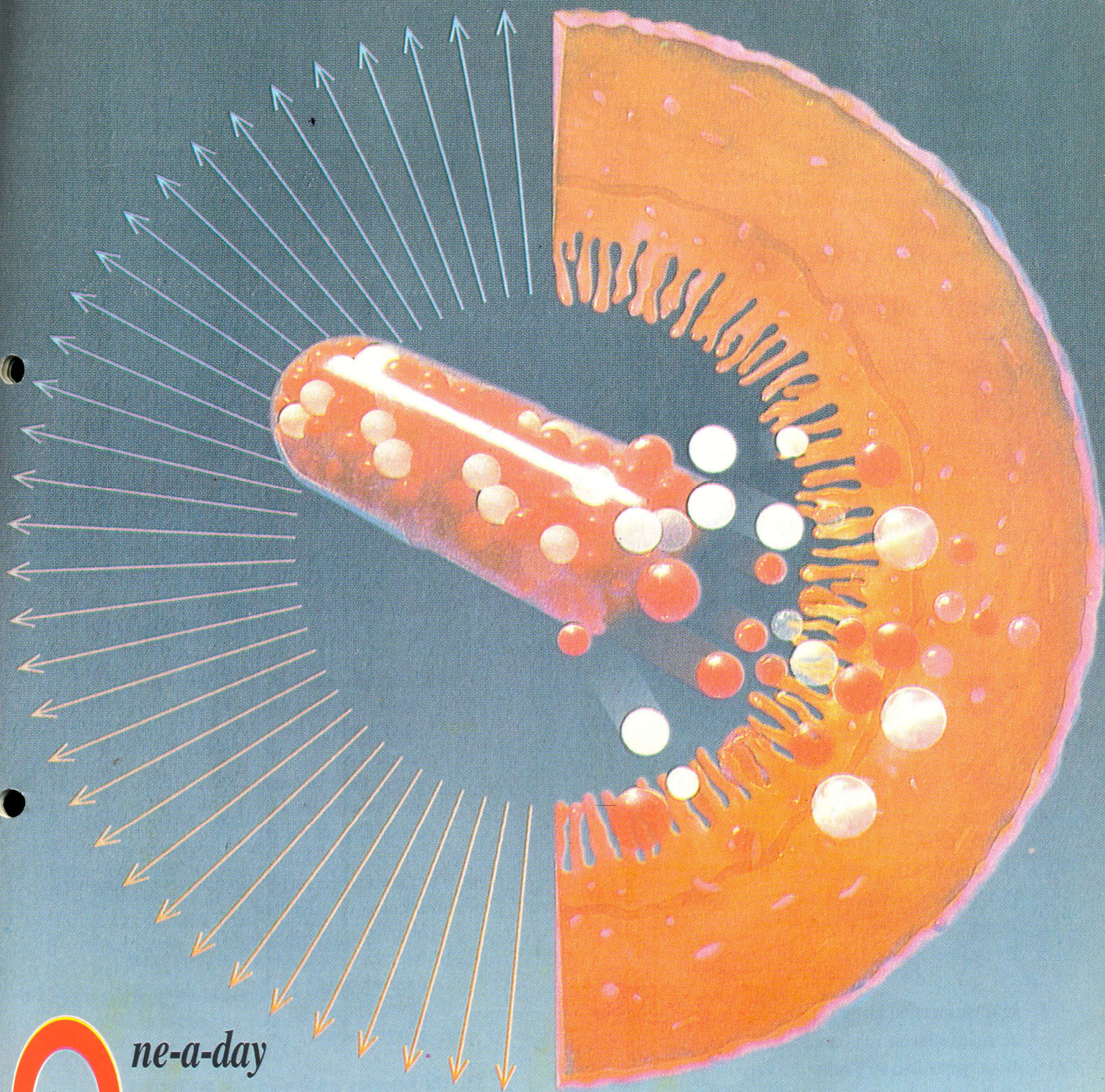
A 20-years-old college student, newly arrived in USA, was evaluated for severe abdominal pain. What is the diagnosis?

Answer will be published in the next issue of "The ORION".

Indian J Paed 1998; 65



# Better Approach in NSAID Therapy



**O**ne-a-day  
**rfenac-TR**

Diclofenac Sodium 100 mg  
Timed Release Capsule

...A Balanced dosage form for  
Smooth Absorption and  
Sustained Action



# M E D I 3 Q U I Z

1. De Quervain's thyroiditis is commonly associated with
  - A elevated ESR
  - B painless goitre
  - C dense fibrosis involving the thyroid and adjacent structures
  - D hyperthyroidism
  - E increased thyroid uptake of  $^{99m}$  technetium
2. In a 10 year old girl
  - A a positive Heaf test indicates immunity to tuberculosis
  - B repeated chest infections are likely to be due to chronic bronchitis
  - C inhaled corticosteroids are contraindicated as treatment for asthma
  - D asthma is usually associated with positive skin prick tests to common allergens
  - E cystic fibrosis may be diagnosed for the first time
3. Hepatitis C virus
  - A accounts for >90% of post transfusional hepatitis
  - B less than 30% of patients will progress to chronic liver disease
  - C aplastic anaemia is a recognised complication
  - D 50% of patients treated with interferon will relapse on stopping treatment
  - E has an incubation period of less than 6 weeks
4. Munchausen's syndrome is characterised by
  - A female sex
  - B delusions of illness
  - C obsessional personality
  - D folie á deux
  - E recovery after surgical intervention
5. IgM rheumatoid factor
  - A reacts with the Fab component of IgG
  - B is synthesised by T cells
  - C fixes complement
  - D is the predominant rheumatoid factor assayed by the Rose-Waaler reaction
  - E is diagnostic of rheumatoid arthritis
6. Myoclonus
  - A is a sign seen in metabolic encephalopathy
  - B is a feature of the Gilles de la Tourette syndrome
  - C with dementia is a feature of Creutzfeldt-Jacob disease
  - D may occur with childhood epilepsy
  - E is a feature of chronic anoxic encephalopathy
7. Interleukin-1
  - A is a lymphocyte activating factor
  - B is an endogenous pyrogen
  - C inhibits fibroblast proliferation
  - D stimulates the synthesis of acute phase proteins in the liver
  - E is not synthesised by macrophages
8. During normal inspiration
  - A right arterial pressure increases
  - B pulmonary venous flow increases
  - C systemic arterial pressure increases
  - D heart rate decreases
  - E splitting of the second heart sound is increased
9. A 1 year old child would be expected to
  - A uncover an object (which was covered before the infant could grasp it)
  - B grasp a raisin
  - C play a simple ball game
  - D feed himself a biscuit
  - E put three words together
10. The following are recognised features of pulmonary involvement by sarcoidosis
  - A obstructive ventilatory defect
  - B inspiratory crackles heard on auscultation
  - C finger clubbing
  - D pleural effusion
  - E hypercalcaemia
11. The following anatomical data are correct
  - A opponens pollicis muscle is innervated by the ulnar nerve
  - B abductor pollicis brevis is supplied by the median nerve
  - C the diaphragm is innervated by C3, C4 and C5





- D lower cord of the brachial plexus comprises C8, T1 and T2
- E the knee jerk is innervated by L3 and L4 segments

**12. Tunnel vision is seen with**

- A Vitamin A deficiency
- B acute glaucoma
- C papilloedema
- D exophthalmic ophthalmoplegia
- E hysteria

**13. CD4+ T cells:**

- A Are cytotoxic for virally infected cells.
- B Are restricted in antigen recognition by MHC class II molecules.
- C Release cytokines in response to antigen stimulation.
- D Are a major target cell for infection with HIV.
- E Are involved in delayed type hypersensitivity.

**14. Indications for urgent dialysis in uraemic patients include**

- A asterixis
- B itching
- C pericarditis
- D peripheral neuropathy
- E hiccoughing

**15. Pseudomembranous colitis**

- A typically spares the rectum
- B may occur after metronidazole
- C is caused by toxin produced by *Clostridium difficile*
- D is best treated with intravenous vancomycin
- E relapses is very uncommon after treatment

**16. The response of the kidney to an acid load**

- A involves an increase in urinary free hydrogen ion

secretion until a minimum pH of 3.8 is achieved

B leads to an increase in the chloride-anion gap

C results in the generation of  $H_2PO_4$  ions in the urine

D leads to increased synthesis of glutamic acid in the cells of the distal tubule

E is hampered by the respiratory response

**17. Atrial myxomas**

- A are more common in the right atrium than in the left atrium
- B do not recur after resection
- C may mimic infective endocarditis
- D are poorly visualised on echocardiography
- E usually arise from a pedicle near to the fossa ovalis

**18. Features of VIPoma syndrome include**

- A hypokalaemia
- B alkalosis
- C hypoglycaemia
- D increased gastric acid secretion
- E provocation of VIP releases by somatostatin

**19. Neuroleptic malignant syndrome**

- A is characterised by hyperthermia and muscular rigidity
- B can occur when tricyclics alone are administered
- C most commonly occurs after haloperidol treatment
- D is usually fatal
- E responds to treatment with tetrabenzine

**20. Extraparadidal rigidity may be caused by**

- A butyrophenone tranquilisers
- B vitamin B<sub>12</sub> deficiency
- C abuse of synthetic pethidine derivatives
- D carbon monoxide poisoning
- E the neuroleptic malignant syndrome

**Please Use the Answer Sheet Opposite Page No. 28**  
**Answers to MediQuiz 3 must reach us within 31st July 1999**



# MediQuiz - 2 Winners

WE ARE HAPPY TO ANNOUNCE THE LUCKY WINNERS OF  
MEDIQUIZ - 2. OUR CONGRATULATIONS GOES TO THE  
WINNERS AND THANKS TO THE PARTICIPANTS.

THE WINNERS OF THE MEDIQUIZ - 2 ARE:

1. **Dr Sk Amir Hossain Amu** MBBS DTCD FCPS (Med, Part II)  
723/'A' Block  
BSMMU  
Dhaka
2. **Dr Ahad-ur-Rahman** MBBS  
401, Internee Hostel  
JIMCH  
Bajitpur  
Kishoreganj
3. **Dr Zerín Rahman** MBBS  
H# 15, R# 23, Sector# 7  
Uttara Model Town  
Dhaka
4. **Dr AKM Rafiqul Bari** MBBS  
20 Monipuripara  
Sangsad Avenue  
Tejgaon  
Dhaka
5. **Dr Kaniz Moula** MBBS FCPS (Med)  
Padma Diagnostic Centre  
Malibagh  
Dhaka
6. **Dr Kazi Atiqur Rahman** MBBS MD (USA) MD (Card Part II)  
H# 1270  
East Shewrapara  
Mirpur  
Dhaka
7. **Dr. Menoka Ferdhous** MBBS  
Medical Officer  
Thana Health Complex  
Savar  
Dhaka
8. **Dr Deb Prosad Bairagi** MBBS DCH (Vienna) MAMS (Vienna)  
45 Shamsur Rahman Road  
Khulna
9. **Dr. Iffat Shams** MBBS  
Operational Researcher  
Operational Research Section  
ICDDR,B  
Mohakhali  
Dhaka
10. **Dr Mahbubul Haque** MBBS  
A/R, MU - V  
DMCH  
Dhaka

THE WINNERS WILL BE CONTACTED INDIVIDUALLY  
AND AWARDED A FULL SET OF CECIL'S TEXTBOOK OF  
MEDICINE LATEST EDITION EACH.



# MediNews

## Brain cells can regenerate

Scientists have proved that human neurons are able to regenerate. Dr Fred Gage and colleagues at the Salk Institute for Biological Studies in California, together with doctors at the Sahlgrenska University Hospital in Sweden, have shown that new neurons do develop after birth.

This flies in the face of conventional wisdom which suggests that brain cells, unlike all other cell types, do not reproduce.

Dr Gage's team took postmortem brain tissue from five patients who had received an intravenous injection of bromodeoxyuridine as part of their treatment for squamous cell carcinoma. This drug is a thymidine analogue and is therefore taken up into the newly synthesised DNA of dividing cells.

Because of this property, bromodeoxyuridine is sometimes used to check for tumour cell proliferation. The researchers surmised that if neurons could reproduce then any new neurons, if present, would also take up bromodeoxyuridine.

Using immunofluorescence techniques and a laser microscope, which can optically section through individual cells, the team was able to detect the presence of bromodeoxyuridine in all five postmortem specimens.

In addition to showing that new cells were present in the brain, the team also confirmed that these cells were neurons by looking for two other markers which can differentiate between neuronal cells and glial cells (*Nature Medicine* 1998;4:1313-7).

The brain tissue studied by Dr Gage's team comes from the dentate gyrus, the part of the brain which acts as a relay station between the cortex and the hippocampus and is important in memory and learning. As yet Dr Gage has no idea whether the new cells identified in these sections are fully functional or under what sort of conditions new cells would be introduced. "There may be a replacement phenomenon going on, but we have no clear answers as to whether or not there is cell death over time," he said.

Plasticity and autologous repair may also have to be reexamined in the light of these findings.

In diseases such as Alzheimer's, Parkinson's and multiple sclerosis, neuronal death obviously occurs, but there may be something about disease process itself that prevents what might now be considered "normal" neurogenesis from taking place.

Clearly, the factors that stimulate and limit neurogenesis will have to be better understood before any mechanisms for showing or reversing neuronal loss can hope to offer benefit to people with these neurodegenerative diseases.

*BMJ* 1998; 317:1272

## Food and Drugs alter response to anaesthesia

Common food and widely used prescription and over the counter drugs may alter patients' response to muscle relaxants and anaesthetic agents,

according to studies presented at the American Association of Anaesthesiologists' meeting in Orlando, Florida, USA.

Potatoes, tomatoes, and aubergines contain solanaceous glycoalkaloids that even in small amounts may greatly slow the metabolism of muscle relaxants and anaesthetic agents such as suxamethonium, mivacurium, and cocaine, said Daniel McGehee of the department of anaesthesia and critical care at the University of Chicago, USA.

Solanaceous glycoalkaloids remain in the body for several days and are not altered by cooking. The compounds inhibit butyryl cholinesterase, which breaks down many anaesthetic agents, and acetylcholinesterase,

which breaks down acetylcholine and is necessary for normal nerve and muscle function. When these enzymes are blocked, anaesthetics and muscle relaxants remain in the body longer. Patients with a mutant form of butyryl cholinesterase may take 5-10 hours to recover from anaesthesia instead of the usual 40-90 minutes, said Dr McGehee.

There is no simple clinical tests for solanaceous glycoalkaloid levels, but anaesthesiologists may want to add questions on diet when taking a patient's history, the Chicago researchers suggest.

Another problem for anaesthesiologists is that patients may be taking prescription and over the counter drugs that may interact in unknown ways with anaesthetic agents. In an anonymous study at the

department of anaesthesia and critical care at Tulane University School of Medicine, New Orleans, USA 169 patients aged over 21 who were scheduled for elective surgery were asked to circle drugs on a list of 33 drugs known to affect central nervous system.

"We were very surprised to find 43% of patients were on a psychiatric drug," said Dr Corey Scher. "Many psychiatric drugs are coming on the market, and many are prescribed for non-psychiatric reasons: fluoxetine (PROZAC) for dieting, lithium for tremors, melatonin for sleep. We really don't know anything about the interaction of drugs our patients are taking and anaesthesia."

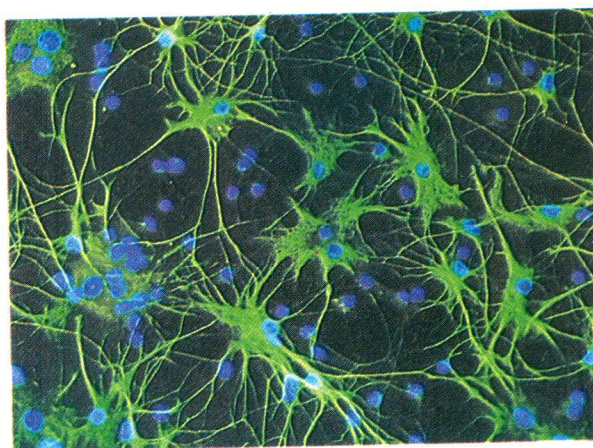
*BMJ* 1998; 317:1102

## Antibiotics may prevent heart attack

Infections, particularly *Chlamydia pneumoniae*, have been suggested as causes or contributing factors in atherosclerosis and heart attacks. Now indirect evidence shows that antibiotics, taken to treat common infections, may protect against first time myocardial infarction (*JAMA* 1999;281:427-31).

Patients who had taken tetracyclines were at significantly lower risk of having a heart attack than those who had not, according to retrospective analysis of data from 350 general practices in the United Kingdom's General Practice Research Database, which includes about three million patients.

The study, by the Boston Collaborative Drug Surveillance Program at Boston University, Massachusetts, USA identified patients in the



Neurons : Divide or not to divide?



database who had a first heart attack between 1 January 1992 and 31 October 1997. Patients were excluded who were older than 75 or who had risk factors such as a history of ischaemic heart disease.

Each patient was matched with controls from the same practice, also excluding those with risk factors. The study identified 3315 patients with heart attacks and these were matched with 13 139 controls.

Some heart attack patients and some control patients had received antibiotics. However, more patients who had not a heart attack had received antibiotics, compared with those who had had one.

This finding suggested that taking antibiotics somehow protected against heart attacks.

Compared with patients who received no antibiotics, those who received tetracyclines had an odds ratio of 0.7 (confidence interval 0.55 to 0.90) and those who had an odds ratio of 0.45 (0.21 to 0.95). Those who received macrolides (mainly erythromycin which is not very effective against *C. pneumoniae*), sulphonamides, penicillins, or cephalosporins were not "protected" against a heart attack.

The authors concluded that their findings indirectly support the hypothesis that certain chronic bacterial infections may have a role in the aetiology of ischaemic heart disease and that use of tetracyclines or quinolones might alter the course of such chronic infections and thereby reduce the risk of heart attack.

Not so fast to the prescription pad, argued Dr Aaron Folsom of the School of Public Health at the University of Minnesota, Minneapolis, USA (*JAMA* 1999; 281:461-2). While *C. pneumoniae* and *Helicobacter pylori* as well as herpes virus, cytomegalovirus, and periodontal infections may contribute to atherosclerosis, the mechanism is unclear. He pointed out that caution in antibiotic prescribing is needed to prevent development of drug resistant bacteria.

BMJ 1999; 318:417

### **$\beta$ -catenin identified as epithelial signal that induces hair morphogenesis**

Elaine Fuchs and co-workers of Howard Hughes Institute, University of Chicago, Illinois, USA report that transgenic mice expressing a stabilised  $\beta$ -catenin in their skin continue to produce many new follicles with sebaceous glands and dermal papilla after birth (*Cell* 1998;95:605-14). The result indicates that  $\beta$ -catenin can induce adult epithelial cells to differentiate into active hair follicles, a process that normally occurs only in embryonic skin. The finding raises the possibility of a cure for baldness.

This is "really exciting discovery", says Angela Christiano (Columbia University, New York, USA), "because, up to now, we've always assumed that you're stuck with the number of hair follicles you're born with. If it becomes possible to regenerate new hair follicles in adult, this would create opportunities to treat many types of hair loss such as alopecia areata and male-pattern baldness".

But it is early days. Hairs produced by follicles formed after birth in the transgenic mice were angled randomly, producing a rough coat, and the endless supply of  $\beta$ -catenin led to a high incidence of hair-follicle

tumours. By 3-4 months, the mice had many hair-follicle-covered epitheloid cysts resembling human trichofolliculomas. And as the mice aged, they developed larger, more obvious tumours. These were less differentiated than trichofolliculomas and resembled human pilomatricomas, tumours of the hair matrix.

The development of such tumours is likely to be a major stumbling block to the development of a  $\beta$ -catenin-based treatment for alopecia, but their occurrence reveals that misregulation of  $\beta$ -catenin in vivo has a specific role in hair follicle carcinogenesis. Autosomal dominant mutations in  $\beta$ -catenin occur in some colorectal cancer-cell lines and "our findings might explain why some patients with colon cancer also exhibit a tendency to develop hair-follicle tumours", says Fuchs.

Lancet 1998; 352: 1761

### **Low-tech acute myocardial infarction intervention gets new lease of life**

An infusion of glucose, insulin, and potassium (GIK) could be an important adjuvant for the immediate treatment of patients with acute myocardial infarction. In a placebo-controlled, randomised trial of 407 patients from six South American countries, a combination of traditional reperfusion therapy and GIK (given over 24 hours) reduced mortality after acute myocardial infarction from 15.2% to 5.2%.

"If these results are confirmed by larger clinical trials, GIK might become a promising therapy", says Leopoldo Piegas, one of the researchers involved in the trial, of Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil.

GIK infusion was first proposed as a metabolic way to protect the ischaemic myocardium in 1962, but since then no conclusion has been reached about the efficacy of the approach.

In the current study, patients were given either 2.4 l GIK solution (containing 25% glucose, 50 IU insulin, and 80 mmol/l potassium chloride), 1.8 l GIK solution, or no GIK. Because of the small number of patients, there were no significant differences in adverse effects or benefits between the high and low-dose groups, and the trialists reported their results as a comparison between GIK therapy and no GIK (*Circulation* 1998; 98:2227-34).

As Piegas notes, the trial was designed to investigate the safety of the method. However, the trialists reported a significant reduction in mortality (relative risk in patients given GIK compared with controls was 0.34 [95% confidence interval of 0.15 to 0.78]). Side-effects were rare and minor.

The Estudios Cardiológicos Latinoamérica Collaborative Group is now doing a 10 000-patient study of GIK infusion. Piegas, a member of the group, says that if the treatment proves to be an effective adjuvant option for treatment of acute myocardial infarction, it will have an impact on survival in both developed and developing countries, since it requires few human resources. "And it's very cheap, probably less than US\$ 5 per patient", he adds.

Lancet 1998; 352:1833



*Werner Zoege von Manteuffel was born in 1857 in northern Estonia and became professor of surgery at Tartu University, Estonia, in 1899. He was the first surgeon to advocate the use of boiled, sterilised rubber gloves to protect the patient from infection during surgery and published the first paper on sterilised rubber gloves in 1897. At that time most surgeons were operating with their bare hands, although some had experimented with silk or cotton gloves, which proved impossible to sterilise. To wear boiled rubber gloves, he said, was to have "boiled hands."*

BMJ 1998;317:1330



## Answer to MediQuiz 3 (Page no. 24 & 25)

Answer to MediQuiz 3 must reach us within 31st July 1999.

**10 PRIZES  
FOR ALL  
CORRECT  
ANSWERS**

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Please write the **true** stem(s) of a question in its respective box as shown below:

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fold

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- How satisfactory is the presentation of the Journal?  
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- To what extent the Journal is beneficial for upgrading medical knowledge?  
☐ Excellent    ☐ Good    ☐ Fair
- Do you have any suggestion or comments?

If any, please feel free to write down in the space on the opposite side.

Second  
fold

### ANSWERS

MediQuiz 2

- Roth spot
  - Infective endocarditis, leukaemia, severe anaemia
- Soft-tissue calcification
  - Systemic sclerosis, dermatomyositis etc.
- Surgical emphysema
  - Pleural aspiration/biopsy
- Splenomegaly
  - Lymphoma, leukaemia, hyposplenism (ITP unlikely)

Please give your mailing address and some personal information so that we can keep in touch with you (you may also attach your visiting card):

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Qualification .....

Year and Institution of Graduation .....

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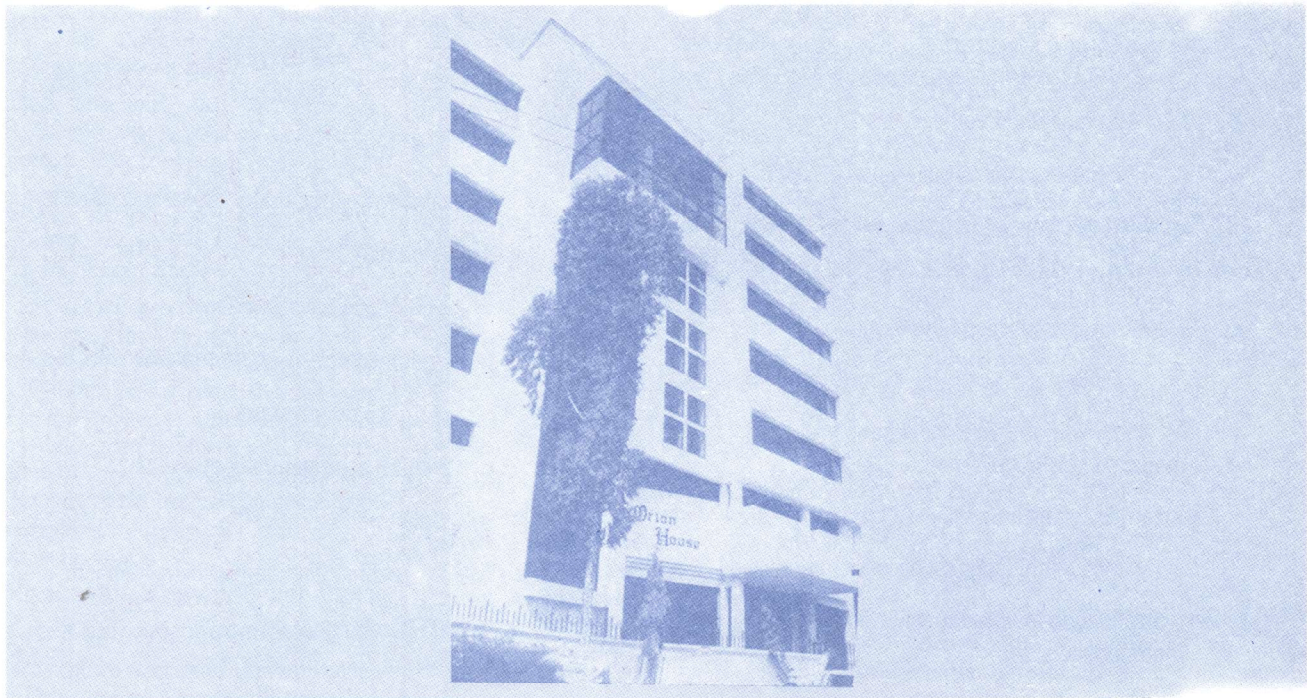
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*Space for Comments and Suggestions*



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