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JOURNAL OF BANGLADESH COLLEGE OF PHYSICIANS AND SURGEONS

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EDITORIAL

Dengue Syndrome: Yesterday, Today and Tomorrow

On these days of 2003 our country has entered in fourth year since documentation of the emergence of dengue as a public health problem in 2000. With an initial period of aback possibly the froth has been settled to look back and forward to review the whole affair in this behalf. Needless to pointing that no other communicable disease has been imputed for such a community response positively and negatively, in contemporary period. When dengue outbreak occurred in 2000 it poised itself a new entity non familiar both for the profession and the people alike. On the locus standii of today it is necessary to review the yesterday for shaping the tomorrow. This is because dengue is different on many counts. We have to agree with the statement of Gertrude Stein that 'A difference must a make difference to be a difference'[1]. Indeed dengue is this.

Dengue is special because of so many Nos, the so called 'Nos of Dengue'. There is no specific clinical feature, no specific user-friendly diagnostic lab test, no specific therapy and not the least no specific preventive measure. On the other hand it is a communicable vector borne viral febrile illness with high morbidity and panic stricken mortality with seasonal preponderance. The inherent peculiarities of the vector mosquitoes make them relatively beyond the reach of all conventional anti-vector measures which are highly related with some apparently non modifiable socio-economic-cultural-habitat issues[2].

During yesterdays of 1996-97 it was documented for the first time in a scientific manner the presence of dengue in our country[3]. The apparent naive data foresaw outbreaks in near future within few years. A value of 13.7% seropositivity in a group of under 15 children with fever attending Pediatric Out Patient Department of Chittagong Medical College Hospital over a period of one year with the evidence of 3 sero types of virus and more secondary infection pattern than primary revealed that significant numbers with non specific febrile illness was due to dengue with low grade continuation of transmission and outbreak potential. These harbinger data didnot get the attention it deserved. An entomological survey for vector showed at that time a figure, less than 20% by all 3 indicators, which could not be interpreted because of absence of any previous data in this regard and hence might be taken as baseline[4]. Given with this lab and entomological data possibly the situation was grooming for more maturation of other factors to culminate in an outbreak and later on turning to be a public health problem. A new addition to the list of public problems of our country.

In 2000 when the outbreak became a reality in the face of ambiguous community responses professionals and national control program personnel were in great difficulties at the outset because of respective 'Nos of Dengue'. This transient period of inerrancy passed off quickly. Borrowed knowledge from WHO and other dengue endemic countries mention worthy of which was Thailand, provided the initial alma matter for case management and of course control endeavors. Within a very short period medical professionals commanded the grip over the situation. Moreover internists and pediatricians could able to identify the elements which were not appropriate in the borrowed management guidelines in country

perspective. Through a national consensus consultative meeting internists and pediatricians of the country endorsed a `National Guidelines for the Clinical Management of Dengue Syndrome'[5]. The term `Dengue Syndrome' was adopted to cover all overlapping and sometimes indistinguishable presentations of dengue viral infection. This syndromic approach over emphasizes the target of management of reducing the mortality and morbidity as well, through the so called and popular 'Early Diagnosis and Prompt Treatment' approach.

While clinicians of the country have been engaged in their efforts to case management, some operational research have been initiated to gather readily applicable data. These are: relevance of case definition in terms of specificity, sensitivity and predictive values, pattern of viral serotypes and, estimation of proportion of dengue infection among febrile cases. The entomological counter part has also been initiated to document the various indices of vector. These are activities to make the dengue management more evidence based and appropriate. In these efforts of National Control Program, WHO and WHO collaborative centers in Thailand have been providing generous logistic and technical supports.

Compilation of published, being published and unpublished on-process data demand crucial review. The toll of dengue as documented by the National Control Program was 5551, 2617 and 6104 cases in 2000, 2001 and 2002 respectively with DHF frequency of 21.0%, 16.9% and 7.1% and case fatality rate of 1.7%, 1.6% and 0.9%[6]. Most cases in order of frequency was reported from Dhaka, Khulna and Chittagong metropolis. It has been found that possibly outbreaks will occur in even years in highly populated metropolitan cities in sequence, hemorrhagic fever will be more in alternate outbreaks increasing base line incidence to about 3-4 folds with parallel increase of vector indices. But relationship of vector indices to clinical incidence was not in agreement[7]. Initial multiple serotypes except D_1 that was found in early serosurvey has been changed. Only one type of viral serotype is now evident in subsequent outbreaks, which is D_3. The sensitivity and specificity of case definition provided by national guidelines in use by the doctors were found to be 83% and 75% respectively. The over all incidences during outbreaks were found to be around 3 fold rise than the base line of non outbreak years. Interestingly though there is incremental increase in incidence but the DHF proportion and case fatality are decreasing. But this is too early to comment emphatically.

Dengue experience moulded some of the usual clinical practice in terms of approach, choice of lab tests, management and reorientation of some forgotten skill. Out of these, approach to fever and use of antipyretics are more notable. Because of the clinical navigation provided by fever of the clinical course in dengue syndrome complete induced afebrile state is not warranted. The use of analgesics as antipyretic in the form of NSAIDs is forbidden, though both people and professional are long accustomed to use in this behalf. Scientifically fever is a protective response of the body and hence should only be addressed when it is intolerable or becomes a reason for further direct complication like convulsion in children. This scientific approach to fever was not readily acceptable to people in pre dengue. era, but now it has been gaining fast acceptance. The craze ushered by dengue outbreak for doing dengue specific lab test like RDT, blood and platelet transfusion, usage of steroid and other non specific remedies, and most noteworthy the use of antibiotic, are fast declining. The forgotten clinical test's.' like Capillary Refilling Time and Capillary Fragility are now becoming a common practice with its due applause for dengue diagnosis and management. Moreover the intensive management that is,

required for a DSS patient and the confident evidence based approach to DHF providing the health care professional with knowledge, skill and attitude which can be utilized for any other critical and potentially critical patient.

Dengue is an example where absence of knowledge can be supplemented by wisdom. In the sea of Nos in this regard of specific clinical attributes the epidemiological, based permutation and combinations of non specific parameters even provided reasonable operational case definition for suspicion and management with high index of specificity, sensitivity and confidence interval[8]. In documented series we found the sensitivity and specificity of Positive Tourniquet Test, Leucopenia and Leucopenia plus Positive Tourniquet Test respectively 65% and 55%, 95% and 55%, and, 85% and 80%[9]. Farthur enhancement of these can only be done through continuation of appropriately designed scientific operational studies for country perspective customization and training on guidelines.

The diagnosis and management of dengue is fairly simple for most cases if one adheres to the national guidelines, can able to suspect the condition at early period and refrain from overdoing. The keyword is therefore 'Early Diagnosis and Prompt Treatment' a time tested approach of national control program. Early detection and appropriate simple management may prevent the masquerading of the downhill process of DHF and DSS even. But this is not so simple because of many factors. Both the professional and patients should be able to comply and complement based on awareness, confidence and the scientific pursuits. The tragedy of science is that it cannot be practiced always. Here in this case in a patient with high continued fever or bleeding it may be difficult for both to adhere consistently the scientific approach in absence of reciprocal trust based on knowledge, skill and attitude. So the prime need is the fast orientation of the people and the profession and, growth of confidence on scientific evidence based approach. All the maladies which occurred in the form of mortality off dengue so far was mostly due to the over doing and lack of confidence on evidence based approach.

The community response that is poised by dengue is unique in the contemporary history of any communicable disease in this country. But the intense community response which was initially ambivalent has been later on turned into some really positive direction in terms of awareness, community empowerment and dynamic global movement. This is very pertinent for the control of dengue, because of the predisposing factors for the vector to thrive and increase in magnitude are highly linked with socio, economic, habitat and cultural factors that are beyond the reach of health authorities. On the other hand appropriate community empowerment may make the practice of scientific medicine in this regard through early diagnosis and prompt treatment thereby reducing mortality and morbidity much more conducive and easier. In this context the role of the community may be envisaged as, measures to reduce the habitat of vector mosquito and their proliferation, reduce man-mosquito contact and early suspicion of a case and the first aid. But prime target is to take individual measures of protection at the present day scale.

Documentation and reporting of dengue cases is far more important for any control endeavor. Appropriate compilation of data can provide information not only about the toll but also can predict the future outbreak, the clinical pattern and morbidity. This can therefore make the measures appropriate in readiness before the outbreak and can therefore efficiently contain the outbreak and reduce the morbidity and mortality. The practice of reporting as per national guidelines is sufficed to achieve this aspect. Indeed dengue is one of the examples of successful documentation by national control program form the very beginning even with some lapses. The most important lapse in this regard is the failure to pick up data from the health care outlets which are not run by

the public sector. Notwithstanding this the documentation lack the uniformity, comprehensive clinical attributes that should be in this behalf.

Dengue is a challenge package for the community, for the professional and for the national control endeavor because of its peculiarities. The concurrent evidence that, in countries where dengue entered never left and causing cyclical outbreaks with heavy tolls in terms of morbidity and socio-economic burden. This attribute is important for a country like us which is at the beginning with the experience of dengue. At this point of period therefore pragmatic programs are needed to face the menace of which scientific exercises and proactive clinical role are the most warranted matter. In short the public and the profession should be oriented to 'learn to live with dengue'[10].

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(J Bangladesh Coll Phys Surg 2002; 20 : 111-114)

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Presentation of Invasive Cervical Cancer

F SOBHAN, FCPS[a], KJ MAULA, DGO[b]

Summary :

Objective : To determine how patients with invasive cervical cancer present.

Method : A prospective study was carried out on 110 patients with invasive cervical cancer attending Gynae Outpatient Department of National Institute of Cancer Research & Hospital, Dhaka between January 27, 2001 & June 10, 2001.

Results : 6 patients (5.45%) had Stage 1 disease, 77 (70%) were in Stage 11, 25 (22.73%) in Stage 111 & 2 (1.82%) in Stage 1V. 55.45% of patients presented with abnormal vaginal bleeding, 25.45% presented with vaginal discharge, 14.54% with pain, 1.8% with abnormal Pap smear & 2.7% presented with other symptoms. The growth was ulcerative in 40% cases, exophytic in 38.18% & endophytic in 18.18%. The tumour size was > 4cm in 52.73% cases and < 4cm in 47.27% cases. 90.91% of patients had squamous cell carcinoma & 9.09% had either adenocarcinoma or adenosquamous carcinoma.

Conclusion : Most of the patients in this study had locally advanced or regionally advanced invasive cervical cancer. Abnormal Pap smear was not a common presentation. These findings underscore that cervical screening programmes should be given priority in our health care delivery system.

(J Bangladesh Coll Phys Surg 2002; 20 : 115-119)

Introduction :

There has been a substantial decrease in the incidence & mortality from cervical cancer in North America, the Nordic countries & the UK[1,2,3]. However, it continues to remain the commonest cancer affecting females in the developing countries[4]. A large proportion of women present with advanced disease & are in a poor nutritional state. In India, cervical cancer is the commonest cause of death in women aged 35-45 years[5]. Data of different hospitals show that cervical cancer is the leading female malignancy in Bangladesh[6,7]. A community-based study reported its prevalence to be about 26%. Since cervical cancer is an important cause of premature disability & death of women in Bangladesh, it was decided to carryout this study to determine the various presentations of this disease.

Materials and Methods :

110 patients with invasive cervical carcinoma attending Gynae Outpatient Department of National Institute of Cancer Research and Hospital (NICR&H), Dhaka between January 27, 2001 and June 10, 2001 were included in this study. Medical interview, physical examinations including pelvic examination, relevant investigations were done in each case. Diagnosis was confirmed by histology. Data collected included age at diagnosis, parity, menopausal status, presentation, histology, size & stage of the cancer. Staging was done according to International Federation of Gynaecology and Obstetrics (FIGO) classification. In cases where there was more than one presenting symptom, the presentation assigned was the one that prompted the patient to seek the services of National Institute of Cancer Research and Hospital (NICR&H), Dhaka.

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Results :

The age range of the 110 patients was 24-80 years & the median age was 45.5 years. 65% patients were in the age group of 45 - 60 years. The peak incidence was between 40 to 49 years (Fig. I). About forty-three percent women in this series were postmenopausal. Mean parity was 6. Around sixty-nine percent women were grandmultiparae. Only one patient (.9%) amongst 110 women was nulliparous. Six women (5.54%) were in Stage I, seventy-seven (70%) in Stage II, twenty-five (23.27%) in Stage III and two (1.8%) in Stage IV.

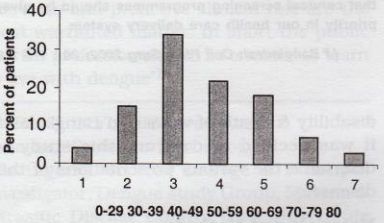

Fig.-1 : *Age distribution of patients of invasive cervical cancer*

Table-I

Presentation of cervical cancer

	No. of patients
Presentation	
Abnormal vaginal bleeding	61 (55.45%)
Postmenopausal bleeding	25 (22.72%)
Irregular bleeding	26 (23.63%)
Postcoital bleeding	10 (9%)
Vaginal discharge	28 (25.45%)
Pain	16 (14.54%)
Abnormal Pap smear	2 (1.8%)
Other	3 (2.7%)
Total	110 (100%)

The presentation of the study population is summarized in Table I. Sixty-one (55.45%) patients presented with abnormal vaginal bleeding. Of these 61 patients, 26 were postmenopausal & 35 premenopausal. Post coital bleeding occurred in 10 patients, 9 of whom were premenopausal. Twenty-eight (25.54%) presented with vaginal discharge & sixteen (14.54%) with pain. Two (1.8%) presented with abnormal Pap smears. One patient each presented with a pelvic mass, with acute urinary retention & with enlarged supraclavicular lymph nodes.

Table II summarizes the association of presentation with stage of disease. Abnormal Pap smear was the presentation in stage I only. Pain was present in more advanced cases.

Table II

Association of presentation with stage

	Stage		
Presentation	I	II	III and IV
Abnormal bleeding	3(4.92%)	47(77.05%)	11 (18.03%)
Vaginal discharge	1(3.57%)	22(78.57%)	5 (17.86%)
Pain	0	8(50%)	8 (50%)
Abnormal Pap smear	2(100%)	0	0
Other	0	0	3 (100%)

Table III shows the gross appearance of the cervix. Ulcerative tumours were present in forty-four (40%) cases and exophytic growth in forty-two (38.18%) cases. Endophytic growth was present in twenty (18.18%) cases. No visible tumour was detected in four (3.63%) cases.

Table-III

Gross appearance of cervix

Description	No. of Patients
Ulcerative growth	44 (40%)
Exophytic growth	42 (38.18%)
Endophytic growth	20 (18.18%)
No visible tumour	4 (3.64%)
Total	110 (100%)

Table-IV

Association of appearance of cervix (type of tumour) with stage

Appearance of cervix	Stage I	Stage II	Stage III	Stage IV
Ulcerative growth	1 (2.27%)	33 (75%)	8 (18.18%)	2 (4.54%)
Exophytic growth	1 (2.38%)	33 (78.57%)	8 (19.04%)	0
Endophytic growth	0	11 (55%)	9 (45%)	0
No visible tumour	4 (100%)	0	0	0

Table V

Association of stage with histologic grade

Stage	Grade 1 well differentiated	Grade 2 moderately differentiated	Grade 3 poorly differentiated
I	2 (33.33%)	3 (50%)	1 (16.67%)
II	11 (14.28%)	47 (61.04%)	19 (24.67%)
III	3 (12%)	13 (52%)	9 (36%)
IV	0	1 (50%)	1 (50%)

The association between gross appearance of cervix (type of tumour) and stage of cancer is shown in Table IV. The distribution of exophytic & ulcerative tumours was similar in stage I, stage II & stage III cancers. In four (66.66%) of six cases of stage 1 cancers, no growth was visible on the cervix.

Among 110 patients, the tumour size was > 4cm in fifty-eight (52.73%) cases and < 4cm in fifty-two (47.27%) cases.

Hundred (91%) women had squamous cell carcinoma & ten ((9%) had either adenocarcinoma or adenosquamous carcinoma. The association between stage and histological grade of tumour is summarized in Table V. Moderately differentiated tumours (Grade 2) were the predominant variety in stage I, stage 11 and stage III cancers.

Discussion :

The age distribution of patients in this series is similar to that of other studies[8]. The peak incidence was in the fifth decade & the rate declined after age 65. Another study found the rate to decline after age 60[9].

Parity six was associated with the largest proportion (20%) of cervical cancer cases, followed by parity seven (16%) and parity eight (13%). Some authors have, however, found the incidence to increase from parity six onwards[10]. Of 110 women, only one (.9%) was nulliparous. In contrast, Pretorius[11] had 18% nulliparous women in his study. It may be mentioned that Pretorius had carried out his study in California, USA. .

The epidemiology of cervical cancer has been a subject of numerous studies. Risk factors identified include early age at first marriage, increasing number of marriages, poor personal hygiene, greater number of pregnancies, early age at first intercourse and multiple sexual partners of the women, with the later two factors appearing to be most directly related to the occurrence of the disease[12]. The number of sexual partners of the husband also increases the risk of the wife[13]. In Bangladesh, sexual conduct is

guided by religious and social norms and extra marital sex is not common. This factor possibly accounts for the low incidence of cervical cancer amongst nulliparous in this series.

The clinical stage of cervical cancer at the time of diagnosis & the tumour size are important predictors of the outcome of the disease[14,15]. 70% women in this series had stage 11 disease & 23.72% were in stage 111. The primary tumour was bulky in the majority of cases. The prognosis of most of the patients is therefore likely to be poor.

As has been noted by others, the most common presenting symptom was bleeding[8,11]. Abnormal Pap smear was the presentation in 1.8% cases. In the series of Pretorius[11], abnormal Pap smear was the presentation in 28% cases. The proportion of stage I cases in the current series was 1.8% while it was 53% in Pretorius's series. Comparing the two, it is seen that presentations with abnormal Pap smear is more than twenty nine times higher (28% vs 1.8%) and the number of stage I cases is about ten times higher (52.73% vs 5.45%) in Pretorius's series. The plausible explanation for the difference in presentation lies in the utilization of cervical cancer screening programmes. Pap smear as a screening test for cervical cancer is widely utilized in the developed countries. This has resulted in earlier detection of asymptomatic cases[9] and increased detection of stage I cases[16,17]. The overall effect has been a substantial decline in the incidence of and mortality from cervical cancer in the developed countries. In developing countries, the implementation of organized cytology screening programmes has proved difficult because of labour and fiscal constraints[18]. This is true for Bangladesh also. Hence the observed difference in the proportion of asymptomatic & stage I cases in the two series, carried out in entirely different socio-economic contexts.

In this study, no growth was visible on the cervix in 66.66% of stage I cases. This is an important reminder that a hypertrophied cervix with no obvious growth might in fact be harboring cancer. Many such cases are initially treated as chronic cervicitis & the correct diagnosis made only after inappropriate surgery has been done. Hence, it is essential that all abnormal and suspicious looking cervices are biopsied before undertaking definitive treatment.

The majority of tumours were of the squamous cell type and this is in accord with other studies[8,9]. There are disparate views on the significance of differentiation with regard to prognosis. Some have found that prognosis was more favourable in those with better-differentiated tumours[19], while others have failed to identify a difference[20].

Conclusion :

In this study, the clinical presentations of a number of cervical cancer cases were analyzed. Given the current socio-economic trends, it is unlikely that there will be an appreciable decline in the incidence of cervical cancer in Bangladesh in the coming years. Hence, the need is to educate women about the symptoms of cervical cancer so that they seek early medical consultation. Renewed focus on cervical screening programme is also required. Since the organization of comprehensive cytology screening progamme has so far proved elusive, consideration may be given to alternate low-cost, low-technology methods of screening such as VIA (visual inspection of the cervix after application of acetic acid).

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Sero Diagnostic Value of Elisa in Tuberculosis

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Abstract :

The Immunoglobulin G (IgG) antibody response to mycobacterium tuberculosis was evaluated in this study to assess it's potential value as a diagnostic aid. 50 healthy volunteers with negative or positive tuberculin test acted as control. Most (98%) of the control scored negative results. About 46% of pulmonary tuberculosis and 32% of extra pulmonary tuberculosis were sensitive to the test. In smear positive patients the test was sensitive in 50% of cases. Thus, this test which detects IgG antibody against mycobacterium tuberculosis has specificity of 98% and sensitivity of about 46% in pulmonary tuberculosis and 32% in cases of extra pulmonary tuberculosis.

(J Bangladesh Coll Phys Surg 2002; 20 : 120-123)

Introduction :

Tuberculosis (TB) is the largest single infectious cause of human mortality[1]. One in every three people on earth is believed to be infected with mycobacterium tuberculosis, leading to seven to eight million cases of active tuberculosis per year and approximately three million deaths annually[2]. The incidence of TB has remained high in most of the developing world including Bangladesh and the disease has recently re-emerged as a public health problem in industrialized countries. The burden of problem has been intensified to a great extent with the increased incidence of tuberculosis in AIDS patients and due to appearance of multi-drug resistant tuberculosis.

The ultimate goal of biomedical TB research is to lessen the public health burden of this disease by developing improved diagnostic, therapeutic and intervention strategies. To overcome the limitations of the conventional laboratory tests for the diagnosis of tuberculosis, attempts have been made to develop a good serodiagnostic test. Enzyme Linked Immunosorbent Assay (ELISA) for estimating antibodies in the serum and other body fluids in cases of tuberculosis have given encouraging results[3].

The aim of this study is to detect the specificity and sensitivity of ELISA in detection of pulmonary and extrapulmonary tuberculosis.

Materials and Methods :

Fifty three patients (40 males and 13 females) with tuberculosis (28 pulmonary and 25 extrapulmonary) were studied retrospectively. Age of the patients ranged from 18 years to 79 years (mean age 43.3 years). All the patients belonged to Bangladesh Armed Forces and their family and were admitted to CMH Dhaka during the period of January' 97 to March' 99. Tuberculosis were diagnosed with the help of patients symptoms, clinical observations, CXR, sputum for AFB, tracheobronchial washings and brushings, MT, ESR, pleural fluid and CSF study, biopsy of affected organs, ELISA for TB complex and other appropriate investigations. Fifty healthy volunteers (30 males and 20 females) of different age ranging from 20 to 70 were included in the study as control group.

Blood samples from both patients and 'control group were tested at Armed Forces Institute of Pathology by using commercially available reagents and following the instruction of the kit. ELISA method was applied to detect the IgG antibody against mycobacterial A-60 antigen complex which is an interspecific antigen found in the cytosol of typical and atypical mycobacteria.

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Results :

A total of 53 cases of tuberculous patients were delt. Among 28 pulmonary tuberculosis 13 (46.43%) were IgG positive and among 25 extrapulmonary tuberculosis 8 (32%) were IgG positive. Total number of IgG positive cases were 21(39.62%). Out of 12 smear positive cases 6 (50%) showed positive IgG response. Among 50 control subject only 1 (02%) individual showed positive IgG and 49 (98%) were negative for IgG against tubercular antigen.

Data Analysis :

Table-I

Distribution of study population and IgG positive cases.

Types of TB	Pulmonary (N-28)*	Extrapulmonary TB (N-25)					
Subtypes	-	Pleural N-9	L. Node N-8	Bones N-3	TBM N-2	Urinary N-2	Intestinal N-1
AFB smear positive	12	0	0	0	0	0	0
IgG +ve	13 (6+7)**	3	3	1	1	0	0
Percentage of IgG positivity	46.43%	33.33%	37.5%	33.33%	50%	0%	0%
Overall percentage of positivity	46.43% (13/28)	32% (8/25)					
39.62% (21/53)							

*Endobronchial TB (n-3).
**7 out of 12 smear +ve cases.
7 out of 16 smear negative cases.

Table-II

Distribution of IgG positive cases in smear positive pulmonary TB.

Total N-12	Pulmonary parenchyrnal N-9	Endobronchial N-3
IgG	6(66.66%)	0(0%)
Overall percentage of of positivity	50%(6/12)	

Table –III

Control Group

Total No.	IgG + ve	IgG-ve
50	01(02%)	49(98%)

Discussion :

Serological tests for tuberculosis are a measure of the humoral immune status of the patient. They are not a substitute to AFB or its antigen detection. But, the serological tests by detecting specific mycobacterial antigens and antibodies can be of great help in diagnosing the smear negative tuberculosis as these are rapid, in expensive and simple to perform[3]. IgG antibodies appear when an infection becomes establised. They indicate a good immunological response of the patient to the infection[4]. IgM antibodies are an indication of the beginning of a primary infection (primary complexes). IgA antibodies strengthen the diagnosis in cases of suspected meningitis, pleuresis and pericarditis, renal TB and AIDS patient with TB[5]. In this study, serum IgG level against mycobacterial A-60 antigen complex was detected and following cutoffs have been taken for positive or negative, results.

Results	IgG Sero units
Negative	<125
Dubious	125-225
Positive	>225

Specificity of ELISA was found to be 98% which is comparable to a similar Study (>98%) done at centre MURAZ, pairs[6]. Sensitivity in smear positive cases was 50% as compared to 40% in above study. Another study done at Dept of Microbiology University College of Medical Sciences, Delhi, showed the specificity of ELISA was 87.5% and sensitivity of 77.5%[7] Different studies show a percentage of A-60 seropositivity in healthy people varies between 1.5 and 3%[4].

In 10-20% of individuals the humoral immunologic activity is weak and they may show false negative results[8]. Mycobacteria other than mycobacterium TB (typical TB) may yield positive ELISA tests. It also reacts with antibodies found during leshmaniasis and nocardia infection[9]. Immunosuppressive treatment and AIDS may also alter the immune response[10]. So the result obtained with this test are to be considered in conjunction with clinical observations and the results of other tests.

Conclusion :

This study reveals the specificity of ELISA in detecting mycobacterium tuberculosis is high (98%) but sensitivity is low (- 40%). Its sensitivity is relatively high in pulmonary (- 46%) than extrapulmonary (32%) tuberculosis. From these results we conclude that, ELISA for detection of mycobacterial antigen alone is not sufficiently sensitive to be useful for routine use. It can be used as a complementary technique for the diagnosis of tuberculosis especially when traditional methods fail to arrive a conclusive diagnosis. However, large scale study is required for reconfirmation and finalization of results.

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Avoidable Factors for Maternal Mortality- A Community Based Investigation in Bangladesh

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Summary :

This study was a descriptive one with a cross sectional design. It was done in Gopalganj district from September 1997 to August 1998. Two hundred five maternal deaths from 1994 - 1997 were investigated. The study was done with the objective to determine care seeking behaviour of mothers who died, identify causes of delay in "three delay model" and to seek out avoidable factors in those deaths. Data analysis was done using Chi-square test. Only 49 (23.9%) out of 205 mothers who died attended health facility. 77.6 percent families had knowledge about where to go with an Emergency Obstetric (EO) problem and 76.6 percent knew how to reach the health facility. Those patients attended health facility whose families had knowledge about where to go (P=<0.001) and how to go (P=<0.001). Problem unrecognized (45.1%), economic constraints (27..5%) and time constraints (9.9%) acted as barrier in seeking care in families who did not seek care. 71.5 percent maternal deaths at health facility were categorized as avoidable and substandard care was observed in 82.9 percent cases. Underlying medical causes of maternal death are a range of social, economic, cultural and quality of care factors that greatly contribute to women's health before, during and after pregnancy.

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Introduction :

Maternal mortality is a test of the status of women in the society[1,2]. It reflects a woman's basic health status, her access to health care and the quality of service that she receives. In Bangladesh maternal mortality is one of the highest in the world with an estimated rate of 3.9/1000 live births with approximately 3 million births per year[3]. A range of factors influence the outcome in an obstetric emergency and contribute to this high maternal death.

Most obstetric complications cannot be predicted, and there is no way of preventing them. Ensuring access to care has been shown to be an effective intervention for reduction of maternal mortality in Bangladesh circumstances. The chance of surviving an obstetric complication is excellent if a woman receives medical care in time.

Thus it is important for women and their families to recognize signs of pregnancy related complications, realize their seriousness and be confident that they can be addressed through formal health care. To save the lives, of a vast majority of women who develop obstetric complications it is not necessary to build facility in every village and insist that all women deliver there. We do, however, need to assist communities, in developing plans to ensure that, when a complication does develop, quick action can and will be taken so that women in need can reach to appropriate facility in time. In this connection, it is useful to analyze separately each of the three steps that must be considered in order for a woman to get life saving treatment. Delay in any of these three stages can spell death. These delays result from socio-economic constraints, cultural

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conditions, geographic and environmental obstacles, administrative and logistic barriers that exist in every community.

Lack of access to care contribute predominantly to maternal death in developing countries. What is meant by "access" and what are the factors affecting it? Simply establishing services will not make them accessible. A service is accessible if it is within reach, women can get it easily and they are not deterred from using it. Good quality services require that health care providers have adequate clinical skills and are sensitive to women's needs, that facilities have necessary equipment and supplies; and that referral system functions well enough to ensure that women with complications get essential treatment.

The "Three Delays Model" put forward by Deborah Maine et al at Columbia University provides a framework for analyzing the factors that contribute to maternal deaths[4]. The first two delays relate directly to issue of access to care, encompassing factors in the family and community. The third delay relate to factors in the health facility. This study was done to determine the care seeking behaviour of the mothers who died, identify causes of delays in the "Three Delay Model", to determine which maternal deaths were avoidable and to seek out avoidable factors in those deaths and to recommend ways to overcome barriers that cause delays in seeking, reaching and receiving care at health facilities.

Methodology :

The study was a descriptive one with a cross sectional design. The study area was in Gopalganj District covering 5 Thanas, 71 Unions and 592 villages. The district is situated 200 km South of Dhaka, capital of Bangladesh. Maternal deaths that occurred during 1994, 1995, 1996 and 1997 in the above area were investigated. A total of 205 maternal deaths were identified using Family Welfare Visitors (FWVs) registers. FWVs are paramedics stationed at health and family planning centres with an average of 1 per 25,000 population. Retrospective questioning of relatives or associates of the deceased women were done to collect data. This technique of data collection is called Verbal Autopsy Technique. The study period was one year from September 1997 to August 1998. Data analysis was done using software SPSS PC+ version 7.5. The categorical data were presented through univariate and bivariate tables. Chi-square tests at 5% level of significance were attempted to find out the association between different attributes.

No standard definitions were used to classify socio-economic status of the deceased. They were categorized as poor, average and in good social class by asking the family the followings:

Good social class

If the family was able to save money after maintaining food, clothings and housing

Average social class

If the family could maintain food, clothing and housing without depending on others

Poor social class

If the family had to starve or depend on others for food and clothings.

Results :

A total of 205 maternal deaths that occurred in Gopalganj District from 1994 to 1997 were investigated. 91 patients did not seek care and 65 patients decided to seek care but failed to attend health facility. Only 49 (23.9%) patients could attend health facility (Fig.1). Among them 77.6% families had knowledge regarding where to go with an Emergency Obstetric (EO) problem and 76.6% knew how to reach the health facility. Families who had knowledge about where to go and how to reach facility decided and attended the facility (P=<0.001, P=<0.001 respectively) (Table-I). Husband (50%), family members (15%), mother-in-law (12%) in succeeding order were the principal decision makers for seeking care in obstetric emergency.

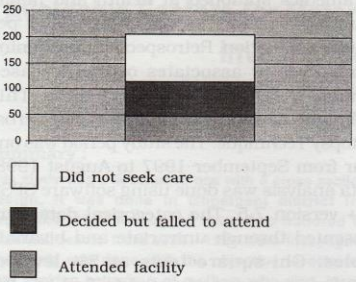


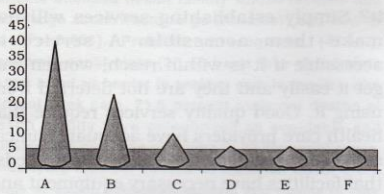
Fig.-1 : Care seeking behaviours of deceased in regards to utilization of health services

Decision to seek care was taken as soon as the problem was recognized in 63.2% cases while in 36.8% cases they were taken only when the condition became serious.

Among families who did not seek care after development of EO problems it was found that 45.1% family could not recognize the problem. Economic constraints (27.5%) and time constraints (9.9%) also acted as barrier in seeking care (Fig.-2). Relating the socio-economic status with the care seeking behaviour in bivariate table it was found the economic constraint was the main reason behind not seeking care in poor class while in average and good class families could not recognize the problem (Table-II). Among the patients who failed to attend facility after decision, time constraints and economic constraints were the main barrier. Time constraints probably was due to delayed perception of seriousness of problem in some cases. 6.2% patient died on way indicating delayed decision for taking the patient to health facility (Fig.-3).

In this study 73.17% families could recognize EO problems. Husband (35%), relatives (23%), village doctors/FWV (12%) recognized the problem in succeeding order. Time between recognition of problem and maternal death was calculated separately for some common obstetric complications. They ranged between 1-17 hours for postpartum hemorrhage, 12-18 hours for ruptured uterus and 28-58 days for heart disease (Table-III)

Majority of the patients were carried by slow moving manually run vehicles to health facility and 51% patients reached health facility after 4 hours of decision. Among the 49 institutional deaths in 51 percent cases, treatment started immediately after reaching the health facility. There was delay



A = Problem unrecognized
B = Economic constraints
C = Time constraints
D = Member not at home
E = Transport problem
F = Parda/superstitions

Fig. 2 *: Reasons behind not seeking care*

in 49 percent cases because of logistic problems. After reaching the first health facility 12 patients needed referral to higher centre for operation, blood and specialist consultation but none were provided with ambulance from the first level of contact. 73.5% patients died after 6 hours of reaching the first health facility. Categorization of death in facility showed that 71.5% deaths could be avoided and in 8.1% cases death could not be categorized.

All deaths which were categorized as avoidable were reviewed in depth to identify the avoidable factors. This was done under broad heading of delay in seeking care, delay in reaching facility and delay in starting treatment. There was considerable overlap in care seeking behaviours. Some patients had delay in all the three stages while others had in two stages or some had delay only in one stage. 82.9% patients had delay in starting treatment and reasons behind were soughted out (Table-4). Thus substandard care was observed in health facility in 82.9% cases in this study.

Table-I

Maternal death by knowledge regarding where and how to go and care seeking behaviours of deceased.

	Care seeking behaviour of deceased		
	Not decided to seek care	Decided but failed to attend	Decided and attended facility
Knowledge regarding where to go			
Yes	50 (54.9%)	60 (92.3%)	49 (100%)
No	41 (45.1 %)	5 (7.7%)	0 (0%)
x^2= 49.042; df = 2; P =<0.001			
Knowledge regarding how to go			
Yes	48 (52.7%)	60 (92.3%)	49 (100%)
No	43 (47.3%)	5 (7.7%)	0 (0%)
X^2= 52.778; df= 2; P =<0.001			

Table-II

Maternal death by socio-economic status and reasons behind not seeking care

	Reasons behind not seeking care			
Socio-economic status	Economic constraints	Problems unrecognized	Time constraints	Others
Poor	20 (80.0%)	21 (52.5%)	6 (66.7%)	74 (56.5%)
Average	5 (20.0%)	16 (40.0%)	3 (33.3%)	51 (38.9%)
Good	0 (0%)	3 (7.5)	0 (0%)	6 (4.6)

Table-III

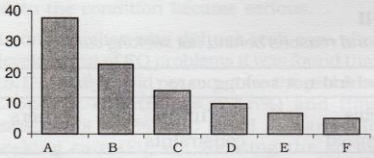
Time between recognition of problem and maternal death

Complication	Hours	Days
Haemorrhage	—	—
Postpartum Haemorrhage	1 -17 hrs.	—
Retained placenta	10 hrs.	4 days
Antepartum Haemorrhage	2 hrs.	6 days
Eclampsia	2 - 12 hrs.	2 - 4 days
Ruptured Uterus	12 - 18 hrs.	
Obstructed labour	—	2 - 4 days
Jaundice	—	6 — 25 days
Severe anaemia	—	14 - 30 days
Heart disease	—	28 - 58 days
Induced abortion	—	3 - 6 days

Table-IV

Avoidable factors in maternal death

Variables	No. of patients n=35	Percentage
Delay in seeking care after decision	21	60%
Delay in reaching facility	25	71.4%
Delay in starting treatment	29	82.9%
a) Delay in seeing the patient by doctor	3	
b) Non arrangement of blood	13	
c) Non availability of medicine	1	
d) Late/non referral of patients from lower to higher center	4	
e) Trial for NVD continued where caesarean section was indicated	8	



A = Time constraints
B = Economic constraints
C = Distance/transport problem
D = Patient condition serious
E = Mother/relatives/husband not willing
F = Died on the way
G = Husband not available

Fig-3 : *Reasons behind not attending facility after decision*

Discussion :

Delay in Seeking Care

76.1 % patients in this study did not seek hospital care. Socioeconomic status was found positively correlated with care seeking behaviour (Table-II). For poor class economic constraint was the main reasons for not seeking care while for average and good social class the problem remain unrecognized. In Ghana, 64% of women who died of pregnancy complications sought help from a traditional healer before going to a health facility and the main reason for not seeking care were cost and their belief that the woman was not ill enough[5]. In table-1 it has been shown that families who knew where to go and how to reach health facility in EO problem attended the facility (P=<0.001, P=<0.001 respectively). Studies have found that husband and mother in law knew very little about pregnancy related complications and their possible fatal consequences[6]. In a previous formative study on KAPP relevant to utilization of EOC series, husband had ,a high knowledge gap about the life threatening consequences of emergency obstetric complications[1]. In this study 34.1% husband could recognize EO problems and they were the principal decision makers in seeking care. This observation suggest that knowledge of EO problem and awareness among community members have a positive impact in safe motherhood problem. It is important for women and their families to recognize the signs of pregnancy related complications and realize their seriousness.

For most complications enough time is available to manage the case. While a serious haemorrahge can kill a woman in less than hour, in many cases women arrive at hospital alive after bleeding for much longer. For other common complications there are usually several days between the time the condition

becomes obvious and death (Table-III). The findings of time between problem recognition and maternal death in this study matched well with the assumption of D Maine[8].

Delay in Reaching Health Facility :

Good road communication, transport and distance to health facilities are important for timely arrival to the facility in obstetric emergencies. In most rural areas, one in three women lives more than 5 km from the nearest health facility and 80% of rural women live more than 5 km from the nearest hospital[9]. The scarcity of vehicles and poor road conditions makes it extremely difficult for women to reach nearby facilities. Walking is the primary mode of transportation even for women in labours[10]. In this study 77.5% patients used slow running manually operated vehicles as transport.

Timely communication with nearest hospital is often the decisive factors between life and death. Villagers are unable to communicate with the hospital. A great time is always lost for arranging transport for shifting patient and on journey. Here it took more than 4 hours after decision to reach health facility in 51 % patients. In rural Tanzania, 84% women who gave birth at home intended to deliver at a health facility, but did not because of distance and lack of transportation[11].

Delay in Receiving Care at Health Facility :

Quality of care is a key factor in ensuring program success in reproductive health. Before implementing health education and effective community mobilization to promote the use of services at health facilities, they need to be capable of meeting increased demand and providing good quality care. MS Angela Kamara of the Regional Prevention of Maternal Mortality Network project says "You have to clean your house before you invite guest in."

The common barriers that contribute to poor quality care include: lack of drugs and supplies, in adequately trained staffs, delays in referral and poor interaction between clients and health care providers. All these are categorized under the broad heading of substandard care. Family members who bring a woman in hospital may be forced to purchase drugs and supplies from outside pharmacies which can cause fatal delays[4,12]. Health staffs may lack life saving and basic skills. They are poorly supervised, underpaid and overworked[13]. In this series there was non arrangement of blood in13 cases and non availability of medicine in one case for which the patient died.

The number of referrals that the woman undergoes before reaching an appropriate health facility is a crucial determinant of survival. The inability of health facilities to deal with obstetric complications and unwillingness to accept potentially serious cases lead to patients being shifted from one facility to another. In addition failure of health workers to identify women suffering from serious pregnancy related complication and to refer them to a higher centre[14] causes delay in referring women from community health facilities to hospitals. The stepwise hierarchical referral system further increases misreferrals and prevent women from receiving care that could save their lives[13]. Staff at the community facilities may not recognize the seriousness of the problem or systems for transporting women to higher centre is not available[15]. In this series similar observations were found. Four patients died due to late/non referral from lower to higher centre. Doctors at community health centre could not recognize the need of caesarean section in patients. None of the patients who needed referral were provided with transport from the health centre.

In this study 71.5% deaths were found avoidable. This findings resembles the findings of 718 maternal deaths in Egypt reported by Kassas M et al where 92% were found avoidable[16]. The deaths which were categorized as avoidable, all had delays of "Three delay model" either alone or in

combination of two or three (Table-4). 82.9% patients had substandard care which was more than Suleiman et al series[17] where 52% patients were identified as victims of substandard care after confidential system of enquiry.

To overcome the barriers that are integrally linked to women's low utilization of available health services the findings of the study suggests

- Increased information, education and communication (IEC) efforts to broaden the knowledge and awareness of community members about the signs of life threatening complications and when and where to shift the patient. There must be community involvement in making transport available for emergencies. Local transport unions and vehicle owners may be sensitized to help women with obstetric complications. Also there must be preparedness of the family for obstetric complications for example saving money from the start of pregnancy or provision of loans to meet the need.
- Decentralize service: Maternal health services need to be available as close to people's homes as possible. In order to make this a reality, facilities need to have supplies and equipment; staff need to be trained in the necessary skills. There must be a functioning referral system to ensure that emergency cases reach a facility capable of managing them. The referring facility will be responsible for the patient until she reaches the referral centre including transportation.

Conclusion :

The underlying medical causes of maternal death are a range of social, cultural, economic and quality of care factors that greatly contribute to women's health before, during and after pregnancy. Good quality services should be delivered through community based models which are likely to be more accessible in terms of distance and cost to larger numbers of people, particularly in rural areas.

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Role of Human Foetal Membranes (Amniotic Membrane) in the Management of Burn Wound

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Summary :

This is a prospective study of 40 patients with deep and deep dermal burn where human foetal membranes (FMs) also called amniotic membrane were used. FMs were used in 25 patients who were not suitable for early burn excision with some degree of infection. Results in respect to formation of granulation tissue were excellent and control of infection was also satisfactory. On the other hand, FMs were used in 15 patients over widely meshed split skin graft where the formation of hypertrophic granulation tissue through the windows of meshgraft preventing coalescence of epithelium and delay healing. In five patients of the second group, FMs were used in split skin graft donor area. Patients complain severe pain and dryness of the area, which was relieved using ointment to moisten the area.

(J Bangladesh Coll Phys Surg 2002; 20 : 132-137)

Introduction :

Treatment of major burn is complex and challenging for plastic surgeons throughout the world. Initial treatment starts with resuscitation of the patient to overcome the hypovolaemic shock. Large amount of fluid & electrolyte comes out of the body. Most of the fluid comes out during the 1st 24 hour and of lesser degree during 2nd 24 hours.

Next step is to take care of the burn wound. Burned skin not only loses its normal function, but also gradually disintegrates and provides media for bacterial colonization. Toxin absorbed from burnt tissue and causes Adult Respiratory Distress Syndrome (ARDS), septicaemic shock, renal failure and ultimately patient die from Multi Organ Dysfunction Syndrome (MODS). So wound care is important. Wound care can be done either by open method or by closed method.

In open method, after cleaning patient remains in room with sterile environment where filtered air with laminar flow and barrier nursing is strictly maintained. But in practice it is impossible to make the environment absolutely free from microorganism. Closed method of wound care is now popular throughout the world where after cleaning; the wound is covered with antimicrobial agent then wrapped with thick cotton wool and gauze. Dressing changed at regular interval.

Recently there is great development in wound care where allograft, amniotic membrane, artificial dermis, synthetic and semi-synthetic dressing materials play an important role. In case of superficial burn, amniotic membrane adheres after application & remains so till epithelialization is complete (fig. 1 a&b). In case of deep and deep dermal burn, the burnt tissue needs to be removed either by total burn excision or tangential excision and wound is covered with autograft. At the same time the burn patients who are not suitable for early excision the raw surface covered with allograft, amniotic membrane or other dressing materials to prevent external contamination with loss of fluid and electrolyte. Later stage, the allograft and

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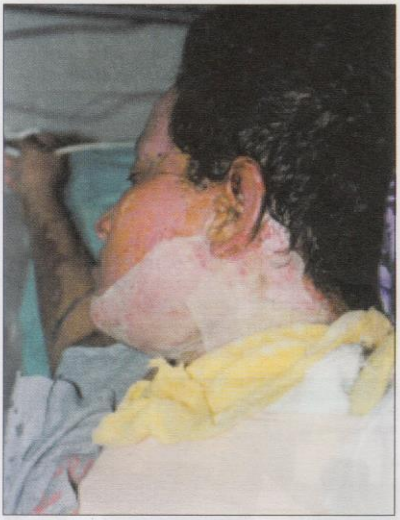

Fig.-1a: *Application of amniotic membrane over superficial burn involving face and neck.*

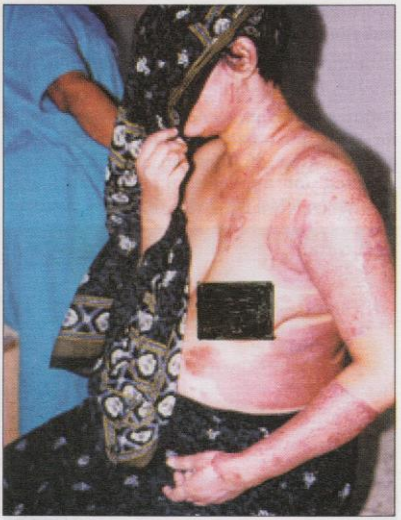

Fig.-1b: *After healing without any surgical intervention in face and neck (same patient).*

amniotic membrane need to be replaced by autograft.

Human foetal membrane was first used as biological skin substitute or dressing about 90 years ago (Davis 1910; Sabella 1913)[1]. FMs are also called amniotic membrane (Robson 1982)[2]. Anatomically FMs consist of two loosely connected layers, inner amnion (A) and outer chorion (Ch). Inner amnion layer composed of cuboidal, flattened epithelial cells and of mesenchymal connective tissue. Outer chorion which is composed of fairly thick transitional epithelium. Amnion is thin and shiny in contrast to chorion which is less homogenous and dull[3]. Foetal membrane can be used in total (amnion + chorion) or only as amnion (epithelium + base membrane)[4]. Amniotic membrane is also compared with honey with good healing effect[5].

Basic properties of human foetal membranes:

i) Absence of immunologic rejection.

ii) Healing effects of FMs, may be due to
   a) Antibacterial
   b) Angiogenetic or other biologic factor and
   c) Biomechanical characteristics of FMs.

Materials and Method :

During the Period of July 2000 to June 2001, 40 patients were studied with deep dermal and deep burn in a private Hospital of Dhaka City, Bangladesh. Human foetal membranes (FMs)[2] were used to cover burn wound in 25 cases, to cover widely meshed skin grafts over freshly excised wounds in 15 cases and skin graft donor area in 5 cases.

Basic Technique :

Human foetal membrane (FMs), was supplied from Institute of Food and Radiation Biology division, Bangladesh Atomic Energy Commission, Savar, Dhaka. They collect FMs in fresh condition from healthy mothers. After cleaning FMs is dried in oven at 40° ± 2°c

overnight and then sterilized by gamma radiation at 25 KGY[6].

Patients of study group were divided into two groups, A & B. (Table -II)

Group A - burn patients who were not suitable for early burn excision and admitted with some degree of infection were the cases selected for application of human foetal membrane (FMs) (fig. 2a&b). Extent of burn was

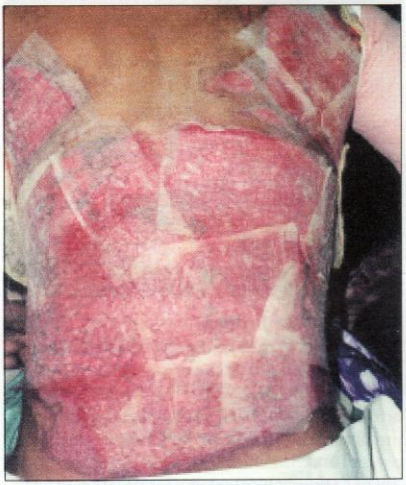

Fig.-2a: *Amniotic membrane applied over the meshed split skin graft following tangential excision.*

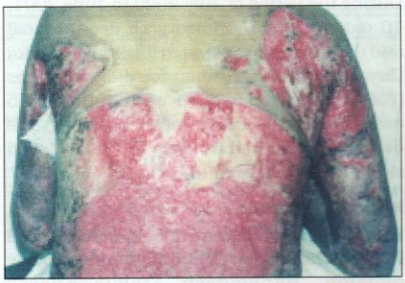

Fig.-2b: *Hypertrophic granulation tissue protruding through the windows of meshed skin graft preventing their coalesces and hiding the original meshed skin (same patient).*

10-36% with mean burn 22% (table -I). During every dressing part of loose slough, excised and covered with FMs. Every alternate day dressing was changed and part of the loose escher excised and covered with FMs. These processes continue till all escher removed and covered with autograft. At the same time the progress of granulation tissue formation was followed. Once healthy granulation tissue formed, wound was covered with meshed split skin graft.

Group -B: Patients who were admitted early and undergone early burn excision and wound cover with 1:3 or 1:6 meshed split skin graft. This meshed skin graft was covered with FMs (fig. 3 a&b).

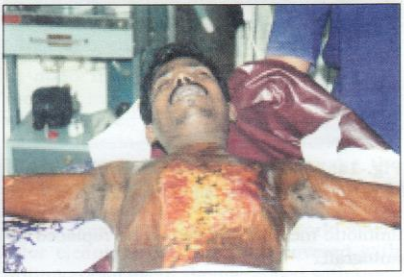

Fig.-3a: *Dressing with amniotic membrane, a patient with infected deep burn.*

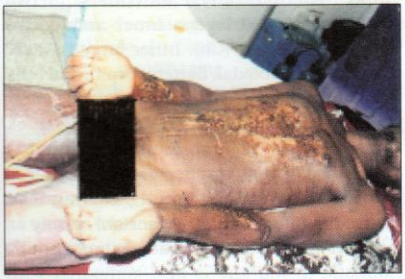

Fig.-3b: *Split thickness skin graft over burn area following granulation of wound on 10th postoperative day (same patient).*

In five patients of group -B, where split skin donor area was covered with human foetal membrane. (table -III a - fig. 4)

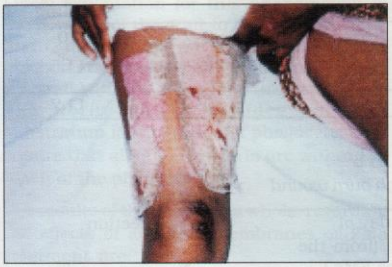

Fig.-4: *Amniotic membrane applied over skin donor area.*

Results :

Group A: Formation of granulation tissue was quick 7-12 days (average 8.7 days) from the time of first application (table-111b). Wound of 10 (ten) patients were grossly infected and infection was controlled within 7-10 days after application of FMs (table-III b).

Group B: In 15 cases FMs were used to cover meshed split skin graft. There was hypertrophic granulation tissue through the window of mesh graft which prevents coalescence of the epithelium of mesh graft and delay healing (table-III c) .

Split skin donor area was covered with FMs or amniotic membrane in 5 (five) patients who complained of severe pain and dryness of the donor area. This pain was relieved temporarily with analgesic but finally with application of ointment to keep the wound moist.

Table -I

Number of patient in age & sex variation with percentage of Burn

Age (in years)	Male			Female		
	Number	%	Average % of burn	Number	%	Average % of burn
0-10	1	2.5	18	3	7.5	21
11-20	3	7.5	23	2	5	22
21-30	5	12.5	21	8	12.5	20
31-40	1	2.5	22	5	12.5	13
.41-50	2	5	21	3	7.5	36
51-60	4	10	26	3	7.5	32
>60	0	0	0	0	0	0

(Mean % of burn -22%)

Table - II

Conditions where amnion use

Sex	Over donor site		Group A (Over deslough wound)		Group B (Over meshed split thickness skin graft)	
	Number	%	Number	%	Number	%
Male	1	2.5	8	20	6	15
Female	4	10	17	42.5	9	22.5
Total	5	12.5	25	62.5	15	37.5

Table - III a

Results in donor area

Sex	N. of Pt.	Severe pain	Dryness	Infection	Average day of healing
Male	1	1	. 1	0	10
Female	4	4	4	0	11.5
Total	5	5	5	0	11.2

Table - III b

Results in deslough burn wound

Sex	Number of Patient	Average day of angiogenesis (from the time of use FMs.)	Infection	
			N	%
Male	8	7.5	1	2.5
Female	17	9.4	3	7.5
Total	25	8.7	4	10

Table - III c

Results over the meshed split thickness skin graft (1: 3) .

Sex	Number of Patient	Hypertrophic granulation tissue protruding through meshed skin	Delay of coalesce of mesh	Infection
Male	6	6	6	0
Female	9	9	9	0
Total	15	15	15	0

Discussion :

Reviewing the available literature concerning the utilization of amniotic membrane (FMs) in the treatment of various skin defects, mainly in superficial burn we have found positive results. First use of amniotic membrane were reported by Sabella (1913)[1], there after on extensive flame burn by Douglas (1952)[7]. The indications, ranged extended on to the donor-sites (Quinby et al, 1982;[8] Robson, 1982; Waikakul et al, 1960) and clean second degree burn (pigeon, 1960). FMs also successfully used in some cases of eye surgery to prevent adhesion, reconstruction in the gynaecology, neurology, urology & vascular disease[3].

The current consensus is that it is the intimate adherent property of the biological dressing to an open wound in some way suppress bacterial proliferation and helps in eliminating existing bacteria[9]. There are a number of factor that may contribute to this effect. In clean surgical wounds the collagen of the graft or biological dressing via its haemostatic properties; will help to stop bleeding and thus prevent subsequent haematomas, which would provide opportunities for bacterial proliferation. In addition, the very close bonding between graft and wound eliminate dead space in which serous exudates could collect that encourage

bacterial growth[10]. On contaminated wounds, grafts or biological dressings can not only suppress bacterial growth but also 'reduce the existing microbial population density[11]. Likely explanation for this phenomenon is the bonding of the graft to the wound bed by fibrin, the bacteria are trapped in the thin fibrin matrix linking the collagen fibers of the graft with the collagen of the wound bed. The fibrin matrix provides an ideal substratum for migration of phagocytes and ensure that all of the bacteria are within the reach of the phagocytes [10].

The results of this study as a whole, regarding the effects of amniotic membranes or FMs treatment are:

i) In deep burn - FMs or amniotic membranes help in wound-debridement, reduce wound infection, help to form rapid granulation tissue.

ii) In cases over the widely meshed split skin graft - hypertrophic granulation tissue through the window of mesh graft hinder coalescence of epithelium and delay healing. This also goes in favour of rapid angiogenesis.

iii) In split skin donor area - patients complain of severe pain. May be due to dryness resulting from irritation of nerve endings.

Conclusions :

The beneficial effects of amniotic membranes or FMs are encouraging mainly from the point of view of cost-effectiveness and the possibility of their use in countries where cadaveric allograft is difficult to procure and pigskin is restricted.

Acknowledgement :

This work was done in co-operation with Division of Food and Radiation Biology, Atomic Energy Commission, Savar, Dhaka, Bangladesh. We give thanks to all of them, specially Md. Mamun Miah, Research officer, for their kind co-operation.

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Making an Effective Oral Presentation

(J Bangladesh Coll Phys Surg 2002; 20 : 138-140)

An essential aspect of any research finding is dissemination of the findings arising from the study.

The best way to organize a scientific paper for oral presentation is to proceed in the same logical sequence that one usually does in writing a scientific paper.

An essential aspect of any research finding is dissemination of the findings arising from the study. The most common way to make others inform and aware of the work is by publishing the results of the study/clinical trials in relevant scientific journals as an article or by presenting the results in a scientific seminar or symposium or by giving an oral or poster presentation, often at a national regional or international meeting. It is to be remembered that oral or poster presentation is the most common and rapid way to; disseminate the new findings. In addition, skills needed to prepare an oral presentation can be used in a variety of other settings such as organizing a seminar, preparing for a thesis/dissertation defense, conducting a job interview, etc. The article presented here deals with issues related-tip, making an effective oral presentation.

Like scientific writing, many times one has to present the scientific information orally in the seminars, symposia or conferences in front of the audience. To make the oral presentation effective, one has to talk low, one has to talk slow and finally, one has to be optimistic and should not talk too much. This strategy is likely to keep the audience in a track and attentive, It is to be remembered that the audience here is the most important factor to be considered to make the 'presentation effective. Therefore, their interest should always be looked for. Thus, only the relevant things should be presented in quickest and shortest possible time, so that, the audience should not feel bored and should not loose interest. Because, this is only effective if there is a good interaction between the speaker and the audience or the participants. If for any reason the communication is one-way, it will be meaningless. On the other hand, two-way' interactions are useful and productive. Many unsolved or; unanswered things would be solved or answered, if there is a good interaction. It is always desired that the interaction should be constructive and contributory to the pertinent field.

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How to proceed for oral presentation :

The best way to organize a scientific paper for oral presentation is to proceed in the same logical sequence that one usually does in writing a scientific paper which has been addressed in the 6th issue of RoMedica, January to March, 2002. One should start with, "what is the problem and what might be the possible solution?" These two things, i.e, the problem and the solution constitute the main issues of oral presentation. However, it is to be remembered that oral presentation of a scientific paper does not constitute publication. If the published paper needs presentation, it should be presented in details along with experimental/clinical protocol. The common form of oral presentation, however, does not contain full details. Extensive citation of the literature is undesirable in an oral presentation.

Time limits for oral presentations :

Most of the oral presentations are short, and the standard time limit for these is 10 minutes. But if full paper is presented, obviously it needs time more than 10 minutes. The theoretical content of the paper

must be trimmed down relative to that of written paper. No matter how well organized, too many ideas if presented too quickly, will be confusing. Therefore, one should talk to the most important point or the result and should stress that. There are, of course, some longer forms of oral presentations, such as presentations in the symposium. A typical time allotted for symposium presentation is 20 minutes. A few are longer. A seminar is usually and normally of one-hour duration. Obviously, one can present, more materials if one have more time. Even so, when more time is available, one should go; slowly and carefully, presenting the main points or themes. If one proceeds too fast, specially at the beginning, the audience will loose the interest. The daydreams will begin and the message of the presentation will be lost.

Aids to effective oral presentation :

The following aids are likely to make an oral or audio-visual presentation highly effective, interactive and meaningful.

Slides :

At small, informal scientific meetings, various types of audio-visual aids may he used, Over-head projectors (OHP), flip charts and even black boards can be used effectively. At most scientific seminars, however, 35-mm slides or transparency through OHP are the common audio-visual aids, which are being practiced. It has been seen that the transparency using OHP are most acceptable to the audience than the 35mm slides used for the purpose. These audio-visual aids are convenient, economic and are the most appropriate instruments for presenting the paper and getting the relevant message from it in all the settings. However, use of laptop and multimedia are more attractive and the presentation would he more effective. But these are expensive and sometimes difficult to arrange. Thus, transparency and 35-mm slides are commonly used. The presentation on the other hand, will be ineffective if there are no studio-visual aids. Furthermore, the audio-visual aids draw the attention of the audience as long as the presentation continues. Every scientist should know how to prepare effective slides. The following points should be considered for preparation of slides:

- Slides should be designed and prepared specifically for use in the oral presentation.
- Slides prepared from graphs that are drawn for journal publication are seldom effective and often are trot even eligible.
- Slides prepared from a typewritten manuscript or from a printed journal or book are almost never effective.
- It should always be remembered that slides should be wide rather than high which is just opposite of the preferred dimension for printed illustrations.
- Slides should he prepared by the professional on at least by use of professional equipment. Slides prepared with standard typewriters are almost never effective, because the lettering is too small. Word processing will be fine if a large size is selected. However, now a day, graphs are generated by the computers, which can be used to make the slides with the help of PowerPoint software.
- It should be remembered, that the lighting in the conference room should be optimum for the slides to be displayed and also the contrasts.
- Slides, should not be crowded. Each slide should be designed to illustrate a particular point or perhaps to summarize a few. A slide is said to be bad if it is not understood within a second or two.
- The slides and other audiovisual aids needed for the seminars should be brought to the hall ahead of the audience. The slide projector, OHP, laptop, multimedia and the lights should be checked before beginning of the seminar. It is to be ensured that the slides are correctly inserted in.

Slides prepared from a typewritten manuscript or from a printed journal or book are almost never effective.

Slides should not be crowded. Each slide should be designed to illustrate a particular point or perhaps to summarize a few. A slide is said to be bad if it is not understood within a second or two.

Oral kpresentation can virtually be destroyed and meaningless if the andience is noisy or wrose, asleep.

The audience can disagree with the speaker's statement. In that case, the speaker should try to explain the reason of disagreement of the audience.

Order of sequence and proper order and should not be upside down or out of focus. Normally, slides should he made simple and should contain visual statements, which are self-explanatory and easily understandable. The slides supplement what the speakers are saying at the time the slide is on-screen. The slide should not simply repeat what the speakers are saying. It is very important to note that one should never read the slide text to the audience. However, slides that are thoughtfully designed and are well prepared can greatly enhance the value of a scientific presentation and make the presentation highly effective.

The Audience:

In a scientific seminar, the audience is the most important element for interaction. The greater the number of audience, the more will be the interaction and more things will be coming out from the paper presented. It has already been stated that the presentation of a paper in a scientific seminar is a two-way interaction or process. Because the material being presented at a scientific conference is likely to be the newest available information in that field, the speaker should present his/her material clearly and effectively so that the audience can understand and learn from the paper being presented. It is almost certain that the audience for an oral presentation will be more diverse than the readership of a scientific paper. Therefore, oral presentation should be pitched at a more general level than would be a written paper. The technical details should be avoided because of the heterogeneous characteristics of the audience.

For communication to be effective, the audience has also certain responsibilities. As for example; the audience should be quiet and attentive. Speakers respond well to an interested, attentive audience. On the other hand, oral presentation can virtually be destroyed and meaningless if the audience is noisy or worse, asleep.

Question and Answer session:

It is customary that following an oral presentation, there will be the session of question answer. This is the most crucial part of the presentation. During this time, members of the audience have the option of raising question/issues/comments, etc. not covered by the speaker. The audience is always encouraged to make comments, constructive criticisms or address the issues, which the speaker has missed and thus, can, enrich the presentation. Such comments/ questions should be stated cautiously. Any question, which is likely to embarrass the speaker, is not expected from the audience. The audience can disagree with the speakers statement. In that case, the speaker should try to explain the reason of disagreement of the audience.

In summary, to make the oral presentation effective and meaningful, the speaker and the audience must have friendly interaction. As for example, the speaker has an obligation to be considerate to the audience. Similarly, the audience has an obligation to be considerate to the speaker. Thus, the interaction is two-way and contributory and reciprocal.

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REVIEW ARTICLE

Chronic Viral B Hepatitis : Update on Management

N AHMAD[a] , M KHAN[b]

(J Bangladesh Coll Phys Surg 2002; 20 : 141-149)

Chronic viral hepatitis is a major cause of liver related morbidity and mortality worldwide. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infection causes the majority cases of chronic viral hepatitis. Natural course of chronic viral hepatitis includes progression to cirrhosis, hepatic failure and hepatocellular carcinoma. Effective treatment will interfere the disease progression and thereby prevent the complications of chronic HBV infection. Considering the relatively high cost of treatment the management of chronic viral B hepatitis demands a rational approach.

Hepatitis B virus :

The Australia antigen, subsequently renamed hepatitis B surface antigen (HBsAg), was discovered by Blumberg and colleagues in 1965[1]. This led to an explosive growth in information about the hepatitis B virus. Serologic and later molecular diagnostic tests for hepatitis B were developed. Most importantly safe and effective vaccines for the prevention of HBV infection were developed. The prevalence of HBV infection varies in different geographical areas. The HBV carrier rate is 0.1%-1% in western countries where it is largely a disease acquired in adulthood in contrast to a carrier rate of 5%-20% in Asian and African countries where it is usually acquired perinatally or, in childhood[2]. Hepatitis B virus is a partially double stranded DNA virus and belongs to the family of hepadnaviruses. The HBV genome is composed of a relaxed circular, partially double-stranded DNA molecule of 3.2 kb. It has a highly compact organization with four partially overlapping open reading frames (ORFs) encoding the envelope (pre-S/S), core (pre-C/C), polymerase (P) and X proteins[3]. The replication cycle of HBV begins with the attachment of the virion to the hepatocyte. Inside the hepatocyte nucleus, synthesis of the plus strand HBV DNA is completed and the viral genome is converted into a covalently closed circular DNA (cccDNA). The cccDNA is the template for the pregenomic RNA, which is reverse transcribed into the minus strand HBV DNA. There are two sources of cccDNA: entry of new virus particles into the hepatocyte and translocation of newly synthesized HBV DNA from the hepatocyte cytoplasm. Most antiviral agents that have been examined so far have little or no effect on cccDNA[4]. This accounts for the rapid reappearance of serum HBV DNA after cessation of antiviral therapy.

HBV mutants :

The HBV genome replicates via the reverse transcription of an RNA intermediate and is therefore prone to mutations. HBV mutants that are detected clinically may have been selected because they confer survival advantage over the wild type virus by evading host immune response or by enhancing virus replication. Mutations in the precore, S and P genes have been most extensively studied.

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The predominant mutation in the precore region is a GA change at nucleotide 1896 (A1896) which leads to premature termination of the precore protein, thus preventing the production of HBeAg[5]. The A1896 mutant was first reported in patients with chronic active hepatitis or fulminant hepatitis[5]. However, recent studies found that the A1896 mutant can also be found in asymptomatic carriers.[6] The precore mutant may replicate more efficiently than the wild type virus[6]. Mutations in the HBV S gene have been reported in infants born to carrier mothers who developed HBV infection despite vaccination[7,8] and in liver transplant recipients who developed HBV reinfection despite prophylaxis with hepatitis B immune globulin (HBIG)[9,10] Although these mutants have diminished binding to anti-HBs, the vast majority can be readily detected by conventional serology assays, in particular assays that use polyclonal anti-HBs. Mutations in the polymerase (P) gene are frequently encountered during antiviral therapy.

Immunopathogenesis :

Understanding of the pathogenesis and natural history, of HBV infection led to the development of antiviral therapies for the treatment of chronic hepatitis B. The host's immune attack against HBV is the cause of the liver injury. It is mediated by a cellular response to small epitopes of HBV proteins, especially HBcAg, presented on the surface of the hepatocyte. HLA class I-restricted CD8+ cells recognize HBV peptide fragments derived from intracellular processing and presentation on the hepatocyte surface by class I molecules. This process leads to direct cell killing by the CD8+ cytotoxic T lymphocyte[11,13]. HLA class II-restricted CD4+ lymphocytes recognize peptide fragments derived from viral proteins presented in the antigen groove of non-hepatic antigen-presenting cells, principally macrophages. The identification of viral protein epitopes by the CD4+ cell leads to the stimulation of T-cell proliferation and cytokine synthesis and provides help for B-cell responses. The different immune responses in patients in whom virus is cleared successfully and those in whom it is not depend on the match between the HBV peptides presented by host major-histocompatibility-complex molecules and the specific T-cell-receptors of the host. If sufficient recognition and activation occur, the immune response is carried to completion, all infected cells are destroyed, viral replication is aborted, and antibodies to HBsAg prevent the reinfection of hepatocytes. If the response is inadequate, the infection continues. For practical purposes, the severity of the hepatocyte injury reflects the vigour of the immune response: the most complete immune response is associated with the greatest likelihood of viral clearance and the most severe liver injury.

Natural history of chronic HBV infection :

The sequelae of HBV infection are complete recovery, chronic carrier state or chronic hepatitis often complicated by cirrhosis or hepatocellular carcinoma. Ninety-five percent of infected neonates with immature immune systems become asymptomatic chronic HBV carriers, as compared with 30 percent of children infected after the neonatal period but before six years of age. Only 3 to 5 percent of adults having acute infections remain chronically infected, the remainder have viral clearance. Depending on virological, biochemical and liver histological characteristics the natural history of chronic HBV infection can be divided in 3 phases. The phase-1 is immunotolerance phase. or replicative phase, phase-2 is immunoclearance phase and phase-3 is latent phase or non-replicative phase. All 3 phases are present in neonatally acquired infection but in childhood or adulthood acquired infection the immunotolerance phase is absent. Phase-1 is present in only neonatally acquired infection and it usually persists up to 20 years of age. In this phase there is high viral load due to active viral

replication, serum HBeAg is +ve and anti-HBe is -ve, serum HBV-DNA is +ve. Serum ALT is low and there is minimal histological activity in the liver. The exact mechanism(s) by which tolerance is induced is not clear. Several mechanisms have been postulated, including clonal deletion of HBV-specific T cells as a consequence of transplacental infection of the developing foetus or transplacental passage of sub-viral antigens such as the soluble HBeAg, and immune exhaustion. However, clinical and immunological studies indicate that the virusspecific T cells are not clonally deleted, as HBV-specific T cell proliferation has been demonstrated in patients who subsequently developed HBeAg seroconversion[14]. Whether the immune response is triggered by maturation of the immune system, loss of tolerance or presentation of new viral epitope(s) is not known. Patients in phase-2 are usually young adults of 20-40 years age. In this phase there is seroconversion from HBeAg to anti-HBe and serum HBV-DNA is low. The ALT is raised or fluctuating and the liver show histology of chronic active hepatitis. Phase-3 is characterized by older age group and very low viral load due to absence of replication. Serum HBeAg is -ve, anti-HBe +ve and serum HBV-DNA is usually negative. Serum ALT is low and there is minimal histological activity or histology of cirrhosis or HCC. The majority of carriers who develop HBeAg seroconversion remain HBeAg negative and anti-HBe positive with normal ALT levels and minimal or no necroinflammation on liver biopsy. This has been referred to as the "inactive carrier state[15-21]. The course and outcome of the inactive HBsAg carrier state is generally but not invariably benign depending on the duration and severity of the preceding chronic hepatitis.

Indications for treatment :

The main aim of treatment of chronic HBV infection is to suppress HBV replication before there is irreversible liver damage. It is not clear if vital 'eradication is an attainable goal because of the difficulty in eliminating cccDNA in the liver and the existence of extra hepatic reservoirs of HBV.

The ideal therapeutic strategy in chronic viral B hepatitis depends on understanding of the natural history of HBV infection. The diagnosis of CHB depends on suggestive clinical features, raised transaminases, rational interpretation of serological markers of HBV and the presence of necroinflammatory changes in liver histology. The rational indications for treatment of chronic HBV infection are evidence of viral replication (HBeAg +ve and/or serum HBV DNA +ve using hybridization assays) and presence of liver disease (abnormal ALT levels). In patients of chronic HBV infection hepatitis B virus may be either nonreplicative or replicative. The replication of HBV is evidenced by the presence of serum HBeAg and/or detectable serum HBV-DNA by unamplified assay (or $>10^5$ copies/ml by PCR). The non-replicative or inactive HBsAg carrier state is characterized by serum HBsAg positivity for at least six months, negative serum HBeAg, undetectable serum HBV-DNA by unamplified assay($<10^5$ copies/ml by PCR), persistently normal serum transaminases and absence of significant hepatitis on liver histology. Patients in the inactive HBsAg carrier state do not require any drug therapy. However, they should be monitored with periodic liver biochemistries as liver disease may become active even after many years of quiescence.

Chronic hepatitis B (CHB) is defined as necroinflammatory changes of the liver caused by HBV infection persisting for more than 6 months. It is characterized by serum HBsAg positivity for at least six months, positive/negative serum HBeAg, detectable serum HBV-DNA by unamplified assay(or> 10^5 copies/ml by PCR), persistent or intermittent elevation in serum transaminases and presence of significant hepatitis on liver histology. Therefore, chronic hepatitis B is

separable into two major forms: HBeAg positive and HBeAg negative. Both forms can lead to cirrhosis and end-stage liver disease. These classical CHB patients are in the phase-2 of chronic HBV infection and need active treatment. In the typical phase-1 infection, there is viral replication but normal aminotransferase levels and there is virtually no progression to cirrhosis. However, during phase-2 infection of cirrhosis develops in approximately 50 percent of patients in five years[22,23]. There 'is little benefit in treating phase1 infection with immunostimulants such as interferon[24], nor is there a need to treat phase-3 infection[25-27]. The goal of treatment is to hasten the progression from phase-2 to phase-3 (seroconversion from HBeAg to anti-HBe), with the clearance of hepatocytes with replicating virus, since they are the prime focus of the liver injury[28]. Spontaneous seroconversion occurs at a rate of approximately 5 percent per year[29].

Efficacy of treatment :

For therapeutic purpose CHB patients may be categorised into classical patients group and problem patients group. Classical patients are those who are in the phase-2 of HBV infection characterised by presence of serum HBeAg, low serum HBV-DNA, raised ALT and histology of active hepatitis. The problem group includes chronic HBV infection with serum HBeAg +ve but normal transaminase levels, precore mutants, HBeAg +ve decompensated cirrhosis and immunosuppressed patients.

Therapeutic agents used for chronic viral B hepatitis fall into two major groups, immunomodulating agents and direct antiviral agents. Immunomodulating agents include interferons, cytokines and therapeutic HBV vaccine. Direct antiviral agents are nucleoside analogues which include lamivudine, famciclovir, lobucavir and adefovir. Interferon stimulates host immune system thereby helps viral clearance. Nucleoside analogue reduces high viral load by inhibiting viral replication and thereby facilitates immune clearance. However, nucleoside analogues lead to the development of viral mutations and drug resistance. Currently interferon-a and lamivudine are the only two therapeutic agents approved by FDA for chronic hepatitis B. The response to therapy is usually defined as loss of HBeAg in patients who were initially HBeAg positive and undetectable serum HBV-DNA by unamplified assays. These end-points are usually accompanied by remission of liver disease as evidenced by normalization of ALT levels and decreased histological activity.

Interferon-α

Chronic hepatitis B patients have deficient responses to endogenous interferon. Recombinant interferons, resembling the naturally occurring cytokines produced in response to viral infections, have immunomodulatory and antiviral effects, inducing the display of HLA class I molecules on hepatocyte membranes, thus promoting lysis by CD8+ cytotoxic lymphocytes and directly inhibiting viral-protein synthesis[30,31]. The, usual dose of interferon for classical group is 5 MU IFN-a subcutaneously thrice in a week for 4-6 months. High pre-treatment ALT and low serum HBV DNA levels are the most important predictors of good response to interferon therapy. A series of clinical trials demonstrated a beneficial effect of IFN-a in patients with HBeAg positive chronic hepatitis. A meta-analysis of reported randomized controlled trials of IFN-a found a significant difference between treated patients and controls in clearance of HBeAg (33% vs 12%), serum HBV DNA (37% vs 17%) and HBsAg (7.8% vs 1.8%)[32]. However, IFN-a is less effective in HBeAg positive patients who have normal ALT levels. These patients have HBeAg clearance rates of <10% with IFN-a therapy[33]. Interferon can suppress HBV replication and induce remission in liver disease in patients with HBeAg negative

chronic hepatitis (precore mutants) but relapse after cessation of treatment is common[34]. Low dose IFN-a can decrease HBV replication in patients with clinical cirrhosis but the risks of serious infections and hepatic failure are very high. Children with HBeAg positive chronic hepatitis have similar response rates to IFN-a as adults and appear to tolerate treatment well[36]. However, as in adults, children who have detectable serum HBV DNA but normal ALT levels have very low response rates. In an attempt to increase the response to IFN-a therapy, several investigators evaluated the effects of prednisolone priming. This strategy was based on observations that steroid withdrawal in patients with chronic hepatitis B was frequently associated with a flare in hepatitis followed by HBeAg seroconversion. A meta-analysis of randomized trials showed that prednisolone priming did not enhance the overall response of IFN-a therapy, although it appeared to have a marginal benefit in a subset of patients[37]. The risk of hepatic failure during steroid withdrawal and the availability of safer therapies have led to the abandonment of this treatment strategy. IFN-a treatment is associated with a wide range of adverse events including flu-like illness, fatigue, myelosuppression, emotional lability and flares in hepatitis. Although the flares in hepatitis during IFN-a treatment are thought to reflect immunemediated lysis of infected hepatocytes and to predict a favourable response, these flares can induce hepatic decompensation in patients with cirrhosis.

Lamivudine :

Lamivudine is an orally administered nucleoside analogue which is highly effective in inhibiting HBV-DNA synthesis. The dose of lamivudine for adult with normal renal function is 100 mg daily orally. Although the duration of lamivudine therapy is not well defined, it is advisable that treatment should be continued until HBeAg seroconversion occurs. However, lamivudine treatment should be administered for a minimum period of one year. High pretreatment ALT is the most important predictor of response to lamivudine therapy. Several randomized clinical trials showed that a 1-yr. course of lamivudine monotherapy induced HBeAg seroconversion in 16-18% of patients and appeared to be similar in efficacy to a 16 week course of IFN-a monotherapy[38-40]. Lamivudine has also been shown to be effective in patients with HBeAg negative chronic hepatitis B and in the re-treatment of patients who previously failed to respond to IFN-a[41] It has also been reported to be safe and effective in improving liver function in patients with decompensated cirrhosis. Lamivudine is also found to be effective in recurrent hepatitis B post-liver transplantation and in preventing HBV reinfection after liver transplantation[38]. Lamivudine is very well tolerated with side effect profiles identical to that of placebo. Mild (2-3 folds) increases in ALT levels may be observed during or after treatment but symptomatic hepatitis or an increase in bilirubin values is extremely rare. A major problem with lamivudine treatment is the development of drug-resistant mutants. There is emergence of lamivudine-resistant mutants in about 14 -32% of treated patients after one year of lamivudine therapy which may be increased to 66% after three years of treatment [38,42-46].

Lamivudine resistance :

Lamivudine therapy leads to the emergence of drug resistant HBV mutants. The two most common mutations include a methionine to valine or isoleucine substitution at codon 204(M204V/I) in the YMDD motif and a leucine to methionine substitution at codon 180(L180M) of the HBV polymerase gene[47,48]. The development of these mutants is usually associated with breakthrough infection but the long-term clinical significance of these mutants is not known. In many patients, serum HBV DNA and ALT levels remain lower than pre-treatment

values, suggesting that there may be a continued suppressive effect of lamivudine on the wild type virus and a lower virulence of the mutant. Indeed, HBeAg seroconversion has been reported in some patients after the development of lamivudineresistant mutations[49]. Adefovir dipivoxil, a nucleotide-analogue is the prodrug of adefovir. It has potent antiviral activity against HBV similar to lamivudine, excellent oral absorption, and an intracellular half-life that permits once-daily dosing[50]. Adefovir dipivoxil has antiviral activity against both wild-type and lamivudine-resistant HBV and is currently in phase III clinical testing[51-55]. High doses of adefovir is associated with significant nephrotoxicity and 10mg daily seems to be safer. To date, there has been no report of emergence of adefovir dipivoxil-resistant forms of HBV[56,57]. However, the optimal dose, durability of the response, and safety of prolonged therapy remain to be determined.

In chronic hepatitis B, if therapy is indicated, one must decide whether to use interferon-a or lamivudine or both. The advantages of interferon-a are that it is given for a limited time, antiviral resistance does not occur, and the quality and long-term durability of responses are excellent. Disadvantages are that interferon is expensive and has significant side effects including some that are rare but serious (induction of autoimmune disease, bacterial infections, depression, and acute psychosis). The advantages of lamivudine therapy are that it is easy to administer and monitor and it is associated with few, if any, side effects.

Disadvantages of lamivudine are that the long-term durability of responses appears to be less than with interferon-a and that prolonged therapy is often needed. Moreover, it is associated with a high rate of viral resistance. Lamivudine and IFN-a have different mechanisms of action. Thus, combination of the two agents may have additive or synergistic effects. However, two recent studies found that combination therapy with lamivudine and IFN-a was not superior to monotherapy with either agent[40, 41].

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Carcinosarcoma of the Endometrium and Cervix of an Adolescent Girl- A Case Report

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Introduction :

Uterine Carcinosarcoma (CS) or Malignant mixed mullarian tumour (MMMT) account for less than half of all uterine corporal malignancies of mesenchymal or mixed epithelial mesenchymal origin and 50% of all uterine sarcoma and 3-6% of all uterine tumour[1,2]. The primary site of origin is in the endometrium and myometrium but rarely can develop in the cervix, fallopian tubes, ovaries[3]. Very rarely they can arises in the vagina, retroperitoneal space, Peritonium and cervical stump after subtotal hysterectomy[4-6]. They are very aggressive neoplasm even when they confined to the uterus and have a poor prognosis. They characteristically occur in post menopausal women in their six and seven decade but rarely occur in reproductive age[2,5]. The presenting symptoms is usually vaginal bleeding but pelvic pain and vaginal discharge are also common symptoms. 'Sometimes, fregmants of necrotic tumour may pass per vaginum or a neoplastic mass prolapse in the vagina. Since the tumour are mainly endometrial in origin about 75% can be accurately diagnosed by D & C. Radiation therapy may be the predisposing factors. Histologically they are highly, anaplastic with many bizarre nuclei and mitotic figures. They spread by continous infiltration of the sorrounding tissue and early lymphatic and haematogenous metastasis is common[2,3]. Treatment of choice is total abdominal hysterectomy with bilateral salpingoophorectomy preceded or followed by adjuvant radiotherapy and/or chemotherapy[2,7]. As because they are highly malignant and rapidly metastasizing even when they apperently confined to the uterus the over all 5 years survival rate is 20% to 30%[1,3,7].

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Case Report :

A 17 years old very pretty girl Miss Emama siddique student of H.S.C from a middle class family was admitted in Gynae department of Mitford hospital on 21.5.02 with the complaints of very foul smelling blood stained discharge per-vagina with lower abdominal pain and backache for last 6 (six) months and her appettite was tremendously decreased for last 3 months.

Her past history revealed that she was reasonably good 5 years back. Her menerche was at the age of 11 years and then menstruation was cyclical for next 2 years. After that irregular bleeding was started lasting for 4 years and became continuous for last 1 (one) year with passage of large to moderate size clots. She was treated for several times by local doctors with oral progestogen (tab. orgametril (5mg) or Primolut -N) and antibiotics but condition was not improved. Uitrasonogram of lower abdomen was done and shows moderate size uterus with multiple fibroid with PID and treated accordingly. For the last 6 months she had profuse blood stained foul smelling P/V discharge with backache and lower abdominal pain. Lastly she consulted with a

gynaecologist and a provisional diagnosis was made that it seems to be a case of infected myomatous polyp from history and a very gentle P/V examination and advised immediate hospitalization for further evaluation and management.

On admission a thorough physical examination was done and found her health and nutritional status was average. She was severely anaemic, normotensive, , slight lower abdominal tenderness and profuse foul smelling P/V discharge present: Rectal mucosa was found free on Per-rectal examination. Simultaneously a pre-operative conservative treatment with-antibiotics, antifungal, blood transfusion was given and all pre-operative investigation including serum CA-125 was done and all report were found within normal range. Then a thorough P/V examination was done under G/A. A large, friable, fungating growth which bleeds on touch and seems to be arising from whole of the cervix was found. The exact size of the uterus & cervix could not be detected properly but all fornics found free. Removal of whole growth was not possible due to profuse bleeding and distorted anatomy. Debulking of the growth was done as far as possible per-vaginally. 3 unit of whole blood was transfused peroperatively and a tight vaginal pack was given. Another 2 units of blood was transfused in post-operative ward. Vaginal pack was removed after 24 hours and bleeding was controlled. Her post operative period was unevenful. Histopathological report of resected tissue shows a rare diagnosis of carcinosarcoma (CS).

Abdomen was woman for revision surgery after 7 days and total abdominal hysterectomy with bilateral salpingoophorectomy was done. Per-operatively uterus was found slightly enlarged, both adnexae was apperently healthy, cervix was grossly enlarged with growth, no palpable lymph node was found and all structure was free from adhesion. A thorough peritoneal wash was given by normal saline and peritoneal lavage sent for Cytological examination. After removal, uterus was bisected and found two polypoid growth about 1.5 cm x 1.5 cm arising from the endometrium. Each half of the specimen was sent for histopathological examination in two laboratory. The report was CS from both laboratory.

Upto 3rd post operative day, she had only complain of backache, bodyache but after that she felt severe pain during defaecation. On 8th post operative day all stiches was removed and abdominal wound found healthy. Patient was discharged on 10th post operative day and referred to Cancer Institute, Mohakhali, Dhaka for further planned follow-up adjuvant therapy.

Discussion :

Uterine CS are among the most lethal neoplasm known to occur in the uterus with an average 5-years survival rate of 25%[7] for all stages. Cervix is the rare site of origin of such tumour[3]. This very rare case report describes CS arising in the cervix as well as in the endometrium of a young adolescent girl of 17 years.

Primary sarcoma of the cervix is also rare, one study shown only 6 were CS among 26 cervical sarcoma[8]. Another very rare case was reported by John H. Farely M.D et al that CS of the Cervical remnant of a 30 years old lady following sub-total hysterectomy[5]. Shintaku-M et al reported one case of CS originate from retro-peritoneal space of a 51 years old women and another case was reported. In the ovary of a 74 years old female who had pelvic irradiation 33 years previously[5,6]. CS of the endometrium sometimes assoclated with other condition such as non-gestational choriocarcinoma, a case was reported in a 71 years 'old. women, another case report was shown that extensive neuroectodermal differentiation occurring in a 54 years old women with CS of the uterus[9,10].

It is established that the metastasis of these tumour is very rapid if it is apparently

confined to the uterus but still angiogenesis of the tumour is unknown. But it is suggested from a study that tumour angiogenesis in the epithelial element may be more active than that of the mesenchymal element and also substantiated the high metastatic potential of the epithelial element in uterine CS. Carcinoma cells thus may play a key role in the angiogenesis of this biphasic neoplasm[11]. Regarding tumour marker serum CA-125 was found within normal level of some reported case and also in our case. But an elevation of serum tissue polypeptide antigen (TPA) a tumour marker was detected in four of five (80%) patients with MMMT shown in one study[12].

The most important prognostic factor with regard to survival is the extent of the disease at the time of Primary surgery[5]. The prognosis is very poor when the tumour extended beyond the uterus[7]. Regarding treatment, the role of adjuvant chemotherapy or radiotherapy (RT) with surgery has yet to impact on long term survival, although ongoing studies are exploring these possibilities[13]. The role of RT is difficult to asses, it favorably impacts tumour control in the pelvis with no influence on overall survival due to extensive metastasis[14]. Platinum-based combination chemotherapy with doxorubicin, Cisplatin, ifosfamide is presently considered to be the most active regimen[7] survival is linked to the surgical stage of the disease. The median survival for all stages is only 18 months[17].

Most recurrence develop within 12 months and at distant sites[16]. Factors associated with recurrence and survival include depth of myometrial invasion, Lymph vascular space invasion (LVSI), adnexal and serosal involvement, Positive Cytology and lymph node metastasis[17].

Conclusion :

CS of the uterus, fallopian tube, ovaries are highly aggressive neoplasm with incompletely understood histogenesis. The major limitation of the cure of such tumour is systemic spread. The high recurrence rate even in stage I disease and the predominance of distant metastasis at relapse indicate a need for adjuvant systemic therapy. The prognosis of these patient is very poor. Extra uterine spread and age of the patient at the time of diagnosis are main prognostic factors. The content of carcinomatous component of serous or clear cell type had a negative influence on survival.

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Molluscum Contagiosum of the Nipple – An uncommon Presentation with Review of the Literature

TIMA FARUQ, FCPS[a], K BEGUM, FCPS[b], I ARA, FCPS[c]

Summary :

Molluscum contagiosum is a viral lesion of the skin and mucus membrane of the face, trunk, hand abdomen genitalia etc. Nipple is a very rare site. The lesions usually undergo spontaneous regression within 6 to 9 months. If not regressed spontaneously may be treated by various chemicals. Surgical curettage is indicated when medical treatment fails.

(J Bangladesh Coll Phys Surg 2002; 20 : 154-157)

Introduction

Molluscum contagiosum, a virally induced skin lesion caused by Molluscum contagiosum virus, a member of the pox virus group, which causes proliferation of epithelial cells. Mollusc (Latin: Molluscus-soft) a soft protuberance on the skin. Infection spreads usually by direct contact but may spread by auto inoculation. Fomites also can be a means of transmission of the disease. The infection is common in children and young adults specially males & commonly occur on the face, trunk , hand and through sexual contact to abdomen and genitalias. Hundreds of lesions may develop in inter-triginous area such as axilla & crural region. Specific antibodies were found in 73 – 87% of cases. Clinically the lesions are smooth, pale, firm nodules about 2-5 mm in diameter with a central depression. Spontaneous regression is common within 6 – 9 months, if not curettage is the best treatment[1].

Case Report :

A 26 years old parous housewife having 3 children (age of last child 4 years) present with the history of gradual swelling on the right nipple along with discharge of milk like substance for 1 year in a private hospital as out patient. She was treated with various antibiotic elsewhere without any benifit.

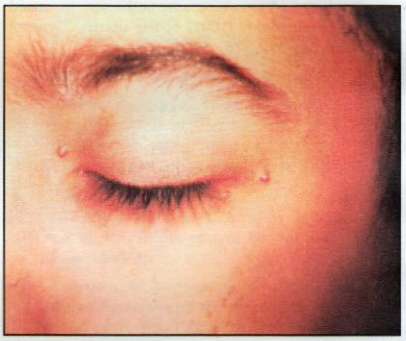

Fig.-1 : *Molluscum contagiosum on the Eye lid*

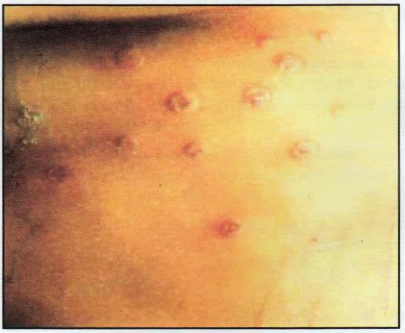

Fig.-2: *Molluscum contagiosum on the trunk*

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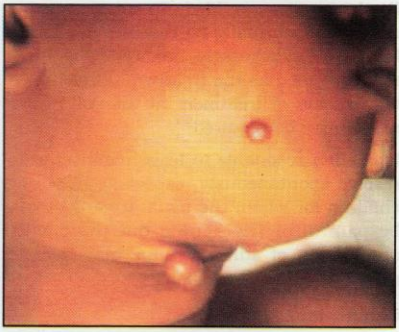

Fig.-3: *Molluscum contagiosum on the face and neck.*

On examination - a small irregular nodular swelling about 1 cm in length situated just under the skin on the right nipple, not so tender , soft in consistency was found. Milk like substance comes out on compression of the nodule, like a discharging sinus. Cytology of the nipple discharge shows only chronic inflammatory cells.

Treatment – Under local anaesthesia enucleation of the nodule was done successfully. An elongated fleshy mass about 1 cm in length

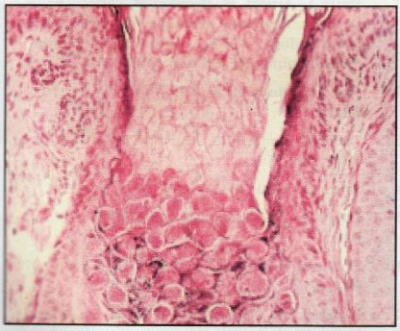

Fig.-4: *Histological appearence of molluscum contagiosum*

comes out very easily without any bleeding. Post operative recovery was uneventful. Follow up after 1 month shows proper healing of the wound.

Histopathology – Histopathological examination reveals features of molluscum contagiosum, characterized by epithelial hyperplasia with epithelial downgrowths in lobules & molluscum bodies in the cells of the epidermis. No malignancy is seen.

Discussion :

Molluscum contagiosum is an infectious disease caused by a poxvirus. The virus occurs throughout the world. Infection is common but the incidence is not reliably known in most areas. The disease is rare under the age of 1 year because of maternally transmitted immunity and a long incubation period[2]. In hot countries where children are lightly dressed and in close contact with one another and where personal hygiene is poor, spread within household is not uncommon. The age of peak incidence is reported as between 2 and 3 in Fiji[2], and between 1 and 4 in Zaire[3]. In new Guinea the annual attack rate for the children under 10 years was 6%[4]. In cooler climates, however spread within households is rare and infection is commoner at a later age. A peak age at 10-12 years was correlated with attendance at swimming bath[2] and two to four folds greater incidence in male[3,5] may be their more frequent use of swimming and communal bathing facilities. A later increase in incidence in young adults is attributable to sexual transmission of the virus[6,7].

There is a clinical impression that molluscum contagiosum is common in patients with atopic eczema[8,9] in the immunosuppressed[10,11,12] and in those in sarcoidosis[13,14]. The duration both of the individual lesion and of the attack is very variable although the most cases are self limiting within 6-9 months, but may persist 3-4 years[15]. The distribution of the lesion is influenced by the mode of infection and by the type of clothing worn and hence by the climate. In the temperate climate they are commonly seen on the neck or on the trunk particularly around the axellae, except in the sexually transmitted infection when the

anogenital region is involved[16,17]. In children in the tropics, lesions are more common on the limbs. However they may also occur on the face particularly on the eyelids and the scalp, lips, tongue, buccal mucous membrane and on any part of the body surface including the soles where the appearance is atypial[16]. Nipple is also a very atypical site. Molluscum contagiosum has reported to occur on the scar[18]. A study on 578 molluscum contagiosum have shown the location of the disease were in head and neck- 34.7% trunk-27%, lower limb-20.7%, upper limb- 8.7%, genitalia- 3.8%, occurs in female patients-56.7%. The age range of the series was 0-19 years[19].

The diagnosis is usually obvious when multiple lesions are present. Single or multiple round domed shaped lesions waxy pink or skin coloured, firm papules with central umbilication and could easily be mistaken by viral warts[20,21,22]. They have a symetrical cup shaped downgrowth of lobules of epidermis, packed with eosinophillic or basophillic intracytoplasmic inclusions[20,21]. Direct microscopical examination of an unstained curetted lesion crushed on a slide establishes the diagnosis.

The solitary molluscum may resemble as a pyogenic granuloma, a keratocarcinoma or an epithelioma and may be difficult to identify. It may also be confused with epidermal cyst, nevocellular nevai, metaplastic ossification, soft fibroma, sebaceus hyperplasia & kaposis sarcoma. The diagnosis is often not made until the lesion is examined histologically but can be carried out rapidly by electron microscopy[22].

Treatment is offered by simple mechanical methods like expression of the contents by squeezing the papule with blunt forceps superficial curettage or shaving off with a sharpened wooden spatula may each suffice, although it is usual to add an application of a silver nitrate stick, phenol or strong iodine solution BP, chemical methods alone, including podophyllin, are less effective. Diathermy is more likely to cause scarring and would normally be reserved for larger lesions. Cryotherapy has recently been recommended as the treatment of choice. A few session of treatment at interval of 2-3 weeks may be required[23].

It is often resonable to leave molluscum to resolve spontaneously, especially in young children for whom the usual treatment can be painful or frightening but the rightly application of adhesive tape may help to remove the smaller lesions[23].

Conclusion :

Molluscum contagiosum is a common skin lesion mainly in the child & young adult spread by close contact & caused by molluscum contagiosum virus of pox virus group. Nipple is an uncommon site of molluscum contagiosum, can be easily mimicked as viral wart , malignant growth etc. Excision , cryosurgery, local application of different chemicals is the treatment of these viral tumour but there is a chance of recurrence also.

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COLLEGE NEWS

(J Bangladesh Coll Phys Surg 2002; 20 : 158-160)

Examination News

The following candidates satisfied the Board of Examiners and are declared to have passed the FCPS Part II and MCPS Examination held in July, 2002 subject to confirmation by the Council of Bangladesh College of Physicians and Surgeons.

FCPS PART II

Roll No.	Name of Candidates	Graduated from	Speciality
3	Dr. Md Abdul Motaleb	Dhaka Medical College	Medicine
6	Dr. Sadhu Uttam Kumar	Dhaka Medical College	Medicine
27	Dr. Shah Habibur Rahman	Dhaka Medical College	Medicine
29	Dr. Shahnoor Sarmin	Chittagong Medical College	Medicine
54	Dr. Mohammad Monir-Uz-Zaman	Sir Salimullah Medical College	Medicine
65	Dr. Kaisar Nasrullah Khan	Sir Salimullah Medical College	Medicine
68	Dr. Jabed Akhtar	Rangpur Medical College	Surgery
75	Dr. S.M. Shameem Waheed	Sher-e-Bangla Medical College	Surgery
77	Dr. Muhammad Khaled Mahmud	Dhaka Medical College	Surgery
83	Dr. Lotay Tshering	Mymensingh Medical College	Surgery
84	Dr. Masroor Hasan	Sir Salimullah Medical College	Surgery
91	Dr. Md. Shaukat Ali	Sir Salimullah Medical College	Surgery
95	Dr. Md. Jahangir Kabir	Dhaka Medical College	Surgery
102	Dr. Md. Saifullah	Dhaka Medical College	Surgery
104	Dr. Subarna Islam	Sir Salimullah Medical College	Surgery
106	Dr. Salma Yesmin Choudhury	Rajshahi Medical College	Surgery
107	Dr. Abu Hena Mahboob	Sylhet Medical College	Surgery
113	Dr. Mohammed Jahangir Kabir Bhuiyan	Sylhet Medical College	Surgery
123	Dr. Md. Nurul Hossain	Dhaka Medical College	Paediatrics
133	Dr. Dilara Alo	Dhaka Medical College	Paediatrics
134	Dr. Md. Shahidul Haque	Chittagong Medical College	Paediatrics
136.	Dr. Nazma A. Chowdhury	Dhaka Medical College	Paediatrics
139	Dr. Shamsun Nahar	Sir Salimullah Medical College	Obs. & Gynae
140	Dr. Mariam Faruqui	Dhaka Medical College	Obs. & Gynae
148	Dr. Farjana Sohael	Rajshahi Medical College	Obs. & Gynae
149	Dr. Mah Zabin Naz	Sir Salimullah Medical College	Obs. & Gynae
155	Dr. Gulshan Ara	Sir Salimullah Medical College	Obs. & Gynae
169	Dr. Biswa Nath Ghosh	Sher-e- Bangla Medical College	Ophthalmology
170	Dr. Amal Kumar Biswas	Sir Salimullah Medical College	Ophthalmology
171	Dr. Uddab Mallick	Rajshahi Medical College	Ophthalmology
181	Dr. Manash Kumar Basu	Chittagong Medical College	Anaesthesiology
183	Dr. Parveen Akhter	Sher-e-Bangla Medical College	Anaesthesiology
187	Dr. Md. Sayedur Rahman	Sir Salimullah Medical College	Radiology
189	Dr. Muhammad Afsar Siddiqui	IPGMR	Dermatology & V.
190	Dr. Md. Shamsul Huda	Rangpur Medical College	Dermatology & V.
196	Dr. Suraiya Akhtar	Dhaka Medical College	Haematology
198	Dr. Yasmin Akter	Mymensingh Medical College	Biochemistry
199	Dr. Farhana Yasmin	Sir Salimullah Medical College	Microbiology
200	Dr. Narjis Maliha Kawsar	Dhaka Medical College	Microbiology

The following candidates satisfied the Board of Examiners and are declared to have passed the MCPS Examinations held in July, 2002 subject to confirmation by the Council of the Bangladesh College of physicians and Surgeons

MCPS

Roll No.	Name of Candidates	Speciality
3	Dr. Md. Shafiul Azam	Medicine
8	Dr. Nausher Azimul Huq	Medicine
10	Dr. Nikhil Chandra Nath	Medicine
12	Dr. Khan Md. Sayeduzzaman	Medicine
23	Dr. Md Alamgir Ahmed Chowdhury	Medicine
24	Dr. Lakhsman Chandra Barai	Medicine
28	Dr. Md, Kafil Uddin	Medicine
37	Dr. Md. Saleh Uddin	Medicine
38	Dr. Md. Obaidul Haque	Medicine
39	Dr Ahmed Ashafuddoula	Medicine
45	Dr. Mohsin Ahmed	Medicine
49	Dr. Md. Kabir Uddin	Medicine
55	Dr. Khandaker Abu Talha	Surgery
72	Dr. Ashis Kumar Das	Paediatrics
74	Dr. Md. Abdur Razzaque	Paediatrics
78	Dr. Mohammed Nurul Alam	Paediatrics
81	Dr. Md. Khalilur Rahman	Obs. & Gynae
94	Dr. Shaheen Sultana	Obs. & Gynae
103	Dr. Ismat Ara	Obs. & Gynae
106	Dr. Fatema Kamrun Naher	Obs. & Gynae
110	Dr. Afroza Akhter	Obs. & Gynae
118	Dr. Mst. Irine Parvin	Obs. & Gynae
140	Dr. Ismatara Bina	Obs. & Gynae
161	Dr. Md. Mostafizur Rahman	Otolaryngology
165	Dr. Mohammad Ali Zulkawsar	Otolaryngology
167	Dr. Dipankar Lodh	Otolaryngology
168	Dr. Md. Badrul Islam	Otolaryngology
169	Dr. Akel Mohammed	Otolaryngology
171	Dr. Md. Tauhidul Islam	Otolaryngology
174	Dr. Chowdhury Md. Ikramul Latif	Psychiatry
177	Dr. Md. Habibul Islam	Anaesthesiology
179	Dr. Md. Idris Ali Bepari	Anaesthesiology
183	Dr. Sunil Kumar Biswas	Anaesthesiology

Roll No.	Name of Candidates	Speciality
188	Dr. Md. Asaduzzaman	Anaesthesiology
193	Dr. Subrata Kumar Roy	Anaesthesiology
200	Dr. Sajjad Mohammad Yusuff	Radiology
203	Dr. Shameem Al Mamun	Dermatology & V.
207	Dr. Mohammad Mukles-ur-Rahman	Dental Surgery
210	Dr. Md. Akteruzzaman Talukder	Forensic Medicine
212	Dr. Md. Humayun Kabir	Forensic Medicine
213	Dr. Md. Shahidul Islam	Forensic Medicine
214	Dr. Md. Nur Hossain	Forensic Medicine
215	Dr. Md. Manjur-Ul-Quader	Forensic Medicine
221	Dr. Md. Mujahid Hossain	Family Medicine
223	Dr. Mohammed Montasir Islam	Family Medicine
231	Dr. Md. Nazrul Islam	Family Medicine
240	Dr. Apurba Kumar Pandit	Family Medicine
243	Dr. Md. Bashidul Islam	Family Medicine
249	Dr. Bandana Chakravorty	Clinical Pathology
250	Dr. Sanjoy Kanti Biswas	Clinical Pathology
253	Dr. S.M. Ashraf Hossain	Clinical Pathology