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JOURNAL OF BANGLADESH COLLEGE OF PHYSICIANS AND SURGEONS

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CONTENTS

EDITORIAL

The Relationship of Pphysical and Mental Health : Co-occurring Mental and Physical Disorders

Developments in biochemistry, immunology, radiographic imaging, endocrinology, and other disciplines have produced an increased overlap between medicine and psychiatry.[1] Primary care physicians have a growing recognition of the benefits of psychiatric consultation and treatment of their patients.

Many reasons account for the lack of recognition of mental disorders. In medical clinics patients with both physical and psychological distress may be unable to or unwilling to discuss emotional symptoms because they believe physical symptoms are the appropriate problems to present to physicians. Of equal importance is the physicians failure to obtain a psychosocial history from the patient. Most internists have had inadequate training in psychiatry, feel uncomfortable with psychiatric patients, and do not understand how mental disorders may manifest with physical symptoms.

Psychiatrists' involvement in specialized medical units has grown during the past two decades.[2] Many patients have both a significant medical illness and a psychiatric disorder. Many such patients are elderly and require a combined medical and psychiatric therapeutic approach.[3] Medical-psychiatric units have been successfully developed in many medical centres in recent years. Patients with depression and a concurrent medical disease are present in all units. Chronically mentally ill patients have a high prevalence of inadequately treated medical diseases. [3, 4, 5]

Over two thirds of people suffering from depression complain of pain with or without reporting psychological symptoms.[6] Many people have trouble expressing internal emotions, consider mental illness to be s stigma, or simply assume depressive symptoms relate to their personal situations and therefore do not seek treatment. Physical symptoms are more prevalent among women, the elderly, the poor, the children, the culturally diverse populations, the medically ill, and the imprisoned.

The frequency in which serious physical diseases are accompanied by emotional and behavioural problems, symptoms and disorders are well established by research publications in the recent past years.[7] It has explored how emotional and behavioural disorders that accompany major physical illnesses are often ignored and even discounted in the development of treatment and prevention plans for cardiovascular diseases, diabetes, gastrointestinal disorders, communicable diseases and other illnesses.

World Federation for Mental Health has identified four specific areas of Co-occurrence of Mental disorders with Diabetes, Cancer, Cardiovascular disorder, and HIV/AIDS. The consequences of emotional and mental problems are many fold including successful treatment and management of diabetes, cancer, cardiovascular disease and HIV/AIDS, including the issues relating to compliance to treatment. The World Federation for Mental Health launched action plan and has provided research based background and fact sheets which include a package of information regarding the health consequences of HIV/AIDS, including the psychosocial impact that HIV/AIDS has on victims, their family and especially on children who are orphaned due to the death of parents infected by HIV/AIDS.

Individuals who have a severe and persistent mental disorders including schizophrenia or depression, very often present a variety of physical health problems, like obesity, high blood pressure, diabetes etc. For many of these individuals, quality medical care for their physical health needs is simply unavailable or inaccessible due to the lack of personal financial resources. In many instances, medical problems may result from negative side effects of medication being taken to manage the mental disorder, in turn, physical health problems may serve to encourage noncompliance with prescribed psychiatric medications.

The Century long ideas of separation between so-called "mental and physical" health has no real

relevance to the scientific understanding of health in the 21st Century; yet the myths and misunderstanding persist.[8] Mental health advocates all over the world have, in almost apologistic posturing said that this false premise should no longer exist and yet these voices continue to go unheard. The time has come to reinforce what we stand for mind and body are inseparable; health is a complete state of well-being and there is no health without mental health.

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10. Alaxandria, Virginia 22302-0810 USA, 1-703-838-7543, info @ wfmh.com.

ORIGINAL ARTICLES

Perception and Practice of Health Care Providers on Asthma Management in the Community of Bangladesh

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Summary :

More than 7% children (4 million) and 5% adults are suffering from asthma in Bangladesh. The management of asthma has already been formulated globally. We need to know the management of asthma at every level of health care facility of the country.

The study was done to look into the current perception and practice of Health Care providers (HCP) on asthma management.

It was a cross sectional survey. Multistage cluster sampling design was followed for the selection of HCPs from all over Bangladesh. A total of 288 HCPs were selected including 120 patients and 69 pharmacists. Data were collected by trained physicians through a structured questionnaire from HCPs with face-to-face interview.

Asthma was considered as a common health problem by all HCPs. All HCPs thought respiratory distress (92.2%-100%) and cough (63.6%- 90%) to be most important features for the diagnosis of asthma. Chest x-ray was the only investigation advised in 49.1%-75% cases to support the diagnosis of asthma. Use of nebuliser was limited to the consultants and RPs (53.5%-86.4%) in acute asthma. Use of rescue course of oral corticosteroids was minimum (14%-45.6%). Antibiotics use was found in 77.7%-100% cases. Oral salbutamol, aminophylline and kitotifen were found very common for asthma management. Use of inhalers by the patients was found low and limited only to salbutamol and beclomethasone. The aspect of asthma education was confined only to advising 'avoiding triggering factors'. HCPs suggested for organization of asthma/ respiratory centers in different health facilities and their training on asthma management.

The modern management of asthma is not widely practiced by the physicians of Bangladesh.

(J Bangladesh Coll Phys Surg 2005; 23 : 3-8)

Introduction :

Asthma is a substantial health problem among children and adults worldwide[1], with high and increasing prevalence rates in many countries like UK and Australia[2,3,4]. It affects approximately one in five children and one in ten adults in Australia[5]. The prevalence of asthma in Bangladesh is also substantial. More than 7% children (4 million) are suffering from asthma (attacks of wheeze in last 12 months) according to the first National Asthma Prevalence Study[6] and the first ever ISAAC study conducted in the schools of Dhaka district by Kabir et al[7]. Asthma is more prevalent in coastal areas than the city/ town areas of Bangladesh[,8,9]. The management of asthma has already been formulated globally. Many countries are now managing asthma in accordance to their own national guidelines[10,11]. Inhalation therapy is the mainstay of management of asthma now recommended for both acute and persistent asthma cases. Salbutamol, ipratropium bromide, sodium chromoglycate, nedocromil sodium, salmeterol, formoterol, beclomethasone, budesonide, fluticasone etc. all are now available and recommended for inhalation therapy. The concept of asthma as a disease characterized by airway inflammation had explored the tremendous role of corticosteroids in the management of asthma even in childhood[12,13]. Systemic corticosteroid therapy is a valuable adjunct in the treatment of acute severe asthma in children responding poorly to treatment with nebulised b_2 agonist. Moreover, antibiotics are not routinely recommended in the management of acute asthma[14]. The Asthma Association of Bangladesh has already formulated a guideline[15]. In the contrary, asthma is being managed in the traditional way in most of our situation by prescribing

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suspension of salbutamol and antibiotics, which has even been recommended in the manual of ESP (Essential Service Package)[16,17].

To optimize the management of asthma it is essential to explore the present situation of asthma treatment all over the country starting from tertiary health care centre down to grass root level community.

Methodology :

It was a cross sectional study conducted during July 2000 to June 2001. Multistage cluster sampling design was followed for selection of the HCPs. Three national level institutions (BSMMU, DSH, NIDCH) and 8 medical colleges selected randomly from 13 govt. medical colleges, 12 districts hospitals from six divisions (the districts where the medical colleges are non-existent) were randomly selected, 12 upazilla health complexes (one from each district was randomly selected), 12 unions (one from each upazilla) and 12 villages (one from each union).

A total of 288 HCPs consultants 103, registered physicians (RPs), like assistant registrars (AR) working at the medical college hospitals 40, medical officers (MO) working at the district hospitals and upazilla health complexes 44, private practitioners (PP) 36 and unregistered physicians like quacks at the village level 57, 120 asthma patients and 69 pharmacists were also interviewed.

Trained physicians took face-to-face interview of HCPs, and asthma patients from aforesaid areas. Data were collected on asthma prevalence, diagnostic features, investigations, drugs prescribed (oral and inhaler), and use of drugs by the patients. Another written questionnaire was used to collect data from local drug dispensers about cost and availability of drugs. All data were double entered into two computers by two data enterers into Epi-info program and subsequently the values were merged to minimize the errors. Analysis was done using SPSS software program.

Results :

Asthma was considered to be a common disorder by every level of HCPs (76.6%-86.6%). For diagnosis of asthma, all categories of HCPs considered respiratory distress (93.2%-100%) and cough (73.7%-90.3%) to be most important features. Wheeze was less recognized by the quacks (26.3%), but night cough waking and chest tightness were also less recognized by the RPs (Table-1). Only investigation of chest x-ray was thought to be required by all level of HCPs (49.1%-76.7%). Spirometry (0%-12.6%) and pulse oximetry (0%-2.5%) were almost non-existent. The use of nebuliser in acute asthma was found to be limited exclusively to RPs and consultants (53.5%-86.4%). Use of rescue course of oral corticosteroids was minimum (14%-45.6%). Other drugs used were salbutamol inhaler (66.7%-96.8%), parenteral hydrocortisone (50.9-94.2%), oxygen (10.5%-80.9%) and parenteral aminophylline (35.1%-75.9%). The quacks mostly (80.7%) referred the cases to better centres for further management (Table-2). The most commonly prescribed preventers were beclomethasone (14%-83.3%), sodium chromoglycate (1.8%-65%) and salmeterol (1.8%-28.2%). Prescription of common oral medications for the management of asthma by the HCPs were salbutamol (88.3%-100%), aminophylline (53.4%-87.7%) and kitotifen (59.2%-82.5%). It was also reflected by the asthma patients experience as to using oral asthma drugs of salbutamol, aminophylline and kitotifen (Table-3). Antibiotics were prescribed by all quacks and RPs but 77.7% of consultants, mostly ampicillin/ amoxicillin (48.5-78.9%).

The most common inhalers available in all areas were reliever salbutamol, and preventer beclomethasone. Spacers were not available in areas beyond medical college and town areas (Table-4). This finding was also substantiated by the asthma patients' experience of using available inhalers of salbutamol and beclomethasone (Table-3).

Almost all HCPs responded positively when asked about providing asthma education to the patients (93%-99%). But the asthma education was limited mostly telling 'to avoiding things' like allergens, cold, food and dust. The education did not cover well the topics like explaining the nature of disease, the technique of using inhalers, importance of long-term use of inhalers and follow up visits (Table-5).

The HCPs identified certain limitations about the barriers of good asthma management. These were limited facility for asthma management at the working health care facility-availability of nebulisers, spirometers, inhalers and poverty on the part of the patients. They also emphasized on the problems of providing asthma education because of ignorance about asthma diagnosis, asthma education to motivate patients about the importance of inhalers, long-term therapy, technique of inhaler use. However, the HCPs suggested for organizing an asthma/ respiratory center in different health facilities and training of HCPs on different aspects of asthma management (Table-6).

Table-I

What were the features HCPs consider for the diagnosis of asthma?

Asthma features	Consultants (103) %	RPs (120) %	Quacks (65) %
Wheeze	93.2	84.1	26.3
Resp distress	93.2	98.3	100
Cough	90.3	74.3	73.7
Night cough waking	72.8	41.7	5.3
Chest tightness	70.9	40.3	12.3

Table-II

How did HCPs manage acute asthma?

Modes of treatment	Consultants (103) %	RPs (120) %	Quacks (65) %
Salbutamol nebuliser	86.4	53.5	00
Ipratropium bromide	36.9	18.5	00
Salbutamol inhaler	93.2	96.8	66.7
Parenteral hydrocort/ oradexone	88.3	94.2	50.9
oral prednisolone/ oradexone	45.6	29.4	14
Inj Aminophylline	55.3	75.9	35.1
Oxygen	74.8	80.9	10.5
Referral	16.5	17.0	80.7

Table-III

Patients' experience about asthma

Modes of treatment	Town / Medical College areas (n=36) %	Upazilla (n=32) %	Villages (n=21) %	Total (89) %
Oral asthma medication				
Salbutamol	100	81.2	85.7	89.8
Aminophylline	38.8	28.1	52.3	38.2
Theophylline	16.6	21.8	4.7	15.7
Kitotifen	38.8	40.6	4.7	31.6
Corticosteroids	36.1	31.2	9.5	28.0
Inhalation therapy				
Salbutamol	50.0	37.5	42.8	43.8
Beclomethasone	22.2	9.3	4.7	13.4

Table-IV

Availability of inhalers as per pharmacists' opinion

Available	Town / Medical College areas (n=16) %	Upazilla (n=22) %	Villages (n=31) %
Relievers			
Salbutamol	100	95	71
Ipratropium bromide	62.5	27.2	00
Preventers			
Sodium chromoglycate	81	59	06.4
Beclomethasone	100	95	55
Salmeterol	94	82	29
Spacers	68.7	21.7	3.2

Table-V

What asthma educations were given by the HCPs to the patients

Asthma education topics	Consultants (103) %	RPs (120) %	Quacks (65) %
Avoid allergens	36.8	35	5.2
Avoid cold	24.2	32.5	43.8
Avoid food	13.5	19.1	26.3
Avoid dust	14.5	45	53.8
Explaining the disease	17.4	6.6	4.6
Technique of use of inhalers	18.4	2.0	00
Long-term use of inhalers	9.7	2.5	00
Follow up visit needed	01	00	00

Table-VI

Suggestions of HCPs to improve the management of asthma

Suggestions	Consultants (103) %	RPs (120) %	Quacks (65) %
Organising center with facilities for management of respiratory/ asthma cases-lung function tests, nebulisers, inhalers	85.5	74.1	24.6
Training of HCPs	87.3	40	33.8
Media coverage on asthma	38.8	18.3	4.6

Discussion :

This is a nationwide study to explore the prevailing situation of asthma management all over the country. All asthma features are not well recognized by all category of HCPs. Use of nebuliser is not widespread in the management of acute asthma. Use of oral asthma drugs are at rampant. Inhaler use is limited only to salbutamol and beclomethasone. Asthma education is at fault with advising only to 'avoid things'. HCPs opined for organization of health centers and training of themselves.

A multi-stage stratified random sampling design was followed for the selection of study population and areas. Trained physicians were involved in taking interviews and filling up of questionnaires in the field with the respiratory physician in the overall supervision. Respiratory physician had to take interview of the senior consultants in order to avoid any scope of cursory interview and difficult situations to be faced by the trained physicians.

HCPs, particularly the registered physicians' inability to recognize the features of asthma like night cough waking and chest tightness was striking. Night cough waking is an important asthma feature[18] and chest tightness[15] also complained by the older group of patients. Because of non-availability of other investigative facilities like spirometer and pulse oximeter, only chest x-ray was considered important for the diagnosis of asthma by the HCPs. Use of salbutamol nebuliser was found limited to consultants and registered physicians to some extent but the quacks were found not at all acquainted with use of this popular therapy of asthma. Salbutamol nebuliser is an integral part of acute asthma management in the modern therapy[15]. The service had not reached to the far-flung areas of Bangladesh. The liberal prescription of the rescue course of prednisolone was not observed in the community. There is an undue fear on the part of the HCPs about the use of corticosteroids, which certainly do not cause much harm to the patients if used for a very short period, than chronic hypoxia resulting from persistent asthma. The popularity of oral medications of asthma in the community might be because of non-compliance for inhalers, which in turn due to poor quality of asthma education and costs of the inhalers. High rate of prescription of antibiotics in asthma might be resulting from confusion about the diagnosis of asthma on the part of the HCPs. Spacers need to be made available to every level of health care facilities so that HCPs have the opportunity to prescribe this to the small asthma kids.

Asthma education was found totally inadequate in our situation. The education was mainly limited 'to avoiding things' and contained very little about explaining the nature of disease, technique of inhaler use, need of long term inhaler and follow up (Table-VI). This might be due to lack of knowledge of HCPs about the aspects of asthma education which covers all aspects of asthma ®. Carefully designed asthma education program for patients can improve parents' and patients' understanding of the condition and its treatment modalities leading to increase in the confidence that the condition can be controlled, thereby increasing the adherence to the treatment regimen and management of symptoms[19].

The HCPs of all levels pointed out the problems faced by them as to limited facility of lung function tests, availability of nebuliser, cost of drugs for poor patients. The quacks did not show their prudence in regard to mentioning the problems faced by them while managing the asthma patients. The HCPs suggested for improvement of asthma management in their respective facility. They suggested for organization of respiratory / asthma centers, facility for lung function tests, availability of nebulisers and inhalers.

Conclusions :

The perception of HCPs about the diagnosis and treatment are not up-to-date and their practice are naturally at fault. The logistics for asthma management are costly and not available everywhere. There is demand for better organization of health care facility and more training of HCPs for asthma management.

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Minimum Inhibitory Concentrations (MICs) for Imipenem of Bacteroides Fragilis - Study of 28 Strains

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Summary :

To determine the Minimum Inhibitory Concentrations (MICs) of imipenem of Bacteroides fragilis, a study was conducted in the Queens Medical Centre, University of Nottingham, England from September 1997 to August 1998. Twenty eight test strains of B. fragilis were tested for MICs of imipenem. Of them, 71.43% of B. fragilis strains showed MIC of < 8mg/L of imipenem.10.715% showed MIC of 8mg/L; 7.14% had 32mg/L and 64mg/L; 10.715% showed MIC of ≥265mg/L. Considering the break point of imipenem resistance as 8mg/L, it could be concluded from this study that 71.43% of B. fragilis strains were sensitive to imipenem.

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Introduction :

Bacteriodes fragilis is a well recognized anaerobic Gram negative human pathogen. It is often isolated from intra abdominal abscess, peritonitis and wound infections associated with large intestine[1]. It is implicated frequently in brain abscess secondary to otitis media[2] and is a major cause of foot ulcer in diabetic patients[3]. Bacteroides species accounts for at least a quarter of all anaerobes isolated from clinical specimens in microbiology laboratories[4].

As most infections involving B. fragilis occur in combination with aerobic pathogens, antibiotic therapy must be directed at both aerobic and anaerobic components. Metronidazole is very effective against anaerobic bacteria and resistance is so uncommon that it is considered as the drug of choice for anaerobic infections[5]. It is usually combined with gentamycin which is widely active against aerobic Gram negative rods.

Most strains of B. fragilis produce B-lactamase which hydrolyses commonly used B-lactam agents including penicillin and ampicillin. However, these antibiotics may be activated by combination with B-lactamase inhibitor B-lactam compounds e.g. clavulanic acid[5].

For monotherapy, B-lactamase stable B-lactams are available, which can be used as a therapeutic agent in the poly microbial infection in which B. fragilis species are involved[5]. These include cefoxitin and the carbapenems-imipenem and meropenem. The lowest concentration of imipenem that completely inhibit the growth of B. fragilis after 48 hours of incubation anaerobically is considered as the MIC of imipenem of B. fragilis. The aim of this study was to determine the MICs of imipenem of B. fragilis strains in the laboratory to find out its sensitivity against these strains.

Materials and Methods :

The study was conducted in the Queens Medical Centre, University of Nottingham, England from September 1997 to August 1998. Twenty nine test strains of B. fragilis were initially selected from the Nottingham Public Health Laboratory, two were originally isolated in Spain and one originated in Japan. In addition, two control strains were used, B. fragilis TAL 3636 which was cfiA (carbapenamase gene) positive and highly resistant to carbapenems[7] and B. fragilis NCTC 9344, a carbapenem sensitive strain known not to produce ß-lactamase.

Brain Heart Infusion supplemented (BHIS) with yeast extract (5g/1), haemin (5mg/L) and menadione (1 mg/L) made according to the Manufacturers instructions was used as a general growth medium. BHIS agar media was obtained by addition of 1.2% Davis agar, (Unipath). The culture plates were incubated in an anaerobic cabinet with an atmosphere of 80% nitrogen, 10% carbon dioxide and 10% hydrogen at 37^0C.

The test strains were identified by use of carbohydrate fermentation, bile tolerance and aesculin hydrolysis. The test strains were grown over night in BHIS broth at 37^0C. An inoculum of 10^6 organisms of each strain were delivered on to agar surface of carbohydrate (glucose, lactose, salicin, trehalose and mannitol) and bile/aesculin test plates with a multipoint inoculator (Denleys Instruments, Billinghurst, Sussex). The plates were examined after 48 hours of anaerobic incubation.

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The antibiotic used was imipenem (Merck, Sharp and Dohme, Hoddeston, Herts). Solutions of imipenem were freshly prepared by dissolving antibiotic powder in sterile distilled water.

Minimum Inhibitory Concentrations were determined by the agar incorporation method. Imipenem in suitable two fold serial concentrations were incorporated in BHIS agar. An inoculum of 10^6 were delivered onto agar surface with a multipoint inoculator. The lowest antibiotic concentration that completely inhibited growth after incubation for forty eight hours at 370C in an anaerobic cabinet was taken as the MIC.

Results :

The Bacteroides fragilis was identified by carbohydrate fermentation, bile tolerance and aesculin hydrolysis. All strains grew on BHIS agar media. There was growth on bileaesculin agar media and black zone around growth indicated aesculin hydrolysis. Four strains fermented salicin, trehalose and mannitol and were not identified as Bacteroides fragilis. So they were excluded from further study. Twenty eight strains were confirmed as B. fragilis as they fermented glucose and lactose but not salicin, trehalose or mannitol. The MIC of the 28 test strains ranged from 0.5 to >256mg/L for imipenem. The following table shows the detailed MICs of the test strains. Twenty (71.43%) B. fragilis strains were sensitive to imipenem showing MIC of <8mg/L of imipenem. Three (10.715%) strains together with the positive control showed a high level of resistance (MIC >256mg/L). It had been estimated that 10.715% of the test strains showed MIC of 8mg/L; 7.14% had 32mg/L and 64 mg/L; 10.715% showed MIC of ≥265mg/L.

Table -I

MICs of imipenem of B. Fragilis test strains

B. fragilis strains	MIC of imipenem (mg/L)	Number (total = 28)	Percentage (N =28)
B. fragilis J8			
" " F10			
" " J1	0.5	5	17.86
" " RB11			
" " R208			
" " A1			
" " 0423			
" " Q7			
" " A3			
" " E10			
" " S1	1	10	35.71
" " R249			
" " R186			
" " 2013E			
" " R240			
" " R97			
" " R251			
" " B89	2	5	17.86
" " E9			
" " 212			
" " 119			
" " 7/5	8	3	10.715
" " T2			
" " 16/16	32		
" " 57	64	2	7.14
" " FS			
" " 288.89	256	3	10.715
" " GAI 30144	>256		

Discussion :

The majority of B. fragilis strains produce typical Bush class 2e ß-lactamase which are the primary mechanism of resistance to most ß-lactam antibiotics with the exception of ß-lactamase stable B-lactam e.g. carbapenem[8]. A minority of strains, however produce ß-lactamase that are metallo enzymes which hydrolyse nearly every class of ß-lactam antibiotic including carbapenem and are not susceptible to inhibition by classical ßlactamase inhibitors such as clavulanic acid[9,10].

In 1992, 1% of B. fragilis isolates have been shown to carry the Zinc dependant carbapenamase gene cfiA[11]. The number of B. fragilis isolates that display B-lactam antibiotic resistance is increasing and reports of carbapenamase production and carbapenem resistance are emerging[12].

The typical MIC of imipenem is 0.06mg/L, whereas the MICs of the test strains in this study ranged from 0.5 to >256 mg/L. Therefore, depending on the MICs of imipenem the isolates are categorized into four groups. Twenty of the test strains showed MIC 0.5-2mg imipenem/L. As the break point of imipenem resistance is 8mg/L, these strains were classified as sensitive, although at least a 10 fold higher antibiotic concentration was required to inhibit these strains compared to fully sensitive B. fragilis strains [13]. Three strains of B. fragilis showed MIC of 8mg/L of imipenem and they were classified as having low resistance. One strain of B. fragilis had MIC of 32mg/L and another one had 64mg/L and were classified as moderately resistant. Four strains of B. fragilis demonstrated high level of resistance with MICs of imipenem of 256mg/L or more. These values are consistent with the previous studies[14,15,16].

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Comparison of the Safety and Efficacy of Intra-vaginal Misoprostol (prostaglandin E_1) with those of Dinoprostone (prostaglandin E_2) for Cervical Ripening and Induction of Labour in a Tertiary Level Hospital

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Summary :

To compare the efficacy and safety of intra vaginal misoprostol (prostaglandin E_1) with those of dinoprostone (prostaglandin E_2) for cervical ripening and induction of labour, a randomized controlled study was done on 74 pregnant women at term with unripe cervix, who had indication for induction of labour in the department of Obstetrics and Gynaecology of Bangabandhu Sheik Mujib Medical University (BSMMU) between the period from July 2002 to June 2003. Seventy-four cases were randomly assigned to receive either 50 µgm intra-vaginal misoprostol or 500 µgm dinoprostone intra-cervically. If labour was not initiated within 6 hours the same dose was repeated every 6 hours to a maximum of 150 µgm of misoprostol or 1.5 mg dinoprostone. The main outcome variables were induction delivery time, number of deliveries within 24 hours, mode of delivery, maternal and neonatal outcome. The mean induction delivery time was significantly shorter in misoprostol group compared with dinoprostone group 11.60±4.5 vs 18.07±. 5.9 hours (P<.0001). There was no difference in cesarean delivery rate between two groups. Uterine hyperstimulation and tachysystol occurred more frequently in misoprostol group than in dinoprostone (16.2% vs 2.7%, P<.05 and 29.7% vs 10.8%, P<.04) respectively. No statistically significant difference was noted between two groups regarding neonatal outcome. Compared to dinoprostone, misoprostol is more effective in cervical ripening and labour induction at term. The frequency of uterine hypercontractility associated with the use of misoprostol did not increase the risk of adverse intrapartum or neonatal outcomes.

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Introduction :

Unripe cervix is well known to cause failure of induction of labour and it is associated with an increased likelihood of prolonged labour and an increased incidence of cesarean delivery.[1] Prostaglandins have been shown to induce cervical ripening and stimulate uterine contraction and have been found to be effective in number of clinical trials at variety of doses and routes of administration[2-3]. Prostaglandin E_2 (dinoprostone) has been widely used for induction of labour[4]. They are most commonly administered intravaginally and in recent years intra-cervically. Intra-cervical approach of PGE_2 was found more effective than intra-vaginal one[5]. Although local application of prostaglandin E_2 (PGE_2) has been considered to be effective in cervical ripening and shortening of delivery time it is very expensive and also sometimes unavailable to obstetrician in developing and underdeveloped countries[6,7]. Misoprostol, a prostaglandin E, analogue, has the advantage of being inexpensive and stable at room temperature. There has been considerable interest in the use of misoprostol for both cervical ripening and labour induction in patients with Bishop score of <4[8-11]. Vaginal administration of misoprostol has been extensively studied and consensus exists as to its efficacy[12]. Safety is the main concern in all studies because of the occurence of extensive uterine contraction on dose related basis[13]. This study was designed to compare the safety and efficacy of intravaginal misoprostol with those of dinoprostone for cervical ripening and induction of labour.

Materials and Methods :

A randomized controlled study was performed on seventy-four pregnant women in department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University who needed induction of

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labour during the period from July 2002 to June 2003. Seventy four women were randomly assigned to receive either 50µgm intra-vaginal misoprostol or 500µgm dinoprostone intra-cervicaly. Inclusion criteria were singleton pregnancy at term (37-42 weeks), cephalic presentation, reassuring foetal heart rate monitor tracing and Bishop score ≤5. Patients were excluded if they had a known hypersensitivity to prostaglandin, history of cesarean section or myomectomy, premature rupture of membrane (PROM), cephalopelvic disproportion (CPD), polyhydramnios, severe oligohydramnios, multiparous women (para 4 or more) and cardiopulmonary disease. After selection for the study a written informed consent was obtained from each participant. For randomization a sequentially numbered sealed envelop were used before induction of labour. Assessment of cervix was done finally before application of medication and documented. The women were randomly selected for two different preparation of prostaglandin for cervical ripening and induction of labour. Tablet of 200µgm misoprostol were divided into 4 parts each part containing 50µgm. Women who were selected for vaginal misoprostol, an initial dose of 50µgm was applied in the posterior vaginal fornix. If labour did not establish within 6 hours subsequent doses of 50µgm were applied 6 hourly maximum up to 3 doses. Subjects who were assigned to receive dinoprostone 500µgm gel was applied intra-cervically. If needed subsequent dose was given every 6 hours maximum up to 3 doses. Study medication was given every 6 hourly until adequate contraction pattern developed (3 contraction in 10 minutes). Oxytocin augmentation if required was begun no sooner than 4 hours after the last dose of medication. Indications of oxytocin augmentation were a protracted or arrested cervical changes for at least 4 hours with inadequate uterine contraction. Following application of prostaglandin foetal cardiac activity was monitored by cardiotochograph (CTG) for at least 30 minutes. Continuous foetal and uterine monitoring was performed in all patients. For foetal heart rate monitoring CTG was done at frequent interval. Artificial rupture of membranes generally performed once cervix became 4 cm dilated. Entry characteristics for the study, including maternal age, parity, gestational age and Bishop score were compared between the treatment groups. Indications for labour induction, maternal and neonatal outcomes were also evaluated. Efficacy and safety were evaluated by the main outcome variables like induction delivery time, vaginal delivery within 24 hours of induction, maternal complications (hyperstimulation syndrome, tachysystol) and neonatal out-come (Apgar score in 5 minutes, admission in neonatal care unit for birth asphyxia or other labour complications).

In case of tachysystol (5 or more contractions in 10 minutes for two consecutive 10 minutes period) and hyper stimulation (tachysystol associated with an abnormal pattern of foetal heart rate tracing) vaginal tablet was removed, maternal position was changed to left lateral side and oxygen was given. Hyperstimulation and abnormal foetal heart rate tracing were indications to discontinue study drug.

Statistical analysis was performed with statistical package for social science (SPSS). For comparison we used unpaired t test and x^2 test. P<.05 was considered significant.

Result:

Total 74 patients were enrolled in this study with 37 patients randomized to each group. Demographic data presented in Table-I. There were no statistically significant differences in maternal age, parity, gestational age and Bishop score between two groups. In addition inductions for induction were similar between two groups (Table- II). Table-III compares intra-partum variables and maternal response to two different type of prostaglandin. Induction delivery time was significantly shorter in vaginal misprostol group than in dinoprostone group (11.60±4.5 hours vs 18.07±5.9 hours, P<.0001). In misoprostol group 64.86% patients delivered within 24 hours of induction compared to 40.54% of patients who received PGE2 for cervical ripening (P=.1). Significantly less patients in misoprostol group required oxytocin augmentation (51.53%) than in dinoprostone group (91.89%), P<.0001. The frequency of hyperstimulation syndrome (16.2% vs 2.7%, P<.05) and tachysystol (29.7% vs 10.8%, P<.04) were significantly higher in misoprostol group than in dinoprostone group. Mode of delivery and indications for cesarean section is compared in Table IV. More patients in misoprostol group (62.2%) delivered vaginally than in dinoprostone group (51.5%) but the difference was not statistically significant. 37.8% patients in misoprostol group and 48.6% patients in PGE2 group needed cesarean

Table I

Demographic Characteristics of the patients

Demographic Characteristics	Vaginal misoprostol	Dinoprostone (n=37)	Significance (n=37)
Maternal age (years) (mean±SD)	24.27 ±3.15	23.45 ±2.66	NS
Parity			
Nulipara	18(48.6)	19(51.4)	NS
Multipara	19(51.4)	18(48.6)	NS
Gestational age (weeks) (mean±SD)	40.13 ±1.45	40.43 ±1.16	NS
Bishop's score (mean±SD)	3.62 ±.79	3.51 ±.83	NS

(Percentage is within parenthesis)

Table-II

Indications of induction

Indications	Vaginal Misoprostol (n=37)	Dinoprostone (n=37)
Postdated pregnancy	24 (64.86)	26 (70.27)
Pregnancy Induced Hypertension (PIH)	8(21.62)	7(18.91)
Elective	3(8.1)	2(5.4)
GDM	2(5.4)	1(2.7)
Rh-isoimmunization	0	1(2.7)

(Percentage is within parenthesis)

Table-III

Maternal response to different Type of prostaglandins

Maternal response	Vaginal misoprostol (n=37)	Dinoprostone (n=37)	Significance
Induction delivery time (Hours) mean±SD	11.60±4.5	18.07±5.9	.0001
Delivery ≤ 24 hours	24(64.86)	15(40.54)	.1
Oxytocin augmentation	19(51.53)	34(91.89)	.0001
Hyperstimulation syndrome	6(16.2)	1(2.7)	.05
Tachysystol	11(29.7)	4(10.8)	.04

(Percentage is within parenthesis)

Table-IV

Mode of delivery and indications of cesarean section

Mode of delivery	Vaginal misoprostol(n=37	Dinoprostone (n=37)	Significance
Normal vaginal delivery	23(62.2)	19(51.5)	NS
Cesarean section	14(37.8)	18(48.6)	NS
Total	37	37	
Indications of cesarean section			
Fetal distress	10(71.4)	3(16.7)	.003
Arrested disorder	2(14.3)	7(38.9)	.23
Failed induction	214.3)	8(44.4)	.12

(Percentage is within parenthesis)

Table-V

Neonatal outcome

Neonatal outcome	Vaginal misoprostol (n=37)	Dinoprostone (n=37)	Significance
Birth weight (Kg) (mean±SD)	2.90±.42	2.88±.35	NS
5 minute Apgar Score <7	10(27)	5(13.5)	.12
Transfer to neonatal ward	7(18.9)	2(5.4)	.07

(Percentage is within parenthesis)

section. Significantly more patients of misoprostol group (71.4% vs 16.7%, P<.003) needed cesarean section due to foetal distress than in dinoprostone group.

Neonatal out-come is compared in table V. Regarding Apgar score it is observed that more neonates in vaginal misoprostol group had score < 7 at 5 minutes than in dinoprostone group (27% vs 13%, P=.12) but the difference was not statistically significant. More neonates of vaginal misoprostol group needed admission in neonatal ward (18.9% vs 5.4%, P=.07).

Discussion :

Labour induction in presence of cervical immaturity is a common indication for the use of prostaglandin particularly infra-cervical PGE_2[14-16]. However in the last 5 years there has been considerable interest in the use of misoprostol, a prostaglandin E_1 analogue for cervical ripening and labour induction[9-11].

In our study we compared the safety and efficacy of vaginal misoprostol with those of intra-cervical dinoprostone for cervical ripening and labour induction. In our result it is seen that vaginal misoprostol is more effective in cervical ripening and labour induction compared with dinoprostone. Induction delivery time was significantly shortened in vaginal misoprostol group (11.60 ± 4.5 vs 18.07 ± 6 hours, P<.0001). Our findings are consistent with previous studies done by Howard et al and Sanchez-Ramos et at[12-17]. In the present study the use of oxytocin was significantly less in vaginal misoprostol group than in dinoprostone group (51.53% vs 91.89%, P<.0001), the findings consistent with that of Fletcher et at and Majoko et al[18-19]. In this study more patients delivered vaginally within 24 hours of induction with misoprostol (64.86% vs 40.54%) but the difference was not statistically significant. When we consider safety of misoprostol uterine tachysystol

and hyper stimulation is the main concern. In this study, it is observed that the incidence of hyperstimulation (16.2% vs 2.7%, P<.05) and tachysystol (29.7 vs 10.8%, P<.04) was significantly more in vaginal misoprostol group than in dinoprostone group. Y.-K. Chang et al in 2003 reported in their study that significantly more patients developed hyper stimulation (18.6% vs 4.7%, P <.05) and tachysystol (25.6% vs 14.0%, P <.05) in misoprostol group than in dinoprostone group, which is consistent with our observation.[5] But in some randomized trial where efficacy and safety of vaginal misoprostol was compared with dinoprostone, it was reported that hyper stimulation was not different and there was no difference in neonatal and maternal out-come [20-22].

Regarding mode of delivery, in our study spontaneous vaginal delivery was more in vaginal misoprostol group (62% vs 51.5%) than in dinoprostone group but the difference was not statistically significant. On the other hand Filomena Nunes et al[14] and Y.-K. Chang et al[5] reported that misoprostol administration did not reduce cesarean delivery rate. In this study though the rate of cesarean section was not statistically different (37.8% vs 48.6%) between two groups, it is observe, that significantly more patients needed cesarean section due to foetal distress in vaginal misoprostol group, 10 out of 14 (71.4%) vs 3 out of 18 (16.7%), P<.003. This might to be due to higher incidence of tachysystol and hyper stimulation in vaginal misoprostol group.

Regarding neonatal out-come, more neonates had Apgar score less than 7 at 5 minutes in vaginal misoprostol group (27% vs13.5%, P=.12) than in dinoprostone group, though the difference was not statistically significant. More number of neonates in misoprostol group needed admission in neonatal ward, 7 out of 37 (18.9%) vs 2 out 37 (5.4%) than in dinoprostone group. Our findings are consistent with those of reported by Rokeya Begum et al[23] but not consistent with the findings reported by Y.-K. Chang et al[5] where no neonate in vaginal misoprostol group required intubation, resuscitation or admission in NICU.

Conclusion:

Administration of vaginal misoprostol appears to be more effective for cervical ripening and labour induction than intra-cervical PGE_2. Regarding safety in this study dinoprostone appears to be safer, as hyperstimulation and tachysystole was significantly less in this group. Close monitoring of labour, intra-partum CTG and maintenance of partogram is mandatory for using these preparations. Further large-scale study using different doses of misoprostol is necessary before one can advocate vaginal misoprostol for cervical ripening and induction of labour.

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Association of ABO Blood Group with Malignancies

S AFROSE

Summary :

ABO blood group of seven hundred and nine patients was documented who had been suffering from malignant neoplastic conditions of different organs and systems from Jan 97 to August 2001 at the Blood transfusion centre of CMCH. The objective was to determine any Association of ABO blood group and malignancy. It was found that, out of these 709 cases, 251 (35.40%) were A group, 219 (30.88%) B group, 204 (28.77%) O group, 35 (4.93%) AB group. It revealed significant association of ABO blood group and malignant lesions for some of the organs and systems. Small sample size precludes firm conclusion and warrants further documentation in the community with larger sample size.

(J Bangladesh Coll Phys Surg 2005; 23 : 18-24)

Introduction :

A blood group system is a group of antigens encoded by alleles at a single gene locus or at gene loci so closely linked that crossing over does not occur or is very rare[1]. Blood group antigens are assigned to a system after being defined immunologically, genetically and biochemically[2].

The ABO blood group system was the first system to be described. Antigenic differences between different species were recognized by Landois in 1985. Landstein was prompted by the work of Landois. He in 1931 first described the serologic differences between red cell of various individuals[3] allowing him to classify people into one of four groups, depending on whether their red cell contained agglutinogen termed A or B. The ABO blood group system is the most important one identified to date.

It has been suggested that the ABO system has evolved under a positive selection pressure. The implication is that certain ABO group provide selective vulnerability to individuals possessing a particular ABO blood group. Some blood groups are found to be associated with certain medical conditions[3-6]. For example blood group "O" associated with increased incidence, of Peptic ulcer and Urinary tract infection. Blood group "A" antigens are more commons in person with cancer of stomach, salivary gland, colon, ovary, uterus, cervix and bladder[5-6,7].

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In Bangladesh, about 200,000 new cases are diagnosed as cancers of different organs[8]. Identifying people at risk to take necessary preventive steps is widely accepted . Establishing association of blood group with malignancy might allow necessary steps to be taken to offer some help for these patients. This prospective study has been designed to record information regarding the association between ABO blood group and malignancy in our population to help manage these victims of malignancy.

Aims and Objectives :

1. To document ABO blood group of patients suffering from malignancies of different organs and systems.
2. To describe the association of different type of malignancies with ABO blood group.

Materials and methods :

This was a prospective observational study. ABO blood grouping of patients attending CMCH with different types of malignancies were done in the Department of Transfusion Medicine. A case record form was used for each patient with entries for Name, age, sex and diagnosis. Compiled data was tabulated and treated with statistical test to see the significance of association of blood group with malignancies.

Results :

A total of 709 patients with different types of malignancies were recorded. Blood group was done and recorded separately for individual patient. Among them 483 were male and 226 were female. Male to female ratio 2.13:1. Table-l : show distribution of patients with different malignancies and their blood group.

Table-l

Showing Distribution of patients with cancer of different Organs according to ABO blood Groups

Organ / System	Total patients	Blood Groups A	B	O	AB
ALL ORGANS	709	251	219	204	35
GIT	322	110	107	90	15
Stomach	235	90	69	66	10
Colon	38	7	19	9	3
Rectum	19	4	4	10	1
Oesophagus	30	9	15	5	1
Hepato biliary	40	16	12	8	4
Liver	22	7	7	6	2
Gall bladder	6	0	3	1	2
Pancreas	12	9	2	1	0
Urinary System	47	21	9	12	5
Kidney	12	4	2	2	4
U. Bladder	25	11	4	9	1
Ca Prostate	10	6	3	1	0
Female genital tract	52	28	11	11	2
Ovary	16	10	2	4	0
Cervix	28	14	7	6	1
Ca uterus	8	4	2	1	1
Breast	46	12	17	16	1
Bronchus	49	10	16	19	4
Lymphomas & Leukaemias	101	36	29	33	3
NHL	26	14	5	6	
HD	5	2	3	0	0
ALL	33	8	14	11	0
AML	28	5	7	14	2
CML	9	7	0	2	0
Oral & upper airway	32	15	9	8	0
Cheek	9	3	3	3	0
Tongue	6	2	2	2	0
Tonsil	8	4	2	2	0
Larynx	4	4	0	0	0
Naso pharynx	4	1	2	1	0
Nostril	1	11	0	0	0
Miscelenius	20	3	9	7	1
MM	8	2	3	2	1
Bone	7	0	5	2	0
Neuroblastoma	2	0	1	1	0
Retinoblastoma	2	0	0	2	0
Skin	1	1	0	0	0

About half (323 / 709) of the patients recorded in the series had malignancies of gastrointestinal system mostly of stomach. 49 patients had Carcinoma of bronchus 46 patients were admitted with carcinoma of breast. Lymphomas and leukaemias accounted for 101 patients 47 patients had involvement of urinary system and 40 had lesions of hepatobliary system.

In total there were 251 (35.4%) in group "A" 219 (30.88%) in group "B" and 204 (28.77%) in "O" group. Only 35 patients (4.93%) were from group "AB". Table-II shows, different distributions and relative frequency in population (study conducted at Chittagong) and their significance. It appears that Blood group "A" people have significantly higher incidence of malignancies.

GIT malignancies

There were 322 cases of GIT malignancies recorded in this study. Of these 110 (34.1%) patients had blood group "A" 107 (33.2%) had group "B" and 15 (4.6%) from group "AB". Among the different groups Blood group "A" had significantly higher proportion of patients. Most patients in this study had carcinoma of stomach 235 of 322 (73%) followed by malignant lesions of colon and rectum 57 (18%) and oesophagus 35 (10%). Association of different blood group among these individual malignancies were calculated and presented in Table -3 and 4. It appears that incidence of carcinoma of stomach is significantly higher in Blood group "A" people. On the other hand Carcinoma oesophagus is significantly high in group "B" and low in Group "O". Malignancies of colon and rectum show no significant change among different blood groups.

Table – II

Showing Distribution of cancer patients (irrespective of types) according to blood group and their significance (n = 709)

Blood Group	Number & Percentage of patients in Group	Frequency in population in Group	P value
A	251 (35.40)	24.82	<.05*
B	219 (30.88)	30.23	>.5
O	204 (28.77)	37.71	> .1
AB	35 (4.93)	7.24	>.1

Table – III

Showing Distribution of patients with cancer of GIT according to blood group and their significance (n = 322)

Blood Group	Number of patients in Group	Frequency in patients	Frequency in population in Group	P value
A	110	34. 16	24.82	< .05*
B	107	33.22	30.23	> . 1
O	90	27.95	37.71	>.1
AB	15	4.65	7.24	> . 1

Table - IV

Showing Distribution of cancer patients with Carcinoma of Different parts of GIT according to blood group and their significance

Blood Groups and frequency in population	Frequencies of different GIT Malignancies and their significance					
	Ca Stomach (235)		Ca Oesophagus (30)		Ca Colon & Rectum (57)	
	Frequency	P value	Frequency	P value	Frequency	P value
A (24.&2)	90(38.29)	<.01*	9(30)	> .1	11(19.3)	<.1
B (30.23)	69(29.36)	> .5	15(50)	<.041*	23 (40.3)	<.05*
O (37.71)	66 (27.65)	>.I	5(16.6)	<.001*	19(33.3)	<. 5
AB (7.24)	10(4.25)	>. 1	1 (3.34)	>.1	4(7.1)	>.5

Hepatobiliary System :
Forty cases of malignancies involving liver, gall bladder & pancreas were included in this study. Of these twenty two patients had hepatocelular carcinoma, six had carcinoma of gall bladder and twelve carcinoma pancreas. (16 of 40) 40% patients was in group A, 12 (30%) and 8 (20%) were in group O. Group A patients have significantly higher and Group O patints have significanly low incidence of malignancies involving hepatobiliary system. Considering hepatocellular carcinoma, Group O have significantly low incidence. Table-V shows distribution in details.

Female genital tract :
Fifty two women were included with carcinoma of cervix and carcinoma ovaries. Of them 28 (53%) were in group A, 11 in both B and O group and two in Group AB. Group "A" was found be associated with significantly higher incidence of malignant lesions of female genital tract. On the other hand Group O showed significantly lower incidence. Carcinoma of cervix was also found similar higher incidence in Group A and low in Group O patients. Distribution of patients with malignancies of female genital tract according to different blood groups is presented in table VI.

Carcinoma bronchus is a common malignant tumor. 49 patients were included during this study. 46 cases of carcinoma breast and 47 cases of malignant lesions of urinary bladder, prostate and kidneys. Out of 49 cases of Bronchogenic carcinoma, 10(20.4%) were of Group A, 16 (32 %) of Group B, 19 (38%) of Group O and only

Table – V

Showing Distribution of patients of Hepatocellular carcinoma according to blood group and their significance

	Malignancies of Hepatobiliary System (N = 40)		Hepatocellular carcinoma (N =22)	
Blood Group & Frequency in population	Number & Percentage of patients in Group	P value	Number & Percentage of patients in Group	P value
A (24.82)	16(40)	<.01*	7(31.81)	> .1
B (30.23)	12(30)	> .5	7(31.81)	> .5
O (37.71)	8(20	<. 01 *	6(27.27)	> .05*
AB (7.24)	4(10)	>.1	2(9.09)	>.1

Table – VI

Showing Distribution of patients with carcinoma of female genital tract & cervix according to blood group and their significance

	Female genital tract (N = 52)		Carcinoma Cervix (n=28)	
Blood Group Frequency in population	Number & Percentage of patients in Group	P value	Number & Percentage of patients in Group	P value
A (24.82)	28 (53.8)	<.001 *	14	<.001
B (30.23)	11 (21.1)	>.05	7	>.1
O (37.71)	11(21.1)	<.01*	6	<.01*
AB (7.24)	2(3.84) I	>.1	1	>.1

four were in Group AB. There was no significant change in distribution (Table-VII).

Almost similar distribution was observed among 46 patients of carcinoma breast included in this study. Significantly higher incidence of urological malignancy was observed in Group A patients. 21 of 47 patients included were of Group A. On the other hand incidence was significantly low in Group B and Group O.

Lymphoma and Leukaemia :

During this study 31 cases of lymphoma were recorded. Among them 16 (51 %) were of blood group A, 8 (25%) were Group B, 6 (19 %) in Group O. Significantly higher incidence of lymphoma was observed in group A patients.

In total 70 patients in this study had leukaemia including AML, ALL and CML. 33 patients had ALL and 28 patients had AML.

20 (28 %) of 70 patients of leukaemia were in Group A, 21 (30%) in Group B, 27 (38%) were in Group O and only two in AB group. There was no significant change in distribution. But in ALL blood Group B had significantly higher incidence and in AML Blood group O had significantly higher incidence. Distribution of patients of leukaemia in different blood group is presented in table IX.

Table –VII

Showing Distribution of patients with Carcinoma of Bronchus, Breast and Urological Malignancies according to blood group and their significance

	Urological Malignancies System (N=47)		Carcinoma Breast (N = 46)		Carcinoma Bronchus (N=49)	
Blood Group & Frequency in population	Number & Percentage of patients in Group	P value	Number & Percentage of patients in Group	P value	Number & Percentage of patients in Group	P value
A (24.82	21(44.7)	<.001	12(26.1)	>.1	10(20.4	>. 1
B (30.23)	9(19.1)	<.05*	17(36.9)	>.1	16(32.6)	>.5
O (37.71) 1	12(25.5)	< .05*	16(34.7)	>.5	19(38.7)	>.5
AB (7.24)	5(10.6)	>.1	1(02.1)	>.05*	4(8.1)	>.5

Table - VIII

Showing Distribution of cancer patients with Lymphomas according to blood group and their significance (n =31)

Blood Group	Number & Percentage of Patients in Group	Frequency in population in Group	X^2 lue	P value
A	16 (51.61)	24.82	28.92	<.001*
B	8 (25.81)	30.23	.65	> . 5
0	6 (19.35)	37.71	8.94	<.O1
AB	1 (3.23)	7.24	2.22	>.I

Table – IX

Showing Distribution of cancer patients with Leukaemia according to blood group and their significance (n = 70)

Blood Group & Frequency in population	Leukaemias (N=70) Number & Percentage of patients in Group	P value	ALL (N= 33) Number & Percentage of patients in Group	P value	AML (N=28) Number & Percentage of patients in Group	P value
A (42.82)	20(28.57)	>.1	8(24.2)	>.5	5(17.8)	>.1
B (30.23)	21(30) j	>.5	14(42.4)	<.05*	7(25)	>.1
O (37.71)	27(38.57)	>.5	11(33.4)	>.1	14(50)	< .05*
AB (7.24)	2 (2.86)	>.1	0	-	2(7.2)	>.5

Discussion :

In this study out of 709 patients with different types of malignancy 483 were male and 226 were female. Male and female ratio is 2.13:1. This ratio almost exactly correspond to the ratio of previous study [9] of our country, where the ratio was 2.07:1. But it does not correspond to the ratio of previous study[10] made by Alam et al which was 1.48· 1.

In this series, among 709 patient of malignancy of different types 251(35.4 %) are of blood group A, 219 (30.8%) are of blood group B, 204 (37.71) are of blood group O and 35 (4.93) are of blood group AB. But frequency of individual blood group in population conducted in Chittagong [12] is A (24.82), B (30.23), O (37.71) and AB (7.24) which is quiet different from blood group frequency in malignancy patients. This indicates statistically significant increased incidence of malignancy in blood Group A population.

Out of 235 cases of carcinoma of stomach included in this study, 90 (38.29%) is in A group, 69 (29.36%) is B group, 66 (27.65%) is O group and rest 10 (4.25%) is AB group. Incidence is found to be significantly high in A group individuals which co-relates with previous findings[4,5]. Ca oesophagus is also found significantly higher in A blood group individuals, 15 (50 %) of 30 patients were blood group A, and lower 5 (16.6%) in blood group O. Ca colon and rectum is found to be significantly higher in Blood group B in this study. This association has not been reported.

In Hepato-biliary carcinoma out of 40 patients 16 (40%) are of A group, 12 (30%) are of B group, 8 (20%) are of O group and only 4 (10%) are of AB group. In these patients group A patient is found significantly higher and group 0 patient found significantly lower. 52 patients were included in this series had carcinoma of cervix and ovary. Out of them 28 (53%) were in group A, 11 in both B and O and 2 were in group AB. Group A was found to be associated with significantly higher incidence of malignant lesions of female genital tract and on the other hand group O showed significantly lower incidence. Findings in this study is similar to other studies reported [4.5,11].

49 carcinoma bronchus patients were included in this study. 10 (20.4%) were group A, 16 (32%) were group B, 19 (38%) of group O and only 4 (8.1%) were of group AB. Distribution was found similar to distribution in population. Earlier studies also did not report any of the blood groups to be associated with decrease or increase in frequency of carcinoma bronchus.[4,5.11]

Out of 46 patients of breast carcinoma 12 (26.1%) are of group A, 17 (36.9%) a of group B, 16 (34.7%) O group, and 1 patient (2.3%) is of group AB. Only group AB patient is found significantly lower. No other group shows any association with Ca breast.

Significantly higher incidence of urological malignancy was observed in Group A patients. 21 out

of 47 patients included were of Group A. Similar finding was reported before[11]. On the other hand incidence were significantly low in group B and Group O.

During this study 31 cases of lymphoma were recorded. Among them 16 (51%) were blood group A, 8 (25%) were group B, 6 (19%) in Group O. Significantly higher incidence of lymphoma was observed in group A. No association of lymphoma with group A patient was reported earlier.

In total 70 patients in this study had leukemia including AML, ALL and CML. 33 patients had ALL, 28 had AML, rest 9 patients had CML. 20 (28%) out of 70 patients of leukemia were Group A, 21 (30%) in group B, 27 (38%) were in Group O and only 2 (4%) in AB. No significant difference in distribution of patients was observed than distribution in population.

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REVIEW ARTICLES

DELIVERY ROOM MANAGEMENT OF NEWBORN - A REVIEW

RRB RAHMAN

Summary :

Five million neonatal deaths happen each year world-wide. Birth asphyxia alone shares 19% of these deaths. It is estimated that neonatal outcome might be improved for more than 1 million infants by implementing simple resuscitative techniques. In this article the patho-physiology of birth asphyxia has been revised briefly. The current views and techniques of neonatal resuscitation have been reviewed here. These include rapid assessment and basic steps of initial stabilization of the neonate immediately after delivery, the initiation of artificial ventilation using bag-mask and bag-tube and maintenance of circulation including techniques of chest compression. Management of meconium - stained baby has been briefly reviewed. Finally administration of medications and fluids and glucose homeostasis have also been summarized for better understanding in delivery room management of newly born baby.

(J Bangladesh Coll Phys Surg 2005; 23 : 25-29)

Introduction :

Every birth should be taken as a medical emergency. Perinatal hypoxia is the leading cause of infant mortality and neurological handicaps both in term and preterm infants. The purpose of delivery room management is to support the newborn's respiratory and circulatory system in order to prevent the consequences of perinatal hypoxia. The health professionals working in this area should have adequate knowledge and ability to work as a team. A discussion of delivery room management integrates the basic elements of resuscitation as well as some more advanced procedures.

Physiology

Effective regular respiration should be initiated within 30 to 45 seconds of delivery. The change in PaO_2 and $PaCO_2$ resulting from clamping the umbilical cord affects chemoreceptors and aid in the reflexive initiation of respiration. Immediately after birth the hostile physical environment comprising light, cold, air current provides respiratory drive by operating through different sensory receptors. The initial breath may generate from 20 to 70 cm of H2O of negative intrathoracic pressure to expand the collapsed alveoli[1]. A rapid decrease in pulmonary vascular resistance and increase in pulmonary blood flow occur after initial lung expansion[2]. Higher colloidal osmotic pressure and lower postnatal hydrostatic pressure of blood within the pulmonary circuit assist in absorbing alveolar fluid after delivery. Fetal right-to-left shunts through the ductus arteriosus and foramen ovale gradually close during this process and by 24 hours of age it becomes functionally insignificant.

Asphyxia and apnea

Asphyxia is defined as inadequate tissue perfusion, which fails to meet the metabolic demand of the tissues for oxygenation and waste removal. Hypoxic tissues begin anaerobic metabolism, producing metabolic acids that are initially buffered by bicarbonate. When bicarbonate fails, acidosis occurs. Asphyxia may occur in utero or postnatal. In either circumstances, there follows a well defined series of events. After a brief period of rapid breathing, respiratory movement ceases and a period of apnea designated as primary apnea follows. At the same time, heart rate falls and neuromotor tone diminishes. If the asphyxic insult continues, the heart rate falls further, blood pressure falls and a series of spontaneous deep gasps occurs. After the last gasp

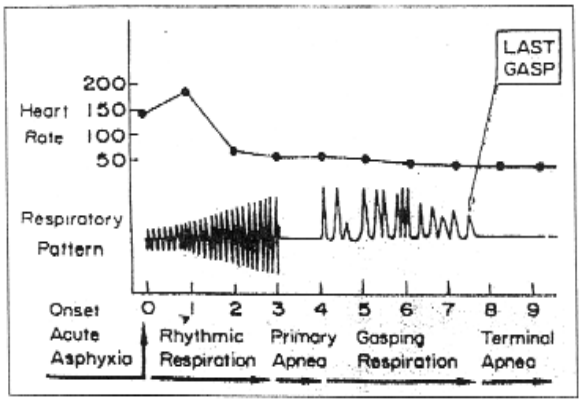

Fig.-1 : *Schematic representation of sequence of events of respiratory failure in experimental animals*[5]

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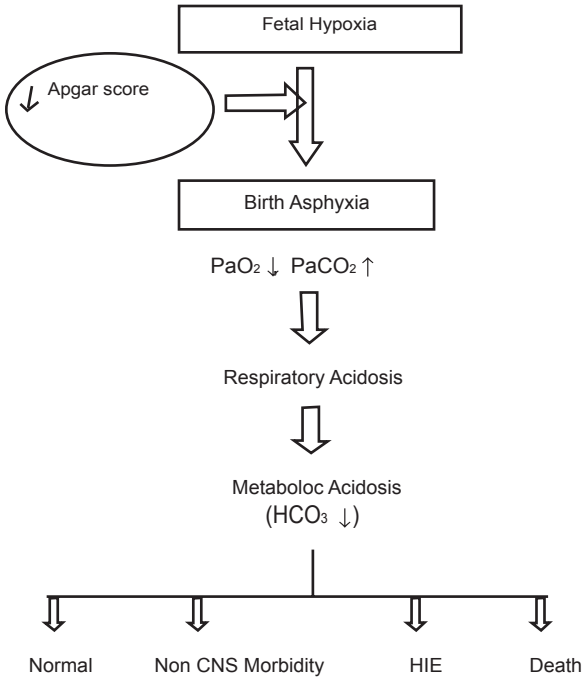
occurs, there begins a period of apnea known as secondary apnea[3]. If an infant is in primary apnea, exposure to oxygen and stimulation will usually induce respiration. If delivery occurs during secondary apnea, the infant will not respond to stimulation. Spontaneous respiration will not resume until resuscitation is initiated with oxygen, assisted ventilation is rarely required. Birth asphyxia should be diagnosed when "baby has gasping and inadequate breathing or no breathing at 1-min". Severe asphyxia corresponds to 1-min Apgar score of 3 or less. Premature infants of less than 37 weeks gestation may develop apnea without any identifiable cause known as Apnea of Prematurity (AOP). This is characterized by ceasation of breathing associated with bradycardia and/or cyanosis and attributable to immaturity of respiratory system and CNS[4].



PaO_2, partial pressure of arterial O_2
$PaCO_2$, partial pressur eof arterial CO_2
HIE, hypoxic - ischemic encephalopathy

Fig.-2 : *Sequence of events following birth asphyxia[6]*

Conditions That May Require Immediate Resuscitation at Delivery

Intrapartum Problems
- Fetal distress
- Persistent late decelerations
- Severe variable decelerations without baseline variability
- Scalp pH < 7.25
- Meconium- stained amniotic fluid
- Cord prolapse
- Premature rupture of membrane (>12 hrs)
- Prolonged or difficult labor (>24 hrs)
- Prolonged 2nd stage of labor (>2hrs)

Medical / Obstetric / Genetic Problems
- Diabetes mellitus
- Suspected or confirmed maternal infection
- Third trimester bleeding
- Pregnancy induced hypertension
- Prolonged rupture of membrane
- Low- birth- weight infant
- Prematurity
- Isoimmunization
- Fetal congenital abnormalities
- Drug therapy- Mg^{++}, ß-blocker

Neonatal Resuscitation

The steps of neonatal resuscitation follow the standard ABCDs for resuscitation:

A- Airway
B- Breathing
C- Circulation
D- Drugs

With the ABCDs as an overall frame work for neonatal resuscitation, the components of the procedure can be explained sequentially:

A. Establishment of an airway
   Positioning
   Suction of mouth, nose, and trachea (in some cases)

B- Initial breathing
   Tactile stimulation
   Positive pressure ventilation

C- Maintainance of circulation
   Chest compression

D- Drugs or Medications

Apgar score

The Apgar score, developed by Dr. Virginia Apgar in 1952, provides a compreshensive and objective measure of the infant's condition in the first minute after birth. Though Apgar score has limitations; Apgar score should be assigned at 1 and 5 minutes and every 5 minutes thereafter until the score is 7. Apgar score between 4 to 7 needs active resuscitation, but less than 4 demands endotracheal intubation, positive-pressure ventilation and supportive medications.

	Sign	Score 0	1	2
1.	Appearance (color)	Blue, pale	Baby pink Extremities blue	Completely pink
2.	Heart rate	Absent	<1 00 beat / min	>1 00 beat / min
3.	Grimace (reflex irritability to suctioning)	No response	Grimace	Cough or sneezing
4.	Activity (muscle tone)	Limp	Some flexion	Well flexed
5.	Respiration (breathing efforts)	Absent	Weak, irregular	Strong cry

Practical epigram of Apgar score

Initial Steps of Resuscitation

a. Prevention of heat loss
b. Clearing the airway (positioning and suctioning) - if needed
c. Initiation of breathing by tactile stimulation or bag-mask ventilation, and
d. Evaluation of the infant.

a. Prevention of heat loss

The majority of the heat loss is due to evaporation of amniotic fluid from the baby's skin surface. Hypothermia frequently results in hypotonia, bradycardia, respiratory depression and acidosis. To prevent the heat loss

- Place the infant under a radiant heat source or over a heated water mattress
- Dry the infant thoroughly and remove the wet linens

b. Clear the airway

- Position the infant supine flat with the neck slightly extended. A rolled blanked or towel may be used under the shoulder.
- Suction the mouth, and then nose to clear the airway. Suction pressure should not exceed negative pressure of 100 mm Hg and suction should not be continued longer than 10s at a time.
- Turn the head to the side to allow secretions to pool in the cheek.
- Deep pharyngeal suction should not be performed during the first few minutes after birth to avoid vagal depression and resultant bradycardia.

c. Initiation of breathing

- Provide tactile stimulation by rubbing the back or gently slapping the feet.
- If the infant remains apneic even after stimulating once or twice and heart rate less than 100 beat / min begin bag-mask ventilation immediately.
- Continue gentle rubbing of trunk, extremities or head to support early respiratory efforts in a depressant infant.
- If the neonate remains apneic or has gasping respiration intubate and continue positive pressure ventilation. Other indications of endotracheal intubations are,

  = ineffective bag-mask ventilation
  - meconium aspiration
  - Apgar score less than 4
  - suspected diaphragmatic hernia.

d. Evaluation of the infant

At each step of the resuscitation procedure the neonate is to be evaluated based on respiration, heart rate, and colour.

Maintenance of circulation

If heart rate is < 100 beats / min, positive pressure ventilation has to be begun even though the infant may have spontaneous respirations. If after 15 to 30 seconds of positive-pressure ventilation with 100 % oxygen the heart rate is < 60 / min, intubation is to be considered and emergency drugs should be prepared. 100 % oxygen

at 5 1 / min provides 80 % to 100 % oxygen to the infant when delivered via a mask or tubing held ½ inch from the nares and surrounded by a cupped hand.

Chest compression

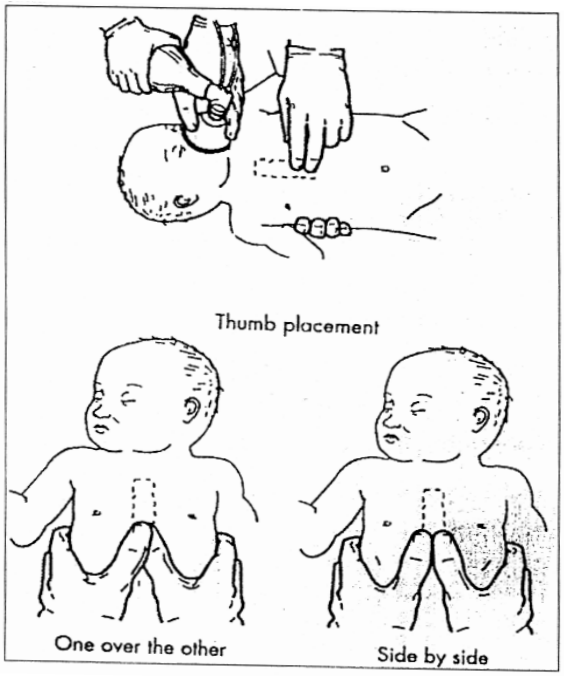
Indications for chest compression include a heart rate of < 60 beats / min, and a heart rate between 60 and 80 beats / min and not increasing despite ventilation for 15 to 30 seconds with 100% oxygen. Following steps should be performed:

- Position the infant supine with the neck slightly extended.
- Provide firm support for the back.
- Perform compression by two-finger or thumb method (Figure 3)
  - Position: lower- third of sternum
  - Rate : 90 times / min
  - Depth : 1/2 to 3/4 inch
  - Support: encircling fingers or hand under the back.
- Provide 90 compression / min and interpose 30 breaths / min with a 3:1 ratio of compression to breath (intubated).
- Continue compression until the heart rate is >80 beat / min.

Medications

The indications for drugs during resuscitation include the followings: Epinephrine: heart rate <80 beats / min despite at least 30 seconds of adequate ventilation with 100 % oxygen and chest compression; heart rate is zero.

Two finger method : Use the tips of two fingers of one hand to compress the steonum, and use your hand or a very from surface to support the infants back.



Sodium bi-carbonate: documented or suspected metabolic acidosis in the presence of adequate ventilation.

Naloxne hydrochloride: severe respiratory depression and narcotic administration to mother in the last 4 hours.

Volume expander: signs of hypovolemia and poor response to other resuscitative measures.

Table-I

Medications for Neonatal Resuscitation

Medication	Concentration	Dosage / Route	Remarks
Adrenaline	1: 10,000	0.1- 0.3 ml / kg i.v,ET(in absence of IV line)	Dilute with normal saline to 1-2 ml for ET administration[8,9]
Sodium bi-carbonate	4.2 % solution 0.5 mEq / ml	2 mEq / kg i.v.	Slowly over 2 min
Naloxone	0.4 mg / ml 1.0 mg / ml	0.1 mg /kg i.v,ET,i.m,s.c.	i.v, ET preferable i.m, s.c. acceptable
Volume expander	5% Albumin Normal saline Ringer's lactate	10 mg / kg i.v.	Over 5-10 min
Glucose	D_{10} W	2 ml / kg i.v. 2-8 mg/kg/min	Slowly
	D_5W	30-60 ml	Orally

ET, Endotracheal tube

Steps of Resuscitation with Meconium-Stained Amniotic Fluid.

Acute fetal hypoxia or "fetal distress" may be associated with passage of meconium into the amniotic fluid[10]. Severe fetal acidosis can result in fetal gasping, leading to in utero meconium aspiration[11]. Suctioning of mouth and hypopharynx at delivery of head should be done to prevent aspiration of meconium with first-breath[12]. If the infant is depressed or the meconium is thick and particulate, suctioning of trachea under direct visualization using an endotracheal tube should be undertaken immediately. Clearing of residual meconium from the stomach also to be done in order to prevent the postnatal regurgitation and aspiration.

Glucose Homeostasis

Fetal glucose concentration varies directly with maternal concentration and is usually 70% of the maternal value. The most common clinical situation in which hyperinsulinemia occurs is the diabetes mellitus. In utero, the fetus becomes hyperglycemic because of the increased transfer of glucose across the placenta from the hyperglycemic mother. Thefetal pancreatic beta cells are stimulated by the increased fetal glucose concentration to produce increased quantities of insulin[13]. After delivery, however, the source of glucose is abruptly removed while the hyperinsulinemia persists, producing hypoglycemia. Neonates with hypoglycaemia tend to develop seizures and should be treated immediately with intravenous glucose infusion to avoid worst neurological sequele. Hypoglycemic neonates may also suffer from various neurological deficits including lower IQ scores at 5 to 7 years of age[14].

Maternal Risk Factors for Neonatal Hypoglycemia

- Diabetes or abnormal glucose tolerance test
- Pregnancy induced or essential hypertension
- Substance abuse
- Antepartum administration of IV glucose

Hypoglycemia was defined previously as a whole blood glucose concentration of less than 35 mg / dl in term infant or less than 25 mg / dl in the preterm infant. The incidence of hypoglycemia is increased in preterm infants, with estimates ranging from 1.5 % to 5.5%

Conclusion

The survival and outcome of distressed newborns depend on timely and effective intervention in the first few minutes after birth. When an infant fails to respond to intensive resuscitative measures in the delivery room, the decision must be made when to stop support. If the Apgar score remains less than 4 at 20 minutes, the probability of cerebral palsy in surviving infant is more than 50 %. If no heart beat has been obtained by 10 minutes or the heart rate remains less than 100 after 20 minutes of maximum resuscitative efforts, consideration should be made to discontinue supportive measures. Parents should have the opportunity to take part in making the decision.

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Role of FNA Cytology in the Diagnosis of Lymph Node Diseases

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Summary :

FNA cytology is indicated for any enlarged abnormal lymph node in any anatomical site. The FNA of deep nodes and other inaccessible lesion can be done by .Applying various radiological imaging techniques. As a rule cytological examination can decide whether the lymphadenopathy is due to reactive hyperplasia, granulomatous inflammation, metastatic malignancy or malignant lymphoma Lymph node clinically suspected of metastatic malignancy constitute one of the commonest indication for FNA

Diagnostic accuracy not only depends on the representativeness of aspirate but also on the quality of tile cytological preparation. Diagnostic sensitivity of tile metastatic malignancy and recurring malignancy is usually above 95% Diagnostic sensitivity has generally been found to be significantly lower for lymphoma than for metastatic malignancy. if the cytological diagnosis is malignant lymphoma or suspicious of lymphoma this must be confirmed by open biopsy and histopathological examination and also by immune marker studies necessary for define diagnosis and subtyping that is necessary to select the appropriate treatment regimen. To recall the several advantages of FNA cytology, it can be concluded that FNA cytology should be the first line investigation in a patient with unexplained lymphadenopathy

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Introduction:

Fine needle aspiration cytology (FNAC) is a simple traumatic invasive procedure that involves aspirating cells and attendant fluid with a small bore needle followed by cytological examination[1].

This method is applicable to lesion that are easily palpable for example superficial growth of skin, subcutis and soft tissue and organs such as lymph node, thyroid, breast & salivary gland. Aspirates may also be taken from lung, the prostate, and the abdominal, and retroperitoneal organs and tissues by applying internal radiological imaging techniques.

FNA of lymph nodes has been practised in central Europe and in Scandinavia for many years, particularly by haematologists in conjunction with aspiration of bone marrow and spleen. It took longer for the method to become widely accepted in the Anglo-American World. Martin & Ellis of the Memorial Hospital in NewYork were pioneers in this field .[3] Thereafter their work was followed up by Bestill & Hajdu[4].

Fine needle aspiration cytology (FNAC) has its application in lymph node pathology in three major clinical setting: Primary diagnosis, staging of disease and follow up[5].

Primary diagnosis made on FNAC in patient with lymphadenopathy may be requested for:

1. Anatomical purposes (e.g. confirming that the nodule at the angle of mandible is a hyperplastic lymph node, and not a salivary gland lesion).
2. Confirmation of suspected clinical condition. (e.g. metastatic carcinoma).
3. First -line investigation in a patient with lymphadenopathy of unknown cause.

Staging of disease is usually undertaken in patient with known primary tumour (e.g. lymphoma) to establish the extent of disease (e.g. subdiaphramatic)

Follow-up of patients with a history of malignancy (e.g. carcinoma of the breast) provide accurate confirmation of recurrence.

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Thus any enlarged abnormal lymph node in any site constitutes an indication for FNA biopsy. Lymph node clinically suspected of metastatic malignancy constitute one of the commonest indications for FNA biopsy. The accuracy of FNA of lymph node in the diagnosis of metastatic malignancy is influenced by many factors such as the size and site of node, fibrosis, previous irradiation and number of punctures made. As a rule, cytological examination can decide whether the lymphadenopathy is due to reactive hyperplasia, metastatic malignancy or malignant lymphoma. Despite newfound support for using needle aspiration for evaluating unexplained lymphadenopathy, there remains resistance to this application for both pathologists and clinicians. This is related to:

1. Lack of clinician's understanding regarding the application of FNA in the management of lymphadenopathy.
2. Inexperience on the part of the pathologists, who interpret lymph node aspirates (resulting in both false- negative and false-positive interpretations).
3. The relative paucity of reliable, well-defined cytomorphologic criteria for the evaluation of lymph node specimens.
4. A failure to obtain and accurately correlate clinical data with cytologic findings when making the final diagnosis.

Barbara F. Atkinson's experience and as the recent literature suggests, when these factors are controlled, the sensitivity and specificity of lymph node aspiration diagnoses are dramatically improved[6]. There are several advantages to using FNA in the evaluation of unexplained lymphadenopathy:

1. It is an easy, reliable office procedure.
2. It is cost -effective and safe.
3. It helps to distinguish benign from malignant disease
4. It assists in patient management.
5. It reduces patient anxiety.
6. It provides material for additional studies (e.g. surface markers, special stains, culture and flow cytometry).
7. It provides data for appropriate therapy.
8. It eliminates the need for open biopsy in most cases of RLNH.

Morphologic characteristics of lymph node aspirates: The following are the useful morphologic features when evaluating aspiration of lymph node. The single most important feature is lymph node interpretation is the pattern of lymphoid elements present on smear. Since both T and B lymphocytes undergo functional changes when stimulated that produce morphologically distinct cell types of varying maturities, reactive nodes usually contain a mixed or polymorphus population of cells. It is the relative proportion of these cells in the overall pattern that gives one of the best criteria for benignity. These population pattern can best be visualized on Romanovsky-stained slide on low power because of flattening of cells during airdrying. In a benign population, except a greater percentage of small round lymphocyte (either mature mantle B cells or paracortical T cells) than follicular centre cells. (Small cleaved and large non-cleaved) or immunoblast and plasmacytoid cells. This ratio however, is dependent upon the stage of the reaction. In other patterns of reactive lymph node hyperplasia there is a greater relative proportion of immunoblast and plasma cells and a smaller relative proportion of small round and small cleaved lymphocyte. Accurately characterizing this lymphoid population and determining the relative of mix of these cells is the first critical step in interpretating lymph node aspirates[7]. The presence of lymphohistiocytic aggregates (LHAs) is also a significant diagnostic features when defining reactive lymph node hyperplasia. These aggregates are actually fragments of hyperplastic follicles that are held together by dendritic and fibroblastic reticular cells. These reticular cells have oval, histiocyte-like nuclei with micronucleoli and long fragile cytoplasmic processes. Another component of LHAs is the tingible body macrophage (TBM). These phagocytic mobile histiocytes generally have cell debris in their cytoplasm; are easily recognized in lymph node aspirates and are usually but not always associated with benign nodes[8]. Scattered in this LHAs is a mixed population of lymphoid cells, usually follicular central cells varying in size from small round to large non-cleaved cells and rarely plasmacytoid cells. Although LHAs is usually indicate a benign follicular

hyperplasia, they are sometimes associated with some lymphomatous processes (e.g. Burkitt lymphoma) especially in partially involved nodes[9]. Background changes in lymph nodes aspirates are helpful when evaluating reactive process because they may assist in further defining both the type of reaction occurring and the causative agent[10]. Identifying a background of neutrophils suggests a suppurative process perhaps from the microabscesses seen in cat-scratch disease or the abscess associated with and unidentified bacterial infection. The presence or absence of caseating necrosis, with or without giant cell formation and epithelioid cells, is associated with a panorama of granuloma producing processes including tuberculosis, sarcoidosis, toxoplasmosis and tularemia. Culture and special stains are indicated when either of these background patterns predominates.

Lymphoglandular bodies (fragments of lymphocyte cytoplasm) are seen in nearly every Romanovsky-stained aspirate containing lymphocytes and are useful in distinguishing malignant epithelial from lymphoid (benign or malignant) processes. It is important to be able to recognize and distinguish other nonlymphoid and lymphoid cell types in lymph node aspirates since they help distinguish benign from malignant processes and assist in specifying the aetiology of RLNH. These cell types include ephitheloid-histiocytes, giant cells (e.g. Warthin-Finkeldey and Langhans), eosinophil, plasmacytoid cells and mast cells.

Technical considerations: Both reactive nodes and nodes involved by metastatic malignancy or lymphoma are highly cellular and moderately vascular tissues. Sufficient material is therefore easily obtained using a 27-23 Gauze needle, except in the presence of fibrosis. Multiple pricking of the needle in different direction within the node for wider sampling do not usually cause admixture with blood to the same extent as when aspiration is used. An abundance of blood in the sample adversely affects cell fixation and tends to distort the cells. During aspiration syringe should be mounted in a pristol grip so that one hand is free to hold the node firmly during puncture. Local anaesthetic is not used and simple skin disinfection as for an injection is adequate. Two or more samples may be necessary to secure enough material for both smears and for special investigations and to reduce sampling error in focal disease. The use of gloves and extreme care in handling the used needles are important safety precautions in many circumstances. The FNA of deep nodes and other inaccessible lesion can be done by applying various radiological imaging techniques. The major internal imaging techniques are computed tomography (CT) and ultrasonography (US) and more recently magnetic resonance imaging (MRI), plus development of stereotactic guidance, particularly for brain and breast biopsies.

If the standard technique does not yield sufficient material, for example due to fibrosis (nodular sclerosing Hodgkin's disease and some sclerosing non-Hodgkin's lymphomas, a 22 Gauze cutting core needle may be tried[11]. An airdried smear has to dry quickly for optimal fixation and therefore has to made thin. The smearing pressure must be finely balanced to obtain a thin smear and at the same time avoid crush artefacts. This can be achieved by pulling the cell sample behind the smearing cover glass. If the flat of the glass is used as in subsequent steps, the movement should be quick and no pressure applied. A wet-fixed smear must be fixed immediately to minimise drying artefacts. Only those part of the smears in which the cells are evenly dispersed, well fixed and not distorted by the trauma of smearing should be chosen for diagnostic evaluation. Areas in which cells show crush and/or drying artefacts, usually at the tail of smear are better ignored. Whenever possible, both airdried and wet fixed smears should be made. Extra smears to allow special stains are often of great value. Staining for microorganisms (Ziehl-Neelsen, PAS, silver impregnation techniques etc.), for mucin (PAS/D, alcian blue), for melanin (Masson, Formalin-induced fluorescence), for acid phosphatase, and for immunocytochemical purposes are those most commonly used. Immunocytochemical staining for demonstration of a variety of tissue specific cell product is one of the most useful "special stains" in diagnostic cytology. Immunocytochemistry is helpful in tracing the origin of metastatic malignancy, in the differentiation of lymphoma from reactive process and from anaplastic carcinoma or melanoma and in the classification of lymphoma[12].

Accuracy of lymph node disease diagnosis: Diagnostic accuracy not only depends on the representativeness of aspirate but also on the quality of the cytological preparations. This is particularly the case in the diagnosis of certain reactive lymphadenopathies and in the diagnosis and classification of lymphoma, which depends on the study of fine cytological detail and on an estimate of proportions of various cell types in the smear[13]. If the biopsy material is adequate, diagnostic sensitivity is occasionally limited by the fact that small metastatic deposits, metastases confined to the subcapsular sinus and single cell metastases can be missed even by multiple aspiration. However, early (micro) metastases rarely produce significant lymph node enlargement and if a lymph node is palpable it is likely to contain enough tumour tissue to be easily detectable by FNA. Although the diagnostic sensitivity of metastatic and recurring malignancy reported in the literature varies, it is usually above 95%[14]. Failure to obtain a representative sample is no doubt responsible for most false negative diagnosis. Interpretation of a representative aspirate can be a problem, but by far more often in lymphoma than in metastatic malignancy. For example, without immunophenotyping follicular lymphoma can be mistaken for reactive follicular hyperplasia[15]. Thus, although a negative cytological report makes malignancy unlikely, it cannot be taken as diagnostic on its own[16] and if the lymphadenopathy does not show sign of regression within a few weeks of observation, FNA should be repeated or a node should be excised for histology. Diagnostic specificity, on the other hand is high. False positive diagnoses are rare[17] if particular caution is observed in the interpretation of smears from nodes in the fields of previous irradiation and in the presence of necrosis. Most false positive diagnoses reported in the literature are the cases of reactive lymphadenopathy reported as suspicious of lymphoma. Conflicting opinions are expressed in the literature regarding the accuracy of cytological diagnosis and of typing of malignant lymphoma[18]. Diagnostic sensitivity has generally been found to be significantly lower for lymphoma than for metastatic malignancy[19]. If the cytological diagnosis is malignant lymphoma or suspicious of lymphoma, this must be followed by surgical excision of the node. The exact diagnosis and classification of malignant lymphoma is necessary to select the appropriate treatment regimen can in most cases only be reached by histological and immunological examination of whole node. As a rule FNA biopsies from malignant lymphoma are cellular. If indicated, an extensive immune marker typing can be performed on cytospin preparations of suspected cells to prove the neoplastic or reactive nature of a nodal or extranodal lymphoid proliferation. Other supplementary techniques such as cytogenetic analysis, morphometry, and gene rearrangement studies may be applied to cell samples obtained by FNA[20].

Cytological findings: FNA samples of lymphoid tissue, nodal or extranodal, benign or malignant are as a rule characterised by a very high cell content. This is obvious to naked eye as the aspirate is smeared. It appears as a film of slimy material which becomes grey on drying. The cytoplasm of lymphoid cell is fragile. Many cells appear as naked nuclei or with a small rim of cytoplasm and a variable number of round cytoplasmic fragments measuring up to 8 micrometer in diameter are seen in the background. Such cytoplasmic fragments - so called 'lymphoid globules' or 'lymphoglandular bodies' which stain an even pale-blue with Giemsa stain, are characteristic of lymphoid tissue, both neoplastic and non-neoplastic. The recognition of 'lymphoid globule' is of great diagnostic value, for example in distinction of lymphoma from anaplastic carcinoma. Most of the lymphoid cells in smears are seen as single cells but dense clumps or aggregates may also occur especially in bloody smear. Cell detail is obscured in such clumps and they are of no diagnostic value as they can be found in both reactive and malignant nodes. However a characteristic aggregation of cells tends to occur in some follicular centre cell lymphomas[21] or CD30 positive large cell lymphomas[22].

A. The cytological features of reactive lymphadenopathy: The reactive pattern is variable depending on the degree of stimulation, the number and size of germinal centres and on whether the sample derives mainly from a germinal centre, or from interfollicular or paracortical tissue. A smear which derives mainly from interfollicular tissue consists predominantly of lymphocyte with a variable

number of scattered immunoblast, plasma cell, non-specific histiocytes and endothelial cells. Germinal centre tissue is represented by poorly defined loose tissue fragments. These fragments include centroblasts, centrocytes, and a smaller number of lymphocytes which adhere to the syncytial cytoplasm of dendritic reticulam cells. The following criteria are used for the diagnosis of reactive lymphadenopathy.

1. A mixed population of lymphoid cells.
2. A predominance of small lymphocytes.
3. Centroblasts, centrocytes, immunoblasts and plasma cells in variable but 'logical' proportion.
4. Dendritic reticulam cells associated with centroblasts and centrocytes (representative germinal centres)

Scattered histiocytes with intracytoplasmic nuclear debris (tingible body macrophages)

6. Pale histiocytes, interdigitating cells, endothelial cells, eosinophils and neutrophils (variable).

The important features which distinguished a reactive process from lymphoma are:

I. A mixed population of lymphoid cells representating the whole range of lymphocyte transformaton from small lymphocytes to immunoblasts and plasma cells.

II. A predominance of small sometimes slightly larger 'stimulated lymphocytes' which have small round nuclei and a characteristic chromatin pattern of large ill-defined chromatin condensations.

III. Centroblasts and centrocytes associated with dendritic reticulam cells derived from germinal centres and tingible body macrophage[23].

The presence of macrophages with tingible bodies favour reactive hyperplasia but does not rule out lymphoma. Especially in high grade lymphomas like Burkitt's lymphoma with a high turnover of cells, a considerable number of starry sky macrophage may be present. The cytological pattern of reactive hyperplasia in which plasma cells are prominent but without other distinguishing features can be seen for example in cases of secondary syphilis and of rheumatoid arthritis.

The differential diagnosis between follicular hyperplasia and follicular lymphoma of mixed cell type (centroblastic/centrocytic) can be very difficult in FNA smear. In follicular lymphoma the predominant cell type may appear small but the nucleus is of intermediate size and has an irregular shape and more granular chromatin similar to centrocytes. Immunoblasts, plasma cells and tingible body macrophages are usually absent or few in number. The difficulty in distinguishing the two conditions is largely due to the fact that the dendritic reticulam cells associated with centroblasts and centrocytes are seen in both and that interfollicular areas in lymphoma may contain large number of small lymphocytes. Immunological demonstration of poly or monoclonality may be necessary to solve the problem. A prominent immunoblastic and plasmacellular reaction is found in several conditions. In viral lymphadenitis particularly in infectious mononucleosis, immunoblasts, plasmacytoid cells, mature plasma cells and atypical lymphocytes can be numerous[24].

Immunoblastic cells can cause differential diagnostic problems; the main differential diagnoses are T-cell immunoblastic lymphoma and Hodgkin's disease (atypical binucleate immunoblasts closely resembling Reed-Sternberg cells can occasionally can be seen). In mononucleosis, the diagnosis is usually already suggested by the clinical presentation and can be confirmed by serological tests. Prominent immunoblasts and sometimes Reed-Sternberg like cells also occur in postvaccinal lymphadenitis and dilantin hypersensitivity. Immunobalstic reaction such as angioimmunoblastic lymphadenopathy (AILD) are difficult to distinguish from T-cell lymphoma and in many cases progress to lymphoma. An increased number of histiocytes without specific features can be seen in smears from non-specific reactive nodes, perhaps indicating some degree of sinus histiocytosis. Histiocytes are particularly prominent in nodes sampled within a few days of lymphangiographic examination. Their cytoplasm contains lipid droplets, multinucleated histiocytic giant cells are common and there is often a conspicuous number of eosinophils. Another condition with prominent histiocytes and multinucleated giant cells as a reaction to foreign materials is silicon lymphadenopathy, occasionally seen in axillary nodes of women with silicon breast

prostheses. Scattered small cluster of histiocytes which have ovoid, pale nuclei and resemble epithelioid cells with a background of follicular hyperplasia are suggestive of toxoplasmosis. The cytological pattern is not diagnostic in itself and needs to be confirmed by serological tests. Microcysts and organisms are hardly ever seen in smear[25].

Numerous non-chohesive, pale histiocyte -like cells are present in dermatopathic lymphadenopathy. Some macrophages contain pigment-either haemosiderin or melanin. These have smaller and more consistently oval-non-folded- nuclei and have a better defined cytoplasm. Some eosinophils are usually present. The background is predominantly of small lymphocytes which may appear slightly atypical with small pale, central nucleoli and blast forms are less common.

In histiocytosis X and malignant histiocytosis, the nuclei of Langerhans histiocytes are large and can have a very irregular shape: folded convoluted, lobulated and grooved. Mitotic activity may be seen and sometimes necrosis. Such cells seen in lymph node

aspirate especially in absence of eosinophils may raise a suspicion of metastatic malignancy such as melanoma. However the nuclear chromatin of Langerhans histiocytes is bland and finely granular. If suspected, the diagnosis may be confirmed by immunochemistry[27] and/or by EM. The cytological finding in sinus histiocytosis with massive lymphadenopathy have been described by Lampert and Lennert and by Van Heerde[28.] They diagnosed the entity by observing large histiocytes with intracytoplasmic lymphocytes and plasma cells.

B. The cytological features of granulomatous lymphadenitis: The criteria used for the diagnosis of granulomatous lymphadenitis includes.

I. Histiocytes of epithelioid type forming cohesive cluster.

II. Multinucleated giant cells of Langhans type.

III. With or without necrosis (Caseous type).

Epithelioid cells are quite characteristic seen in smear from lymph node. They have elongated nuclei, the shape of which can be described as resembling the sole of a shoe. The nuclear chromatin is finely granular and pale. The cytoplasm is pale without distinct cell borders. The most commonly encountered granulomatous lymphadenitis with necrosis is tuberculous. The tuberculous lymphadenitis contains aggregates of epithelioid cells, multinucleated giant cells against a necrotic (caseous) 'dirty' background. The FNA procedure should include sending material for culture. Ziehl-Neelsen stain shows sparse acid-fast bacilli particularly within necrotic areas. Caseous material appears granular and eosinophilic in smear and usually lacks recognizable cell remnants. Smear from tuberculous lymph node may sometimes show only polymorphs and necrotic debris without histiocytes particularly in immunocompromised patients. Cohesive clusters of epithelioid cells in absence of necrosis are suggestive but not diagnostic of sarcoidosis. However, tuberculosis remains in the differential diagnosis whether necrosis is present or not.

Cat scratch disease often present as a rapidly developing swelling in preauricular area and neck region of children[29]. FNA reveals a 'dirty' aspirate composed of a mixture of lymphocytes, plasma cells, eosinophils and a number of polymorph in a necrotic background. Aggregation of epithelioid and/or giant cells can be seen. Warthin-starry stain can be attempted to demonstrate causative bacteria. Sometimes only a few epithelioid cells are found in small groups or as a single cells or the histiocytes may not quite have the typical appearance of epithelioid cells. The pattern then approaches that of non-specific, reactive lymphadenitis with prominent histiocytes. This may be the case in toxoplasma lymphadenitis and in the early stage of sarcoidosis. Lymphogranuloma venereum clinically present as enlarged inguinal lymph node. FNA shows 'active histiocytic' cells scattered in background of neutrophils and debris. Endothelial cells can sometimes also closely resemble epithelioid histiocyte. Also deposits of kaposi's sarcoma in lymph node may be mistaken for granulomatous lymphadenitis, although the nuclei are more elongated and spindle shaped and the nuclear chromatin is darker and coarser than in epithelioid histiocytes[30.] Clusters of epithelioid cells are

sometimes found in cases of malignant lymphoma particularly in Hodgkin's disease and in Lennert's lymphoma. They can also occur in metastatic seminoma and in lymph node regional to carcinoma. One must therefore look carefully for abnormal lymphoid cells and for metastatic cancer cells in smear containing epithelioid histiocyte. Full knowledge of the clinical presentation is obviously essential.

The cytological features of Non-Hodgkin's lymphoma: Cytological subtyping of non-Hodgkin's lymphoma (NHL) in FNA smear is difficult and requires extensive experience. It can only be successful in centre with a team of oncology experts and with a regular flow of material. However, the diagnostic criteria of lymphoma in cytological preparations vary with the histological subtypes. It is therefore necessary to describe the main subtypes in some detail. Of all current classification of non-Hodgkin's lymphoma, the Kiel classification can most readily applied to cytological preparation and is therefore used in this presentation. The various cell types and cytological, histological and immunological patterns of malignant lymphomas were recently illustrated by Van Heerde et al in Amsterdam[31]. The cytological criteria for the diagnosis of non-Hodgkin's lymphoma are as follows:

1. A monotonous population of small lymphoid cells.
2. Mainly round nuclei slightly larger than those of normal small lymphocytes.
3. Characteristically coarse granular nuclear chromatin; nucleoli absent.
4. A varying number of prolymorphocytes; larger size, more cytoplasm, pale chromatin, single central nucleolus.

Immunophenotype: Pan B, faint SIg, CD5 & CD23.

The typical well-differentiated lymphocytic lymphoma of CLL type is readily recognized by monotonous population of cells resembling of small lymphocytes. Difficulties can arise if the process contains numerous proliferation centres with many large and intermediate size cells- paraimmunoblast and prolymorphocytes. A large B-cell lymphoma may develop in patients with B-CLL, the so-called Richter syndrome[32]. Low grade non-Hodgkin's lymphoma yield a monotonous population of small lymphocytes (chronic lymphocytic leukaemia type), lymphocytes with plasmacytoid or plasma cells differentiation (lymphoplasmacytoid type, plasmacytoma), or centrocytes (centrocytic lymphoma) and centroblasts (centrobastic/centrocytic lymphoma).

High grade B-cell lymphomas show a monotonous population of centroblasts (centroblastic non-Hodgkin's lymphoma), lymphoblasts (lymphoblastic, including Burkitt's), or immunoblast (immunoblastic non-Hodgkin's lymphoma). T-cell lymphomas are usually diagnosed after immunochemistry confirm the cell of origin. Of interest is human T-lymphotropic virus type I (HTLV-I) associated cutaneous Tcell lymphoma. FNA smears contain a population of small lymphocytes, eosinophils, small convoluted blasts and plasma cells. Pleomorphic high grade T-cell lymphomas must be distinguished from anaplastic carcinoma and large cell anaplastic CD30 (Ki-I) positive lymphoma by means of immunochemistry[33].

Burkitt's lymphoma is endemic and Epstein-Bar virus associated in African children, the jaws often being involved. In non-African cases most patients present with abdominal localisation. FNA smear of Burkitt's lymphoma show the following characteristic features.

a) A relatively uniform cell population with a high mitotic rate.
b) Round nuclei of variable but predominantly intermediate size.
c) A granular or speckled chromatin pattern; multiple small but prominent nucleoli.
d) A variable, mostly thin rim of dense blue cytoplasms with small lipid vacuoles (MGG).
e) Starry Sky macrophages often prominent.

In true histiocytic lymphoma, it is difficult to recognize correctly in routine cytological smears. A very pleomorphic cell population with multilobed nuclei and multinucleated cells which may resemble Reed-Sternberg cells are usually present. The main differential diagnosis include large cell non-Hodgkin's lymphoma (especially large cell anaplastic CD30 positive lymphoma) and Hodgkin's disease.

There are certain problems in diagnosis of lymphoma. The problems are :

a) Suboptimal cytological preparation.

b) Variable pattern in one node.

c) Distinction from reactive lymphadenopathy.

d) ML with few neopalstic cells in a dominant population of reactive lymphoid[34]cells, e.g. T-cell rich B lymphomas.

e) Small cell anaplastic carcinoma and other small cell tumours particularly versus ML mantle cell and lymphoblastic type.

f) Large cell undifferentiated carcinoma and melanoma versus large cell lymphoma, especially ML CD30 positive.

g) Effects of chemotherapy and radiotherapy.

Direct smears must be made expertly, since poor preparation makes accurate diagnosis impossible. It has been emphasized that suboptimal smear are the commonest cause of diagnostic difficulties and misinterpretations. In general airdried MGG-stained smears are recommended for the diagnosis of lymphoproliferative lesions, but a combination with alcohol fixed smear stained by Pap or by H&E provide complementary information. Smears of a cell suspension prepared in the cytocentrifuge, in addition to routine smears are very helpful in the diagnosis and classification of NHL and are well suited for immune marker studies[35]. The difference between normal lymphocyte and the neoplastic cells of ML lymphocytic lymphoma (well differentiated) is relatively subtle and the most obvious diagnostic features is the monotomy of the cell population. However, a sample including proliferation centres does not appear monotonous since there can be many cells of intermediate and large size (prolymorphocytes and paraimmunoblast) mixed with the typical cells of CLL type[36]. Such a case can be mistaken for reactive lymphadenopathy unless close attention is paid to the cytological detail of the lymphocyte and the result of immunocytology. ML lymphoplasmacytoid can also be mistaken for reactive lymphadenopathy in view of the sometimes pleomorphic character of the smear population. Immunocytochemical, clinical and biochemical data are of utmost diagnostic importance. In ML centrobastic/centrocytic there may be high proportion of small lymphocytes to suggest a benign reactive process. However, the small cleaved cells of some follicular lymphomas can be difficult to distinguish from lymphocytes in a reactive process particularly if smears are not technically optimal. Nuclei must be studied carefully in high power to appreciate the slightly larger size, irregular shape and granular chromatin. Occasionally, non-Hodgkin's lymphoma of larger cell type may have few neoplastic cells scattered in a background of reactive lymphoid cells[37]. In FNA smears, large centrocytic lymphoma cells have a tendency to clump together into aggregates showing some moulding of nuclei. Rows and Palisades of closely apposed, ovoid nuclei which appear columnar through moulding may simulate small cell anaplastic carcinoma or even adenocarcinoma. However, the proportion of isolated cells is usually larger in lymphoma and may of these have the typical appearance of lymphoid cells with the rim of basophilic cytoplasm and a nuclear chromatin pattern which is different from that of carcinoma cells. Importantly, nuclei of lymphoma cells of a similar size to those of small cell anaplastic carcinoma usually have prominent nucleoli. This is a helpful but not infallible features: nuclei of large centrocytes and of small cell carcinoma of intermediate type may be very similar in size and may have similar nucleoli. Nuclear moulding and well-formed single files of tumour cells are more obvious in small cell carcinoma and other metastatic small cell tumours. The pale-blue, uniformly rounded cytoplasmic fragments characteristic of lymphoid tissue (lymphoid globules/lymphoglandular bodies) are different from the cytoplasmic and nuclear fragments of tumour necrosis in smears of carcinomas[38].

Immunocytochemical staining for cytokeratin and panleukocyte marker can usually solve the problem of distinguishing between small cell carcinoma and lymphoma in difficult cases. Smears of large cell undifferentiated carcinoma and of melanoma may show total dissociation of the tumour cells, nuclei may be larger, with fine chromatin, prominent nucleoli and abundant basophilic cytoplasm. This pattern can be indistinguishable from large cell

lymphoma particularly from immunoblastic or large anaplastic CD30 positive lymphoma and from Hodgkin's disease. The presence of cytoplasmic fragments (lymphoid globules) in lymphoma and lobulated nuclei is helpful. Well-formed sharply delineated aggregates of tumour cells are not seen in lymphoma. Again in difficult cases, immunological staining for cytokeratin and lymphoid markers is usually decisive. However, the commonly used immune markers may not solve the problem of distinguishing large cell anaplastic CD30 positive lymphoma from large cell carcinoma and this may require extensive immune marker studies or even electron microscopical examination[39].

Chemotherapy and radiotherapy may cause changes to lymphoma cells which render typing more difficult. In particular, treatment seems to cause an increased irregularity of the nuclear shapes.

The cytological criteria for the diagnosis of Hodgkin's disease: Hodgkin's disease (HD) is a malignancy of lymphoid tissue characterised by the Reed-Sternberg (R-S) cell or a variant of R-S cell (atypical mononuclear cells/Hodgkin's cells). Usually a background of reactive lymphoid cells, granulocytes (especially eosoniphils), plasma cells and histiocytes is present. The R-S cell is of unknown origin, but some data previously suggests origin in the dendritic reticulum cells. Recently the cell of origin is very probably a lymphocyte. The lymphocyte predominant subtype is in fact a B-cell proliferations, sternberg ('Popcorn') cells and most of the small lymphocytes being B-cells. The other subtypes nodular sclerosing, mixed cellularity and lymphocyte depletion variants - are called classic Hodgkin's disease in which the background lymphocytes are T cells. According to the recent immune marker analysis, the lymphocyte depletion subtype appeared to be a large cell anaplastic CD30 positive non-Hodgkin's lymphoma in most instances[40]. The patients with Hodgkin's disease usually present with painless lymphadenopathy (subdiaphragmatic in 90%, cervical >> mediastinal > axillary), fever, night sweats, pruritus, malaise or weight loss. Later in the course patients have retroperitoneal lymph node, spleen, liver and/or bone involvement. About 50% of the cases occur in patients between 20 & 40 years of age. Less than 10% of cases occur before the age 10 and less than 10% after age of 60. The male to female ratio is 4:3 (males also have worse prognosis). Hodgkin's disease accounts for 30 to 40% of all lymphomas.

The following cytologic criteria are recognized as diagnosis of Hodgkin's disease.

1. Reed-sternberg cells
2. Atypical mononuclear cells (Hodgkin's cells)

A variable number of eosinophils, plasma cells and histiocytes.

A background population of lymphocytes.

5. Immunophenotype: 'classic' Hodgkin's disease: Reed-sternberg cells CD30, CD 15; small lymphocytes pan T. Lymphocyte predominant type: Reedsternberg cells pan B, CD45, EMA; small lymphocyte pan B.

A confident diagnosis of Hodgkin's disease can only be made in the presence of typical Reed-sternberg cells with a background of lymphocyte and reactive cells (e.g. eosinophil, plasma cell and histiocytes). Reed-sternberg cells have large lobulated nuclei which may appear symmetrically double (mirror nuclei) or complex and multiple. The nuclear chromatin is coarse and irregularly distributed in a reticular fashion with clear areas in between which give the nucleus an overall pale appearance. Nucleoli are large often huge, eosinophilic in H&E preparations; pale or basophilic in MGG-stained smear. The cytoplasm is abundant and pale so that nucleus often appears to be surrounded by an empty spaces. Sometimes the characteristic nucleoli are not well demonstrated and in some cases only mononuclear Hodgkin's cells which have a nuclear structure similar to the typical Reed-sternberg cells are present. In such cases the definite diagnosis must await histological examination, except in recurrent disease when classic Reed-sternberg cells are not essential for diagnosis.

In lymphocyte-predominant subtype HD, the patient is generally a child with a single large spherical node and no other symptoms. The aspirate contains a monotonous population of slightly irregular small lymphocyte with scattered, scanty large multinucleated giant cells, corresponding to the 'popcorn' cells in histology, usually without distinct

nucleoli. Mixed cellularity HD the nodes are clinically soft and aspirates are very cellular. This variant most readily diagnosed because of presence of numorous R-S cells and their variants scattered in a background of many eosinophil, plasma cell and histiocytes[41]. Lymphocyte depletion HD is the least common type and the affected node may be fibrotic or cellular. It is characterised by very pleomorphic R-S cells in a limited lymphoid background. Nodular sclerosing subtype is the most common variant form of HD. The tough consistency of the node felt with the needle, a scanty aspirate and the presence of fibroblast and collagen fragments in smear are features suggestive of nodular sclerosing type. In this type aspirate contains many typical R-S cells and mononuclear variants. In fibrotic areas the fragile R-S cells often lose their cytoplasm and may present as bare nuclei. The background is usually a population of lymphocyte, eosinophils and plasma cells. Occasional cases have areas of suppurative necrosis.

There are certain problem in the diagnosis of Hodgkin's disease:

1. Poor biopsy yield
2. Reed-sternberg look-alike cells in other conditions.
3. Epithelioid histiocyte suggestive of granulomatous lymphadenitis.

Poor biopsy yield is a problem mainly in the nodular sclerosis subtype. Not in frequently, smear show only a few lymphocytes, fibroblast and fragments of collagen which may suggest a chronic inflammatory process. Multiple biopsies or the use of a cutting core needle may be necessary to obtain sufficient material.

2. Large, multilobated nuclei resembling R-S cells can be seen in a variety of conditions. Atypical immunoblasts in non-neoplastic reactive lymphadenopathy, for example in infectious mononucleosis, in rheumatoid arthritis-associated and drug induced lymphadenopathy may have nuclei of this type. They usually differ from the typical Reed-sternberg cells by having smaller and darker nucleoli, a denser chromatin and a basophilic cytoplasm. Multinucleated giant cells in small or large cell nonHodgkin's lymphoma, e.g. ML lymphoplasmacytoid, ML pleomorphic T-cell and especially large cell anaplastic CD30 positive lymphoma, can also have large nucleoli similar to Reed-sternberg cell4[2.] The distinction is particularly difficult in presence of eosinophils, plasma cells and epithelioid cells which is not unusual in T-cell lymphoma. Immunological studies may be necessary to solve the problem. In some cases of large malignant cells with very large nucleoli and with many eosinophils and reactive lymphoid cells in the background, representating single malignant cells of metastatic especially nasopharyngeal carcinoma, which were misdiagnosed as Hodgkin's disease.
3. Cluster of epithelioid histiocytes are sometimes seen in smears of Hodgkin's disease and in some non-Hodgkin's lymphomas which could suggest granulomatous lymphadenitis. The lymphoid cells must therefore always be carefully scrutinized in lymph node smear containing epithelioid cells.

Cytological criteria for the diagnosis of lymph node necrosis: Extensive or total necrosis /infarction of lymph nodes occur in some inflammatory processes, in metastatic malignancy, in malignant lymphoma and rarely in relation to vasculitis and to trauma. If necrosis is extensive, FNA smears may not include any well-preserve cells necessary for diagnosis. Completely amorphous, granular material without identifiable cell remnants suggest caseous necrosis and smear should be searched for acid-fast bacilli and other microorganism. In acute inflammatory necrosis, the aspirate and smears have a purulent character. Necrotizing lymphadenitits (kikuchi's disease) is a condition of unknown but most probably viral etiology seen in young women, in which there is focal necrosis in cervical lymph node[43]. In FNA smears, the characteristic findings are of large number of pale phagocytosing histiocytes with eccentric nuclei, debris with nuclear fragments, absence of neutrophils and a reactive background of lymphoid cells. The presence of large mononuclear cells in such nodes may cause a suspicion of malignant lymphoma. Smears from areas of coagulation necrosis in lymph nodes show numerous cell shadows, some with preserved but pyknotic nuclei. Unless there is a clear history of trauma, such findings raise a strong

suspicion of either metastatic carcinoma or malignant lymphoma. Nodal metastases of small cell anaplastic carcinoma of lung, melanoma and breast carcinoma are prone to necrosis and the necrotic cells with pyknotic nuclei can be indistinguishable from necrotic lymphoid cells. Extensive necrosis/infarction is not uncommon in malignant lymphoma, both non-Hodgkin's and Hodgkin's. Total infarction of a lymph node can sometimes precede manifest lymphoma[44] FNA biopsy should be repeated, if possible from other abnormal nodes and if a diagnosis can still not be made, surgical excision is indicated.

F. Cytological criteria for the diagnosis of metastatic malignancy: Since clinical enlargement of a lymph node by a metastasis usually invokes more than a fourfold increased in mass, the majority of the node is replaced by metastatic malignancy when it present as lymphadenopathy. Two important criteria are used a diagnostic tool for metastatic malignancy.

1. Foreign cells amongst normal/reactive lymphoid cells
2. Cytological criteria of malignancy.

The cytological pattern seen in routinely stained smear often give clues to the site of primary tumour. Columnar cells with elongated nuclei arranged in palisades, stringy mucus and necrosis suggest a primary in the large bowel; while mucin containing signet ring cells suggest the stomach as the most likely primary site among several other possibilities. Glandular cells, moderately pleomorphic, arranged in a gland-in-gland or cribiform pattern suggest prostatic carcinoma. Large cells with abundant pale, granular or finely vacuolated cytoplasm and a low N:C ratio suggest a renal cell carcinoma. Very large central nucleoli are typical of less well-differentiated forms of this tumour and are also seen in large cell anaplastic carcinoma of lungs and nasopharynx and in hepatocellular carcinoma. Pulmonary and pancreatic adenocarcinoma can have a variety of pattern. They usually show a moderate degree of glandular differentiation, prominent nuclear pleomorphism and obvious mucin secretion. As a rule, the presence of intracytoplasmic mucin excludes renal, adrenal, hepatocellular and thyroid carcinoma. Breast cancer usually displays poor glandular differentiation while cell balls and single files of cells are more common. Some tumours form a monolayer of dispersed cells with intact cytoplasm. Nuclear pleomphism is often relatively mild.

The cells of small cell anaplastic carcinoma of lung are closely packed together in aggregates or as single files with prominent nuclear moulding. Pyknotic nuclei and nuclear debris are commonly seen between preserved cells, in the absence of massive necrosis. 'Tear-drop' nuclear artefacts caused by smearing are characteristic. Smears of malignant melanoma may show total dissociation of cells, well-defined cytoplasm, eccentric nuclei, prominent anisokaryosis, uniformly dense chromatin, often large nucleoli, binucleate cells, intranuclear vacuoles and in most cases some cells with intracytoplasmic pigments or at least a dark staining paranuclear area. Malignant melanoma can occasionally mimic lymphoma in FNA smears. Testicular tumours may clinically occult and present with metastases to pelvic, paraaortic or supraclavicular nodes. The cytological pattern of seminoma is characteristic. The tumour cells are mainly dissociated and are mixed with lymphocytes and epithelioid cells. They have large rounded vesicular nuclei and evenly distributed nuclear chromatin. Nucleoli are prominent. The cytoplasm is pale and both cytoplasm and nuclei are very fragile, the dispersed cytoplasm forming a 'tigroid' background to the nuclei[45]. Cells from a transitional carcinoma may also be dispersed, resembling a large cell lymphoma, or may form solid and sometimes papillary groups. The cells have abundant, relatively dense cytoplasm with distinct borders and pleomorphic nuclei which are often eccentic. A tendency to squamous differentiation or spindle cell pattern may be seen.

Special stains are often helpful and the cell sample can be divided to provide spare slides for this purpose. Squamous differentiation is most obvious in alcohol-fixed papstained smear but can also be distinguished in MGG-stained preparation. The histochemical demonstration of intracytoplasmic mucin droplets is important in adenocarcinoma. Strong positivity for acid phosphatase by the enzymatic method or positive immunocytochemical staining for prostatic acid phosphatase and/or prostatespecific antigen in an adenocarcinoma supports a prostatic origin. Distant

metastases particularly to supraclavicular lymph nodes are sometimes the first manifestation of prostatic cancer preceding any urinary symptoms. Immunocytochemical staining for S 100 and especially HMB45 for melanoma is more reliable. Differential cytokeratines (CK7, CK20) may be helpful in suggesting the origin of metastatic carcinoma. In some cases, electron microscopical examination of the aspirate can be helpful, particularly in small round cell tumour and in some mesenchymal tumours.

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CASE REPORTS

Disseminated Histoplasmosis in Acquired Immunodeficiency Syndrome - A Case Report

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Summary :

A 41-year-old married tribal businessman from Teknaf was seen in a local clinic in Chittagong. He presented with continued high fever, sore throat, oral candidiasis, loose motion, weight loss, lymphadenopathy and hepato-splenomegaly. He had no history of sexual promiscuity, drug abuse or blood transfusion. He visited Myanmar on several occasions where he had done tattoo on his body. He was diagnosed as a case of AIDS with disseminated histoplasmosis.

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Introduction :

Histoplasmosis is an uncommon disease caused by dimorphic fungus H. capsulatum. Though endemic in some parts of North America the disease is uncommon in Asian countries. In the human body the fungus is found as intracellular small budding yeast mainly within the macrophages. The fungus enters the lung by inhalation where neutrophils and macrophages form the earliest host line of defense. Macrophages exert less efficient anti-fungal activity than neutrophils, and the yeast-form can multiply within them leading to lysis of them and infection of new cells. The major defense against the fungi is exerted by T-cell mediated immune response. Mainly the CD4 helper T lymphocytes and to a much lesser degree CD8 cytotoxic T lymphocytes are main cells involved in containing and clearing the infection. CD4 cells are crucial to the healing of infection while CD8 cells have an additive effect to CD4 lymphocytes for the optimal eradication of the organism [1,2].

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In most cases, histoplasmosis is a benign self-limiting disease, particularly in immunocompetent individuals. Disseminated histoplasmosis occurs in immunodeficient patient. In endemic areas, 2% to 5% of human immunodeficiency virus (HIV) infected patients may develop disseminated histoplasmosis[3]. In this communication we describe a case of histoplasmosis in a HIV infected patient.

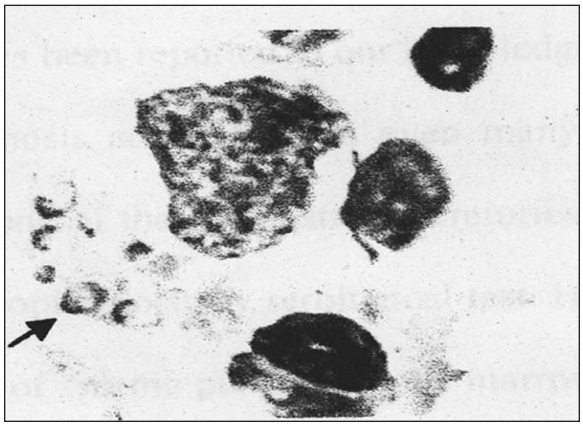
Case History :

Mr. M T, a 41- year-old tribal businessman from Teknaf, Cox's bazar was seen in a local clinic in Chittagong in December 2003. He presented with continued high fever not responding to broad-spectrum antibiotics. He had prostration, anorexia, sore throat and weight loss for six weeks, and loose motion for three days. He had no such history in the recent past. He gave history of visit to Myanmar on several occasions for business purpose. He had no history of exposure, drug abuse or blood transfusion. Clinical examination revealed pallor, dehydration, oral moniliasis, cervical lymphadenopathy, hepatornegaly and splenornegaly, and tattoo marks on the deltoid region of both arms and back of the trunk. His lungs were clear and heart revealed no abnormality. Vital signs were, Pulse-120/min, BP-80/60 mm Hg, Res.- 32/min, Temp-105^0 F.

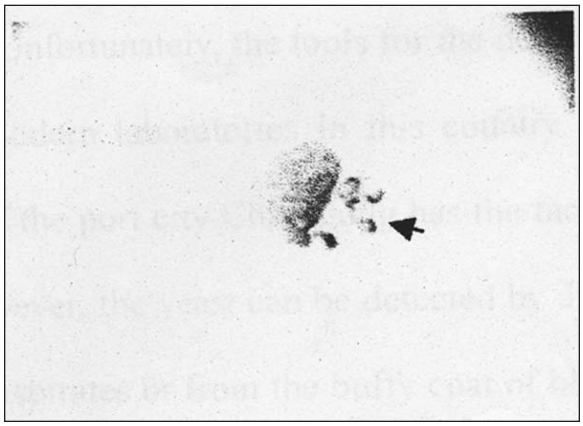
Investigations showed- Hb-7.7 gm/dl, Total WBC - 3800/cumm, Platelet count- 150,000/ cumm, P-85%, L-10%, M-0%; E-01% and myelocytes-04%. Absolute lymphocyte count was 380/cumm. Endoscopy of UGIT revealed moniliasis throughout the whole length of the oesophagus. Bone marrow examination revealed low cellular marrow with both

intracellular and extracellular Histoplasma capsulatum. Anti HIV anti-body was positive (ELISA & Immunochromatography, line-immunoassay).

The patient was diagnosed as a case of Acquired Immunodeficiency Syndrome (AIDS) with disseminated histoplasmosis. He was treated with ceftriaxone, amikacin, metromdazole and itraconazole. Unfortutely the patient died of septicaemic shock two days after the diagnosis.



Histoplasma capsulatum in macrophage of bone marrow smear



Histoplasma capsulatum in macrophage of bone marrow smear

Discussion :

Like other opportunistic infection histoplasmosis is common in immunocompromised individuals. The incidence of histoplasmosis is increasing in AIDS, organ transplants and in those who need prolong immunosuppresive therapy 4. In AIDS the incidence may approach to 25%[5,6].

Fig 1,2: H. capsulatum (1000x) in macrophage of bone marrow smear, Leishman stain In AIDS histoplasmosis occurs as a progressive systemic disease with prolonged high fever, weight loss, mucocutaneous lesions, hepatosplenomegaly, lymphadenopathy, loose motion and pancytopenia etc[7]. Unless treated promptly with systemic anti-fungal drugs the disease is rapidly fatal with 100% mortality.

Histoplasmosis is not common in Bangladesh. Though a few cases have been detected, not a single case of histoplasmosis has ever been reported in Bangladesh among AIDS victims (Personal communication). It rarely affects individual other than immunosuppressed. With the alarming global increased incidence of AIDS it presents a tremendous threat of becoming a not uncommon disease with the progressively increasing incidence of HIV positive cases. The climates are ideal for the growth of the fungi in Bangladesh. Recent AIDS bulletin has recorded 248 cases of HIV infected individual among which were 26 AIDS Patients (DGHS, MOH&FP, December l. 2002). But according to the WHO reports, estimated number of HIV infected cases and AIDS are far more (UNAIDS Global HIVAIDS, 2001). In none of these cases has histoplasmosis been reported to our knowledge. Unfortunately, the tools for the detection of histoplasmosis are lacking in even many modern laboratories in this country. We found that none of the diagnostic laboratories of the port city Chittagong has the facility to detect histoplasmosis by serological test. However, the yeast can be detected by direct examination of splenic puncture, bone marrow aspirates or from the buffy coat of blood. The fungi can also be grown in appropriate artificial culture media. We detect our case by direct examination of bone marrow (Fig-1, 2). As an invasive technique, bone marrow aspiration and splenic puncture is not risk-free particularly in HIV infected cases. Besides, there is always a chance of missing the parasites in cases of low level of parasitaemia.

Unlike the neighboring country like India and Myanmar the prevalence of HIV infection is still low in Bangladesh. Among the reasons for this low incidence is believed that the social customs, religious, values and restricted habit of not practicing sexual promiscuity are important. But tattoo may appear as an important way of contacting HIV infection particularly in those communities where

tattoo is not an uncommon social practice. Though tattoo is a rare practice by Bangladeshi people it is not uncommon among the tribal. Our patient had done his tattoo in Myanmar. As we could not detect any of the common recognized means of contacting HIV infection in our patient we thought that, probably, tattoo by the use of commonly used needle was responsible for the infection. Our patient had visited Myanmar several times where the incidence of HIV infection is very high. Though he did not admit about sexual contact with the Burmese people. Transmission of HIV infection to our patient through sexual contact still remains a possibility.

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Isolated Injury to Appendix : A case report

MM HOSSAIN

Summary :
Trauma involving the vermiform appendix only is rare. A case of blunt abdominal trauma that involved the appendix without involvement of any other intra abdominal organ is reported here. Possibility of trauma to the appendix should always be sought specially when abdominal trauma is in the vicinity of the structure.

(J Bangladesh Coll Phys Surg 2005; 23 : 46-47)

Introduction :
Appendix is not usually involved in most blunt or penetrating abdominal trauma. Its small size and its relatively secured situation in pelvic, retroceacal or para-colic position may contribute to rarity of injury specially when all other organs remain intact. More than forty cases has been reported so far where appendix was injured without involvement of other intra abdominal viscera[1]. Cases have been reported both in blunt and penetrating abdominal trauma where appendix was the only structure involved in an intra abdominal injury. Preoperative diagnosis is only presumptive. Per-operatively diagnosis may be missed without meticulous exploration and may lead to severe morbidity or even mortality.

Case note
Mr. A R, a young man of 35, was admitted in neurosurgery unit of Chittagong Medical College Hospital following a Road Traffic Accident. He also had an abrasion in lower abdomen. His GCS score was 8 and improved in 48 hours from head injury. He started complaining of abdominal pain and distension. He was transferred to surgical unit for abdominal condition.

On clinical assessment patient was found to be haemodynamically stable and conscious. Abdomen was slightly distended, soft and there was no tenderness except over the abrasion 2 to 3 inches above the right inguinal ligament. There was no lump and Liver, Spleen or Kidneys were not palpable. Bowel sounds were audible. A fluctuating haematoma was palpable in right lower quadrant with step like defect implying discontinuity of deeper layers. Movement of right hip was painful. Plain radiograph of abdomen was unremarkable and no sub-diaphragmatic free gas shadow was seen.

Exploration was done through a transverse lower abdominal incision on right side. Muscles of anterior abdominal wall were found disrupted lateral to rectus abdominis along with peritonium. A loop of small intestine was protruding through the peritoneal rent. There was only a little serous collection in the peritoneal cavity and no sign of peritonitis. All solid viscera and gut were found intact. When followed distally appendix was found buried into torn ilio-psoas muscle posteriorly. Distal part of appendix was crushed and devitalized with a small sero-purulent collection in between the torn muscle. Appendicectomy was done. Peritoneum was closed keeping a drain through separate stab wound.

The wound was meticulously explored upto its depth and cleaned of all debries and dead tissue. Complete haemostasis was achieved. Wound was irrigated with antiseptic solution and closed in layers keeping another drain in the parietal wall.

Postoperatively patient had antibiotics and analgesics. He was allowed oral feeding on third postoperative day. Patient returned home on tenth postoperative day after complete recovery. A course of physiotherapy followed.

Discussion :
Isolated injury to appendix is a rare event but still has been reported both in blunt and penetrating abdominal injuries. Factors favouring safety of appendix may be its mobility, relatively smaller size, or placement behind ceacum or terminal ileum or deep in pelvic cavity. A slippery serosal covering may also contribute to escape trauma.

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First report of direct isolated injury came from Fowler[2] in 1936. In 1956 , Gatewood and Russum[3] reported a case of complete transection of the appendix following a blunt trauma in a motor vehicle accident . At operation the appendix was found freely floating along with tear of rectus abdominis muscle and a torn mesentery near terminal ileum. The mechanism is believed to be a force acting against posterior abdominal wall.

Geer et al[4] reported two cases of appendiceal trauma. One of them was due to a penetrating bullet injury causing injury of the appendix. Second case followed blunt trauma due to MVA. This resulted in separation of appendix from mesoappendix. Possible mechanism seem to be a shearing force acting against a fixed retroperitoneum. Edwards[5] and his colleagues reported a case of transection of appendix in a patient of 41 years in Ohio USA due to seat belt injury. Possible mechanism may be a compression of abdominal viscera against pelvic bones. Statter MB, and Coran AG reported a case of appendiceal transection associated with a lap belt restraint in a small child[6]. Paul[7] also reported a case of appendiceal trauma in blunt abdominal injury.

Acute Appendicitis may occur after a blunt abdominal trauma without being directly injured in the event. Serour[1] reported three such cases of acute appendicitis following blunt abdominal trauma. They reviewed the literature in an attempt to find relationship between blunt abdominal trauma and Post-traumatic appendicitis (PTA). They defined it as acute inflammatory process following blunt abdominal trauma in a previously healthy individual, provided the appendix has not been severely injured by the trauma itself. Symptoms appear between 6 and 48 hours after trauma. They identified about forty cases of post traumatic appendicitis from world literature. Hennington also reported two cases of acute appendicitis following abdominal trauma[8]. Suggested mechanisms include ileoceacal haematoma, mesenteric disruption, forceful displacement of stool and gas into appendix with consequent proliferation of bacteria. Resulting occlusion of lumen cause obstructive type of appendicitis.

Conclusion :

Although rare, injury to the appendix may occur both in blunt and penetrating trauma. Search should always include appendix specially when trauma is violent and involves lower abdomen

Acknowledgement :

I am thankful to the Director of Chittagong Medical College hospital for allowing me to publish this report. I am also grateful to my colleagues.

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CORRIGENDUM

The names of authors of article "Study to Document Pre Admission Risk Factors for Development of Severe Malaria and the Spectrum of It and Outcome in Different Categories of Hospitals in Malaria Endemic Zone of Bangladesh" published in the Journal of Bangladesh College of Physicians & Surgeons Vol.-22, No.-3, September 2004 was printed as "EB Yunus" should read as "MA Faiz, EB YUNUS, MR Rahman, MA Hossain, ME Rahman, SN Bhuiyan".

COLLEGE NEWS

(J Bangladesh Coll Phys Surg 2005; 23 : 49)

Fellowship & Membership Examination :

The Fellowship Part-I, Fellowship Part-II (Preliminary), Fellowship Part-II (Final) & Membership Examination of the College for January 2005 has commenced on scheduled from 1st working day of January 2005. 4817 candidates appeared in FCPS Part-I examination in various specialitis of which 986 qualified. 456 candidates appeared in FCPS Part-II examination & 213 candidates appeared in MCPS examination of different specialitis.

As in previous years a number of senior and reputed academicians of Royal Colleges of United Kingdom (UK), Ireland, Saudi Council, College of Physicians and Surgeons Pakistan have been invited to examine the students of the above mentioned examinations along with their Bangladeshi counterpart.

Annual General Meeting :

The annual general meeting of the college for 2005 will be held on 25th February 2005 at the college premises. A number of agenda along with the annual budget will be placed before the meeting.

Election of the Councillors :

Biennal election of the college to elect eight councillors will be held on the same day of annual general meeting. Fellows of the college will elect eight new councillors for coming four years. The newly elected councillors will join the existing 12 councillors to form the 20 members college council.

Publications :

1. College council has published a pocket diary of the college for 2005. The diary has been sent to the fellows at their addresses available in the college. The fellows yet not received the diary are requested to contact the college office.
2. The council has decided to publish an updated fellow's directory of 2005. In this regard a prescribed form of information details has been sent to the fellows. The fellows are requests to fill up the form & send it back by 31st January 2005