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CONTENTS

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Articles are accepted for publication on the condition that they are contributed solely to this journal. Paper should be as brief as possible consistent with the subject. Short case reports are accepted provided this do not exceed two full pages in the journal (usually around five typewritten pages). Authors should estimate space occupied by title, authors illustrations and references so as to keep within the two-page limit.

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Examples of References:

Journal article, one author:

1. Lloyd JR: The etiology of gastrointestinal perforations. J Pediatr Surg 4:77 85, 1983.

Journal article, two or three authors:

2. Kilpatrick RM, Aseron CA: Radioisotope detection of Meckel's diverticulum causing instestinal bleeding, Z. Kinderchis 13, 210-217, 1973.

(See page 22)

ABDOMINAL INCISIONAL HERNIA

Abdul Hadi[1], Abu Siddique[2], Mirza Mazharul Islam[3].

Key Words:

Incisional Hernia, ventral hernia.

Summary:

54 cases of abdominal incisional hernia are reported. The predisposing factors in the development of incisional hernia were identifiable in 41 cases and in 13 the hernia complicated a wound that had healed primarily. This study discusses the predisposing factors as seen at the Dhaka Medical College Hospital and offers suggestions for reducing the incidence and associated complications.

Introduction:

Incisional hernia, one of the late complications of abdominal surgery, occurs through a week scar of a previous operation. Various factors that affect wound healing and abdominal wound dehiscence are discussed by different authors in the literature (1, 3, 4, 6, 8, 9, 10) and these may contribute to the development of incisional hernia.

1. Abdul Hadi, Associate Professor of Surgery.
2. Abu Siddique, Assistan Registrar,
3. Mirza Mazharul Islam, Ex-Professor and Head of the Dept. of Surgery, Dhaka Medical College & Hospital, Dhaka.

The literature on incisional hernia in Bangladesh is not present. The purpose of this retrospective study is to consider the possible predisposing factors in the development of incisional hernia as seen in our patients and to offer suggestions for reducing the incidence and associated complications.

Materials and Methods:

We treated 54 patients for incisional hernia in two of the surgical units of Dhaka Medical College Hospital from January, 1981 to December, 1985. The case notes of these patients were studied to obtain information regarding the previous laparotomy taking into account such factors that might have contributed to the eventual development of incisional hernia; age and sex, initial pathology, type of incision and technique of repair, post-operative complications and grade of operating surgeons.

Table I summarizes the age distribution. The age ranged from 4 to 56 years. The maximum age incidence is in the third, four thand fifth decades of life. The youngest patient was a 4-year-old girl who was operated for intussusception and the oldest was a 56-year-old lady who had elective cholecystectomy and gastroenterostomy for

Table 1

Incisional hernias: age distributions.

Age group (years)	No. of cases	%
0-10	2	3.7
11-20	1	1.8
21-30	17	31 5
31-40	11	20.4
41-50	16	29.6
51-60	7	13.0
Total	54	100

cholelithiasis and chronic duodenal ulcer. In this series, there were 16 males and 38 females as shown in Table-II. The male to female ratio was 1 : 2.4.

Table-II

Incisional hernias : sex incidence.

Sex	No. of cases	%
Male	16	29.6
Female	38	70.4
Total	54	100

36 patients (66.7%) of the previous laparotomies were emergency and eighteen (33.3%) were elective. The indications for the initial laparotomies are listed in Table-III.

Table—III

Ineisional hernias: Indications for initial laparotomies.

Indication:	No. of casses Elective	Emergency	%
Gynaecological:			
Caeserian section	—	18	33.3
Hysterectomy	7	—	13.0
Tubectomy	2	—	3.7
Surgical:			
Perforated duodenal ulcer	—	5	9.3
Chronic duodenal ulcer	3	—	5.6
Cholecystectomy	3	—	5.6
Typhoid perforation	—	3	5.6
Intestinal obstruction:			
Intussusception	—	1	1.8
Ascariasis	—	1	1.8
Fibrous adhesions	—	2	3.7
Iliocaecal tuberculosis	—	1	1.8
Sigmoid volvulus	—	2	3.7
Appendicular abscess	—	1	1.8
Penetrating abdominal injury	—	2	3.7
Nephrectomy	2	—	3.7
Prostatectomy	1	—	1.8
Total	18	36	100

The frequency of obstetrical and gynaecological operations (50%) explains the female preponderance (70.4%). Primary infective conditions were significant in the list and 94.4% of the incisions used were vertical as shown in Table—IV.

Table—IV.

Incisional hernias : types of incision.

Incision	No. of cases	%
Subumbilical midline	29	53.7
Paramedian	15	27.8
Epigastric midline	7	13.0
Lumber Incision	2	3.7
Inguinal	1	1.8
Total	54	100

The predisposing factors identifiable in 41 patients (76%) are shown in Table—V.

Table—V.

Incisionol hernias: post operative predisposing factors.

Factors	No. of cases	%
Wound infection	23	42.6
Cough	15	27.8
Wound dehiscence	8	14.8
Distension	6	11.1
Drain	3	5.5
Previous Caeserian section	2	3.7
Constipation	2	3.7
Asthma	1	1.8
Pulmonary tuberculosis	1	1.8
Dysentry	1	1.8

N. B. 17 cases had more than one factors.

13 patients (24%) had an uneventful post-operative period. Wound infection was the single most common factor and occurred in 23 patients (43%). The second highest factor was persistent post-operative cough which was found in 15 patients (28%). Eight patients (15%) had wound dehiscence out of which three had resuturing of burst abdomen. Six patients had post-operative abdominal distension. Five elective cases were complicated by wound infection.

Table—VI shown the time lag between laparotomy and development of incisional hernia. 27 patients (50%) developed the hernia within three months and by six months 41 patients (76%) had developed hernia. No special feature was identifiable in the remaining 13 patients (24%) who developed hernia later than six months after laparotomy.

Table—VI

Incisional hernias : onset of hernia.

Time lapse (Months)	No. of cases	%
1	8	14·8
2	8	14·8
3	11	20·4
4	2	3·7
5	3	5·5
6	9	16·7
7-12	6	11·1
13-24	4	7·4
25-36	2	3·7
37-48	1	1·8
Total	54	100

An attempt was made to relate the experience of the operating surgeon to the frequency of incisional hernia. Emergency laparotomies were mostly performed by the registrars and assistant registrars. Two tubectomies for sterilisation were done in a family planning clinic, but the grade of the surgeon could not be known. Poor surgical technique may be a contributory factor in the development of incisional hernia in a few cases in this series.

42 patients had anatomical repair. The "Keel"s procedure was used by one of us* in 12 patients. Twenty patients were followed up for atleast six months by one of us* with recurrence recorded in one case.

Discussion:

The incidence of incisional hernia complicating laparotomies varies according to the operations and the underlying pathology. A careful study of the literature dealing with this subject reveals an incidence varying from 3·8% to 3·9%.

Incisional hernia usually occurs after defective wound healing. Various factors that affect abdominal wound healing and wound disruption have been studied extensively (1, 3, 4, 6, 8, 9, 10). They are classified into local factors which include blood supply, local infection, apposition of wound edges, absence of movement and tension, irradiation & technique of wound closure, and general factors such as the age of the patient, presence of anaemia, malignant disease, diabetes, systemic infection, jaundice, uraemia, protein, vitamin C deficiency, the use of steroids and cytotoxic drugs (4·8). In our series we could identify factor or combination of factors that were responsible for defective wound healing and hence incisional hernia in 41 patients. However, the wound that has healed primarily are not immune from developing hernia. We had thirteen patients with a normal post-operative period that developed incisional hernia. It is, of course, known that an incisional hernia may start as a symptomless, partial disruption of the deeper layers of a laparotomy wound during the immediate or very early post-operative period. Often the event passes unnoticed if the skin wound remains intact after the stitches have been removed([12]).

Incisional hernia occurs in either sex at any age with higher incidence in elderly patients. The age distribution in our series varies from 4 to 56 years with peak incidence in the third, fourth and fifth decades of life. The sex incidence shows a predominence for females. This is due to the increased number of obstetrical and gynaecological operations and also reflected in the age distribution with half of the female patients in child bearing age group (20—40 yrs). Incisional hernia is related to the type of incision employed in the primary operation and statistics reveal that upper abdominal vertical incisions and more especially midline ones, both epigastric and subumbilical, are more prone to incisional hernia than any other. Surgeons in Bangladesh most commonly use vertical incisions because they save time and give adequate exposure. This is also confirmed by the finding that vertical incisions constituted 94·4%. The McBurney and transverse incisions have always afforded a high degree of protection and hernia following these incisions is rare. One appendicectomy in this series was done through the McBurney incision indicating that appendicectomy wounds also herniate ([11]).

* Abdul Hadi

Of the initial laparotomies, 67% were performed as emergency in circumstances which were usually not ideal from aseptic point of view and 19% of these had infective pathology. Thus a combination of emergency surgery and infective condition was associated with greater morbidity. This explains the occurrence of wound infection in 23 patients (43%) and wound dehiscence in eight (15%). Wound infection commonly occurs in patients with typhoid and late peptic ulcer perforations—an association well known in Bangladesh. Our rate of wound infection and wound dehiscence is very high inspite of routine use of antibiotics in all types of post-operative patients. Antibiotic afford undue sense of security and diagnosis of collection of pus is, therefore, often delayed. The earlier suppuration is diagnosed and the pus is evacuated, the lesser becomes the chance of infection(²).

Increased post-operative abdominal pressure due to persistent post-operative cough and continuous distention imposes upon freshly sutured abdominal wounds stress which is sufficient at times to cause wound disruption and post-operative hernia. In our series, fifteen patients had persistent post-operative cough and six had distension which might have contributed to the incisional hernia.

Incisional hernia is often found in cases that have been drained. The very necessity of drainage indicates that the patient is sufferlng from intrabdominal suppuration with texaemia which is often held responsible for a comparatively high incidence of wound infection and later on hernia,

Like other hernias, incisional hernia may give rise to complications such as obstruction, gangrene, perforation, spontaneous rupture with possible mortality (7). It is desirable that its incidence be reduced and that where it occurs, its repair be undertaken electively.

Most of the indications for laparotomy like peptic ulcer perforation, typhoid perforation and emergency caeserian section are preventable with good medical and antenatal care. The prevention of post-operative hernia also depends upon the anaesthetist, the surgeen, the nature of the disease and the patient's diet. The anaesthetist by his skill can reduce post-operative cough and vomiting ; he can give adequate relaxation to the abdominal wall for gentle handling and easy suturing of the wound by the surgeon. The surgeon by his scrupulous and aseptic technique must ensure firm and secure apposition of the edges of the wound, he must remember the post-operative requirements for abundant proteins and Vitamin C by his patients who may also suffer from protein or Vitamin C deficiency. Since most incisional hernias develop within six months of laparotomy adequate followup of patients and early elective repair are recommended.

Acknowledgement :

The authors express their gratitude to the Director, Dhaka Medical College Hospital, Dhaka, for his permission to use hospital records for publication of this paper.

References :

1. *Annotation :* Burst abdomen ; Lancet : 1 : 28, 1977.
2. Asiruddin M, *Pathophysiology in Surgery :* Ist Ed. Modern Publishers Ltd., Dhaka, P: 123, 1972.

3. Doughlas, D. M.: *Repairs of incised wounds.* J. Roy. Coll. Surg., Edin ; 13, 92, 1968.

4. Ehrilich, H. P. & Hunt, T. K: *Effect of Cortisone on wound healing.* Ann. Surgery. 167 : 324. 1968.

5. Grace R.H., COXS : *Incidence of Incisional hernia after dehiscence of the abdominal wound.* Am. J. Surg. : 131 : 210, 1976.

6. Greenburg AG. Saik RP, Pesken GW: *Wound dehiscence, Pathophysiology and prevention.* Arch Surg : 114 : 143, 1979.

7. Hamilton RW: *Spontaneous rupture of an Incisional hernia.* Br. J. Surg. 53(5): 477, 1966.

8. Irvin, TT. *Abdominal wound healing in jaundiced patients.* Br. J. Surg. : 65 : 521, 1978.

9. Levenson, S.M., Stein, J.M. and Grossblatt, N. : *Wound healing, proceedings of a workshop.* Washington, National Academy of Sciences National Research Counoil.

10. Penninck FM and others: *Abdominal wound dehiscence in gastroenterological surgery.* Ann Surg. 189 : 345, 1979.

11. Pollet J.: *Appendicectomy wounds do herniote.* J. Roy. Coll. Sur. Edin. 22(4): 274, 1977.

12. Rains, AJH, Ritchie, HD. *Bailey ond Love's—Short practice of Surgery.* 19th Ed. H.K. Lewis & Co. Ltd. London, P : 1095, 1984.

'ABDOMINAL COCOON' A PECULIAR CLINICO-PATHOLOGICAL ENTITY : EXPERIENCE OF SEVEN PATIENTS IN DHAKA

A. N. Md. Atai Rabbi

Key Words:
Abdominal Cocoon.

Summary:

This is a report of seven patients who revealed cocoonic feature at laparotomy: six were female of adolescent age group and one elderly male. The patient presented either with asymptomatic abdominal lump or features of subacute or chronic intestinal obstruction. Following different surgical procedures, short term follow up revealed no recurrence of symptoms.

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Introduction:

Abdominal cocoon is a new term, first described by K. T. Foo et al. in 1979. This is a condition characterized by thick

membrane formation encasing the intestine. This has been reported from South East Asia and India. Similar pathological manifestations have also been reported from Western world, but aetiological background appears to be different. This condition has been observed in adolescent females mainly.

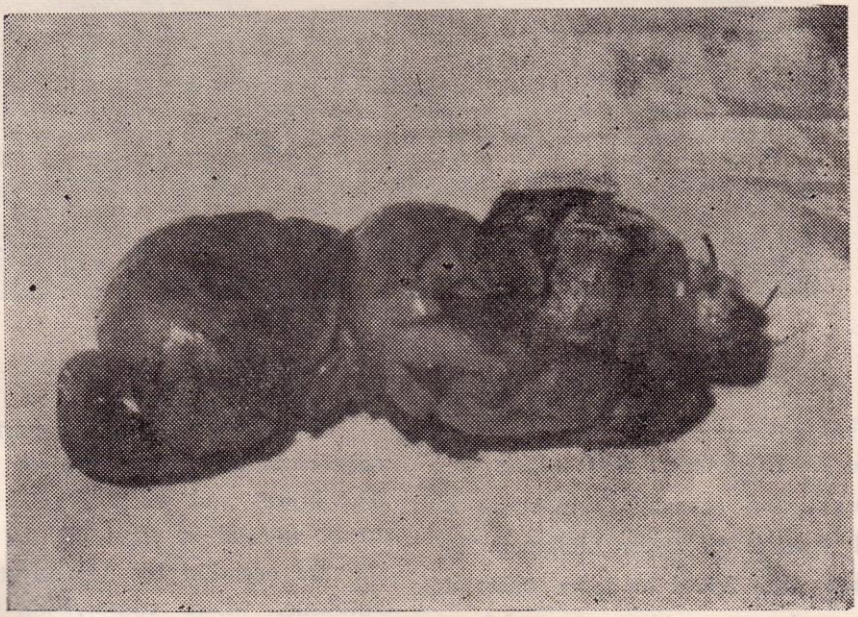
Patients and Presentations:

There are seven patients in our series. They either reported for abdominal lump to the gynaecologist who provisionally diagnosed it to be ovarian cyst or to a general surgeon with intestinal obstructive features.

Classical finding could be seen only after exploration of abdomen. Of our seven patients six were adoleseent female, age ranging from thirteen to eighteen and one was 55 years old male.

Two patients presented with right lower abdominal mass which were diagnosed as ovarian tumours and were treated by gynaecologists initially.

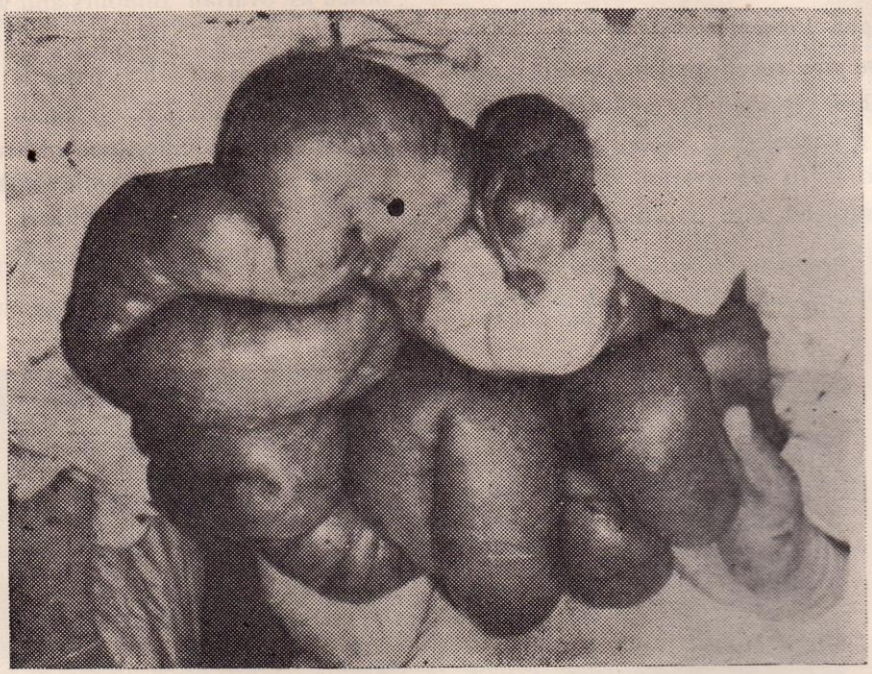
The rest of the patients came for surgical consultation, of whom three were having chronic intestinal obstructive features. Two patients with intestinal obstruction had vomiting, loss of weight, abdominal distension and visible peristalsis.



In one of the patients of chronic small bowel obstruction, small bowel enema revealed dilated small intestine. In these patients encased intestines were found to be grossly coiled up and compressed. The proximal free intestine were found to have

dilatation. The male patient who had this cocoonic feature gave history of spontaneous cure of inguinal hernia, subsequently developed an abdominal lump and chronic intestinal obstructive features.

The basic change we have observed in these patients, a fibrous sheet formation, ensheathing part or whole of intestines. The intestines which were inside the shell coiled up and aggregated in a small area,



The fibrous sheet coverings were about paper thick. The sheet was thicker towards pelvis and gradually thinner as it extended towards the upper abdomen. As it encased the bowel in some cases it formed a cystic mass. Along the periphery of the affection, the sheath seems to be continuous with the parietal peritoneum. The intestine inside the sheath were loosely adherent with each other and also with covering sheath.

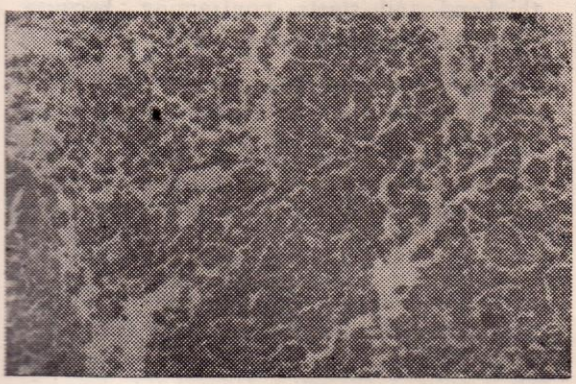
After resection of the part, the cross section looked like multiple diverticuli. The bowel wall when freed were found to be normal in most of the part but on rare occasion the sequestrated part of intestine, where compression was gross, looked scarred and stenosed.

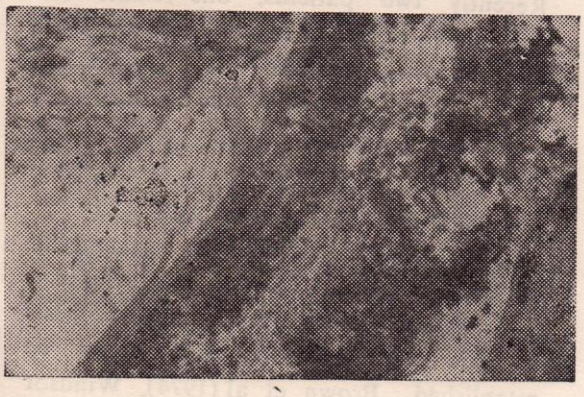
Histological features: Tissue was taken from regional lymphnode, wall of the intestine and the covering membrane. In the lymph node the normal architecture was found to be preserved. The lymphatic

TABLE—I

Sl. No.	Age	Age of Menstruation	Symptoms with duration	abdominal mass and other sign	Type of obstruction	Operative Findings,	Operative proceedures	Resul
1.	18 yrs.	12 yrs.	Pain abdomen, lower abdominal swelling—6 months	Mass in the Rt. lliac region.	None	lleo-caecal encased mass	Rt. hemicolec-tomy	uneventfu post-opera period.
2.	16 yrs.	13 yrs.	pain abdomen—8 months. constipation, swelling lower abdo-men—3 months.	mass at iliac fossa and hypogastrium	None	affection of whole small bowel.	lysis of adhesion by cutting along the antimesen-teric border.	Do
3.	14 yrs.	12 yrs.	pain lower abdomen, swelling of lower abdomen-6 moths.	lump in the Rt. iliac fossa.	Chronic intesti-nal obstruction.	plastic adhesien of licum forming a mass	Resection of affected part of bowel.	Do
4.	14 yrs.	12 yrs.	Colicky pain, vomi ting—2monhs, swelling lower abdomen, loss of weight—6 months.	visible peristal-sis, mass Rt. iliac fossa.	subacute intestinal obstruction	ileo-caecal encased mass	Rt. hemicolec-tomy	Do
5.	15 yrs.	12 yrs.	Abdominal swelling, vomiting, loss of weight, constipation	Tense abdomen, visible peristalsis, low general condition	subacute intesti-nal obstruction	plastic adhesion of terminal ileum forming lump	segmental resec-tion and lysis of adhesion.	Do
6.	17 yrs.	12 yrs.	pain abdomen 12 yrs. vomiting since 10 days	Abdominal disten-sion, visible peris-talsis, diffuse lump	subacute intes-tinal obstruction	plastic adhesion of terminal coils of small intesti-nes & caecum.	lysis of adhesion and release of bowel from sac.	Relieved symptom
7.	55 yrs.	Male	pain abdomen, lump, constipation, H/O reduction of Hernia	circumscribed lump around umbilicus	Chr. intestinal obstruction	plastic adhesion of small intestine & part of large gut.	lysis of adhe-sion and re-lease of bowel.	Relieved symptom

sinusoids were dilated with diffuse infiltration of histiocytes. Section of gut wall revealed moderate infiltration of chronic inflammatory cells predominantly lymphocyts in all coats. The membrane showed marked fibrosis and adhesion with gut wall.





We had to decide on the table about the procedure in consideration of type, grade and site of affection. In two cases right hemicolectomy was done and in another to cases conservative segmental resection and lysis of adhesion. One case where there was total affection of small bowel, incision along the antimesenteric border and then peeling off the adhesion were tried. As such it was possible to make the gut free from these as well as from other gut. It was a short of delivery of small bowel from the encased sheath. In the rest of the patients no resection of bowel were done and only delivery of bowel from encased shealh were practised.

There were no mortality and post-operative gross complications in this short series. Immediate post operative results were good, symptoms were reduced or diminished but follow up could not be done in all cases. One of the patients who had right hemicelectomy, reported three months after surgery. There was no recurrence of symptom : she complained of vague mild abdominal pain. One patient who had total affection of small bowel had mild wound sepsis but subsequently was lost from our follow up. The rest of the patients who had surgery during the last three months of the report to have gained weight since operation.

Recently two patients, one female and one male reported to us and they are almost normal for the last one and half year. There was no feature of recurrence or adhesion and obstruction.

Discussion :

This condition is likely to be the result of low grade peritonitis of unknown aetiology. There have been many hypothesis in this regard but nothing could be established. Brown et al (1974), Windsor et al (1975) and Eleriningham et al (1977) described similar cases of intestinal obstruction due to sclerosis in patients who had history of long term use of practolol (a beta adrenergic blocker) K. T. Foo et al (1978) suggested that the adherent fibrous membrane can result from granulomatous peritonitis, as one of his patients had epitheliomatous granuloma on histopathology. The fact was suggestive of tuberculous infection but culture of the membrane could not establish the aetiology. Fowler (1971) had suggested possibility of viral pathogen in the primary peritonitis. Presence of lymphocytes and plasma cells in the organised fibrous exudate suggest the possibilities of viral pathogens.

K. T. Foo et al also thought that it could be due to retrograde menstruation and it starts as a low grade chemical peritonitis resulting in fibrous sheet formation. In his series of ten patients all were within two years of menarche. This fits with our series, where age ranged from twelve to eighteen, one being male of fifty an exception.

It appears from our observation that whatever may be the cause the disease started in the pelvis as pathological changes looked more mature in the pelvis. This is how we presume retograde infections probably initiated the pathology. Female genital tract being open helps the pathogenesis. As a sequele low grade peritonitis starts with fibrinous deposit over the peritoneum. Initially this is more diffuse and in course of time this starts healing by fibrosis and the sheet gradually become thickend and starts contracting because of collagenous structure. This is how it encages the intestine and intestine coils up in small area to accommodate bigger segments. As such its presentation depends on its mechanical effects of anatomical involvement and its physiological effects.

Low grade peritonitis is the predecessor of abdominal cocoon. The fact is further revealed from the history and feature of our last patient who was a male. He gave history of spontaneous cure of inguinal hernia following acute feature of irreducibity for short period and pain. As the obstructed loops of intestine was reduced, it has some visceral peritoneal trauma and subsequently inflammation and low grade peritonitis. This finally lead to cocoonic change.

In fine, we can assume that this abdominal cocoon is an atypical abdominal adhesion characterised by either localised or diffuse encaging of intestine by fibrous sheet. Here the loops of intestine is sequestrated out from peritoneal cavity. It differs from usual abdominal adhesion as it does not have bands and fringes, rather a smooth surface.

Abdominal cocoon being prevalent in particular sex, particular age group, having particular geographic distribution should have some particular cause and predis-

posing factor in the a etiology. This is yet to be found out. Retrograde menstruation or infection fits with our personal series and with the series of K. T. Foo et al. But it is not proved beyond doubt. Practolol has been proved to have sclerosing effect but there is no history of practolol therapy in our series and in the series of K. T. Foo.

One common feature still prevails in these practolol peritonitis that these patients were also female but they were middle aged and elderly.

About the treatment it is now suggested, procedure should be more conservative than drastic resection. Simple peeling of the gut from the adhesive sac most of the time release the gut from the trap and relieve the patient. As the gut within the sac are loosely adherent peeling is not very difficult, whether this type of lysis may cause further adhesion in the subsequent life is not yet established. In our series we could not follow the patients for more than one and a half year. So inference can not be made about subsequent complications and recurrence.

Reference:

1. Brown P., Badieley H., Read AE; *Sclerosing peritonitis, an unusuul reaction to a β—adrenergic blocking drug (practolol)* Lancet 1974 2, 1 77-1481.
2. Foo K. T. et al; *Unusual small intestinal obstruction in adolescent girls, "The abdominal cocoon";* B. J. Surg. vol 65 (1979) 427-430.
3. Fowler R.; *Primary peritonitis—changing aspects* 1965-1970. Aust. Paediatr 7: 73-83, 1977.
4. Rao PL NG et al; *Abdominal cocoon—a cause of Intestinal obstruction in a 4 year old girl;* Indian Paediatrics, vol XIV Number 11, 1047-48.
5. Tobe, T.; *Inapparent virus infection as trigger of appendicitis.* Lancet 21, 1342-1346, 1965.
6. Windsor CWO et al/*"Fibrinous peritonitis"; a complication of practolol therapy.* Br Med J, 2:68 1975.

PATHOPHYSIOLOGY OF INVOLUTIONAL OSTEOPOROSIS

Dr. Sharmeen Ahmed, Dr. A. K. M. Khorshed Alam

Key words:

Involutional osteoporosis, osteopenia, vitamin D, calcium, parathormone (PTH), skeletal intermediary organization, modeling, remodeling, microdamage physiology.

1. Dr. Sharmeen Ahmed, Deptt. of Clinical Pathology, DMCH.
2. Dr. A. K. M. Khorshed Alam, Asstt. Prof. of Medicine IPGMR.

Summary:

This article presents the most current concept of primary osteoporosis based on 59 references. Osteoporosis has been defined and classified. The patho-physiology and pathomechanics of osteoporosis has been described in details. The two types of involutional osteoporosis have been compared and contrasted.

Definition and Classification:

Osteoporosis is the common metabolic bone disease. It is characterized by (i) osteopenia, i.e, a reduction in bone mass per unit volume of bone, and (ii) mechanical incompetence of bone (Frost, 1985a). Reduction in bone mass includes reeduction of both osteoid tissue as well as mineral content of bone, and mechanical incompetence of bone means a skeleton that hurts and/or fractures during normal mechanical usage.

Involutional osteoporosis is the commonest type of osteoporosis in clinical practice. Osteoporosis may also be secondary to many diseases. Very rarely, a form of juvenile osteoporosis also occurs. Involutional osteoporosis is divided into two groups: postmenopausal and senile. Riggs et al. (1983) coined the terms Type I and Type II osteoporosis for the two types of involutional osteoporosis. The complete classification of osteoporosis is given below (Modified from Kelley et al., 1985; Frame & McKenna, 1985; Riggs et al., 1983).

Classification of osteoporosis:

A. PRIMARY OSTEOPOROSIS

1. Involutional Osteoporosis
   - Type I: Postmenopausal Osteoporosis
   - Type II: Senile Osteoporosis
2. Juvenile Osteoporosis

B. SECONDARY OSTEOPOROSIS

1. Endocrine Abnormality
   - Hyperparathyroidism
   - Cushing's Syndrome
   - Hypogonadism
   - Thyrotoxicosis
   - Diabetes Mellitus
2. Genetic Abnormality
   - Osteogenesis Imperfecta
   - Homocystinuria
   - Ehlers-Danlos Syndrome
   - Menkes' Syndrome
   - Marfan's Syndrome
3. Haematologic Disorders
   - Multiple Myeloma
   - Leukaemia
   - Lymphoma
   - Systemic Mastocytosis
4. Immobilization, e g., Paralysis
5. Iatrogenic Causes
   - Glucocorticoids Therapy
   - Thyroid Hormone Therapy (Excessive Dose)
   - Heparin Therapy
   - Bilateral Oophorectomy
6. Miscellaneous Causes
   - Alcoholism
   - Primary Biliary Cirrhosis
   - Rheumatoid Arthritis
   - Scurvy

The Skeletal Intermediary Organization:

To understand the pathophysiology of osteoporosis one should be cognizant of the skeletal intermediary organization described elsewhere (Frost, 1985a, 1985b, 1983; Heany & Barger-Lux, 1985). Like any machines (such as cars) having master plans, the mammalian skeleton has an analogous master plan, but its Manufacturer did not publish a manual for it. So scientists are trying to discover its features by research. Current concept is that bone is not a static organ as one may think of due to its toughest nature, but is in a constant dynamic homoeostatic balance. It has been found that the skeletal

intermediary organization (10) has three major levels and many specialized mechanism which, in turn, provide special functions that underlie skeletal health and disease, including osteoporosis. Malfunctions of three of those mechanisms/functions, (i) modeling, (ii) remodeling, and (iii) microdamage physiology, in the direct sense cause the features osteoporotic skeleton, and so the ultimate medical causes of osteoporosis must somehow affect them.

Modeling : Modeling controls the microarchitecture, shapes and proportions of bone including outside bone diameter, marrow cavity diameter, and cortical thickness. It primarily affects periosteal and corticoendosteal surfaces. Two (10) mechanisms provide the bone modeling function: (i) the resorption drift, and (ii) the formation drift. They move bone surfaces through tissue space, the former by eroding them, and the latter by adding new circumferential lamellar bone to them. Stereotyped patterns of drifts maintain a bone's shape as it grows from infant to adult size and they can correct deformities due to malunion.

Remodeling: Bone remodeling signifies a turnover of hard tissue in packets, known as basic multicellular units (BMUs) that couple in time and space an initial focal resorption process to an ensuing formation one. Remodeling also occurs throug hout life; but unlike modeling, it is not coupled with general body growth. Various hormones, nutrients, biochemical substances and mechanical influences can modify the amounts resorbed and formed per typical completed BMU. Osteoporosis is the result of unequal bone resorption and formation whereby net bone gain is less than net bone loss. In healthy adults each remodeling unit replaces about 0.05 to 0.10mm^3 of bone and requires about three months to complete its task. Each packet of renewed bone remains intact for an average of 10 years. The remodeling time lengthens to 4 to 6 months in older adults, and in some bony regions of older osteporotric patients, it has been found to be as long as 30 months.

Microdamage Physiology: Bone microdamage physiology (MDx) implies that physical microcracks occur in human bone during life due to mechanical fatigue phenomenon, which BMU-based remodeling normally repairs. The MDx 'burden' in a given skeleton reflects the balance between its production and repair. If there is increased MDx production or impaired MDx repair, or both, bones become fragile and undergo spontaneous fractures. Known examples of such fractures include the march or stress fractures of adults, including osteoporotic persons.

The exact mechanism of osteoporosis at the cellular level is unknown, but it is believed to be the uncoupling of osteoclastic-osteoblastic activity, with osteoclastic activity predominating (Avioli, 1983).

Involutional Osteoporosis:

Bone responds to adverse stimuli in a limited number of ways. One of these ways is development of osteoporosis. Thus, osteoporosis may be the final common response of bone loss from various types of abnormalities in bone metabolism. Involutional osteoporosis seems to be a heterogeneous disorder. Type I osteoporosis occurs in a relatively small subset of postmenopausal women who are 51 to 65 years of age. Less frequently, a similar

syndrome occurs in men of comparable age. Type II osteoporosis occurs in a large proportion of women or men who are older than 75 years of age. Osteoporosis occuring in the decade from 66 to 75 years may represent a combination (Riggs et al., 1983).

Type I Or Postmenopausal Osteoporosis :

This classic form of disease was originally described in 1940 by Dr. Fuller Albright and his associates and was first objectively confirmed in the 1960s (Nordin et al., 1966). It characteristically occurs in women within 10 to 15 years of menopause. These women appear to have lost disproportionately large amounts of trabecular bone from the axial skeleton (Riggs et al., 1981). Vertebral comprression fracture is the main clinical manifestation of this type of osteoporosis, but Colle's fracture of distal radius occurs frequently (Riggs et al., 1983). Oestrogen deficiency is generally believed to be the main aetiologic factor (Lindsay et al., 1976). Less commonly, a similar disorder occurs in men of comparable age and the female : male ratio is 8 : 1 (Riggs, 1984).

For Type I osteoporosis, the predilection for women and the temporal proximity of the menopause implicate oestrogen deficiency as an aetiologic agent. There is no reasonable room for doubt that the loss of bone that starts with the menopausal fall in plasma oestrogen levels is associated with a rise in bone resorption (Nordin et al, 1981). Bone formation at this time either increases or remains unchanged. This interpretation is amply confirmed by the relevant biochemic changes associated with the menopause, which include a significant rise in urinary hydroxyproline and in plasma alkaline phosphatase (Crilly et al., 1981, 1980). It has been found that there is also a rise in plasma and urinary calcium in the menopausal state (Nordin et al., 1985). Not only is the plasma calcium higher in post than premenopausal women, but it is higher again in osteoporotic than in normal postmenopausal women, and this is also true of the fasting urinary calcium, although this does not quite reach significance. Rise in fasting plasma and urinary calcium has also been found 3—6 months after hysterectomy with bilateral oophorectomy (Gallagher et al., 1972).

Therefore, postmenopausal osteoporosis is the result of increased bone resorption associated with menopause or oophorectomy. It has been suggested that a decline in plasma oestrogen levels causes an increase in bone sensitivity to the resorptive action of parathyroid hormone (Gallagher et al , 1980). However, this concept of increased bone responsiveness to circulating endogenous PTH by oestrogen deficiency in menopause was originally theorized by Heany (1965) and Nordin's group (Jasani et al., 1965). Direct evidence supporting this mechanism was provided by demonstration of Riggs et al. (1972) that oestrogen treatment of women with Type I osteoporosis decreaaed bone resorption (assessed by microradiography of biopsy specimens), but increased serum iPTH. The oestrogen effect may be mediated by calcitonin, a hormone secreted by C cells of the thyroid, which lowers plasma calcium and phosphate, and inhibits bone resorption. It has been suggested that menopause decreases calcitonin secretion (Hillyard et al., 1978) ; if so, this would be an additional factor

which exacerbates bone loss. Some authors have reported that calcitonin level in post-menopausal patients increases with oestrogen therapy (Stevenson et al., 1981 ; Morimoto et al., 1980). Others have stated that oestrogen does not affect basal calcitonin levels on a long term basis and they question the role of calcitonin in the aetiology of post-menopausal osteoporosis (Leggate et al., 1984). It has been found that parathyroid function is decreased or normal in most patients with Type I osteoporosis (Gallagher et al., 1979) ; others have found consistently low levels of serum iPTH in postmenopausal osteoporosis (Franchimont and Heymen, 1976 ; Riggs et al., 1973 . But this low serum iPTH in post-menopausal osteoporosis does not preclude a permissive sustaining role for PTH in maintaining bone resorption, however, because when oestrogen is deficient, bone resorption is enhaced.

With one exception (Avioli et al., 1965), all studies have consistently shown that patients with osteoporosis have low calcium abosrption when compared with age matched control subjects (Gallagher et al., 1979, 1973 ; Szymender et al , 1972 ; Riggs et al., 1967 ; Caniggia et al., 1963). This calcium malabsorption has been attributed to a deficiency of serum 1,25 $(OH)_2D$ (Gallagher et al., 1979). However, results of measurement of serum $1,25(OH)_2D$ in postmenopausal osteoporosis have been conflicting. Initially Gallagher et al (1972) reported that serum $1,25(OH)_2D$ was decreased in patients with postmenopausal ostdoporosis as compared with age and sex-matched control subjects. Subsequently, several other investigators have also consistently found lower values for serum $1,25(OH)_2D$ in postmenopausal osteoporosis (Sorensen et al., 1982 ; Lund et al., 1989 ; Riggs et al., 1981 ; Bishop et al., 1980 ; Lawoyin et al., 1980 ; Orimo and Shiraki, 1979). Not all investigators, however, have found that serum $1,25(OH)_2D$ is lower in postmenopausal osteoporosis. Haussler and McCain (1977) found that the concentration of 1,25 $(OH)_2D$ in serum from women with postmenopausal osteoporosis was normal. Christiansen (1982) and Nordin et al (1985) also found no significant difference in serum 1,25 $(OH)_2D$ levels in normal and osteoporotic women matched for age. However, decreased production of 1,25 $(OH)_2D$ in postmenopausal osteoporosis does not appear to be a primary (intrinsic) defect of renal 25-OH-D 10 hydroxylase activity ; as it has been found that following administration of parathyroid extract, the increase in serum $1,25(OH)_2D$ was similar in both control and Type I osteoporotic subjects (Riggs et al., 1981).

Because all postmenopausal women are relatively oestrogen deficient but only some develop osteoporosis, factors in addition to menopause must determine individual susceptibility. In a matched group of postmenopausal women with and without vertebral compression fractures, Davidson et al (1983) were unable to find significant difference in serum concentrations of a battery of 12 different hormones, including free oestrone, free testosterone and androstenedione. However Longcope et al (1984) and Aloia et al (1985) have found that serum adrenal androgens such as androstenedione and dehydroepiandrosterone (DHA) are significantly lower in osteoporotic than in normal women of similar age.

Although all of these findings have not been confirmed uniformly, they are sufficiently consistent to suggest the model shown below for Type I osteoporosis. The resultant changes in vitamin D and calcium metabolism, therefore, are the secondary consequences of increased bone loss.

Type I Osteoporosis
(Postmenopausal Osteoporosis)

Oestrogen Deficiency → Increased bone loss
Other Factors → Increased bone loss
Increased bone loss → Decreased PTH secretion
Decreased PTH secretion → Decreased 1,25 $(OH)_2$ D production
Decreased 1,25 $(OH)_2$ D production → Decreased calcium absorption

(After Riggs et al., 1983; Riggs, 1984)

Type II Osteoporosis or Senile Osteoporosis:

Senile osteoporosis occurs in persons of 75 years of age or older and differs clinically from the type previously described. Bone loss is proportionate for both cortical and trabecular bone and is only slightly more for patients with fracture than for the rest of the aging population (Riggs, 1984). Hip fracture, which is uncommon in patients with postmenopausal osteoporosis, assumes great clinical importance in those with senile osteoporosis (Nordin et al., 1980). The female: male ratio of affected persons decreases to 2:1, and the disorder is much more prevalent (Riggs, 1984). Only about 5 to 10% of postmenopausal women have fractures caused by osteoporosis before the age of 65 years (Smith et al, 1960), whereas by 90 years, the cumulative incidence of fractures of the hip is 32% (Gallagher et al., 1980) and of the vertebrae is about 50% (Riggs, 1984).

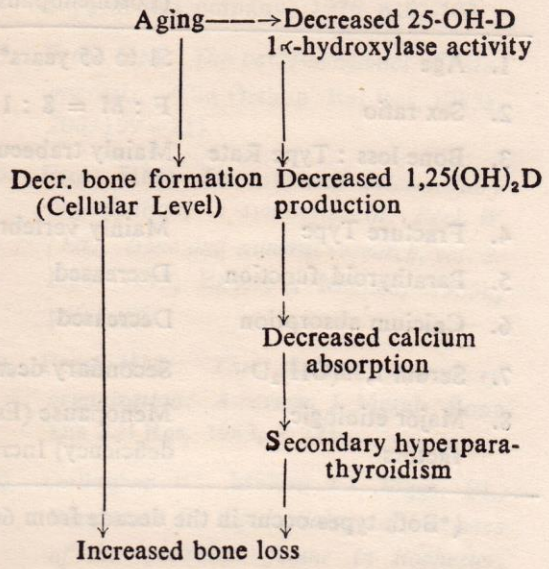
Most likely, multiple factors, including senescence of bone cells, contribute to senile osteoporosis. Impaired bone formation appears to be one of the major causes of Type II osteoporosis. From the fourth decade of life onward, less bone is formed than is resorbed at individual remodeling foci, and this imbalance increases with aging (Lips et al., 1978). Again a decrease in calcium absorption may be one of these contributing factors. Many studies using either radioactive calcium (Gallagher et al., 1979 ; Alevizaki et al., 1973 ; Bullamore et al., 1970 ; Caniggia et al., 1963) or metabolic balance (Nordin et al., 1976) techniques have shown that intestinal calcium absorption decreases with aging In both sexes. Although estrogen affects calcium and vitamin D metabolism, it seems unlikely that the menopause alone could account for the observed progressive linear decrease in calcium absorption that continues into the 10th decade of life, and of course, it could not account for the decrease in males, which is almost as large as that which occurs in postmenopausal women. In contrast to postmenopausal osteoporosis in which serum iPTH is low, in senile osteoporosis all investigators who have measured serum iPTH as a function of age have, in fact, found that it increasses (Gallagher et al., 1980; Wiske et al., 1979 : Berlyne et al., 1975). Also, Delmas et al. (1982) reported that three indices of bone turnover—serum bone Gla protein (osteocalcin), serum alkaline phosphatase and urinary hydroxyproline—increased significantly with aging and are

positively correlated with serum iPTH. These findings are consistent with the hypothesis that impaired calcium absorption contributes to bone loss.

Decreased calcium absorption in elderly persons could result from either an intrinsic abnormality of calcium absorption or impaired metabolism of vitamin D to 1,25 $(OH)_2$ D, its physiologically active form. Several studies (Gallagher et al., 1979 ; Manolagas et al., 1982) have found significantly decreased levels of serum 1,25 $(OH)_2$ D (associated with normal levels of serum 25-OH-D) with aging rather than increased levels, which could be expected if an intrinsic defect in calcium absorption was present. Lund et al. (1982) however, failed to find a decrease in serum 1,25$(OH)_2$D in 194 men and women whose ages ranged from 15 to 90 years. Slovik et al. (1981), however, found that six young normal subjects had a greater increase in serum 1,25$(OH)_2$D after infusion of PTH than did five older patients with osteoporosis. In the main, therefore, these findings suggest that elderly persons may have decreased renal 25-OH-D 1α-hydroxylase activity, analogous to findings documented for aging rats (Horst et al., 1978 ; Armbrecht et al., 1980).

Thus, the apparent abnormality in vitamin D and calcium metabolism for Type II osteoporosis would correspond to the following model.

TYPE II OSTEOPOROSIS
(Senile Osteoporosis)



(After Riggs et al., 1983 ; Riggs, 1984)

Osteoporosis occuring in women within the first 10-15 years after menopause and that occuring in men and women older than 75 years of age differs with respect to epidemiology, patterns of cortical and trabecular bone loss, parathyroid function, calcium and vitamin D metabolism, and cause. The differences may be summarized in Table I (Riggs et al., 1983 ; Riggs, 1984).

Table—1

Summary of Differences between Type I Osteoporosis and Type II Osteoporosis

	Type I Osteoporosis (Postmenopausal Osteoporosis)	Type II Osteoporosis (Senile Osteoporosis)
1. Age	51 to 65 years*	75 years*
2. Sex ratio	F : M = 8 : 1	F : M = 2 : 1
3. Bone loss : Type Rate	Mainly trabecular Accelerated	Trabecular and cortical Not accelerated
4. Fracture Type	Mainly vertebral	Both vertebral & hip
5. Parathyroid function	Decreased	Increased
6. Calcium absorption	Decreased	Decreased
7. Serum $1,25(OH)_2D$	Secondary decrease	Primary decrease
8. Major etiologic factors	Menopause (Estrogen deficiency) Increased bone loss	Decreased bone formation Sec. hyperparathyroidisn

(*Both types occur in the decade from 66 to 75 years of age)

Reference :

1. Avioli LV : *Osteoporsis.* In, Peck WA (Ed), *Bone and mineral research annual.* Annual l. Amsterdam, Excerpta Medica, 1983, 280—318.
2. Avioli LV, McDonald JE, Lee SW: *The influence of age on the intestinal absorption of 47-Ca absorption in post-menopausal osteoporosis.* J Clin Invest, 1965, 44, 1960-1967.
3. Albright F, Bloomberg E & Smith PH: *Postmenopausal osteoporosis.* Trans Assoc Am Physicians, 1940, 55, 298—305.
4. Aloia JF, Coh SH, Vaswani A, Yeh TK, Yuen K, Ellis K: *Risk factors for postmenopausal osteoporosis.* Am J Med, 1985, 78, 95.
5. Alevizaki CC, Ikkos DG, Singhelakis P: *Progressive decrease of true intestinal calcium absorption with age in normal man.* J Nucl Med, 1973, 14, 760—762.
6. Armbrecht HJ, Zenser TV, Davis BB: *Effect of age on the conversion of 25-OH-D_3 to 1,25$(OH)_2D_3$ by kidney of rat.* J Clin Invest, 1980, 66, 1111—1123.
7. Berlyne GM, Ben-Ari J, Kushelevsky A, Idelmen A, Galinsky D, Hirsch M, Shainkin R, Yagil R, Zlotnik M: *The etiology of senile osteoporosis: secondary hyperparathyroidism due to renal failure.* Q J Med; 1975, 44, 505—521.
8. Bullamore JR, Gallagher JC, Wilkinson R, Nordin BEC, Marshal DH; *Effect*

of age on calcium absorption. Lancet, 1970, 2, 535—537.

9 Bishop JE, Norman AW, Coburn JW, Roberts PA, Henry HL: *Studies on the metabolism of calciferol.* XVI : *Determination of the concentration of 25-hydroxy vitamin D, 24, 25-dihydroxy vitamin D, and I,25-dihydroxy vitamin D in a single 2 milliliter plasma sample.* Min Elec Metab, 1980, 3, 181—189.

10. Caniggia A, Gennari C, Bianchi V, Guideri R: *Intestinal absorption of 45-Ca in senile osteoporosis.* Acta Med Scan, 1963, 173, 613—617.

11. Crilly RG, J Ones MM, Horsman A, Nordin BEC: *Rise in plasma alkaline phosphatase at the menopanse.* Clin Sci, 1980, 58, 341.

12. Crilly RG, Francis RM, Nordin BEC: *Steroid hormones, aging and bone.* Clin Endocr Metab, 1981, 10, 115.

13. Christiansen C : *Osteoporsis and vitamin D metabolites. A status report.* In: *Norman AW, Schaefer K, Herrath DV, Grigoleit* H-G *(Eds), Vitamin D, chemical, biochemical and clinical endocrinology of calcium metabolism.* Berlin, Walter de Gruyter, 1982, p915—920.

14. Delmas PD, Stenner D, Wahner HW, Mann KG, Riggs BL: *Serum bone gla protein increases with aging in normal women: implications for age-related bone loss (abstract).* Calcified Tissuu Res, 1982, 34, S4.

15. Frame B and McKenna MJ: Osteoporosis: *Postmenopausal or secondary ?* Hosp Pract, 1985, 20 (10A), 37—46.

16. Franchimont P, Heynen G (Eds): *Parathormone ond calcitonin radioimmunoassay in various medical and osteoarticular disorders.* Philadelphia, J. B. Lippincott Company, 1976, p101-107.

17. Frost HM: *The pathomechanics of osteoporosis.* Clin Orthop Rel Res, 1985a, 200, 199—223.

18. Frost HM: *The skeletal intermediary organization: A synthesis. In: Peck W (Ed), Bone and mineral research, vol. 3.* New York, Excerpta Medica, 1985b, p49—108.

19. Frost HM : *The skeletal intemdicry organization: A review.* J Metab Bone Dis Rel Res, 1983, 4, 281.

20. Gallagher JC, Melton LJ, Siggs, BL, Bergstrath E: *Epidemiology of fractutes of the proximal femur in Rochester, Minnesota.* Cin Orthop, 1980, 150 163 —171.

21. Gallagher JC, Young MM, Nordin BEC: *Effects of artificial menopause on plasma and urine calcium and phosphate.* Clin Endocr, 1972, 1, 57.

22. Gallagher JC, Riggs BL, Jerpbak CM, Arnaud CD: *The effect of age on serum immunoreactive parathyroid hormone in normal and osteoporotic women.* J Lab Clin Med, 1980, 95, 373—385.

23. Gallagher JC, Aaren J, Horsman A, Wilkinson R, Nordin BEC: *Corticostroid osteoporosis.* Clin Endocrinol Metab, 1973, 2, 355—368.

24. Gallagher JC, Riggs BL, Eisman J, Hamstra A, Arnaud SB, DeLuca HF: *Intestinal calcium absorption and serum vitamin D metaboiites in normal sub-*

jects and osteoporotic patients: Effect of age and dietary calcium. J Clin Invest, 1979, 64, 729—736.

25. Haussler MR, McCain TA: *Basic and clinical concepts related to vitamin D metabolism and action (parts 1 & 2).* N Engl J Med, 1977, 297, 974—983.

26. Hillyard CJ, Stevenson JC and MacIntyre I: *Relative deficiency of plasma calcitonin in normal women.* Lancet, 1978, 1, 961.

27. Heany RP: *A unified concept of osteoporosis.* Am J Med, 1965, 39, 877.

28. Heany RP & Barger—Lux MJ: *Calcium, bone metabolism, and structural failure.* Triangle, 1985, 24(3/4), 91—100.

29. Horst RL, DeLuca HF, Jorgeman NA: *The effect of age on calcium absorption and accumulation of 1,25$(OH)_2D$ in intestinal mucosa of rats.* Metab Bone Dis Relat Res, 1978, 1, 29—33.

30. Jasani C, Nordin BEC, Smith DA, Swanson I; *Spinal osteoporosis and the menopause.* Proc Royal Soc Med, 1965, 58, 441.

31. Kelly WN, Harris ED, Ruddy SA, Seldge BC (Eds): *Text book of rheumatology, vol. 2.* Philadelphia, W. B. Saunders Company, 1985, 1657-1662.

32. Lindsay R, Hart DM, Aitken JM. MacDonald EB, Anderson JB, Clarke AC: *Long term prevention of postmenopausal osteoporosis by oestrogen: evidence for an increased bone mass after delayed onset of oestrogen treatment.* Lancet, 1976, 1, 1038—1041.

33. Lawoyin S, Zerwekh JE, Glass K, Pak CYC: *Ability of 25-hydroxy vitamin D_3 therapy to augment serum 1, 25—and 24,25—dihydroxy vitamin D_3 in postmenopausal osteoporosis.* J Clin Endrocrinol Metab, 1980, 50, 593—596.

34. Lund B, Sorensen OH, Lund B, Agner E: *Serum 1,25—dihydroxy vitamin D in normal subjects and in patients with postmenopausal osteopenia: Influenee of age, renal function and estrogen therapy.* Horm Metab Res, 1982, 14, 271—274.

35. Lips P, Courpron P, Muenier PJ: *Mean wall thickness of trabecular bone packets in the human iliac crest: Changes with age.* Calcified Tissue Res, 1978, 26, 13.

35. Leggate J, Farish E, Fletcher CD, McIntosh W, Hart DM, Sommerville JM: *Calcitonin and postmenopausal osteoporosis.* Clin Endocrinol, 1984, 20, 85—92.

37. Longcope C, Baker RS, Hui SL, Johnston CC Jr: *Androgen and estrogen dynamics in women with vertebral crush fractures.* Maturitas, 1984, 6, 309.

38. Manolagas SC, Howard J, Culler F, Catherwood BD, Deftos LJ: *Cytoreceptor assay for 1,25 $(OH)_2D$: A simple, rapid and reliable test for clinical application (abstract).* Clin Res, 1982, 30, 527A.

39. Morimoto S, Tsuji M, Okada Y, Onishi T, Kumahara Y: *The effect of estrogens on human calcitonin secretion after calcium infusion in elderly female subjects.* Clin Endocrinol, 1980, 13, 135—145.

40. Nordin BEC, Need Ag, Morris HA, Aorowitz M: *New approaches to problems of osteoporosis.* Clin Orthop Related Res, 1985, 200, 184—197.

41. Nordin BEC, Aaron J, Speed R, Crilly RG: *Bone formation and resorption as the determinants of trabecular bone volumes in postmenopausal osteoporosis.* Lancet, 1981, 2, 277.

42. Nordin BEC, Heyburn PJ, Peacock M, Horsman A, Marshall D, Crilly RG: *Osteoporosis and osteomalacia.* Clin Endocrinol Metam, 1980, 9, 177—205.

43. Nordin BEC, Wilkinson R, Marshall DH, Gallagher JC, Williama A, Peacock M: *Calcium absortion in the elderly.* Calcified Tissue Res, 1976, 21 (Suppl), 442—451.

44. Nordin BEC, MacGregor J and Smith DA: *The incidence* of *osteoporosis in normal women: Its relation to age and menopause.* Q J Med, 1966, 35, 25.

45. Crimo H, Shiraki M: *Role of calcium regulating hormones in the pathogenesis of senile osteoporosis.* Endocrinol Jpn. 1979, 26(Suppl), 1—6.

46. Riggs BL : *Vitamin D and involntional osteoporosis In: Kumar R (Ed), Vitamin D.* Boston, Martinus Nijhoff Publishers, 1984, p560—577.

47. Riggs BL and Melton III LJ: *Evidence for two distinct syndromes of involutional osteoporosis.* The Am J Med, 1983, 75(6), 899—901.

48. Riggs BL, Melton III LJ, Wahner HW: Heterogeneity of involutional osteoporsis: *Evidence for two distinct osteoporosis syndromes. In: Frame B, Potts JT Jr (Eds), Clinical disorders of bone and mineral metabolism.* Amsterdam, Exerpta Medica, 1983, p 337-342.

49. Riggs BL, Wahner HW, Dunn WL, Mazess RB, Offord KP, Melton LJ III: *Differential changes in bone mineral density of the appendicular and axial skeleton with aging: Relationship to spinal osteoporosis.* J Clin Invest, 1981, 67, 328-335.

50. Riggs BL, Arnaud CD, Jowsey J, Goldmith RS, Kelly PJ: *Parathyroid function in primary osteporisis.* J. Clin Invest, 1973, 52, 181-184.

51. Riggs BL, Hamstra A, Deluca HF: *Assessment of 25-hydroxy vitamin D 1α-hydroxylase reserve in postmenopausal osteoporosis by administration of parathyroid extract.* J Clin Endocrinol Metab, 1981, 53, 833—835.

52. Riggs BL, Jowsey J, Goldsmith RS Kelly PJ, Hoffman DL and Arnaud CD: *Short and long-term effects of estrogen and synthetic anabolic hormone in postmenopausal osteoporosis.* J Clin Invest, 1972, 51, 1659—1663.

53. Riggs BL, Kelly PJ, Kinrey VR, Scholz DA, Bianco AJ Jr: *Calcium deficiency and osteoporosis. Observation in one hundred and sixty-six patients and critical review of literature.* J Bone Joint Surg, 1967, 49A, 915—924.

54. Sorensen OH, Lumholtz B, Lund B, Hjelmstrand IL, Mosekilde L, Melsent F, Bishop JE. Norman AW: *Acute effects of parathyroid hormone on vitamin D metabolism in patients with bone loss of aging.* J Clin Endocrinol Metab, 1982, 54, 1258—1261.

55. Slovik DM, Adams JS, Neer RM, Holick MF, Potts JT Jr: *Deficient production of 1,25(OH)$_2$D in elderly osteoporotic patients.* N Engl J Med, 1981, 305, 372—374.

56 Stevenson JC, Abeyasekera C, Hyllyard CJ, et al.: *Calcitonin and calcium regulating hormones in postmenopausal women ; Effect of estrogens.* Lancet, 1981, 1(8222), 693—695.

57. Szymendra J, Heany RP, Saville PD: Intestinal calcium absorption; *Concurrent use of oral and intravenous tracers and calculation by the inverse convolution method.* J Lab Clin Med, 1972, 79, 570—578.

58. Smith RW Jr, Eyler WR, Mellenger RC: *On the incidence of senile osteoporosis.* Ann Intern Med, 1960, 52, 773-781.

59. Wiske PS. Epstein S, Bell NH, Queener SF, Edmondson J, Johnston CC Jr: *Increases in immunoreactive parathyroid hormone with age.* N Engl J Med, 1979, 300, 1414—1421.

(Continued from front inside cover)

Journal article, more than 3 authors :

3. Filler RM, Eraklis AJ, Das JB, et al: Total intravenous nutrition. AM J Surg 121 : 454—458, 1976.

Complete Book :

4. Golligher JR. Medical care of the Addolescent (ed.2). New York, Appleton 1966, p, 208—216.

Chapter of book :

5. Nixon HH: Intestinal obstruction in the newborn, in RobC,Smith R(eds). Clinical Surgery, chap 16, London, Butterworth, 1966, p, 168—172.

Chapter of book that is part of published meeting:

6. Natving JB., Kunkel HG, Gedde-Dahl T Jr. : Chain sub-groups of G Globulin, in Killander J (ed) : Gamma Globulins proceedings of the Third Nobel Symposium, New York, Wiley, 1967, pp, 37—54.

7. Okamatsu T, Takayama H, Nakata K, et al : Omphalocele surgery, presented at the meeting of the Pacific Association of Pediatric Surgeons, San Diego, April 1973.

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CALCIUM ANTAGONISTS—A REVIEW

M. A. Jalil Chowdhury

Key Words:
Calcium antagonists :

Summary:

Calcium antagonists are a new group of drugs of considerable importance in Ischaemic heart disease. They are now being used with success in the managment of angina, supraventricular tachycardia, hypertension including hypertensive emergencies and hypertrophic cardiomyopathy. A direct action on transmembrane Ca^{++} influx is the active principle of calcium channel blockers. In addition to this group, some Ca^{++} antagonists also have an effect on intracellular calcium mechanism. The calcium antagonists reduce the strength of myocardial contraction, reduce oxygen consumption, cause coronary dilation and reduce peripheral resistance.

Introduction :

Drugs like Nitrates, Beta-adrenoreceptor blocking agents, Dipyridamole etc., are now being widely used as antianginal agents[1–2]. Calcium antagonists represent a new class of drugs which have been found valuable in the treatment of angina pectoris and various other cardiovascular disorders and so are of considerable clinical importance[3].

Calcium antagonist, as implied by the name, interfere with the normal functions of Ca^{++} in the body, including that in the excitation-contraction coupling in the smooth muscle and in cardiac muscle. Their effect, according to Fleckenstein[4], is explained by a selective blockade of the slow channel of the cell membrane i.e., by interference with the transmembrane Ca^{++} influx.

Caleium ions are recognised as playing an important role in the contractile process of the heart, smooth muscle, and skeletal muscle, in glandular secretions and in the release of neurotransmitters. In view of this, it is rather surprising that cacium antagonists can be used therapeutically, having apparently a rather selective action on the cardiovascular system, without important side effects.

How Ca^{++} acts intracellularly :

The calcium ions are necessary for the activation of the myofibrillary ATP-ase, an enzyme that converts the energy rich compound ATP into cyclic AMP, with a consequent release of energy. The chemical energy bound in ATP is converted into mechanical work in the form of myofibrillary contraction. There are intracellular receptor protein for calcium ions called "Calmodulin", which acts as an intracellular link through which Ca^{++} produces myofibrillary contraction. In the presence of calcium ions, "Calmodulin" binds to enzyme and activates them.

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Physiology of Calcium antagonists :

Pure calcium channel blockers (Prototype: Nifedipine):— These group of compounds selectively inhibit the slow calcium influx through the cell membrane without having significant effect on the rapid Na^+ influx which is responsible for the production of action potentials[3]. Other member of this group-with minor reservations are verapamol and diltiazem

Calcium antagonists acting by calcium channel blockade an intracellular action (Prototype : Fendiline) :— The result of recent research have shown that some Ca^{++} antagonists have additional intracellular sites of action. They inerfere with the availability of Ca^{++} for contraction of vascular smooth muscle and cardiac muscle mainly intracellularrly by inhibiting the release of Ca^{++} from various pools[3].

Some other antianginal drugs such as Perhexiline and Prenylamine have some calcium-blocking properties but these probably do not explain their activity[2].

Pharmacology of Calcium antagonists :

o They reduce the strength of myocardial contraction without marked effect on the action potential ("electro-mechanical coupling")

o Reduces the consumption of energy rich phosphates in the contractile system.

o Leading to reduction in oxygen consumption.

o Increase in oxygen availability due to coronary dilatation as consequences of relaxation of smooth muscle cells in the coronary arteries.

o Calcium antagonists increase blood flow, not only in coronary but also in mesenteric, renal and femoral vessels.

o Various calcium antagonists were found to decrease systemic vascular resistance[5-6]. In addition pulmonary arterial pressure was reported to be lowered[7].

o Reduction of infarct size and enhanced development of collateral circulation was claimed by some studies[8-9].

o Slowing the AV conduction and increasing the refractory period of the AV node have been suggested as the principal mechanism for anti-arrythmic effect of some of the calcium antagonists like verapamil[3].

o Diltiazem was found to increase sodium diuresis to a great extent that could be explained by its effect in enhancing renal blood flow[10].

Therapeutic use :

Table I lists the clinical situations where calcium antagonists could be used:—

Table—1

Clinical indications of calcium antagonists

Angina pectoris
Prinzmetal's Variant angina
Post-myocardial infarction angina
Arrythmia—Supraventricular tachycardia
Hypertension
Hypertensive crisis
Hypertensive cardiomyopathy

Most of the clinical studies were concerned with the use of calcium antagonists in angina pectoris. The fact that these drugs increase coronary blood flow but at the same time reduce oxygen consumption by reducing the consumption of ATP, decrease arterial pressure would suggest their value

as antianginal agent. Further, in contrast to propranolol, these drugs could also be used in patients with bronchospasm. Rather calcium antagonists inhibit the secretions of mediators of bronchospasm[11]. In addition to uncontrolled clinical trials, there were some double-blind studies which indicated these drugs superior to plecebo in reducing the number of daily attack, in necessiating less nitroglycerine comsumption, and in improvement of exercise tolerence[12-14]. None of the studies has proven superiority of calcium antagonist over propranolol, in the prevention of anginal attack[12,14]. The most convincing results with calcium antagonists were obtained in variant angina[15]. The effectiveness of calcium antagonists in variant angina can be explained by the ability to prevent coronary vasospasm. Clinical experience in the treatment of arrythmia is confined mainly to verapamil given intravenously. This drug was shown, in several studies, to be effective in causing termination of Paroxysmal supraventricular tachycardia when given intravenously and in preventing their recurrences of attack when given orally[16]. In atrial fibrillation and ventricular arrythmias, however, verapamil is not so effective.

Calcium antagonists have gained an important place in the treatment of mild hypertension[17]. Sublingual administration of Nifedepine has been shown to produce a rapid fall of blood pressure and seems to be useful in the managment of hypertensive emergencies including hypertensive encephalopathy[5,18].

Hypertrophic cardiomyopathy may be another indication for the use of calcium antagonist, as verapamil was reported to improve exercise capacity in these patients[19].

Side effects:

Common side effects are headache, dizziness, nausea or vomitting. Some 20-30% patients on nefedipine develope peripheral edema as a result of vasodilatation[1]. In some patients, angina is made worse by nifedipine. Nifedipine has recently been reported to cause cataract in some patients also[20].

References :

1. Julian DG: *Cardiology (4th. edn.)*. London, ELBS, 1983, p. 138-139.
2. Girdwood RH: *Clinical Pharmacology (24th ed.)*. London, Bailliers Tindall, 1979, p. 176.
3. Zsoter T : *Calcium antagonists*. Am heart Jour. 99: 805-809, 1980.
4. Fleckenstein A: *Specific pharmacology of calcium in myocardium, cardiac pacemakers, and vascular smooth muscle*. Ann. Rev. Pharmacol. Toxicol. 17:149, 1977.
5. Guazzi M, Olivari MT, Polese A, et al: *Nifedipine, a new antihypertensive with rapid action*. Clin. Pharmacol. Ther. 22:528, 1977.
6. Aoki K, Kondo S, Mochizuki A, et al: *Antihypertensive effect of cardiovascular Ca^{++} antagonist in hypertensive patients in the absence and presence of beta-adrenergic blockade*. Am. Heart J. 96: 218, 1978.
7. Landmark K, Refsum AM, Simonson S, et al: *Verapamil and pulmonary hypertension*. Acta Med. Scand. 204:299, 1978.
8. Schmier J, Bruckner VB, Mittmann V, et al: *Intercoronary collateral and intramyocardial blood distribution in dogs following nifedipine administration com-*

pared with controls, in Jatane AD and Lichtlen PR: Third International Adalat Symposium, Amsterdam, 1976, Excerpta Mediea, p. 42.

9. Reimer KA, Lowe FE and Jennings RE: *Effect of the calcium antagonist verapamil on necrosis following temporay coronary artery occlusion in dogs.* Circulation 55:581, 1977.

10. Kinoshita M, Kushuka R, Shimono Y, et al: *Effect of diltiazem hydrochoride on renal haemodynamic and urinary excretion.* Jap. Clin. J. 42:553, 1978.

11. Kay AB: *Specific and nonspecific triggers in bronchial asthma (report).* J. Royal Soc. Med. 78 (1):82-84, 1985.

12. Sandler G, Clayton GA, and Thornicroft SG: *Clinical evaluation of verapamil in angina pectoris.* Br. Med. J. 3: 224, 1968.

13. Islam MM, Zafar A, Malik A, et al: *Clinical evaluation of Sensit (Fendiline HCL) in angina pectoris and post infarction angina.* Bang. Heart J. 1:52-55, 1986.

14. Livesley B, Catley PF, Campbell RC, et al: *Double blind evaluation of verapamil, propranolol and isosorbide dinitrate against a plecebo in the treatment of angina pectoris.* Br. Med. J. 1:375, 1973.

15. Hosada S and Kimura E: *Efficacy of nifedipine in the variant form of angina pectoris, in Jatene AD and Lichtlen PR*: Third international Adalat Symposium, Amstrdum 1976, Excerpta Medica, p. 195.

16. Singh BN, Eilrodt G and Peter CT: Verapamil: *A review of its pharmacological properties and therapeutic use.* Drugs 15:169, 1978.

17. Breckenridge A: *Treating mild hypertension (editorial).* Br. Med. J 291:89-90, 1985.

18. Sirajul Hoque KMHS, Masud MA, Altaf Hussain SM, et al: *Efficacy of sublingual Nifedipine in the emergency Treatment of se ere Hypertension.* Journal of BCPS 3:19-23, 1986.

19. Rosing DR, Kenneth M, Maron BJ, et al: *Verapamil therapy, a new approach to the pharmacologic treatment of hypertrophic cardiomyopathy II.* Circulation 60:1208, 19.9,

20. Heyningen R, and Harding JJ : *Do Aspirin-Like analgesics protect against Cataract?* Lancet, 17 May:1111-1113, 1986.

AMYLOID TUMOUR OF THE BREAST : A CASE REPORT AND REVIEW OF LITERATURE

Syed Azim Ihtesham Ally[1], Dharam P. Alrenga[2]

Key Words :

Amyloid tumour; amyloidosis ; breast; Congo red, methyl violet & thioflavine T stains; electron microscopy.

Summary:

A case of solitary amyloid tumour of the breast with rheumatoid arthritis is reported.

Introduction:

Amyloidosis is usually a systemic disorder characterized by deposition of amyloid in several organs. It is either primary or secondary to an inflammatory, autoimmune or neoplastic disease. Rarely, isolated tumour-like amyloid deposits (amyloid tumour) have been reported in single organs such as larynx, lung, skin, and urinary bladder (Kyle & Bayrd, 1975). Deposition of amyloid in mammary tissue, either as a part of systemic disease or as an amyloid tumour is rare. Only six cases of amyloid tumour of the breast have been reported in the English literature (Fernandez & Hernandez, 1973; Sadeghee & Moore, 1974; Lipper & Kahn, 1978; Hardy & Myerowitz, 1979; Walker & Fechner, 1982; Cetti, et al., 1983). Another case is documented in this report.

1. Dr. Syed Azim Ihtesham Ally. M. D. Fellow Deptt. of Pathology, Univrsity of Maryland, USA.

2. Dr. Dharam P. Alrenga, Residency Program Director, Cook County Hospital, Chicago, USA

Case Report:

A 76 year-old black female presented with two painless masses in the right breast. One mass was noted approximately one year ago and it was slowly increasing in size; the second one had appeared only recently and had prompted the patient to seek medical advice. She had a history of rheumatoid arthritis involving her shoulders, elbows, wrists, knees ankles and toes for more than 20 years. She was almost continuously under anti-arthritic therapy including acetylsalicylic acid and indomethacin in recent years. Physical examination revealed an afebrile, poorly nourished black female wiht a pulse rate of 80/minute, blood pressure of 170/90 mm. of Hg., and respiratory rate of 24/minute. The right breast had a 2 cm. diameter mass in the upper lateral quadrant and a 1 cm. diameter mass in the upper medial quadrant. Both masses were hard, non-tender and freely mobile. The left breast was normal. The axillary lymph nodes were not enlarged. Systemic examination was normal except for a grade one "functional" systolic murmur at the left lower sternal border. Liver, spleen, heart and tongue were not enlarged. The extremities showed muscular atrophy and advanced arthritic deformities with periarticular swelling in fingers, wrists, elbows, feet and knees.

Laboratory studies revealed mild normocytic and hypochromic anaemia, normal

leucocyte and platelet counts and normal urinalysis. Renal and liver profile tests were within normal range. Serum albumin, globulins, and gamma globulins were 4.5 gm/dl, 2 6 gm/dl, and 1.5 gm/dl respectively. An electrocardiogram revealed sinus rhythm and nonspecific T-wave changes. The chest X-ray was normal. The X-rays of hands showed changes consistent with advanced rheumatoid arthritis. The clinical diagnoses included carcinoma of right breast, rheumatoid arthritis, and anaemia of chronic disease. An excisional biopsy of the right breast was performed and the larger of the two masses was removed.

Pathology: The specimen consisted of a 2.5x2x2 cm. piece of mammary tissue enclosing a firm, circumscribed, gray and waxy nodule which measured 1.1. cm. in diameter. Microscopically, the nodule consisted of large and confluent globular deposits of eosinophilic acellular material (Fig 1), which showed strong affinity for Congo red stain and intense metachromasia with methyl violet stain. In the Congo red stained sections, the acellular material showed apple-green birefringence under polarised light. In a thioflavine-T stained section examined with the fluorescent microscope it showed bright yellow fluorescence. Electron microscopic study showed closely packed, randomly oriented nonbranching linear fibrils which measured 80 Ang stroms in diameter and lacked peri-

Fig. 1. *Large deposits of amyloid around mammary ducts (haematoxylin and eosin, X150).*

odicity (Fig. 2). These tinctorial and ultrastructural characteristics are considered to be pathognomonic for amyloid. At the periphery of the nodule, amyloid deposits were seen around the mammary ducts and in the walls of small veins. Small aggregates of lymphocytes and mature plasma cells, and occasional foreign-body type multinucleated giant cells were seen adjacent to some of the amyloid deposits.

A diagnosis of amyloid tumour of the breast was made, The patient left the hospital before further tests to document the presence of amyloid deposits in other tissues or to document the presence of plasma cell dyscrasia could be initiated. She was subsequently lost to follow up.

Fig. 2. *Extracellular fibrils of amyloid and a few collagen fibres,* (*X35, 300*).

Discussion:

Although systemic amyloidosis could not be excluded in this patient, it was considered unlikely because of the absence of its recognized clinical manifestations such as macroglossia, hepatosplenomegaly, cardiomegaly, congestive heart failure, cardiac conduction disturbances and proteinuria. Even if this patient had subclinical systemic amyloidosis, involvment of the breast as palpable amyloid tumour is unusual.

A review of English literature revealed only six previously documented cases of amyloid tumour of the breast (Table 1).

Table—1

Amyloid tumor of the breast (organized according to the age of the patient).

No.	Year of publication	Authors	Age (years)	Laterality	Size	Associated conditions
1.	1983	Cetti et al	45	Right	2cm	Rheumatoid arthritis ; renal and rectal amyloidosis
2.	1978	Lipper & Kahn	47	Right	small	None
3.	1979	Hardy et al	55	Bilateral	up to 1 cm	Plasmacytosis gammapathy, systemic amyloidosis.
4.	1982	Walker et al	55	Left	0.6cm	None
5.	1974	Sadeghee and Moore	60	Bilateral	6cm 3cm	Rheumatoid arthritis; cutaneous amyloidosis.
6.	1973	Fernandez and Hernandez	62	Right	3cm	None
7.	Present case	Ally and Alrenga	76	Right	1.1cm	Rheumatoid arthritis

All the patients were middle-aged or elderly females. When unilateral, the right breast was involved more frequently; the amyloid tumours were bilateral in two patients. The tumours ranged from 0.6 cm to 6 cm in the largest diameter, were firm to hard in consistency, and mimicked breast carcinoma. In three patients, amyloid deposits were present in one or more tissues other than the breast. Three patients did not have any associated disease. One patient had nonmyelomatous plasmacytosis and k-chain monoclonal gammopathy. Rheumatoid arthritis was present in three patients; it is considered to be one of the common chronic conditions complicated by systemic amyloidosis (Teilum & Lindahl, 1954; Missen & Taylor, 1956). Missen and Taylor (1956) found amyloidosis in 15% of 374 autopsied cases of rheumatoid arthritis. The study of Ozdemir et al. (1971) is of interest in this context. They did not find any significant difference in frequency, distribution and amount of amyloid between 47 autopsied cases of severe and long standing rheumatoid arthritis and 47 appropriately matched controls.

Some authors (Patil et al.. 1970; Carstens et al., 1972) have noted amyloid material in the stroma of breast carcinoma. Others (Tremblay, 1974) however, have not been able to substantiate this observation.

In summary, amyloid deposition in the breast in clinically detectable form as amyloid tumour is rare. It may be unilateral

or bilateral, solitary or multiple, isolated or a part of systemic amyloidosis and may clinically mimic carcinoma of breast.

References :

1. Carstens PHB, Huvos AG, Foote FW, et al.: *Tubular carcinoma of the breast.* Amer J Clin Path, 1972, 58, 231-238.
2. Cetti R, Reuther K, Hansen JPH, and Shiodt T: *Amyloid tumour of the breast.* Danish Med Bull, 1983, 30, 34-35.
3. Fernandez BB, and Hernandez FJ : *Amyloid tumour of the breast. Arch Pathol,* 1973, 95, 102-104.
4. Hardy TJ, Myerowitz RL, Bender BL: *Diffuse parenchymal amyloidosis of lungs and breast.* Arch Pathol Lab Med, 1979, 103, 583-585.
5. Kyle RA & Bayrd ED : *Amyloidosis. Review of 236 cases.* Medicine, 1975, 54, 271-299.
6. Lipper S & Kahn LB: *Amyloid tumour. A clinicopathologic study of four cases.* Amer J Surg Path, 1978, 2, 141-145.
7. Missen GAK, & Taylor JD: *Amyloidosis in rheumatoid arthritis.* J Pathol Bacteriol, 1956, 71, 179-192.
8. Ozdemir AI, Wright JR, & Calkins E: *Influence of rheumatoid arthritis on amyloidosis of aging.* N Engl J Med, 1971, 285, 534-538.
9. Patil SD, Joshy BG, & Datar KG : *Amyloid deposit in the carcinoma of the breast.* Indian J Cancer, 1970, 7, 60-62.
10. Sadeghee SA & Moore SW: *Rheumatoid arthritis, bilateral amyloid tumour of the breast and multiple cutaueons amyloid nodules.* Amer J Clin Path, 1974, 62, 472-476.
11. Teilum G & Lindahl A: *Frequency and distribution of amyloid changes in rheumatoid arthritis.* Acta Med Scand, 1954, 149, 449-455.
12. Tremblay G: *Elastosis in tubular carcinoma of the breast.* Arch Pathol, 1974, 98, 302-307.
13. Walker AN, Fechner RE, Callicott JH: *Amyloid tumour of the breast.* Diag Gyn Obs, 1982, 4, 339-341.

PRIMARY MEDIASTINAL SEMINOMA-A CASE REPORT

G. Rasul[1], Alimuzzaman[2]

Key Words :

Mediastinal tumours, Seminoma, Mediastinal seminoma, Mediastinal germinoma.

Primary mediastinal germinoma of the seminomatous type is a rare malignant germ cell tumour that is histologically identical to testicular seminoma. Fewer than 100 cases have been reported in the world literature (Bush et al 1981). Bush et al reported a series of 13 patients treated at Stansford University Medical Centre between 1961-1976. Hurt et al (1982) reported another series of 17 patients of pure seminoma and four patients of mixed germ cell tumours from the Mayo Clinic. Here we report a case of anterior mediastinal seminoma which we came across in 1986.

Case Report:

A 28 years old male patient presented with a history of progressively swollen neck, dry cough and dyspnoea, worse on lying down, of three months duration. There was swelling of the neck and upper chest wall with swollen veins. Trachea was central and chest wall moved well with respiration. Breathing was vesicular with no added sounds. Apex beat in left 5th intercostal space medial to midclavicular line. No lymphadenopathy or hepato-splenomegaly. Testes were normal. No neurological or muscular signs present.

1. Professor of Surgery, IPGMR, Dhaka.
2. Asstt. Professor of Surgery. ICVD, Dhaka

Total WBC count 7500/c.mm N-62%, L-30% ; M-2% ; E-6% ; B-0% ; platelet 200,000/c.mm Hb-70% ; BUN-9 mg%; FBS 123 mg% ; serum Na-138.4meq., K-4.52meq and Cl-97 meq.

Chest X-ray showed a globular, dense opacity in the superior mediastenum, more to the right of the mid-line. Radio-iodine uptake was 3% at 2 hrs and 10% at 24 hrs, all concentrated at the normal thyroid position, none withitn the tumour mass.

A median sternotomy was done on 31.8.86 and superior mediastinum opened. A very firm globular mass was found occupying the space, enclosing the superior vena cava, trachea and aorta with roots of great vessels within it. With much painstaking and risky dissection more than half of the tumour bulk was removed from around the superior vena cava & trachea. It was a firm, greyish white, uniformly solid mass. This procedure removed his vena caval and trecheal obstruction, which became apparent at the first post-operative day. Patient was relieved of his symptoms and anxiety. No testicular biopsy was taken.

Histological examination revealed a typical seminoma. He was referred to the Radiotherapist colleague who started radiotherapy on the eighth post-operative day. Chest x-ray after three months showed a clear superior mediastinum, and patient free of all symptoms (Fig. 1 & 2).

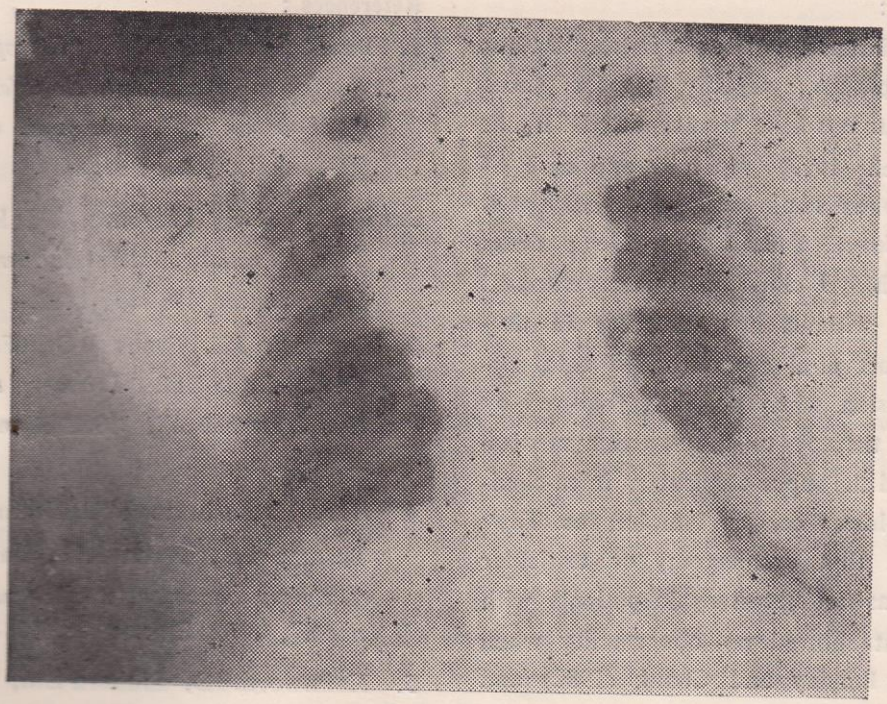


Fig. 1. *Pre-operative Chest X-Ray.*

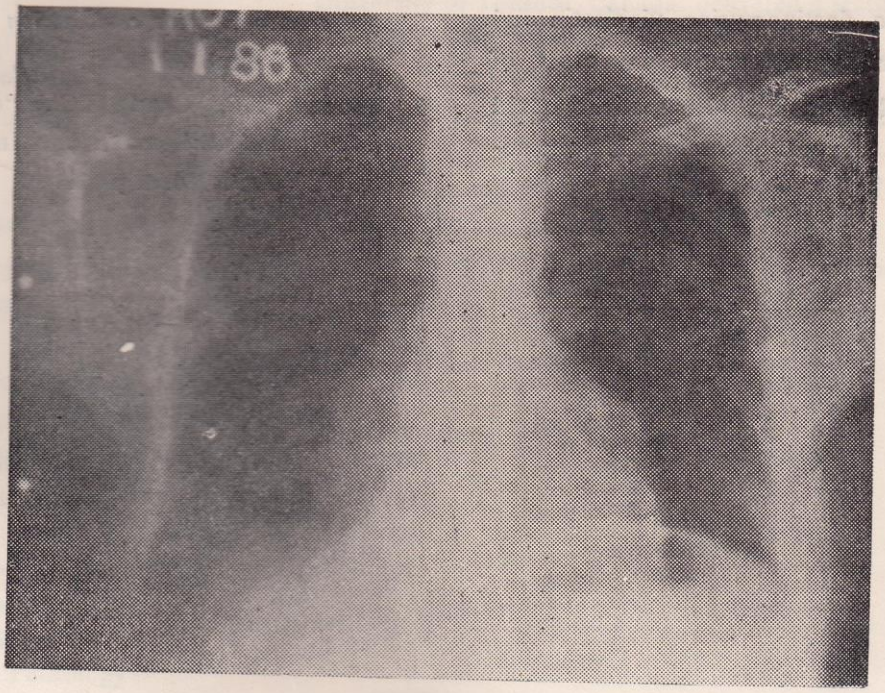


Fig. 2. *Post-operative and Post irradiation Chest X-Ray three months later*

Discussion:

Germinomas can occur in places other than the gonads especially in those places where teratomas have been reported. Banik and Magell (1979) reported one case of retroperitoneal seminoma and Bushkirk et al (1982) reviewed a series of twelve patients from the Mayo clinic with retroperitoneal seminoma without any testicular involvement. Hurt et al recommended total surgical excision when possible, followed by radiation therapy to the superior mediastinum and the supra-clavicular, infra-clavicular and lower cervical lymphnodes. They concluded that orchiectomy or testicular biopsy was not necessary in patients with testes that showed no abnormality when palpated. Panday and Chang (1982) and Hainsworth et al (1982) claimed that combination chemotherapy with cyclophosphamide, dactinomycine, vinblastin and cis-platinum were curative in cases of mediastinal seminoma. Our patient could not afford the cost of combination chemotherapy.

References :

1. Banik, S and Magell, J. *"Retroperitoneol Seminoma presenting with inferior viva caval obstruction"*, The Jour. of Urol. 1979, Voll. 122, p-564.
2. Bush, S. E., Martinez, A, Bagshow, MA. *"Primary Mediastinal Seminoma"*, 1979, Cancer, 48: 1877-1882.
3. Bushkirk JS., Evans RG., Farrow GM., Rode JD. *"Primary retroperitoneal seminoma"*, 1982 Cancer 49 : 1934-1936.
4. Hurt RD., Bruckman JE, Ferrow GM., Bernatz PE., Hahn RG., Earle JD., *"Primary anterior mediastenal seminoma"*, 1982, Cancer 49: 1658-1663.
5. Hainsworth JD, Einhorn LM, Williams SD., Stewart M, Cerio A. *"Advanced extragonadal germ cell tumours: successful treatment with combination chemotherapy"* Ann. Int, Med, 1982, 97:7-11,
6. Panday KJ., Chang YC., *"Cure of Mediastinal seminoma"*, Ann, Int. Med. 1982, Vol. 97 No. 4. p-618.

COLLEGE NEWS

Continuing Medical Education Programme :

September 25, 1986 — Dr. Mahmud Hasan
Assoc. Prof. of Gastroenterology IPGMR,
delivered a lecture on Duodenal Ulcer in Bangladesh.

November 27, 1985 — Dr. Md. Sirazul Islam
Assoc. Prof. of Child Health
Bangladesh Institute of Child Health
Dhaka Shishu Hospital, Dhaka delivered a lecture on Hospital care of Childrens in China; a Comparative analysis in the perspective of Bangladesh.

December 8, 1986 — Mr. W. J. Virgin
First Principal-cum-Superintendent
Dhaka Medical College Hospital, Dhaka
delivered a lecture on "Postgraduate Medical Education and Training Programme in Canada today.

December 28, 1986 — Prof. P. K. Basu
Prof. of Ophthalmology
University of Toranto, Canada delivered a lecture on "Ocular Toxicology".

Examination News :

Results of FCPS I, FCPS II and MCPS Examination held in January, 1987 are given below.

262 candidates appeared in FCPS I Examination in different subjects of which 49 candidates came out successful. Subject wise results are as follows :

Subject	Number appeared	Number Passed
Medicine	62	18
Surgery	61	9
Obstetrics & Gynae	33	9
Paediatrics	39	3
Ophthalmology	18	3
Psychiatry	11	4
ENTD	11	1
Radiology	1	1
Radiotherapy	4	0
Anaesthesiology	15	1
Clinical Pathology	7	0
	262	49

61 candidates appeared in FCPS II Examination in different subjects. List of candidates who satisfied the Board of Examiners are as follows :

Roll No.	Name	Name of Medical College from where graduated	Subject
1	Dr. Md. Abu Sayeed	Chittagong Medical College	Medicine
2	Dr. Shamim Ahmed	Dhaka Medical College	Medicine
13	Dr. Md. Mamtaz Hossain	Rangpur Medical College	Medicine
19	Dr. Chandan Kanti Bhattacharjee	Mymensingh Medical College	Medicine
25	Dr. Majibar Rahman Khan	Dhaka Medical College	Surgery
33	Dr. Tushar Kanti Halder	Dhaka Medical College	Surgery
34	Dr. Md. Mazibar Rahman	Rajshahi Medical College	Surgery
39	Dr. Ahmed Sayeed	Mymensingh Medical College	Surgery
47	Dr. Atika Begum	Rangpur Medical College	Obst. & Gynae
55	Dr. A. S. M. Bazlul Karim	Dhaka Medical College	Paediatrics
61	Dr. U. H. Shahera Khatun	Sir Salimulla Medicalh College	Anaesthesiology

41 candidates appeared in MCPS Examination in different subjects. List of candidates who satisfied the Board of examiners are as follows:

Roll	Name	Name of Medical College from where graduated	Subject
4	Dr. Md. Abul Bashar	Dhaka Medical College	Medicine
16	Dr. Bidyut Mazumder	Chittagong Medical College	Surgery
26	Dr. Nasima Yusuff	Chittagong Medical College	Obst. & Gynae
27	Dr. Nayeema Ahmed	Dhaka Medical College	Obst. & Gynae
28	Dr. Priti Barua	Chittagong Medical College	Obst. & Gynae
32	Dr. Amina Khan	Rajshahi Medical College	Obst. & Gynae
44	Dr. Md. Anwar Hossain	Rajshahi Medical College	ENT
46	Dr. Dewan AKM Abdur Rahim	Mymensingh Medical College	Psychiatry
49	Dr. Md. Didarul Alam	Dhaka Medical College	Anaesthesiology

Fellowship without Examination

Dr. M. A. Mannan, MBBS, FRCP, Professor of Neurology, IPGMR, Dhaka and Dr. Habibur Rahman Ansary, Professor of Pharmacology, Sher-e-Bangla Medical College,Barisal were admitted as Fellow without examination for the year 1986.

Lumpsum subscription of Tk. 5,000/- for life Membership :

It is decided in the Council meeting of the BCPS that henceforth a Fellow must clear up his arrear dues to the College befor he is eligible to become a life-member on payment of Tk. 5,000/- at a time.

Recognition of Training

The Council of the BCPS has decided to provisionally recognise the training of doctors in the department of (1) Medicine, (2) Surgery (3) Obst. & Gynae (4) ENTD and (5) Ophthalmology in teaching hospitals under Tribhuvan University, Nepal for a period of 2 years i.e. from January, 1987 as a prerequisite for appearing in Fellowship examination of the BCPS.

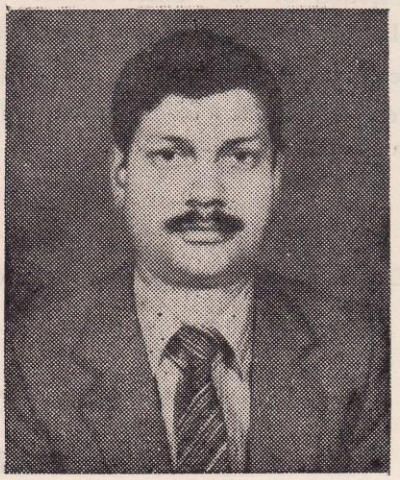
3rd Convocation of the College :

The 3rd Convocation of the College which was a remarkable event for the College was held on 26th Fedruary '87 where Janab H M. Ershad, President of the People's Republic of Bangladesh distributed diplomas to the Fellows and Members. The doctors who qualified in the FCPS and MCPS examination of the College from July 1982 to January 1987 were the participants of the Convocation. Total 121 Fellows and 37 Members received their diploma certificates in the Convocation.

Ashab Gold Medal

There exists a fund in the BCPS for the award of a Gold Medal of the above name to a Fellow securing at least 70% marks in FCPS Part I Examination and passing Part II (Final) Examination in one chance without any break. Dr. Mahmud Hasan (Fellow) who fulfilled these requirements got the Ashab Gold Medal which was awarded to him by President H. M. Ershad in the Third Convocation of the College held on 26th February 1987.

Dr. Mahmud Hasan now posted as Associate Professor of Gastroentrology in IPGMR is the only Fellow of the College to get this award since it was declared in 1975.



Dr. Mahmud Hasan

Annual General Meeting

The 14th Annual General Meeting of the BCPS was held on 27.2.87. Honorary Secretary Dr. T. A. Chowdhury presented his report on activities of the College during the last year. Dr. Ruhul Amin, Treasurer of the College presented Annual Budget for financial year 1987-88 which was accepted by the College. It was followed by a contributory annual Dinner at College primises to which spouses of the Fellows were also praticipated.

Election News

8 (eight) new Councillors were elected in an election of Councillors of the College held on 27.2 87 for a term of four yaers.

New Councillors

1. Dr. A. H. M. Towhidul Anowar Chowdhury
2. Dr. Golam Rasul
3. Dr. S. A. Ashraf
4. Dr. A. K. M. Mahbubur Rahman
5. Dr. Mahmud Hasan
6. Dr. Rashid-E-Mahbub
7. Dr. Nazmun Nahar
8. Dr. S. G. M. Chowdhury

Election of the Office-Bearers of the College was held on 12-3-87. The new Executive Committee will hold Office for 2 years with effect from March, 1987. The new Committee is as follows :

1. President	Dr. S A Ashraf
2. Sr. Vice-President	Dr. Mazhar Ali Quaderi
3. Vice-President	Dr. Golam Rasul
4. Treasurer	Dr. A H M Ahsanullah
5. Members	Dr. A H M Towhidul Anowar Chowdhury
	Dr. Nazmun Nahar

Dr. A H M Towhidul Anowar Chowdhury is acting as Honoray Secretary of the Collage.

Formation of Various Committees and Faculties of the BCPS

Examination Committee :

1. Dr. Golam Rasul	—	Chairman
2. A H M Ahsanullah	—	Member
3. Dr. S G M Chowdhury	—	,,
4. Dr. Nazmun Nahar	—	,,
5. Dr. T A Chowdhury	—	,,
6. Dr. Md. Abdul Hadi	—	,,
7. Dr. S I M G Mannan	—	,,

Reference Committee:

1. Dr. M A Quaderi	—	Chairman
2. Dr. Md. Tahir	—	Member
3. Dr. A S M Fazlul Karim	—	,,
4. Dr. Md. Nurul Amin	—	,,
5. Dr. M R Khan	—	,,
6. Dr. Rashid-E-Mahbub	—	,,

Finance Committee and Tender Committee :

1. Dr. A Quashem	—	Chairman
2. Dr. A H M Ahsanullah	—	Member
3. Dr. Ruhul Amin	—	,,
4. Brig. A Malik	—	,,
5. Dr. A K M N. Chowdhury	—	,,
6. Dr. A K M Anowarul Azim	—	,,

Library Committee :

1.	Dr. M A Jalil	—	Chairman
2.	Mahmud Hasan	—	member
3.	Dr. Md. Humayun Kabir	—	,,
4.	Dr. Kazi Mashiur Rahman	—	,,
5.	Dr. Md. Nurul Islam	—	,,
6.	Dr. Chowdhury Ali Kawsar	—	,,

Journal Committee :

1.	Dr. A K Azad Khan	—	Chairman
2.	Dr. Golam Rasul	—	member
3.	Dr. K M H S Sirajul Haque	—	,,
4.	Dr. A N Md. Atai Rabbi	—	,,
5.	Dr. Md. Shafiqul Hoque	—	,,
6.	Dr. Zafar Ahmed Latif	—	,,

Museum Committee :

1.	Dr. K M Nazrul Islam	—	Chairman
2.	Dr. Golam Rasul	—	member
3.	Dr. M H Mullick	—	,,
4.	Dr. Faruque Azim	—	,,
5.	Dr Shahid Hossain	—	,,

Fellows Welfare Committee :

1.	Dr. Waliullah	—	Chairman
2.	Dr. A K M Mahbubur Rahman	—	member
3.	Dr. Satyendra Nath Aditya	—	,,
4.	Dr. Nazrul Islam	—	,,
5.	Dr. A S M Fazlul Karim	—	,,
6.	Dr. Tofayel Ahmed	—	,,
7.	Dr. Rashid-E-Mahbub	—	,,

Continuing Medical Education Programme Committee :

1.	Dr. S A Shakur	—	Chairman
2.	Maj. Gen. A R Khan (Retd)	—	member
3.	Dr. Shamsuddin Ahmed	—	,,
4.	Dr. Mahbub Kamal Chowdhury		,,
5.	Dr. S A M Golam Kibria	—	,,
6.	Dr. Emran Bin Yunus	—	,,

Faculty of Basic Medical Sciences :

1.	Dr. S I M G Mannan	—	Chairman
2.	Dr. K M Rahman	—	member
3.	Dr. M H Mullick	—	,,
4.	Dr. K M Nazrul Islam	—	,,
5.	Dr. M R Choudhury	—	,,
6.	Dr. K M Fariduddin	—	,,

Faculty of Medicine :

1.	Dr. S G M Chowdhury	—	Chairman
2.	Dr. R K Khandaker	—	member
3.	Dr. Quamrul Huda	—	,,
4.	Dr. Md. Nurul Islam	—	,,
5.	Dr. Tahir	—	,,
6.	Dr. A K M N Chowdhury	—	,,
7.	Dr. Nurul Islam	—	,,

Faculty of Surgery :

1.	Dr. Golam Rasul	—	Chairman
2.	Dr. md. Nurul Amin	—	member
3.	Dr. Fazlul Huq	—	,,
4.	Dr. S A Sobhan	—	,,
5.	Dr. M N Huda	—	,,
6.	Dr. S N Samad Chowdhury	—	,,

Faculty of Obst. & Gynae :

1.	Dr. T A Chowdhury	—	Chairman
2.	Dr. S F Begum	—	member
3.	Dr. Abdul Bayes Bhuiyan	—	,,
4.	Dr. A K M Anowarul Azim	—	,,
5.	Dr. Syed Ershad Ali	—	,,
6.	Dr. Latifa Shamsuddin	—	,,

These Committee and Faculties will function for 2 years from March, 1987.

The President and the Secretary of the College will be the ex-officio member of all Committees.