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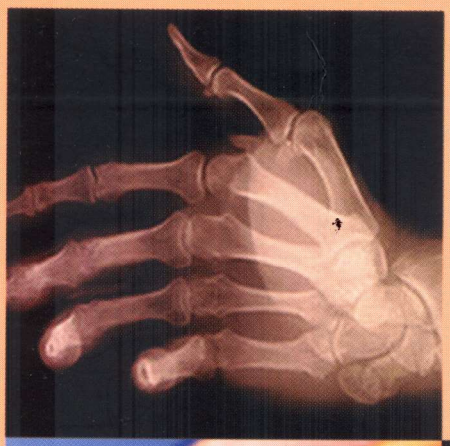

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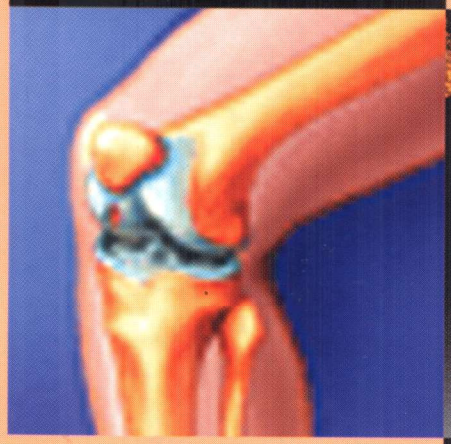

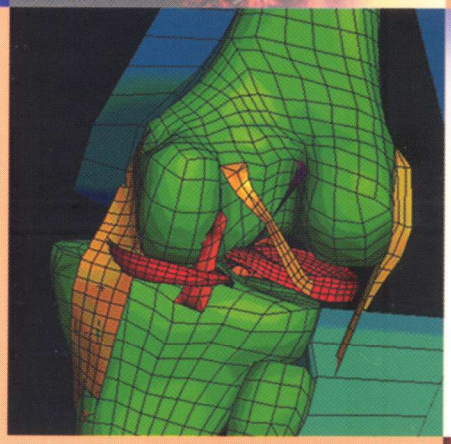

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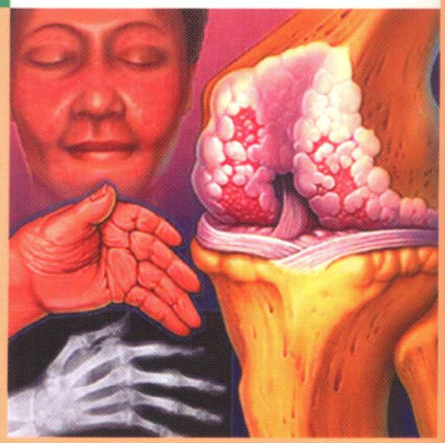

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The ORION Medical journal

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Editor's Choice

One and All

This issue of The ORION is made up of streams of materials that flow at very different rates. This volume seems to have everything: An editorial points out the present situation of 'Depression' in our community and the importance of its treatment (P-66); a review article on 'Dengue' reveals elaborately on pathophysiology, clinical manifestation, treatment & prevention of dengue (P-67-70); another review article on 'Cleft lips' is highlighted on the several surgical approaches for the management of cleft lips (P-71-72).

The review articles: `Hyperemesis Gravidarum' (P-78-79) confers specially on fluid management of the condition and 'Postpartum Heamorrhage' (P-82) states the recent advancement of it's treatment.

The concept of cardiac failure and it's prospect is nicely demonstrated in the article of 'Cardiac Failure' (P-73-77); the article 'Stroke and it's Management'(P-80-81) gives an updated management profile of stroke. The article of 'Peri-operative fluid therapy: In the context of stress response' (P-83-85) is a continuation of previous issue (volume-14;P-56-58).

The review article on `Febrile Seizure' (P-91) flushes the overall idea on the condition and the article on 'Psoriasis' (P-86-88) is mainly focused on the contemporary treatment portrait of psoriasis. An urban study evaluates the treatment benefit of intra-articular injection therapy in frozen shoulder (P-89-90) and the case report on `Carcinoma of breast' (P-92) is accentuating the telepathological practices in Bangladesh.

All of our valued readers should able to extract something from this rich menu that will help them ameliorate their professional knowledge.

The opinions and suggestion of the readers are always appreciated to make The ORION journal richer day by day.

May the Almighty bless all in the spirit of good health.

The ORION wishes all a very happy and prosperous Bangla New Year (Shuvo Novoborsho)-1410.

DR. MOHAMMAD ZAKIRUL KARIM
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Depression and importance of its treatment

Islam H[1]

The Orion 2003; 15: 66

Psychiatric disorders remains unrecognized in vast majority of cases in medical practice in Bangladesh. This is mainly due to inadequate exposure and training and lack of importance in the examination system in the under graduate classes. This is further aggravated by insufficient training during internship period where placement in psychiatry is not taken very seriously by interms. As a result, doctors come out of their teaching institute with negligible amount of knowlede, skill and ability to diagnose and deal with Psychiatric problems in medical practice. To improve this situation Psychiatric team of medical colleges should take more active and dynamic role to create interest among the students and newly qualitical doctor's.

It is commonly believed that psychiatric problems are the problems of developed western society. Different studies all over the world, including Bangladesh have found repeatedly that psychiatric disorders are as common in our country and other developing countries of the world as in developed countries. Differences are in the presentations and at times expression of symptomatolgy of the discase process.The causative factors may be the genes, neurotransmitters, biochemical, metabolic, endodocrines, neuro developmental anomalies, organic, psychosocial, personality or environmental factors.

Depression is fairly common in medical and psychiatric specialty practice. Point prevetance of depression in western countries is between 1.8 and 3.2% for men and between 2.0 and 9.3 for women. In our country in one study by Prof. Chowdhry found 2.9% in a rural area, women suffering three times more than men. In another study (unpublished) women in Savar area 8.9% were found to be suffering from depression. Point prevelance of depressive symptoms are much higher.

In one study by Prof. N. Alam it was observed that 10% of his medical practice patient had depression.

Another study under my supervission in Dhaka city G.P's prescribe antidepressant consciously in 4.5% their patients and anxiolytic drugs at a much higher rate, some time missing depression as anxiety state.

A review by the author it was found that practice pattern of psychiatrists and psychiatric centers in Bangladesh over the last four decades that 15 to 30% the patients attending those facilities are suffering from depression.

Recognition of depression is very impotant because if it remains unrecognized or in adequately treatreated it leads to immense suffering to the individual leading to disabilities.

In on study by WHO in 1990 it was found that Unipolar Major Depression caused 10.7% of the total disability due to all disease and Bipolar disorders causes 3% disability, of the 10 leading causes of disability due to all diseases psychiatric disorders are five among the 10 leading causes of disability. It is for this reason doctors should be competant to deal with phychiatric problems.

Recognition of Depressive disorders by the medical profession is very important as this is one of the condition which if recognized early and treated adequately in appropriate doses for sufficient length of time most of the Patients improve very satisfactoritly. Only 5-15% remains non-responsive or refractory to medicaltreatment. Treatment of depression can be professionlally very satisfying, at times it can be emotionally very disturbing if patients treatment.

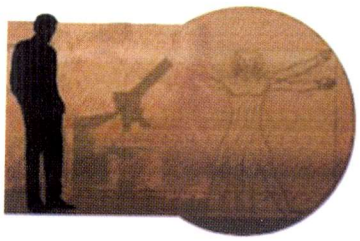
1. Prof. Hidayetul Islam, MBBS (Dhaka), D.P.M. (England)
Founder & Director: Institute of Community Mental Health
Dhaka Monorog Clinic.

Treatment of depression can be professionlally very satisfying, at times it can be emotionally very disturbing if patients under care of the physician or phychiatrists either attempts or commits suicide one review on USA 1988 found suicide rates among patients suffers from depresssion varied 15-30%.

Medical treatment of Depression have improved considerably over the last two decades due to a availability of newer and more effective drugs with less or minimal side effects. This has almost resotoformatised treatment of depression at present.
It is very important that all medical practitioners should be familiar thoroughly with the doses and side effects of the drugs and should treat patients with confidence and should have holistic approach to the patient care remembering that in addition to drug treatment most patient will benefit from psychological and soical support.

A doctor should remember that, he is not only treating the disease, but he is treating a person who is acting and reacting with personal, social and environmental influences. He should not only heal to the person suffering from the disease process he should also provide peace of mind. This should be practiced consciously, wisely, with a benevolent attitude towards the well being of the patient.

Research suggests virus may play role in Depression



New research from Germany indicates some cases of serious depression may be caused by a virus. "We think that there is ... a lot of evidence that Borna virus has clinical significance for this type of disease," said Dr. Liv Bode of the Robert Koch Institute in Berlin. In the United States, at least 17 million people have some form of clinical depression -- not just a passing case of the blues, but a disabling and often long-term disease. Scientists are still unraveling the causes of the disease: genetics, stress and possibly a virus. The virus was first identified in the late 1800s among horses near the town of Borna, Germany. The horses stopped eating, walked in circles and got sick. Some even killed themselves. Autopsies led scientists to the virus in the region of the horses' brains that controls emotions. Researchers in Berlin have found a similar strain in humans. "I think it is supporting our hypothesis that this virus, this particular agent, has really something to do with this type of disorder," Bode said. The anti-viral drug amantadine, used to treat Parkinson's disease, has been found to relieve some cases of depression. A trial is now under way. "I think I'm one of the most skeptical people around ... but I have to face the fact that for about a year now, we've been treating patients and we've been seeing responses to amantadine," said Dr. Ron Ferszt of the Free University of Berlin. German patient Rosemarie Wenzlaff, who suffered from depression for 10 years, says the medication changed her life. "I didn't take care of myself when I was depressed; I couldn't eat," she said. "Now I'm thinking of cooking marmalade. I listen to music now. I watch TV. It's a totally different life." Scientists in the United States say these early findings are interesting, but not conclusive. Results are expected later this year from clinical trials in Berlin that might demonstrate a link between the Borna virus and depression.

Dengue : Recent Health Problem in Bangladesh

Uddin K N [1], Muhsin W M [2]

The Orion 2003 ; 15 : 67-70

Introduction

Dengue is found in tropical and subtropical regions around the world,predominantly urban and periurban areas.It is endemic in more than 100 countries in America, Africa,south east asia and western pacific areas.
WHO[1] estimates there may be 50 million cases of Dengue infection worldwide every year.

Virus

It is an RNA-containing flavi virus. All it's four serotypes can cause Dengue hemorrhagic fever (DHF) / Dengue shock syndrome (DSS).Severe disease is common with Den-2 and Den-3.

Transmission

Dengue is transmitted to human being through the bites of infective female aedes egyptii mosquitoes.Mosquitoes acquire the virus while feeding on an infected individual. Once infected, the mosquito transmit the virus throughout it's life, it transmits it to next generation through transovarian transmission

Incubition period

Average incubition period is 3 -13 days.

Primary infection

Once the virus enter the human body ,the virus is taken by the monocyte- macrophagereplication of virus occurs within these cells.Cells are destroyed and virus released in the circulation(viremia).

Secondary infection

In secondary infection there occurs antibody dependant enhancement of infection whereby crossreactive but nonneutralising antibodies from a previous infection bind to a new infective serotype and facilitate virus entry into cells resulting in higher peak viral titres.In primary and secondary infections higher viral titres are associated with severe infections.

Viremia

Viremia is present for about 24 hours prior the onset of illness and for an average of 5 days after the onset of illness.It usually coincides with the period of fever.During this time humans are infective to vector mosquitoes.

Pathogenesis of DF and DSS

- Agent: Dengue Virus (Den-1, Den-2, Den-3, Den-4)

Viral antigen

A. Enveloped antigen 'E' having
   1. Hem agglutination epitope.
   2. Viral neutralization epitope
   3. Antibody enhanced infection epitope.

B. Nonstructural protein NS1

C. Membrain Protein M--Pre M
   1. Confer Protective immunity.
   2. May have important role in vaccine production.

Vector

Aedes egyptii. Other aedes compatible of transmmision include A. albopictus, A polynensiensis, A.scutellaris complexes.

A. egyptii can transmits dengue infection either immudiately by a change of host when its feeding is interrupted or after an inclubation perid of 8 to 10 days. Patients is infective to mosquito during viramemia which is present from few hours before the onset of symptoms to an average of 5 days after the onset of symptoms.

- When an individual is infected with any one of the four serotype of dengue virus (DEN-1, DEN-2, DEN-3, DEN-4) for the first time, he/she may develop dengue fever.This is primary infection.
- Primary infection confers lefelong homotropic immunity

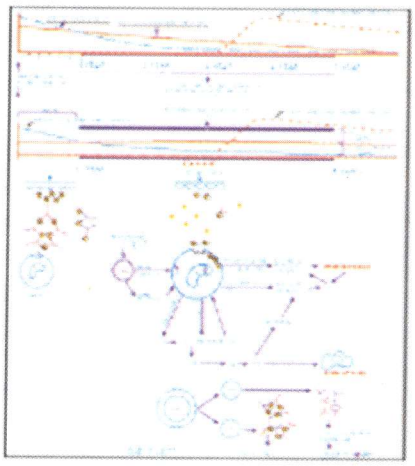


Figure I : Immune pathogenesis of DHF by secondary infection

- This also confers variable heterotropic immunity againist other three serotyps of dengue virus for two to twelve months (Fig.I)
- In a critical time period (from one year to five year after primary infection) when antibody titer reaches sub-neutralizing level, second infection with any other virulserotypes can cause antibody hanged infection giving rise to secindary infection that is called dengue hemorrhagic fever (Fig.I)
- Third and forth dengue viral infection seldom cause symptoms.

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- After single attack of DHF, the chance of second attactk of DHF is only 5%.
- In fetus - with maternal anti dengue IgG can cause DHF with primary viral infection during critical time period (From third to seventh month after birth) when IgG reaches sub-nutrilizing concentration (Fig-II)

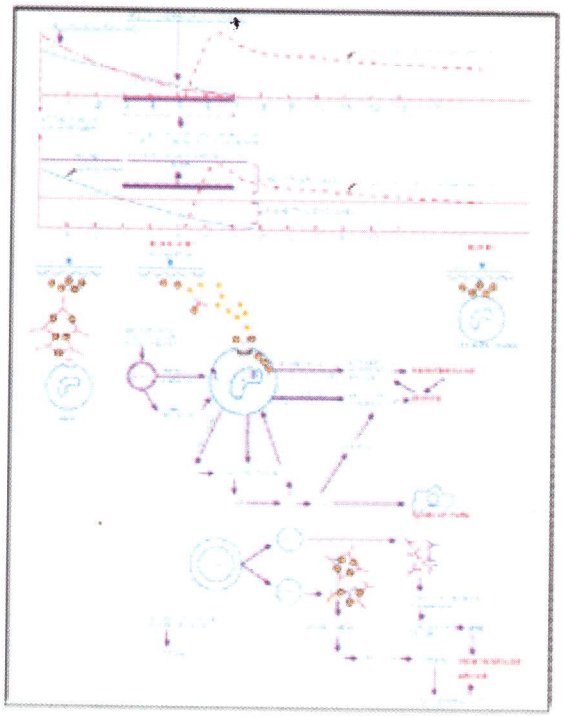

Figure II : Immune pathogenesis of DHF in infant

- T lymphocytes are activited and produce gamma interferon and interleukin-2 during DF and DHF.
- CD-4 T cells are activated at higher level in DHF than DF.
- CD-8 T Cells are significantly activated only in DHF.
- Rapid release of cytokines and chemicals mediators caused by T cell activation and by cytotoxic T cell mediated lysis of dengue viral incfected monocytes, togather with complement activation product teakage and coagulation derangement (Fig.I)
- Augmented B cell activation causes increased plasma cell proliferation followed by release of immunoglobulin.
- Immunoglobulin combined with viral protein (antigen-antibody complex) activate complement and causes increased level of C3a and C5a which cause vascular leakage.
- Antibody cross reacted with plasminogen perturbation of coagulation pathway and associated haemostatic mechanism leading to DIC and bleeding.
- Thrombocytopenia and thrombosthenia resulting from early megakaryocyte arrest play and important role by causing bleeding both in DF and DHF.
- DHF/DSS accompanied by the simultaneous and parallel activation of complement and haemostatic system together vascular permeability, The most abnormal valuas are found in most severely ill patients. The blood levels fof C1q, C3, C4, C5-8, C3 pro-activatots may be depressed. C3 catabolic rate is elevated. Findings are compatible with actinavion of complement, both classicals and alternate pathway. There is also prologed bleeding time, elevated prothrobmib time, Prolonged silicon clotting time, reduction in factor II, V, VII, X, Hypo Fibrinogenmia and increased FDP.
- The more reduction of plasma TXA_2 / PGI_2 ratioleads to more overt and serious manifestation of the disease (One of the cause not to give aspirin or alike drugs in gengue).
- High level of NS -1 is found in acute phase serume of serologically proven secondary infection NS -1 could not be detected in serologically confirmed primary infection. These suggests that NS-1 Contributes significantly to the formation f circulating immune complexes that may play an important role in the pathologinesis of service dengue disease.
- Severity of dengue disease correlates with the following factors:
  - High Viremia titer.
  - Secondary dengue virus infection.
  - DEN-2 virus type.
  - Age of patients (in adult hemorrhage and in children shock predominate)
  - Genetic background of patients.
  - Sex of the patients (Femaile are more susceptible).
  - Time interval between two infection (1-5 years)
  - Sequence of infection (Severe disease DEN-1 & DEN-2, less severe disease DEN-2 & DEN-1)

Histopathological Changes

- Vascular change include vasodilatation, congestion, perivascular hemorrhage and edema of artirial wall.
- Proliferation of reticuloendithlial cells with accelerated phagocytic activities observed frequently. The lymphoid tissue shows inceasing activity of B Lymphocyte system with activity proliferation of plasma cell and lyphoblastiod cells.
- In the liver there is fical necrosis of the hepatic and kupffer cells with formation of councilman like bodies.

Clinical features

Dengue fever is a severe form of flue like illness.

Menifestations

It may be

1. Symptomatic and
2. Asymptomatic

Symptomatic patients may again be with

a)Undifferentiated fever
b)Classical dengue fever(DF)
c)Dengue hemorrhagic fever(DHF)
d)Dengue shock syndrome(DSS)
e)Unusual syndrome such as encephalopathy and fulminant liver failure.

Phases
1. Febrile phase(2-7)days
2. Afebrile phase or critical phase(2-3)days-phase for the risk of developing DHF/DSS.
3. Convalescence phase-persists for 7-10 days after critical phase.

Classical Dengue
Fever
High rise of temperature(104-105^0 F).Fever usually persists for 2-7 days with two peaks during this illness giving saddle back appearance of temperature curve.

Constitutional features of DF
Headache,retroorbital pain,bodyache,muscle pain,joint and bone pain,flushed face.

Rash
Four types of rashes in dengue.
A. Diffuse flushing
B. Fleeting pinpoint eruptions-they develop in first half of illness.
C. Maculopapular or scarletiniform rashes appear on 3rd or 4th day of fever on face and trunk and spread to extrimities.
D. Convalescent confluent petechiae-this is typical rash of dengue,appears on 6th day.

Other features
Hemorrhage,bradycardia ,enlarged liver (tender),raised hepatic enzymes, leukopenia, normal platelet count and hematocrits. Hemorrhage can occur in classical dengue fever i.e fever with hemorrhage does not always mean DHF.

Dengue hemorrhagic fever
All the features of Dengue fever with followings[2]

Hemorrhagic menifestations
Shown by positive tourniquet test, petechiae, ecchymoses or purpura or bleeding from mucosa, gastrointestinal tract, injection sites or other locations :

Platelet count $\leq$100000/mm^3.

Objective signs of plasma leakage due to increased vascular permeability shown by fluctuation of packed cell volume(Hct) by $\geq$20% during the course of illness and recovery or clinical signs of plasma leakage such as ascites,pleural effusion or hypoproteinemia.

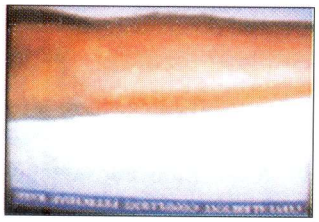

Figure III : Convalescent complement petechie. Petechie all over with itches of normal skin. (Typical dengue rash)

Grades of DHF
Grade-I: Features of DF plus positive tourniquet test
Grade-II: Above signs plus spontaneous bleeding
Grade-III: Signs of either grade- I or grade-II DHF plus featuresof circulatoryfailure viz rapid weak pulse,hypotension apprehension.

Grade-IV: DHF with undetectable BP and pulse.

DSS[2]
Grade III and grade IV together also called Dengue shock syndrome(DSS).A patient is said to have dengue shock syndrome if it has the criteria for dengue hemorrhagic fever and either pulse pressure <20 mm Hg or hypotension defined as systolic pressure < 80 mmHg for those aged < 5 yrs or< 90 mm Hg for those $\geq$ 5.

A patient with pulse pressure less than 20 even with normal systolic or diastolic pressure may be in DSS.

DHF/DSS usually devolop when patient is in afebrile period.

Diagnosis
It is described in three ways
1. Suspected diagnosis 2. Probable diagnosis 3. Confirmed diagnosis.

Suspected diagnosis
For purpose of treatmentsuspicion by a clinician is sufficient.It is not difficult during the period of outbreak. So in our setting during the period of outbreak(July-October)we can take any febrile patient as Dengue provided we do not forget malaria,typhoid,rickettsias which are common in our clinical practice.

Laboratory investigations
Virus is detectable only in febrile period. Antibodies may not be positive in early stages.It may be false positive in other flavi virus infection . Antibody tests should not be done before 4th day of infection. It is wise to do it after 7th day .Complete blood picture including PC, Hct, MP (malarial parasite), LFT(SGOT/SGPT) should be donein early part of infection(3rd or 4th day preferable).

Probable diagnosis
At least one of the followings
- Supportive serology on single serum sample titre>1280 with hemagglutination inhibition test(HIT),comparableIgG titre with ELISA or positive for IgM antibody test.
- Occurence at same location and time as confirmed cases of Dengue fever.

Confirmed diagnosis
At least one of the followings:
- Isolation of dengue virus from serum or autopsy samples
- Fourfold or greater increase in serum IgG (by Hct)or increase in IgM[3] antibody specific to dengue virus
- Detection of dengue virus in tissue,serum,or cerebrospinal fluid by immunohistochemistry, immunofluorescenceor enzymelinked immunosorbent assay(ELISA).

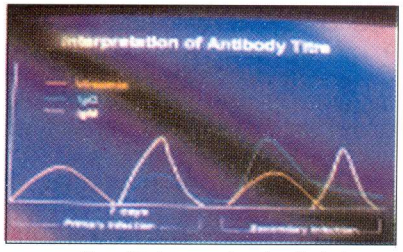

Figure IV :Interpretation of antibody titre

- Detection of dengue virus genomic sequences by reverse transcription-polymerasechain reaction

Exclusion of other diagnosis
A. Febrile phase
1. Complete blood picture including MP

a. Leukocytosis : A very high leukocyte count virtually exclude the diagnosis of a viral disease.

b. Leukopenia : A leukopenia or normal blood count having normal platelet count suggests enteric fever, rickettsiosis or other viral disease.

c. If duration of fever persists for more than 7 days other serological tests for dengue and others are justified (if PC is low and Hct is higher). Fever persisting for more than

two weeks exclude the dignosis of dengue. In the situation of prolonged fever with normal blood picture enteric fever,ricketsiosis should be excluded as these diseases are common in our country.

2. Patients presenting with pain abdomen

Gasritis and hepatitis is the main cause of pain abdomen in dengue.Pancreatitis is a possibility of acute abdomen in dengue,which should be excluded. In case of children rapid distension of abdomen due to ascites may be confused with acute abdomen and an urgent USG abdomen may help.

3. Other investigations

USG abdomen may exclude ascites and effusion(also chest x-ray).Liver function tests, renal function tests,electrolytes should be done in DHF cases.To find out hemorrhagic disorders prothrombintime, APTT, FDP, d-Dimer and fibrinogen level may need to be estimated.

B. Afebrile phase

In this phase DHF patients are at risk, so monitoring should meticulous for 2-3 days.

Monitoring

Four hourly monitoring of blood pressure, pulse,maintenance of intake and output is mandatory during critical period. At least once a day PC and Hct should be available.This will help prevention of DSS and overhydration as well.

Management of Dengue

A. Febrile phase

DF and DHF can't be differentiated initially. DF does not progress to DHF or DHF never begins with DF.Initially management is similar.

1. Reduction of temperature with paracetamol(no other medicine),sponging and adequate rehydration
2. Maintenance of fluid balance and nutrition.
3. Monitoring:Care should be taken about fluid intake from the begining
4. Rest

Reduction of temperature

1. Aim should be to keep temperature <100^{0}F.Paracetamol may be needed in maximum dose(80 mg/Kg/day) in four divided doses.Rectal route works rapidly.
2. Nontherapeutic means:Sponging with cold water(not ice),regular bathe,nursing in cool open space,thin cloths(avoid woolen blanket)helps reducing temperature.
3. Hydration
   Adequate hydration is a must.About 3L/day(100ml/Kg for children) may be a good amount. Plain water, Oralsaline, dabwater, fruitjuice(helps nutrition)-all serve purpose.

Clinical clues like repeated vomitting,persistant abdominal pain apprehension/restlessness, severe epigastric tenderness are good indicator for DHF.

In DHF grade I and II OPD or home management may be adequate provided bleeding is not severe and adequate fluid and monitoring is ensured.Ranitidine/Sucralfate/omipr azole/misoprostol all can help. Domperidone may be used for nausea and vomitting.

B. Afebrile phase

In this phase risk of devoloping DHF is higher so monitoring should be geared .

In DHF III and IV management should be at hospital. Monitoring of the vital signs and maintenance of near normal blood pressure is the goal.Overenthusiastic or panic parenteral fluid and blood/blood product administration is the most serious mistake happens in these phases.

IV fluid

Normal saline is the best fluid. ICU management was not proved superior for DHF IV patients.[4]

Fluid can started @ 3ml/Kg/hr and changed according to need(BP).In practice if facilities available ,fluid can be started from the beginning (grade I) @ 8drops/min and tailored according to need. Oral fluid should always be encouraged along with IV.

Blood/Blood products

If there is excess bleeding(hematemesis,melaena,PV bleeding etc),the Hct is below normal whole fresh blood is indicated.Blood test for grouping should routinely be done for DHF cases. Appraisal of party about group and probable necessity of blood/blood product transfusion before hand should be a routine practice for clinicians,Gum bleeding skin hemorrhages does not need special treatment.Plateletcount less than 10000 and higher hematocrit may be an indication for transfusion of platelet concentrate.Platelet concentrate is costly(2500 BDT) and preparation is time consuming (6 hours).

Other drugs

Antibiotics has no role,though severe neutropenia is common accompaiment prophylactic antibiotics are not indicated. Corticosteroids[1],pressor agents (viz dopamine etc), antivirals, antileaks (carbazocram)have no role.

C. Convalescence

Most of(even DSS cases) the patients become alright on third day. Patient is discharged when: a.General condition is acceptable b.Afebrile c.PC becomes> 50000. Prolonged fever(hospitalstay) may occur in cases with liver necrosis(high S GOT),combined infection(malaria,typhoid, rickettsiosis, hepatitis has been found positive in some of our cases),co-morbid illnesses.

Prevention

May be described in two ways-

1. Primary, 2. Secondary

1. Primary prevention

a. Vaccine

Dengue occurs only in humans,lack of a dengue animal model is an obstacle for vaccine devolopment. Phenomenon of antibody dependent enhancement demand the development of a tetravalent vaccine.Live attenuated tetravalent vaccines are being evaluated in phase 2 trials.

b) Mosquito is our target (to date) for prevention.It is also a difficult task owing to it's intimacy with human.Prevention from mosquito bite is the goal.Mosquito breedig should be prevented by killing larva and destroying receptors for larva viz container /canisters/discarded tyres/small water reservoirs of construction places by not encouraging storage for more than five days. These demands involvement of whole community.

2. Secondary prevention

Adequate management of DHF I and DHF II may prevent development of DSS, thus reduce the mortality in Dengue. Medical persons have great role in secondary prevention.

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Cleft lip and Its managment

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The Orion 2003 ; 15 : 71-72

Introduction

Cleft lips with or without cleft palates is a major social problem and more so in our part of the world. With a mean incidence of 2.1 in 1000 live births among the oriental population the impact of the problem is significant. Caucasians have an incidence of 1 in 1000 live births.

Embryology

The adult facial features develop from the frontonasal prominence and the paired maxillary and mandibular prominences predominantly between the 4th and 8th weeks[7,8]. The migration of ectomesenchyme[1] along the natural cleavage planes between the mesoderm, ectoderm and endoderm around the head is essential for the development of these facial processes. A failure of fusion among these prominences result in facial clefts.

Commonly failure in fusion of the medial nasal prominence and maxillary prominence on one side results in unilateral cleft lip. A bilateral cleft lip results from failure of fusion of the merged medial nasal prominences with the maxillary prominences on either side. The unrestrained growth of the merged medial nasal prominences leads to the anterior overprojection of the premaxilla and prolabium commonly observed in bilateral cleft lips.

Aetiology

Oral clefting is generally considered to be multifactorial. Some factors that have been implicated as contributing factors are

1. Reduced facial mesenchyme
2. Increased facial width
3. Oloigohydramnios
4. Persistent high position of the tongue
5. Failure or delayed occurrence of neck extension
6. Medications during the formative stages
   e.g steroids,anticonvulsants,diazepam, aminopterin
7. Infections in early pregnancy e.g Rubella, Toxoplasmosis and other virus
8. Growth hormone deficiency
9. Hypothalamo-pituitaryhormone deficiency
10. Genetic factors

They may be syndromic or non-syndromic. About 3% of all cleft lips with or without cleft palate are syndromic. Syndromes are more common in isolated cleft palates than in cleft lips with cleft palates. Among these the Pierre-Robin syndrome and the Van der Woude syndrome are common.

The genetic predisposition

The risks of an unborn child having a cleft lip with or without cleft palate has been well summarized by Fraser as[5]

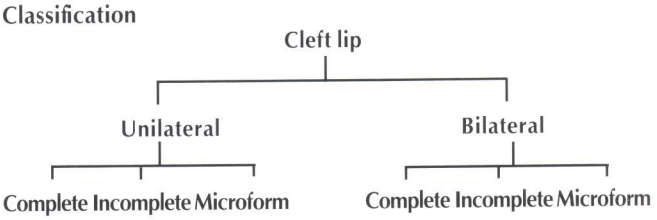
A.If both parents are unaffected but have an affected child the probabilities of the next child being born with a cleft lip (with or without cleft palate) is

1. If there are no relatives affected ----------4%
2. If there is an affected relative ---------- 4%
3. If the affected child has another malformation (Syndromic) - 2%
4. If the parents are related ----------4%
5. If two previous children are affected ----------9%

B. If one of the parents are affected the probabilities of the next child being born with a cleft lip (with or without cleft palate) is

1. If no previous child is affected ---------- 4%
2. If a previous child is affected ---------- 17%

Classification



Cleft lips may be found alone or in any combination with alveolar and palatal clefts.[3]

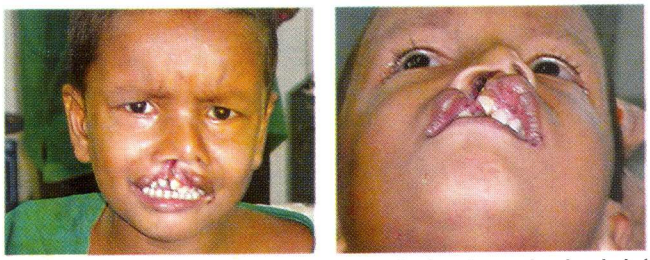


Figure I: Unilateral complete cleft lip with alveolar and palatal cleft

The deformities

The deformities that occur in a cleft lip may be outlined as[2]

1. The premaxilla is rotated outwards and upwards and the lateral maxillary elements are often retropositioned
2. The inferior edge of the septum is dislocated out of the vomer groove and presents with the nasal spine in the floor of the normal nostril.
3. The collumela is shortened on the cleft side
4. The lower lateral cartilage is attenuated and malpositioned
5. The alar base of the cleft side is rotated outwardly in a flare
6. The alar rim is distorted by a skin curtain that droops over the alar rim like a web
7. The vestibular lining is deficient on the cleft side
8. The orbicularis oris muscle is usually hypoplastic and malinserted into the alar wing on the cleft side and base of the collumela on the non cleft side
9. The philtral height is shortened
10. The bilateral cleft deformities are essentially the same as that of the unilateral cleft except the collumela is typically more shortened and there is absence of philtral remnants and muscle elements in the grossly hypoplastic prolabium.

Feeding and Timing of Surgery

Infants with only clefts of the lip (Complete and Incomplete) can be breast fed with some difficulty and that is to be encouraged.

Patients with associated clefts of the palate have difficulties with sucking and consequently breast feeding[2]. Nasogastric feeding, spoon feeding and use of the cleft palate bottle are the options available. Prolonged use of nasogastric feeding invites URTI and is advocated to be avoided.

Foetal surgery is being practiced in certain specialized centers with promising results but the associated complications has prevented its widespread acclaim and the options are yet to be available in this part of the world.

Presurgical orthodontic treatment of collapsed alveolus is initiated in the first or second week following birth.

The initial procedure of lip repair is deferred till 10-12 weeks of age.

Indications for a prior lip adhesion in the first few weeks of infancy are debated but has been found to be helpful in wide complete cleft lips with poorly aligned maxillary segments.

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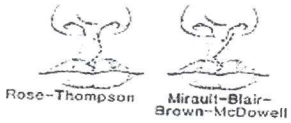
Surgical maneuvers

The repair of the unilateral cleft lip may be categorized on the application of the Z-plasty principle[6]. A mention of the different procedures is made here without going into the details of the procedures.

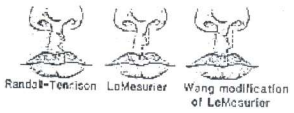
1.Straight line closure :
a. Rose-Thompson
b. Mirault-Blair-Brown-McDowe

Straight line



2.Lower Lip Z-plasty :
a. Randall-Tennison
b. LeMesurier
c. Wang modification of Le Mesurier

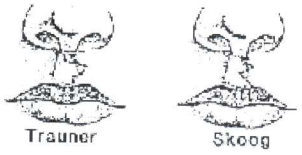
Lower Lip Z-plasties



3.Upper Lip Z-plasty :
a. Millard
b. Wynn

Upper Lip Z-plasties

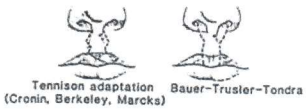
4.Upper and lower Lip Z-plasty : Upper and lower Lip Z-plasties
a. Trauner
b. Skoog



The bilateral cleft lip repair may be similarly outlined as

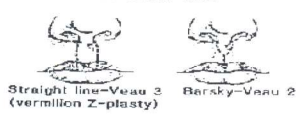
1.Straight line repair
a. Veau 3
b. Barsky-Veau 2

Straight line



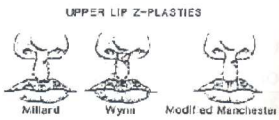
2.Lower Lip Z-plasty :
a. Tennison adaptation (Cronin, Berkeley, Marcks)
b. Bauer-Trusler-Tondra

Lower Lip Z-plasties



3.Upper Lip Z-plasties :
a. Millard
b. Wynn
c. Modified Manchester

Upper Lip Z-plasties



4. Upper and Lower lip Z-plasties : Upper and Lower lip Z-plasties
a. Skoog

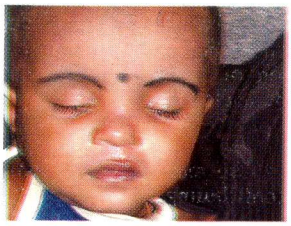


Figure II :
A postoperativeunilateralcleft lip

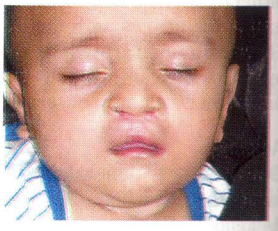


Figure III :
A postoperative bilateral cleft lip

Conclusion

In conclusion it is to be understood that the care of the cleft patient is not a sporadic surgery and requires a systematic program with a team approach. That each case is to be treated on its own merit and the devastating psycho-trauma of the family in general and parents in particular requires due consideration in the planning of a total treatment program for each individual.

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Cardiac Failure: The Concept and the Prospect

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Definition

Cardiac failure is a clinical state resulting from the inability of the heart to provide sufficient blood for tissue metabolic needs, resulting with symptoms of breathlessness, fatigue and intolerance.

*Refractory heart failure is the condition that persists or deteriorates despite intensive therapy.
*Intractable heart failure means when the condition is resistant to all regular therapeutic means.

Regulation of Cardiac Function

In the intact heart there are three principal determinants of the stroke volume (Fig. I).

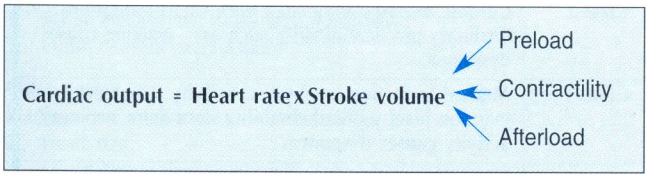

Figure I : Principal determinants of the stroke volume.

Preload

Preload is determined by the volume of blood in the ventricle at the end of diastole. The left ventricular end diastolic pressure (left atrial or let ventricular filling pressure) closely follows the left ventricular end- diastolic volume and is often used as an expression of preload. An increase in preload results in an increase in stroke volume ejected.

Contractility

Contractility is the force of ventricular contraction which is independent of loading; it depends on the interaction of the contractile proteins myosin and actin.

After load

After load is an expression of the resistance which a ventricle must overcome to eject the stroke volume. The total vascular resistance is the sum of the proximal resistance in the aorta (impedance) and the peripheral vascular resistance which is a reflection of the cross sectional area of the systemic vascular beds. If the vascular resistance is reduced ventricular ejection is facilitated and the cardiac output augmented. An increased peripheral vascular resistance leads to an increase in ventricular systolic pressure and wall stress and increases the radius of the ventricle. This leads to increased myocardial oxygen consumption and reduced ejection fraction (Fig. II).

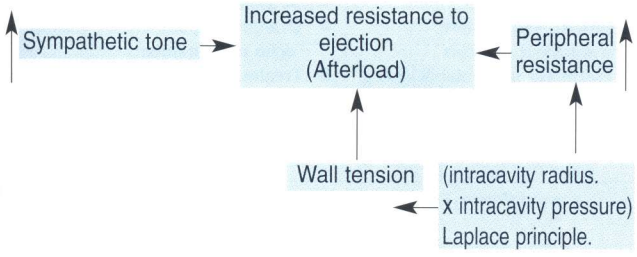

Figure II : Factors affecting afterload in cardiac failure.

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Pathophysiology

The pathophophysiological changes which result in cardiac failure in an individual depend on the mechanism and the resulting effects on the factors regulating cardiac function as mentioned in Table I.

Compensatory mechanism in cardiac failure

Mechanisms come into play to maintain cardiac output and organ perfusion pressure (mean arterial pressure)

Cardiac Mechanisms

1. Heart rate : Tachycardia may occur when the stroke volume is reduced.

2. Ventricular dilatation : As the ventricular volume increases (preload) the cardiac output is increased (Fig.II). The beneficial effects are lost when volume is greater than twice normal.

3. Ventricular hypertrophy: If an increased systolic load is sustained, compensatory ventricular hypertrophy occurs to maintain pump function.

Extracardiac Mechanisms

1.Following reduction in cardiac output, arterial pressure falls. This leads to stimulation of sympathetic nervous activity and withdrawal of vagal tone. Sympathetic activity has an advantageous effect by increasing the heart rate and contractility. Venoconstriction increases venous return and increases preload.

Arterial venoconstriction occurs with regional redistribution of peripheral blood flow to maintain the blood supply to skeletal muscle and heart. Although this vasoconstriction and redistribution is a useful short-term change a secondary reduction in cardiac output follows this increase in afterload (Fig. III).

Table-I : Causes of cardiac failure

Pressure load	
Left ventricle	Right ventricle
Aortic stenosis	Pulmonary stenosis
Hypertrophic obstructive Cardiomyopath	Pulmonary Hypertension
Hypertension	

Volume overload	
Left ventricle	Right ventricle
Aortic valve regurgitation	Atrial septal defect
Mitral valve regurgitation	Ventricular septal defect
Arteriovenous fistula	Pulmonary valve regurgitation
	Tricuspid valve regurgitation

Myocardial disease
Coronary artery disease
Congestive cardiomyopathy
Secondary cardiomypathy
Myocarditis

High output cardiac failure
Hyperthyroidism
Beri beri
Paget`s disease
Pulmonary emphysema

Renin - angiotensin- aldosterone system (RAAS)
Sympathetic stimulation via β_1 adrenorecptore, renal artey hypotension and decreased sodium delivery to the distal tubules stimulate the release of renin by kidney. Renin once in circulation, acts on $\propto_2$ globulin to release angiotensin-I. Angiotenisn-I has no apparent physiological effect. In a single passage through the pulmonary circulation angiotensin-I is to converted by a angiotensin converting enzyme (ACE) to octapeptide angiotensin-II a very potent vasoconstrictor and regulator of renal sodium reabsorption. Angiotensin-II also stimulate release of aldosterone, which promotes the reasorption of sodium and water by renal tubules. This Biochemical cascade is called RAAS. Neuroerdiocrione factors such as cytokines, endothelin and noradrenalin as produced greatly in heart failure. With these changes in RAAS and neuroendocrine system, leads to reduced cardiac output and increased in afterload (Fig. IV)

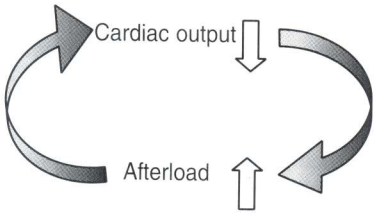

Figure III : The vicious circle in heart failure

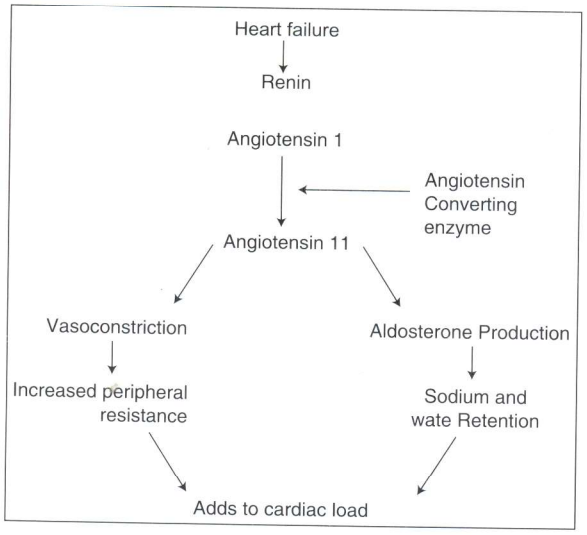

Figure IV : Mode of action of angiotensin-converting enzyme inhibitors.

Left Heart Failure

Symptoms

Dyspnoea

An increased awareness is the usual presenting symptom of left heart failure. Extertional dyspnoea is caused by increasing pulmonary vascular engorgement with decreased compliance secondary to inadequate emptying of the left ventricle. This leads to increased pressure in the left atrium and pulmonary veins. The New York Heart Association classification is useful in assessing the patient's symptomatic awareness (Table II). The patient may be dyspnoic when lying down (orthopnoea) and this may be relived by sitting in an upright posture. Paroxysmal nocturnal dyspnoea may occur as the first manifestation of hypertensive heart disease, aortic disease or mitral valve disease.

Acute Pulmonary Oedema

Acute left ventricular failure may be a dramatic illness which may lead to pulmonary oedema .
This results from rapid development of pulmonary capillary hypertension with an acute and marked transudation of fluid into the pulmonary alveoli. When the pulmonary capillary pressure reaches alveoli greater than the plasma oncotic pressure (25-30 mmHg) then transudation of fluid occurs and pulmonary oedema develops. Acute respiratory distress results with marked ventilatory impairment secondary to reduced gas exchange and increased work associated with breathing. Hypoxia occurs secondary to an increased resistance to air flow in and out of the alveoli. In addition there is alveolar flooding which reduces diffusion of gases from alveolar air into capillary blood. The sensation of dyspnoea may be

Table II : Functional status according to NYHA

Class-1	Patients with cardiac diseases but without limitation during ordinary physical activity.
Class-2	Cardiac diseases associated with slight limitations. Ordinary physical activity such as walking causes dyspnoea.
Class-3	Marked limitation in physical activity. Unable to walk even on level without disability; less than ordinary activity causes dyspnoea.
Class-4	Inability to carry on any physical activity. dyspnoea at rest.

extreme due to increased work in breathing. The mucous membranes are also engorged by oedema fluid leading to bronchocon striction (cardiac asthma). Increased mucus production may occur with precipitation of coughing and blood-tinged sputum may be produced secondary to small haemorrhages from congested bronchial mucosa.

Exertional Fatigue and Weakness

These may be manifestations of poor muscle and organ perfusion. Incresed vascular stiffness, secondary to fluid retention prevents a maximal increase in skeletal mascle blood flow despite maximal metabolic vasodilatation during exercise.

Table III : The Differential Diagnosis of Systolic Heart Failure and Heart Failure with Normal Systolic Function (Diastolic Heart Failure)

Systolic Heart Failure	Diastolic Heart Failure
• Large, dilated heart	• Small LV cavity
• Normal or low blood pressure	• Concentric LV hypertrophy
• Broad age group; more common in men	• Systemic hypertension
• Low ejection fraction	• Elderly women more common
	• Normal or increased ejection fraction
• S3 gallop	• S4 gallop
• Systolic and diastolic impairment by echo	• Diastolic impairment by various echo measurements
• Treatment well established	• Treatment not well established
• Poor prognosis	• Prognosis not as poor
• Role of myocardial ischemia	• Myocardial ischemia common
• Important in selected cases	

Signs

The rate, rhythm and quality of the pulse may be altered. The position and character of the cardiac apex. The quality and intensity of the heart sounds may be altered.
Nonspecific signs include tachycardia with pulsus alternans, cardiomegaly, gallop rhythm with third or fourth heart sounds and basal crackles.

Right Heart Failure

Right ventricular failure may occur secondary to left ventricular failure or develop from a primary intracardiac cause including mitral stenosis, polmonary valve stenosis, tricuspid regurgitation or congenital heart disease. The symptoms of right heart failure are secondary to an increase in the pulmonary artery pressure with resulting systemic venous distension, result into anoreia, right hypochondrial pain and leg edema. Clinical signs include elevated jugular venous pressure and evidence of functional tricuspid regurgitation may be present. A right parasternal heave of right ventricular hypertrophy is usually evident and a loud pulmonary second sound confirms pulmonary hypertension. Hepatomegaly is usually present.

Investigation

Electrocardiagraphy (ECG)

Routine ECG may give evdence of:

1. Myocardial infarction or ischaema.
2. Cardiac rhythm abnormality - brady cardia or tachy cardia.
3. Right or left venticular hypertrophy.

Blood

1. Serum electrolytes, blood urea, creatinine.
2. Other relevant examinations.

Chest x-ray

Routine chest x-ray is useful in confirming.

1. Heart size.
2. Qualitative indication of cardiac chamber enlargement.
3. The aorrtic and pulmonary artery dilatation may be of value.
4. Valvular calcification may be seen.
5. Pulmonary congestion may be evident with upper- lobe blood diversion and kerleys b lines.

Echocardiography

Noninvasive teachnique for assessment of:

1. Chamber dilatation
2. Valular diseases
3. Shunt anomaly.
4. Left ventricular function.

Management

The treatment of cardiac failure is determined by the severity of the clinical presentation, Which may very from life threatening pulmonary oedama to mild congestive changes with peripheral oedema. In many instances, particularly in the presence of congenital heart disease or valvular lesions, the enventual treatment will be surgical.

The general approach should include identification and treatment of precipitating factors; introduction of general measures and specific antifailure regimens; and a plan for long - term management.

Precipitating Factors

The factors listed in Table IV may affect the heart itself or increase peripheral circulatory or metabolic requirements

Table IV : Precipitating factors for cardiac failure.

Direct cardiac effects	Extracardiac effects
• Myocardial infarction • Arrhythmia: 1. Tachycardia 2. Bradycardia • Bacterial endocarditis • Drugs with negative inotripic activity, e.g. beta- adrenoreceptor- blocking compounds, antiarrhythmics. • Pulmonary embolism • Noncompliance with antifailure therapy	• Infection • Anaemia • Thyrotoxicosis • Excessive fluid transfusion • Physical or emotional stress

Precipitating causes (Table IV) should be treated vigorously as a previously stable clinical situation may be reestablished.

General Treatment

The major aims of treatment are to augment cardiac output and to reverse the pathophysiological changes which led to cardiac decompensation. The therapeutic approaches attempt to: 1. Increase salt and water excretion using diuretics 2. Enhance the contractility of the heart by the use of inotropic agents and 3. Nelieve pressure and volume overload by the use of compounds with arterial or venous dilating properties.

Supportive Measures

Rest

Bed rest with the patient in the semirecumbent position will reduce cardiac work and improve diuresis. Passive or active leg exercises should be encouraged to prevent the development of deep venous thrombosis. The early use of the commode for toilet requirements is of value and is helpful on psychological grounds. Progressive ambulation and full rehabilitation depend on an individual`s motivation and occupation.

Diet

Small, bland and attractive meals should be given with vitamin supplementation when required. In severe cases sodium restriction may be required.

Diuretic Therapy

Diureties inhibit sodium reabsorption by the kidney, reduce intravascular volume and hence the left ventricular volume. This reduction in preload reduces the back pressure effects of cardiac decompensation. In addition a reduction in the sodium content of arteriolar walls cause reduced impedance and a degree of afterload reduction.

Loop diuretics are very potent and have a prompt onset of action. They inhibit sodium and chloride transport in the ascending limb of the loop of Henle. It is active by both the iv and oral route. It has a wide therapeutic range and its effects are proportionate to dosage. A dose of up to 500 mg may be effective when the glomerular filtration rate is less than 20 ml/min. In cardiac failure, the oral bioavailability may be reduced and a diuresis may be obtained by changing to iv administration.

Aldosterone Antagonists

Spironolactone is a competitive antagonist of aldosterone, the most potent endogenous mineralocorticoid. It is useful in the management of congestive cardiac failure particularly particularly in the presence of hepatic congestion when secondary hyperaldosteronism can occur. Spironolactone antagonizes potassium excretion and may be a useful adjunctive therapy in patients who are hypokalaemic on other diuretic therapy. It is effective in an average daily dose of 100 mg given in divided doses. The onset of action may be at least 48-72 hours.

Vasodilators

The most important recent innovation in the treatment of cardiac failure has been the use of compounds with vasodilating (Table V).Vasodilators may benefit cardiac failure by reduction of afrerlaod and of preload. When the systemic vascular resistance is reduced and impedance to left ventricular ejection lowered, then an enhanced ejection fraction and stroke volume result. In most patients with congestive cardiac the haemodynamic changes are a combination of a low cardiac output and high ventricular filling pressure, and hence therapy with compounds which have both arteriolar and venous dilating effects have been used. Patients with severe cardiac failure and resistant cedema, combination therapy with diuretics with different modes of action is indicated. The most prominent of the vasodilation currently at use are ACE-I.

The ACE-I an useful in heart failure by decreased production of angiotensin II, ircreased production of bradykinin, excretion of salt and water, attenuation of aldostrone effect, decreases sympathetic nerve actively and decrease in plasma eatecholamines. Furthermore ACE-I prevent & reverses remodeling of heart. Macroscopic changes of remodeling of heart are end-diastolic volume end systolic volume, change of ventricular morphology towards spherical shape and increase in LV mass. Microscopically, chargesassociated with cardiac remodeling are interstitial fibrosis, myocyte hypertrophy, apoptosis.

Table V: Vasodilator drugs used in cardiac failure.

Drug	Route of administration	Mode and site of action
Nitrates	IV. oral, sublingual transdermal	Direct effects on veins: High dosage may reduce arterial pressure. Predominant effect on venous capacitance vessels with reduction in preload.
Prazosin	Oral	Postsynaptic alphareceptor- blocking agent. Mixed venous and arteriolar activity.
ACE-I Captopril Lisinopril Ramipril enalapril	Oral	Angiotensin - converting enzyme inhibitor (ACE) Exhibits mixed venous and arteriolar dilataion leading to dpreload and afterload.

Inotropic Agents

The ideal inotropic agent should have:

1. Efficacy There should be adequate cardiac stimulation without detrimintal peripheral vasoconstriction or oxygen - Wasting tachycardia from reflex or direct stimulation.
2. Rapid onset of action with a wide therapeutic ratio, few side effects and persistent activity with absence of tachyphylaxis .
3. Intravenous and oral formulations to allow acute and long-term therapy to be administered.

Although many compounds are available none fulfil the criteria.

Cardiac Glycosides

The mainstay of inotropic treatment remains the cardiac glycosides.Their principal indication is the presence of congestive cardiac failure with associated atrial fibrillation, Where slowing the ventricular rate is probably more beneficial than direct inotropic activity. Controversy remains concerning the role in patients who remain in sinus rhythm. In high- output states such as thyrotoxicosis and in pulmonary heart diseases, the response to digoxin (Lanoxin) may be disappointing. Digoxin is the most commonly used and can be given by the parenteral or oral route. The onset of action is 15-30minutes, its peak effecct 2-5 hours and elimination half life is 36 hours. Elimination is predominantly determined by glomerular filtration and renal excretion of the unchanged molecule. With digoxin the major determinant of the elimination half- life, is renal function. The maintenance dose must be reduced if renal function is subnormal. There is a narrow therapeutic ratio, the normal therapeutic range being 1-2 ng/ml potassium and glycosides compete for myocardial binding sites and hypokalaemia can exaggerate the toxic effects of glycosides. In patients with marked renal inpairment, digitoxin may be of use in view of its hepatic route of excretion.

β-blockers in Heart Failure

In CHF, there is our enormous increase in noradrceline concentration in myocardium, where levels rise ten times more than other organs. Among the deletetrious effects of noradrenaline are myocyte hypertrophy and death, dilatation, ischaemia, and ariythmias. Hence, blocking the adrenergic receptors is rational approach to therapy, depinding on the characteristies of the blocking agent. The adverse effects of noradrenaline are mediateal by there receptor β_1, β_2 and $\propto_1$, with the β_1 and β_2 receptors responsible for most cytotoxic, inotropic and chsonotrophic effects. Selective β_1- receptor blockade reduces contractile support but also increase systemic vascular resistance, effects that can be deleterious in combination.

In CHF there is an imbalance in neuroendorine factors, with an overproduction of growth promoting substances such as cytokines, angiotensin II, endothelin and noradrelanine. The production of balancing factors like natriuretic peptides, bradykinin and nitric oxide, is insufficient to moderate the growth-promoting effects. Hence the therapeutic effects of blocking adrcnergic receptors, allowing for action form the antigrowth factors. Conventional β-blockers such as metoprolol and bisiprolol block the β_1- receptor only. Comprehensive blockade of β_1, β_2 and $\propto_1$ would provide a more extensive protection against the toxic effects of noradrelanine. Carvedilol is a β-blocker which has the property of comprehensive blockade quality of β_1, β_2 and $\propto_1$ receptors and is therefor a drug of choice as a adrenssic blocks for the prevention of catecholamine toxicity, reduction of myocardial ischamics, prevention of coronery Thrombosis, reduction of arrbythings, prevention of remodeling and induction of regression of established remodelling, allowing action from antigrowth factors by depresing, nueroendrocrine substances acute and chronic hemodynamic changes like reduction in mean arterial pressure, systemic vaseular resistanceLV filling presure and vasodilatation antiprahyerative and antitioxidanal effects. Those it may be recommended that patient with CHF due to LV systolic dysfinction, should receive ACE-I in all stage of CHF. and adrenergic - blocker in class II and III CHF unless intolerant or contraincdicated. Patients with AF and CHF should be treaeal with a Combination of carvedilol and digoxin rathem them alane, heside giveng ACE-I.

Alternatives to ACE Inhibitors

Angiotensin II receptor antagonists several ARBs are approved by the FDA for the treatment of hypertension (losartan, valsartan, irbsartan, candesartan, telmisartan and eprosartan) Although trials are in progress involving the use of ARBs alone of in combination with ACE inhibitors in heart failure, none have been approved for this purpose. The present use of ARBs for the treatment of CHF is limited to patients who experience intolerable cough of angiodema while receiving ACE inhibitors. Several small studies have clearly demonstrated the added benefits of combined ARB and ACE inhibition on LV performance, functional capacity, and safety. The addition of ARBs to ACE inhibitors is extremely well tolerated even in patients who do not tolerate high doses of ACE inhibitors because of symptomatic hypotension.

This may be explained by the fact that ARBs are specific vasodilators that lower vascular resistance primarily to essential organs such as the heart, brain, and kidneys. In contrast, as a result of the concomitant increases in kinin levels, ACE inhibitors are also nonspecific vasodilators that lower vascular resistance to cutaneous tissues and splanchnic beds. In addition, ARBs are associated with a greater improvement in plasma fibrinolytic parameters than that achieved by ACE inhibitors. Thus, the effects of angiotensin II can be attenuated clinically by two fundamentally different strategies blocking systemics formation of angiotensin II through ACE-I and blocking the action of angiotensin II at the AT_1 receptor with angiotensin receptor blockers (ARB).

Diastolic Dysfunction

Diastolic dysfunction of the left and right ventricles often leads to all the signs and symptoms of systolic dysfunction, but the therapeutic approach varies for these two condition. Often , there is significant LV hypertrophy present, and aggressive management of systemic hypertension is required. These patients develop significant congestion, and so diuretics are often necessary. Digoxin is probaby of no use unless the patient is in atrial fibrillation. Tachycardia must be avoided. Rate- lowering calcium blockers (verapamil, diltiazem) are useful drugs of choice for reducing elevated blood pressure, keeping the heart rate under control, and improving ventricular compliance, Beta - adrenergic blockers are first line therapy for maintaining relative bradycardia to maintain time for diastolic ventricular filling. Both verapamil and beta blockers can be used with caution in patients with heart failure caused by hypertrophic cardiomyopathy.

Drug therapies under investigation

Natriuretic peptides and their enhancrs: Conventional diuretics are associated with undesirable stimulation of the reninangiotensin axis, sympathetic nervous system, and vasopressin. (ANP) atrial natuivretic prybid and brain natriuretic peptide (BNP) by contrast, induce diuresis and natriuresis while concomitantly suppressing the renin- angiotensin axis with dilation of peripheral vascular beds (atricl natriuretic peptide). Favorable hemodynamic responses have been observed after ANP infusion, including a fall in pulmonary capillary wedge pressure (PCWP), plasma renin activity, and systemic vascular resistance and an increase in cardiac output. Neutral endopeptidase (NEP) inhibitor administration is associated with a rise in endogenous ANP levels resulting from the inhibition of ANP metabolism. The natriuretic properties of NEP inhibitors are mediated by inhibition of sodium reabsorption within the renal tubule, since they do not alter renal hemodynamics (GFR or renal plasma flow) significantly. NEP is also shown to enhance prostacyclin synthesis, excrting natriuretic effect. The natriuretic effect of BNP infusion is surprisingly and significantly more pronounced in-patients with CHF than in normal patients.

Mechanical support of the heart

Indications

In the setting of failure of dobutamine or vasodilator therapy to improve the hemodynamic status of the patient, and of the necessity for other catecholamine therapy to maintain a cardiac output and/of blood pressure, intraaortic balloon counter pulsation may be necessary.

Timing

In the patient with hypoperfusion and pulmonary congestion, no more than 1-2 hours of pharmacologic trial should be permitted and then only with blood pressure being maintained at 90 mm Hg systolic by pressor agents before a decision is made to proceed with intraaortic balloon counter pulsation.

Surgical Treatment

1. Biventricular Cardiac Pacing

Cardiac resynchronization therapy (CRT)

The use of dual- chamber biventricular pacemaker rechnology to treat patients with chronic heart failure has been proposed. It has been proposed that by altering the timing, sequence, and site of cardiac electrical activation in patients with heart failure, hemodynamic abnormalities may be favorably altered.

2. Implantable cardioverter defibrillators

There is some evidence that the effcacy of this device in terminating ventricular tachycardia or ventricular fibrillation may translate into improved survial in patients with heart failure, but no definite proof exists. Studies are in progress that are designed to address this issuses. Data suggest improved survival compared with conventional antiarrhythmic therapy, including amiodarone, in patients with asymptomatic LV dysfunction or mild to moderate heart failure. For patients with sever heart failure effectiveness in this setting has not been proved.

3. Heart transplantation

Heart transplantation is now an accepted mode of treatment for end-stage CHF. Transplantation significantly increases survival, exercise capacity, return to work, and quality of life compared with conventional treatment provided that proper selection criterea are applied. Patients who should be considered for transplantation are those with severe CHF with no alternative form of treatment. The long term outcome is limited predominantly by the consequences of immunosuppression (infection, hypertension, renalfailure, malignany, accelerated progression of heart failure.

Long Term Management

When the symptoms and signs of cardiac failure have been adequately treated, and the patient's general condition stabilized, It is important to determine the exactnature of the underlying cardiac disease, its severity, and whether further investigation should be performed to consider the patient for sugical therapy. This is patients with congenital heart disease and those with ischaemic heart disease when the possibility of the developmint of cardiac aneurysm after myocardial infarction or the development of mitral valve regurgitation secondary to capillary muscle dysfunction must be considered. The long term rehabilitation abviously depends on the patient's occupation, if employed, and the amount of support available if the patient is, for example, a housewife. Adequate symptomatic review and clinical examination should be undertaken and routine biochemical, haematological and drug level monitoring performed where indicated.

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Hyperemesis Gravidarum

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Introduction

Hyperemesis gravidarum (HEG) means excessive or most severe type of vomiting during pregnancy. Different studies showed that nausea occurs in 66-89% of pregnancies and vomiting in 38-57%. The nausea and vomiting associated with pregnancy almost always begins by 8-10 weeks of gestation, peaks at 11-13 weeks, and resolves (in 50% of cases) by 12-14 weeks. In 1-10% of pregnancies, symptoms may continue beyond 20-22 weeks[1].

Nausea and vomiting is very common during pregnancy. HEG is characterized by persistent nausea and vomiting associated with ketosis and weight loss (>5% of prepregnancy weight). HEG may cause volume depletion, altered electrolytes, and even death. Hospitalization is not infrequent.

Incidence

There has been marked fall in the incidence during the last 30 years. It is now rarity in hospital practice (less than 1 in 1000 pregnancies). The reasons are: (a) better application of family planning knowledge which reduces the number of unplanned pregnancies, (b) early visit to the antenatal clinic and (c) potent antihistaminic, antiemetic drugs. Internationally, HEG appears to be more common in westernized industrialized societies and urban areas than rural areas[2].

Etiology

The etiology is obscure but the following are the known facts: 1. It is mostly limited to the first trimester. 2. It is more common in first pregnancy, with a tendency to recure again in subsequent pregnancies. 3. It has a familial history- mother and sister also suffer from the same manifestation. 4. It is more prevalent in hydatidiform mole and multiple pregnancy. 5. It is more common in unplanned pregnancies but much less amongst illegitimate ones.

Pathophysiology

The physiologic basis of HEG is controversial. The following theories have been proposed:

Psychological abnormalities

Early work on the cause of both nausea and vomiting in pregnancy and HEG suggested that women with these symptoms were unable to accept pregnancy, had problems with their relationships with their mothers, or had personality disorders and/or hysteria. However, nausea and vomiting in pregnancy is now recognized as affecting the majority of women3. Some cases of HEG may represent psychiatric illnesses, including Munchausen syndrome, conversion or somatization disorder, and major depression, or they may occur under situations of stress or ambivalence surrounding the pregnancy. However, HEG may occur in the absence of psychological illness or stress.

Hormonal changes

Homology exists between the human chorionic gonadotropin (HCG) molecule and its receptor and the thyroid-stimulating hormone (TSH) molecule and its receptor. HCG can physiologically stimulate the thyroid. HCG levels peak in the first trimester.

HEG appear to have clinical hyperthyroidism. However, in a larger proportion (50-60%), TSH is transiently suppressed and the free thyroxine (T4) index is elevated (40-73%) with no clinical signs of hyperthyroidism, circulating thyroid antibodies, or enlargement of the thyroid[4].

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Some women with HEG appear to have clinical hyperthyroidism. HCG levels were linked to increased levels of immunoglobulin M, complement, and lymphocytes. An immune process may be responsible for increased circulating HCG or isoforms of HCG with a higher activity for the thyroid.

Some studies link high estradiol levels to the severity of nausea and vomiting in patients who are pregnant, while others find no correlation between estrogen levels and the severity of nausea and vomiting in pregnant women. Previous intolerance to oral contraceptives is associated with nausea and vomiting in pregnancy[5]. Progesterone also peaks in the first trimester and decreases smooth muscle activity; however, studies have failed to show any connection between progesterone levels and symptoms of nausea and vomiting in pregnant women.

Gastrointestinal dysfunction

Elevations in female sex hormones during pregnancy may change esophageal, gastric, and small bowel motility. Although progesterone appears to decrease lower-esophageal sphincter pressure, a number of studies have found no decrease in lower-esophageal sphincter pressure during pregnancy. Studies on gastric emptying demonstrate that it is unchanged in pregnancy. However, some studies have correlated alterations in gastric myoelectrical activity in the first trimester of pregnancy with nausea[6]. Small bowel transit time increases in pregnancy, but only in the second and third trimester.

Hepatic dysfunction

Many investigators have targeted changes in liver function as a possible cause of HEG. Patients with HEG often demonstrate abnormalities of liver enzymes. Liver disease can cause symptoms of nausea and vomiting, and abnormalities have been found on liver biopsy samples from patients with pregnancies complicated by HEG. Theories postulate either an increased sensitivity of the liver to the hormonal alterations of pregnancy or abnormalities in steroid inactivation; however, not all patients with HEG show liver abnormalities.

Lipid alterations

Jarnfelt-Samsioe et al found higher levels of triglycerides, total cholesterol, and phospholipids in women with HEG compared to matched, nonvomiting, pregnant and nonpregnant controls. This may be related to the abnormalities in hepatic function in pregnant women.

Infection

Recent studies have found a relationship between infection with Helicobacter pylori and HEG. In a study by Kocak et al of 95 patients with HEG and 116 matched controls, H pylori infection was found in 91% of patients with HEG compared to 45% in controls[7].

Diagnosis

History

The defining symptoms of HEG are gastrointestinal in nature and include nausea and vomiting. Other common symptoms include ptyalism (excessive salivation), fatigue, weakness, and dizziness.

Patients may experience sleep disturbance, hyperolfaction, dysgeusia, decreased gustatory discernment, depression, anxiety, irritability, mood changes, decreased concentration etc. When obtaining history from the patient, present symptoms can be discussed. Information pertaining to the timing, onset, severity, pattern, and alleviating and exacerbating factors (eg, relationship to meals, medications, prenatal vitamins, stress, other triggers) should be obtained.

A thorough review of systems for any symptoms that might suggest other gastrointestinal, renal, endocrine, and central nervous system disorders is vital. Review past medical history, placing emphasis on past medical conditions, surgeries, medications, allergies, adverse drug reactions, family history, social history (including support system), employment, habits, and diets. Obtaining a thorough gynecologic history of symptoms, such as vaginal bleeding or spotting, past pregnancies, past use of oral contraceptives, and response to oral contraceptives used, is important.

Physical examination

The physical examination is usually unremarkable in patients with HEG. The physical examination findings may be more helpful if the patient has unusual complaints suggestive of other disorders (eg, bleeding, abdominal pain).

Attention should be paid to the vital signs, including standing and lying blood pressure and pulse, volume status (eg, mucous membrane condition, skin turgor, neck veins, mental status), general appearance (eg, nutrition, weight), thyroid, abdominal, cardiac and neuralgic examination findings. Signs of dehydration may occur, including ketones in urine, increased hematocrit, increased pulse rate and decreased blood pressure.

Differential diagnosis

Acute renal failure, addison disease, appendicitis, biliary disease, esophagitis, fatty liver, gastroenteritis, gastroesophageal reflux disease, hepatitis,hyperparathyroidism, hyperthyroidism, ileus, nephrolithiasis, acute pancreatitis, peptic ulcer and intracranial lesions.

Management

The treatment goal is to control vomiting, correct dehydration, restore electrolyte balance, correct weight loss and maintain adequate nutrition. Hospitalization should be considered when the following conditions are present:

- vomiting and symptoms of nausea persist
- weight loss is greater than 5%
- fluid and electrolyte replacement

Fluids

Oral feeding is held up for at least 24 hours after the cesation of vomiting. During this period fluid is given preferably intravenous method. The amount of fluid to be infused in 24 hour is calculated as the total amount of fluid approximates 3 litres per day of which 1.5 litre with 5% dextrose and 1.5 litre with 5% dextrose saline. Extra 5% dextrose equal to the amount of vomitus and urine in 24 hours is to be added. With this regime dehydration, keto-acedosis, water and electrolyte imbalance are likely to be corrected. Intravenous potassium supplement should be withheld unless facilities for blood biochemical and ECG monitoring are available. Potassium overloading may result in heart block. Insulin 10 units per bottle of infusion may be helpful to encourage intracellular shift of potassium ion and to facilitate glycogen storage. The drip rate per minute is calculated as number of litres of fluid to be infused in 24 hours x 12.

Other Drugs

No medications to control this condition have been widely accepted for use during pregnancy. However, some antiemetics commonly prescribed to address the symptoms of HEG are Promazine or Diazepam, Phenergan, Metclopramide, Tigan, Vitamin B1, B6, Vitamin C, Vitamin B complex, hydrocotisone (in case of severe hypotension).

Conclusion

HEG in pregnancy is extremely common. When nausea and vomiting is very severe, the patient may need hospital admission with intravenous fluids and IV medications. Rarely, she will require liquid food and nutrients through her veins or via tube into her intestines. Fortunately, this is very uncommon and is reserved for the most severe cases.

Treatment is usually by modification of diet, including eating foods that taste good and do not cause nausea. Additionally, eating many small meals, rather than three large meals, may be helpful. In some cases medications may be used, which are considered safe for use during pregnancy. In rare cases, hospitalization and evaluation for thyroid or other medical problems may be required.

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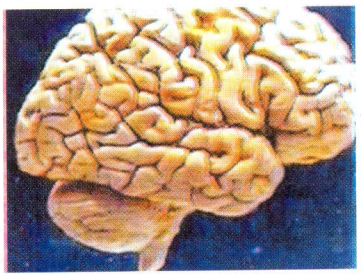
Alzheimer's gene treatment hope

Gene therapy could be used to attack the protein which clumps together into dangerous plaques in the brains of Alzheimer's patients, researchers say. Scientists have also identified a type of brain cell which could also prevent the build up of plaques. In the first study, researchers an enzyme was used to reduce levels of the protein by up to 50% using gene therapy. The neprilysin enzyme naturally reduces the accumulation of the protein beta-amyloid which makes up amyloid plaques in the brain.



Plaques build up in the brains of Alzheimer's patients

Mechanisms

Researchers from the Salk Institute and University College of San Diego and the University of Kentucky carried out the study, published in the Journal of Neuroscience. They used a modified version of the HIV virus to transfer a gene for neprilysin to neurons of genetically modified mice which produced human beta-amyloid. The researchers concentrated on two areas of the brain, the hippocampus and the frontal cortex, areas where plaque formation occurs in humans. Plaques which built up close to where neprilysin was injected were found to be smaller and more compact than in other regions of the brains. In some cases, the so-called plaque "load" was reduced to less than half that found in comparable, untreated areas. The treatment also eliminated damage linked to the build-up of beta-amyloid. Dr Fred Gage, of the Saks Institute, said: "What's significant about this is that neprilysin isn't a drug, but a molecule that controls levels of beta-amyloid naturally.

bbc.com/health

Stroke and it's management.

Hossain S A[1], Abeden Z[2], Begum F[3]

The Orion 2003 ; 15 : 80-81

Acute stroke

It is of no doubt that acute stroke are now a treatable condition and drug treatment and specialist care both influence survival and recovery. In this review article we will be discussing about the early diagnosis of a stroke and it also considers the optimal approaches to diagnosis and early management and lastly stoke medicine and its value in management of stroke.

Conditions requiring referral to hospital

Admit to hospital

- Neurological deficit lasting 1 hour or more
- Dependent patients that is moderate to severe stroke
- Transient inchaemic attack lasting 1 hour or more
- More than one transsient ischaemic attack within a week
- Transient inchaemic attack on anticoagulation
- Patient presenting to hospital
- At request of general practitioner

Refer to cerebrovascular clinic

Independent patient more than 48 hours after stroke (withhold aspirin)

Transient ischaemic attack lasting less than 1 hour (give aspirin)

Symptoms and signs of stroke

Anterior circulation strokes	Posterior circulation stroke
• Unilateral weakness	• Isolated homonymous hemianopia
• Unilatered sensory loss or inattention	• Diplopia and disconjugate eyes
• Isolated dysarthria	• Nausea and vomiting
• Dysphasia	• In coordination and unsteadiness
• Vision:	
Homonymous hemianopia Monocular blindnes Visual inattention	Unilateral or bilateral weak ness and/or sensory loss Non-specific singns • Dysphagia • Incontinence • Loss of consciousness

Stroke is a sudden neurological deficit of vascular origin and is a clinical syndrome manifested by it. The world is putting most of its attention towards the disease like cerebrov cular diseases because of its mortality and morbidity. It is a common and devastating condition that causes death in one third of patients at six months and leaves another third permanently dependent on the help of others. Each year in the United Kingdom there ar 110 000 first strokes and 30 000 recurrent strokes; 10 000 strokes occur in people younger than 65 and 60 000 people die of stroke. Correct management relies on rapid diagnosis and treatment, thorough investigation, and rehabilitation.

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Patients should be assessed at hospital immediately after a stroke. They may need to go straight to hospital rather than wait to see their general practitioner since hyperacute treatments such as thrombolysis must be administered within as little as three hours after stroke. Ambulance crews can be trained to apply simple screening questions to identify likely stroke patients. Stroke is strictly a clinical diagnosis, but brain imaging is required just to distinguish ischaemia from primary intracerebral haemorrhage and to exclude the other diseases that mimic like stroke. The pattern of neurological sings, includin g evidence of motor, sensory, or cortical dysfunction and hemianopia, can be used to diagnose certain clinical subtypes and thus to predict prognosis. Other sings also relate to outcome and may help identify the cause. If neurological symptoms resolve in less than 24 hours, the traditional diagnostic label is "transient ischaemic attack" rather than stroke.

Pathophysiology

There are two types of stroke once subarachnoid haemorrhage has been excluded. Ischaemia accounts for 85% of presentations and primary haemorrhage for 15%. Haemorrhage causes direct neuronal injury, and the pressure effect causes adjacent ischaemia. Primary ischaemia results from atherothrombotic occlusion or an embolism. The usual sources of embolism are the left atrium in patients with atrial fibrillation or the left ventricle in patients with myocardial infarction or heart failure.

Consider stroke if the following symptoms appear :
Sings of stroke at clinical examination

- Conscious level
- Neurological sings
- Blood pressure
- Heart rate and rhythom
- Hear murmurs
- Peripheral pulses
- Systemic signs of infection or neoplasm

Emergency management

Within the first hours after onset of cerebral ischaemia part of the brain is under threat of death. The infarct core may be densely ischaemic and will inevitably die, but there is also tissue with a compromised blood supply balanced on a knife edge between death and recovery. At this stage, oxygenation and haemodynamic and metabolic factors are crucial. The emergency management of stroke requires medical stabilisation and assessment of factors that may lead to complications (such as swallowing and hydration); thrombolysis may be considered. An acute stroke unit concentrates patients, healthcare staff, resources, and expertise into one area, and such units may be associated with a better outcome.

Investigations

Patients with acute stroke should have computed tomography of the brain to distinguish ischaemic and haemorrhagic stroke. This separation is vital since subsequent investigations and treatment differ for the two types. Neuroimaging will also identity conditions mimicking stroke and can helppredict outcome. Ideally, imaging will be performed soon after admission. Magnetic resonance imaging of the brain may eventually replace computed tomography since it not only identifies stroke anatomy but can also assess blood flow and perfusion in the brain, detect whether lesions are new or old, and identify carotid artery stenosis.

Investigation of stroke

All patients

- Computed tomography (ro magnetic resonance imaging)
- Electrocardiography
- Chest radiography
- Full blood count
- Clotting screen
- Electrolyte and creatinine concentrations

Subgroups

- Carotid duplex scanning
- Echocardiography
- Thrombophilia screen
- Immunology screen
- Syphilis serology
- Cerebral angiography (rarely)

Acute intervention

Firm evidence from two large trials has shown that aspirin (160-300 mg daily by mouth, nasogastric tube, or rectum) started within 48 hours of onset of acute ischaemic stroke reduces the risk of subsequent death and disability. However, the effect of aspirin is small and is principally mediated through reducing the risk of early reinfarction. Imaging is recommended before starting aspiring. A large trial of unfractionated heparin in stroke patients found that heparin did not improve outcome, even in patients with presumed embolic stroke. Heparin may still be useful in certain groups of patients.

Thrombolysis with alteplase within three hours of onset of stroke significantly increases the chance of a near complete recovery when administered by specialists. Treatment up to six hours after stroke has been found less effective in meta-analysis of randomized controlled trails.

Patients with a large cerebellar infarct or bleed should be referred for immediate neurosurgical evaluation to facilitate evacuation of the clot or infarct, or shunting for acute hydrocephalus, if required. Anticoagulants should be reversed in patients with primary intracerebral haemorrhage.

Stroke may be complicated by several conditions that can alter outcome adversely. Hyperglycaemia, fever, and hypertension are each associated with a poor prognosis. In the absence of trial evidence, raised glucose concentrations should be normalised and paracetamol given for fever. In contrast, hypertension should not be treated for the first week since some antihypertensive drugs (notably calcium channel blockers) seem to worsen outcome, possibly by reducing regional cerebral blood flow. Large ischaemic strokes are often complicated by oedema, sewllin, and herniation leading to death; no proved treatment is availabe for these complications.

Compications of stroke

Hyperglycaemia, Hypertension, Fever, Infarct extension or rebleeding, Cerebral oedema, herniation, coning, Aspiration, Pneumonia, Urinary tract infection, Cardiac dysrhythmia, Recurrence, Deep vein thrombosis, pulmonary embolism

Rehabilitation

The principal aims of rehabilitaion are to restore function ard reduce the effect of the stroke on patients and their carers. Rehabilitation should start early during recovery with assessment and mobilization while the patient is in the acute stroke unit. Once patients are medically stable, they should be transferred to a stroke rehabilitation unit if further rehabilitation is required. Formal rehabilitation in a stroke unit is associated with reduced death and disability and a shorter stay in hospital. Optimal care is multidisciplinary: doctors, nurses, physiotherapists, occupational therapists, speech and language therapists, dieticians, psychologists, and social workers all have a role.

Secondary prevention

Secondary prevention (apart from blood pressure control) should start shortly after admission. All patients should be offered lifestyle guidance, including advice to stop smoking, reduce saturated fat and salt consumption and alcohol intake, lose weight, and increase exercise. Aspirin started for the treatment of acute ischaemic stroke should be continued indefinitely for secondary prevention.

Stroke management is now supporte by good quality evidence, but many questions remain unanswered. Whenever possible, patients should be given the opportunity to enroll in randomized trials of acute interventions, rehabilitaion, or secondary prevention.

Steps on stroke medicine

Separate subspecialty for stroke

Units should focus on clinical problems rather than diseases.

There are many arguments for stroke management. Many suggest a midification of their proposal. They state correctly that during the past 20 years knowledge of stroke (its course, pathophysiology, effective interventions, etc) has increased greatly. The knowledge base seems likely to continue to grow in the next few years. It is, however, much less certain that there will be an equivalent widespread improvement in service provision. Something needs to be done about this. The creation of a stroke specialty is one option, and the suggestion needs careful consideration. Three points are perhaps woth making. An opportunity now exists to refashion some parts of medical practice, with and increased emphasis on clinical problems rather than diseases. Such an approach would involve identifying what various diseases have in common with each other. Without any doubt stoke medicine should take care of some points.

Prevention

The risk factors for coronary artery diseasse and stroke are similar. Perhaps what is needed is a locality based cardiovascular disease prevention service dealing with such common problems as hypertension, cardiac arrhythmias, and transient ischaemic attacks.

Acute management

Major hospitals might in future have an acute brain damage unit dealing not only with stroke but also perhaps with traumatic brain injury and acute encephalopathies. Such units hould be in a good position to deeal with a wide range of problems (for example, cerebral ischaemia, raised intracranial pressure, convulsions, respiratory difficulties, and nutritional problems)

Rehabilitation

Patients with stroke do better when looked after on a stroke unit.

Acknowledgement:

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Recent Advances in Postpartum Hemorrhage (PPH)

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The Orion 2003 ; 15 : 82

Introduction

Post Partum hemorrhage is one of the important cause of maternal mortality in Bangladesh and in other industrialized and non industrialized countries.[1] No doubt prevention of PPH and active treatment of PPH could bring down the maternal mortality rate (MMR).

One of the primary objective of management of 3rd stage of labour is prevention of PPH, this approach may be active or expectant.[2] Active treatment involves oxytocic therapy at the delivery of anterior shoulder or shortly after delivery of the baby, early cord clamping and placental separation. On the other hand expectant treatment means, nothing is done, Placenta is allowed to deliver spontaneously by maternal effect and sometimes by gravity.[3] Active management is associated with significant about 40% reduction of PPH.

Injectable prostaglandin may be superior to oxytocic in decreasing blood loss but safety data's are still inadequate to recommend. Misoprostol E1 analogue has been reported for prevention of PPH. Oral misoprostol is effective but associated with shivering and pyrexia.[4] Who collaborate trial of misoprostol for management of 3rd stage labour showed much side effect with 600 ug but non with the dose of 400 ug. Rectal Misoprostol is well tolerated and effective to reduce PPH.

Bleeding from episiotonmy may contribute to PPH. Restricted use of episotomy associated with less morbidity of perineal trauma and less blood loss.

Retained placenta may contribute maternal death from bleeding if left untreated, prompt manual removal of placenta under G.A is the treatment option. Other measures include-umbilical injectal of saline and oxytocic. Early sucking and nipple stimulation not shown to be effective to reduce PPH.[5]

Treatment of PPH

Nonsurgical methods involves, uterine massage, oxytocic, placental removal ascertaining of origin of bleeding. Immediate measure include compression of aorta against sacral promontary[6] and bimanual compression of uterus.

Uterine contraction need to be stimulated by uterine massage and injection of oxytocic with or without ergometrin I.V. as a bolus or in drip. If this method fails prostaglandin-F2a 250 μg I.M.[7] is recommended. Rectal misoprostol administration is promising.

Once medical treatment fails, prompt decision of surgery should be taken. Delay in decision may increase maternal mortality. Blood transfusion and early involvement of haematologist is very important. Under G.A uterus, vagina, fornices and cervix need to be explored under good light. Any retained product of conception are removed manually or with ovum forcep. choice intrauterine packing and use of segstaken blaknone tube or folley's catheter with a large bulb depends upon individual surgeon. But these methods are not systematically evaluated. If bleeding is due to rupture-repair or hysterectomy may be needed accordig to the case.

If no tear or trauma, Internal iliac artery ligation or stepwise ligation of uterine and ovarian arteries may be effective when these measures fails subtotal and total hysterectomy is the choice.

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Recently B-lynch or Brace suture may avoid the need of hysterectomy. PPH is an emergency which requires swift action and systemic approach. Successful management of PPH will bring down maternal mortality in Bangladesh.

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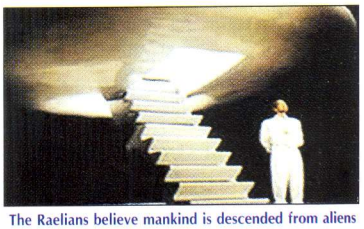
Company shows 'cloned baby'

Previous promises of DNA proof were not followed up

A company claiming to have created the world's first cloned babies has distributed a photograph of one of the "clones" for the first time.

Clonaid said a picture of an infant in an incubator published on its website showed the third of five babies supposedly cloned since December. Many scientists have dismissed Clonaid's claim that any babies were ever cloned at all, pointing to the absence of DNA proof. But the company, which is linked to a sect maintaining that humans were created by aliens, insists the picture shows "the third clone baby", allegedly born in Japan. Its president, Brigitte Boisselier, handed out copies of the photograph on Monday on a visit to Brazil to promote the company.



The Raelians believe mankind is descended from aliens

The Raelians believe mankind is descended from aliens Ms Boisselier, who is also a "bishop" of the Raelian sect, promised to present evidence in the next few days that the child was indeed cloned. The baby's father, she said, would soon travel to Brazil to offer scientists proof that the baby's DNA was identical to that of a deceased sibling. Accompanying Ms Boisselier is Raelian founder and leader Claude Vorilhon, known as Rael. Clonaid says that five babies have been cloned and are all doing well.

bbc.com/health

Peri -operative fluid therapy: In the context of stress response.

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(This article is continued from The Orion 2003; 14: 56-58)

Most operative patients are accompanied by at least one intravenous access to serve as a route for different perioperative drugs and for fluid therapy. Having discussed the context i.e. the stress response of the body, the purpose of the present discussion is to review and outline an easy to follow guideline of perioperative fluid therapy for surgical patients.

Perioperative Fluid management is based on an understanding of the distribution of total body water (Table I) and electrolytes.

Table I: Changes in body weight, body surface & fluid composition with age

	Preterm neonate	Neonate	1yr	3yr	Adult
Weight	1.5	3	10	15	70
BSA(m^2)	0.15	0.2	0.5	0.6	1.7
BSA/wt	0.1	0.07	0.05	0.04	0.02
BW	80	78	65	60	60
ECF(%)	50	45	25	20	20
ICF(%)	30	35	40	40	40

BSA: body surface area, TBW: total body water, ECF: extracellular fluid, ICF: Intracellular fluid

Total body water (TBW) varies with age and sex. Infants (up to 80%), males and thin people (up to 60%) have a higher proportion of their body weight represented by water. When reduced to lean body weight, the proportion of TBW is about 80%, similar to the new-born. The two principal ECF compartments are the interstitial space, which contains about two thirds of the ECF (14% of body weight), and the intra vascular space (IVS), which contains only about 5 percent as plasma water. Smaller amounts of fluid are present in bone and connective tissue and in specialised body compartments, such as cerebrospinal, glandular and ocular spaces. Despite having a similar osmolality (290-320 mosmoles), the electrolyte content of the ECF and ICF are very different. The ECF contains a high concentration of sodium, bicarbonate and chloride whereas, in contrast, ICF has a high concentration of potassium and magnesium. Molecular movement takes place between the various fluid compartments by simple diffusion, facilitated diffusion or active transport whereas water transport between ECF and ICF is by osmosis. The ECF volume is controlled mainly by manipulation of its major cation, sodium through

- ADH release.
- Sympathetic vasoconstriction
- Atrial natriuretic peptide release
- Renin-angiotensin-aldosterone system

The hormonal response to operative injury described earlier sets the stage for a number of iatrogenic abnormalities of fluid and electrolyte balance. As for example if hypotonic fluids are administered to patients during this period to restore plasma volume, hyponatremia is likely to develop.

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Likewise, in the postoperative patient there is a propensity towards developing hypokalemia due to increased insulin secretion and consequent uptake of glucose and potassium into the cell. Hyponatremia, hypokalemia and hypotonicity are the most common abnormalities seen postoperatively[2].

Clinical assessment of fluid balance

An important part of both recognition and management of deranged fluid balance is careful clinical assessment that must begin at the bed site(Table II). Unless a patient is critically ill and must immediately go to the operating room, obtaining his or her admission weight is as essential as measuring blood pressure.

Table II: Use of physical examination to assess extracellular volume

Body Compartments	Volume Depletion	Volume expansion
Intravascular	Mild Supine B P normal Orthostatic fall in BP >15 mm Hg Orthostatic risein pulse>15beats/min Reduced JVP Severe Hypotension Shock	Hypertension S3 gallop Elevated JVP Hepatojugular reflux
Interstitial	Diminished skin turgor	Dependent pitting edema Hepatic congestion
Interstitial(pulmonary)		Rales Wheeze
Transcelluler	Dry mouth & mucous membrane Diminished intraocular pressure Absent axillary sweat	
Other compartments		Ascites, pleural effusion

Derangement of fluid balance may be classified as follows:

a. Volume derangement

The most common is a reduction in volume of ECF, which may occur, in a wide variety of surgical conditions, prior to operation[3].

External and apparent causes

• weeping from raw surfaces • vomiting • diarrhea • hemorrhage • fistula drainage • nasogastric drainage • profuse sweating in hot climate • Diuresis or severe exercise.

Internal redistribution or sequestration

• pleural fluid • peritoneal fluid • lymphoedema • angioneurotic edemaacute sequestered edema (injury, shock, infection).

Major deficits in intravascular volume are readily detectable because they result in hypotension and shock. However, more modest deficits in the volume within the vascular space may not be immediately apparent. One of the most sensitive tests for detecting the presence of volume depletion is measurement of arterial pressure and pulse with the patient in lying and standing position[4]. A fall in systolic pressure greater than 15mmHg or an increase in pulse rates greater than 15 beats/min suggests an intravascular

volume deficit. Another tool to assess intravascular volume is examination of neck veins. In supine position, at a 45-degree angle if the meniscus is no longer visible above the sternal angle, it can be inferred that the jugular venous pressure is less than 7 cm H_2O and suggests volume depletion[5]. Direct measurement of central venous pressure (CVP) by central venous catheter and Swan-Ganz catheter are two other reliable methods to assess volume status6. Volume overload as indicated earlier, can occur at anytime after surgery but is more common in the early postoperative period, when physicians attempt to maintain a large urine flow by aggressive infusion of salt containing fluid.

b.Concentration derangement

Deranged concentration is defined as a disturbance in water balance. When water is lost, as in diabetes insipidus, the electrolytes, which remain behind in the extracellular fluid, are concentrated. When the body gains water, the remaining electrolytes are diluted. In contrast to the evaluation of the volume, which is primarily a bedside determination, the evaluation of concentration disturbances requires measurement of serum electrolytes. Dangerous and perhaps fatal mistakes may be made when electrolyte concentration is evaluated alone without previous consideration of the volume status. As for example hyponatremia can occur in the presence of increased, normal, or decreased volume status. However, it is seen commonly in surgical patients in two circumstances. The first is when surgical losses (either internal or external) which are rich in electrolytes are replaced with dextrose 5% or other hypotonic maintenance type of fluid and the second is the so called TURP syndrome following absorption of irrigating fluid and expansion of intravascular volume during transurethral resection of prostate.

Life threatening hyponatremia has been reported to occur in as many as 4.4 % of post-operative patients and to result in permanent neurological disability in some[7].

c. Disturbed composition

This can be defined as disturbances in the relationship of some of the constituents of body fluids to the other with or without changes of volume and concentration. Acid- base disturbances and imbalance in other ionic constituents such as potassium, calcium and magnesium must also be considered.

All aspects of fluid and electrolyte therapy are guided by the necessity of avoiding either inadequate or excessive administration.

Having mentioned about types and components of disturbances, one needs to be conversant with the different types of fluids available for use during the perioperative period (Table III).

Table III: Composition of some commonly used crystalloids

Solutions	Gl(gm/L)	Na	Cl	HCO_3	K	Ca
Dextrose & Water						
5%	50					
10%	100					
Sodium Chloride						
0.9%NS(normal saline)		154	154			
0.45%(1/2 NS)		77	77			
0.21%(1/4 NS)		34	34			
3% saline		513	513			
Dextrose saline						
D5% in NS	50	154	154			
D5% in1/2 NS	50	77	77			
D5% in 1/4 NS	50	34	34			
Lactated Ringer's or Hartman's solution		130	103	27	4	4

Perioperative fluid and electrolyte administration requires attention to three aspects:

• Preoperative deficits • Ongoing losses • Maintenance.

Maintenance fluids are designed to replace water normally lost through:

• Gastrointestinal tract: 100-200 ml/ day
(Primarily fecal loss)

• The kidneys : 1000ml / day

• Sweat : 100ml / day

• Insensible loss : 600 to 800 ml/day
(Cutaneous & Respiratory evaporation)

In general, a normal adult's daily fluid and electrolyte requirements are approximately 2 to 2.5 litter water, 75 mEq of sodium, and 40 mEq of potassium and at least 100 gm of glucose to provide minimal protein sparing effect.

Normal maintenance requirements can be estimated from Table VII. Solutions like D5 ½ NS, D5 ¼ NS or even D5W are most commonly used as maintenance fluid because daily normal losses are hypotonic (more water loss than sodium loss).

Type, amount and choice of fluid

Intraoperative fluid therapy should include supplying basic fluid requirements and replacing residual preoperative deficit as well as intraoperative losses (blood, fluid redistribution, and evaporation). Healthy normal patients appearing for a surgery after a period of fast will have a preexisting deficit proportionate to the duration of the fast. The deficit can be estimated by multiplying the normal maintenance rate by the length of the fast. As for example, for the average 50kg person fasting for 8hours, this amounts to (40+20 +30) ml/hour for 8 hours or 800ml. This volume of maintenance solution is ideally necessary to correct the deficit. (In reality the deficit will be somewhat less as a result of renal conservation.)

Minor and / or short procedures may not require fluids or transfusion although recent evidence suggests that recovery from anaesthesia is improved when maintenance fluids are provided1 in operations lasting less than 1h, additional fluids are not usually required. The quantity of fluids infused after the first hour depends upon the severity of surgical trauma. Cases with minimal surgical trauma such as ophthalmic surgery, microscopic surgery, or extremity surgery with a tourniquet require only that quantity of fluid for maintenance (2ml kg^{-1} h^{-1}). Patients with severe surgical trauma, such as radical mastectomy, total hip replacement or bowel resection requires as much as 10 $kg^{-1}.h^{-1}$ and may require some colloid. One of the important tasks of the perioperaive physician is to continually monitor and estimate blood loss. While occult bleeding into the wounds or under the drapes complicates estimates, accuracy is important to guide fluid therapy and transfusion. Selection of the overall type of intravenous solution depends upon the surgical procedure and the expected blood loss. For procedure involving minimal blood loss and fluid shifts, maintenance solution can be used. For all other procedures, ringer's lactate solution can be used.

Replacing blood loss

Ideally blood loss should be replaced with crystalloid or colloid solutions to maintain intravascular volume (normovolemia) until the danger of anemia outweighs the risks of transfusion. At that point, further blood loss is replaced with transfusion of red cells to maintain hemoglobin concentration (or hematrocrit) at that level. For most patients, that point corresponds to hemoglobin between 7 and 8g/dl (and a hematocrit of 21-24%). Below a hemoglobin concentration of 7g/dl, the resting cardiac output has to increase greatly to maintain a normal oxygen delivery. A level of 10g/dl is generally used for elderly patients and those with cardiac or pulmonary disease. Higher limits may be used if continuing rapid blood loss is expected. In practice, most clinicians would give lactated Ringers solution in approximately three to four times the volume of the blood lost, or colloid in a 1:1 ratio, until the transfusion point is reached. At that time, blood is replaced unit for unit as it is lost. The transfusion trigger point can be determined preoperatively from the hematocrit and by estimating blood volume. Patients with a normal hematocrit should be generally transfused only after losses greater than 10-20% of their blood volume. The exact point is based on the patient's medical condition and the surgical procedure. The amount of blood loss necessary for the hematocrit to fall to transfusion trigger can be calculated.(Table IV & V).

Table IV: Blood volume as a percentage of body weight[11]

Age	Men(%)	Women(%)
20-40	8.0	7.0
40-60	7.5	6.5
>60	7.0	6.0

Table V:Estimation of allowable blood loss in adult

Estimate red blood cell volume (RBCV) at the preoperative hematocrit (RBC Vpre-op)
Estimate red blood cell volume (RBCV) at 30% hematocrit (RBC V30%)
Calculate red cell volume lost when the Hct is 30%; RBCV lost = RBC Vpre-op _ RBC V30%
Allowable blood loss = RBCV lost X 3

Post operatively, normal volume of maintenance fluid should be given, including any on going third space loss, nasogastric tube drainage, gut fistula, peritoneal drainage, chest drain loss or on going blood loss. Appropriate type of fluid should be chosen depending upon the type of loss. Gut losses are normally replaced in 1:1 ratio with normal saline.

Table VI outlines an approach to replacement therapy for gastrointestinal fluid losses. It should be noted that this table represents a starting point for replacement therapy and that determination of specific fluids may be required.

Table VI: Replacement therapy for gastrointestinal fluid lossess

Sources of loss	Replacement for each liter lost N/S (ml)	D5W (ml)	KCl (mEq)	$NaHCO_3$ (mEq)
Saliva	250	750	20	45
Gastric fluid	250	750	20	0
Upper small bowel fluid	700	300	5	10
Lowe small bowel fluid	750	250	5	20
Pancreatic fluid	500	500	5	90
Biliary fluid	750	250	5	45
Diarrhea	250-500	500-750	35	45

*Normal saline can be replaced with D5 normal saline
*One ampoule of 7.5 % $NaHCO_3$ contains 45 meq of Na and HCO_3^-
*Alkalosis associated gastric drainage results in urinary K^+ loss that must be replaced
*Protein replacement in the form of albumin may be necessary

Fluid and electrolyte management in children

The biggest change in water content of the body takes place during intrauterine gestation and the first three years of life. At birth, a higher percentage of water is in the ECF, unlike older children and adults where the higher proportion is intracellular. At birth, the glomerular filtration rate (GFR) is only 25- 30 % that of adult. However, by 4 weeks of age the kidney achieves 90% maturity. The neonatal kidney has poor concentrating ability and cannot excrete or conserve sodium as well as an older child, causing an increased obligatory water loss. Neonates can increase their urine volume following a fluid load but have a reduced ability to concentrate urine. A healthy new-borne will tolerate a moderate fluid overload much better than moderate dehydration.

Normal fluid and electrolyte requirements

In 1957 Holliday and Segar showed that the water requirement in milliliters was equal to the total energy expanded (i.e. 1000 ml of water is required for every 1000kcal expended.

Table VII: Daily caloric requirement

0-10 kg	100kcal kg^{-1}
10 -20kg	1000kcal+ 50kcal kg^{-1}
(over 10)	
21-70 kg	1500kcal + 20kcal kg^{-1}
(over 20)	

Table VIII: Maintenance fluid requirement

0-10 kg	4ml $kg\text{-}1h^{-1}$
10 -20kg	40ml + 2ml $kg^{-1}h^{-1}$
(over 10)	
21-70 kg	60ml +1 ml $kg^{-1}h^{-1}$
(over 20)	

As is evident from Table I, on a body weight basis, infants have a much higher water requirement than older children and adults. Thus an adult of 70 kg has a daily water requirement of 2.5 liter or 35 ml kg^{-1}.where, as an infant requires 100ml kg^{-1}. The greater fluid requirement in infancy reflects a higher rate of metabolism and growth, a greater surface area to weight ratio resulting a higher insensible water loss and a greater urinary obligatory loss due to a reduced renal concentrating ability. Preterm infants have an even greater rate of insensible loss due to thinner, more permeable, vascularised skin. In infants, fluid management may be complicated by low ambient humidity, use of radiant heaters and phototherapy. Daily requirement of sodium, potassium and chloride are usually quoted as 30, 20, and 20 mol respectively. For every 1000kcal expended. It is evident that this requirement will be met by giving a solution of 0.18% sodium chloride in 4% dextrose with 20 mmol. of added KCl per liter.

Any further electrolyte deficit can ban be corrected by using the formula: Electrolyte deficit (mmol) = weight X (CD - CM) X 0.3. (Where CD = desired plasma concentration and CM= measured plasma concentration). Rationale behind providing 4-5% dextrose in pediatric maintenance fluid is to prevent development of ketosis and not to provide adequate calorie intake. In preterm infants and neonates, solution s containing 10% dextrose is used to prevent hypoglycemia.

Intraoperative fluid management

Deficit

A healthy child coming for elective surgery will have a deficit consisting of hourly fluid requirement multiplied by the numbers of hours of starvation. Of this deficit, 50% should be replaced over the first hour of surgery with the other 50% over next 2 hour.

A sick child coming for emergency surgery may have a further deficit relating to dehydration from existing fever, vomiting or blood loss. The level of dehydration should be assessed and corrected with normal saline or Ringers lactate. A colloid solution may be needed if the extent of dehydration is severe.

Maintenance

Maintenance fluid requirement needs to be given for the duration of surgery to replace insensible water loss and obligatory loss. 5% dextrose during surgery invariably produces hyperglycemia with its untoward effects whereas using IV solution, which contains 1% or 2.5 % dextrose, will correct any pre-operative hypoglycemia and not produce intraoperative hyperglycemia[11].

Intraoperative loss: Intraoperative fluid loss relates to third space loss and blood loss.The volume lost is impossible to measure, but is estimated by the extent of surgery and the clinical response to appropriate fluid replacement.

Table IX : Estimation of normal third space loss

Intra-abdominal surgery	6-10ml kg^{-1} h^{-1}.
Intrathoracic surgery	4-7 ml kg^{-1} h^{-1}.
Eye surgery/ superficial surgery/ neurosurgery	1-2 ml kg^{-1} h^{-1}

It should be replaced with an isotonic fluid such as normal saline or Ringer's lactate. The clinical response to replacement should be sustained and consists of an adequate blood pressure and heart rate, adequate tissue perfusion and a urine output of 1-2 ml kg^{-1} h^{-1}

Blood loss should always be replaced in young children undergoing major surgery. It will need to be replaced with crystalloid, colloid or blood in adequate volume. It is important to have a plan for blood loss replacement based on child's preoperative condition, hematocrit and nature of surgery. The lowest acceptable hematocrit tolerated without needing transfusion has been worked out [10,11].

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Treatment of Psoriasis: An Update

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Introduction

Psoriasis is one of the oldest disease of mankind, history goes as back as 500 B.C. was known as psoralepra and in 19th Century named as Psoriasis as a separate entity.

Psoriasis is a chronic relapsing disease with dull silvery scales on the lesion which usually involve extensors and complicated type are pustular and erythodermic and psoriatic arthritis.

Recently much has been learned about the pathophysiology of psoriasis, and as a result, traditional treatments such as coal tar have been joined by immunosuppressive.

Once considered a hyperproliferative disorder, psoriasis is now recognized as an autoimmune disease involving activation of T cells. As a result, new immunosuppressive agents have significant role in treatment.

During the past decade, investigators have demonstrated that the immune system plays an integral role in the pathogenesis of psoriasis. Activation of T cells, specifically CD4 cells, induces the release of interleukin-2 and alpha interferon, which induce hyperproliferation of keratinocytes.

Although there is no clear inheritance pattern, patients with psoriasis often have a family history of the disease.

Exogenous factors may also play a role. Human papilloma virus and streptococcus can evoke a psoriatic response,

A few medications can trigger the onset of psoriasis, including beta-blockers, lithium, nonsteroidal anti-inflammatory agents, and also corticosteroid withdrawal rebound can provoke Psoriasis.

Management of Psoriasis

Patient should have a total idea about his illness including line of treatment and prognosis of the disease. Treatment planned and prognosis should be explained to the patient.

Psoriasis has got multiple modalities of treatment are widely practiced now topical, systemic, phototherapy, climate therapy and few unusual treatment are practiced.

Topical therapy is generally indicated when psoriasis is limited to less than 20% of the body surface. Agents used include emollients, keratolytics, corticosteroid ointments or creams, coal tar, anthralin, calcipotriene-taza-rotene. and tarcolimus these are used either single and combination.

White petrolium jelly used as a emolient till the date for its soothing and mild keratolytic properties.

Coal tar has been used to treat psoriasis for very long time though; its mechanism of action of action is still not well understood. Some studies have shown that coal tars inhibit DNA synthesis, thus acting as a cytostatic and immunomodulator.

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It is used in combination with ultraviolet B (UVB), 1% crude coal tar in a hydrophilic ointment is applied to the skin before daily phototherapy with minimal erythemal doses of UVB.

Combination reduces the total dose of ultraviolet radiation needed to clear psoriasis; still, the therapeutic effectiveness of this regimen is not significantly superior to that of ultraviolet radiation or tar alone.

Anthralin in paraffin is used for short-contact thereapy to minimize irritation of normal skin. This method involves progressive concentrations ranging from 0.05% to 0.5%; dosage is increased according to patient response. The preparation is applied once or twice a day for 10 to 20 minutes. It should be removed using cotton wool soaked in oil or a mild detergent, followed by showering or bathing. Treatment with anthralin can clear psoriasis leaves a deep brown stain.

Topical corticosteroids are the most widely used treatment for psoriasis, because of their short-term efficacy, high degree of patient acceptability, and relatively low cost. Patient compliance is better than with other topical agents since steroids do not irritate or stain the skin.

Usually potent steroidal agents, are used although milder used for intertiginous areas, such as the axilla or groin. The efficacy topical steroids can be improved by applying a plastic occlusive film over the ointment. A preparation of 0.12% betamethasone valerate was recently approved fro the treatment of scalp psoriasis. It has foam base that liquefies on contact with the skin, depositing the steroid on the scalp. Long-term therapy with topical corticosteroids can cause thinning of the skin, striae, telangactasia, purpura, masking of local infections, hypoigmentation and tachyphylaxis, prolonged use of topical corticosteroids may result in hypothalamicpiuitar-adrenal suppression, particularly in children.

Calcipotriol a vitamine D analogue,

Ointment does not stain clothes, but it is mildly irritating especially on the face and hypercalcemia has been reported after application of twice the recommended maximal weekly dose of 100 gm. Calcipotriol should be used with caution in the elderly and in patients with impaired renal function.

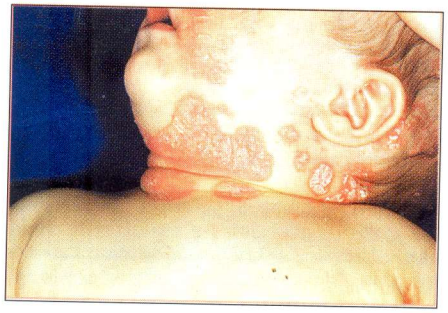

Figure I: Psoriasis in a baby

Tazarotene, available in 0.5% and 0.1% gels, is topical retinoid that was recently introduced for treatment of psoriasis. Although lazarotene has the advantage of not being a corticosteroid, it can irritate normal skin, causing purities and erythematic. Comparison of tazarotene with the corticosteroid flucoinonide has shown that tazarotene

induces longer remission. Among patients with initially successful treatment (50% or greater clearing of psoriasis), relapse occured withi three months of discontinuing treatment in 55% of patients treated with flucinonide, 37% of those treated with tazarotene 0.05% gel, and 18% of the.

Combined Topical Therapy

A mixture of 10% salicylic acid and clobetasol ointment has been found to be highly effective; salicylic acid enhances penefraction of medcation. The combination of calcipoteriene and the steroid applied once a day appears to be superior to either agent applied twice a day. Sequential use of topical corticosteroids and tazarotene may decrease the skin irritation commonly seen with the latter agent may prevent steroid-induced cutaneous atrophy.

Some agents should not be combined. Mixing salicylic acid with calciptrence results in complete inactivation of calcipotriene; combined calcipotriene and hydrocortisone vale rate results in marked deterioration of calcipotriene within a few days.

In addition to coal tar, other topical agents can be combined with phototherapy. When topical calcipotrience is applied after treatment with psoralen methoxalen plus ultraviolet A (PUVA) or UVB, psoriatic lesions are cleared more rapidly and a lower total dose of radiation is needed. The effects of tazarotene are also enhanced when combined with UVB or UVA. Pulse therapy with calcipotriene twice a day on weekdays in conjunction with clobetasol propionate twice a day on weekends may be used to maintain remission after psoriasis has been brought under control.

Phototherapy and Systemic Treatments

Systemic treatment should be reserved for patients with physically, socially, or economically disabling psoriasis that has not responded to topical treatment. Approximately 20% of psoriasis disabling psoriasis that has not responded to topical treatment, either drug or phototherapy more aggressive therapy may be indicated when the disease involves more than 20% of the body surface. The risk: benefit ration for systemic treatment should be determined in each patient.

Broad-band-UVB (wavelengths of 290 to 320 nm) phototherapy has lon had a major role in the management of moderate-to-severe generalized psoriasis. UVB irradation may be used alone or in combination with coal tar UVB immunotherapy is effective for moderate psoriasis (<10% of body surface) that has not responded well to topical therapy. It clears 60% to 80% of lesions.

Narrow-band UVB (TIL-01) phototherapy, which requires a 31 1-nm irradiation ultraviolet bulb, is seeing increased use in the United States. Studies have shown that narrow-band UVB phototherapy is more effective then broad-band UVB, although narrow-band therapy requires longer exposure time. Narrow-band therapy is less effective than PUVA. prospective follow-up studies are required to assess the long-term risks of narrow-band UVB radiation.

PUVA combines ultraviolet A phototherapy (wavelengths of 320 to 400 nm) with psoalen methoxsalen, Methoxsalen, which causes photosensitization, si taken orally two hours before UVA exposure. PUVA's proposed mechanisms of action include 1) intercalation of methoxsalen into DNA, forming cross-links between DNA strands that interfere with DNA synthesis and block cell proliferation, and 2) suppression of cell-mediated immune responses in involved skin.

Candidates for PUVA include patients who have not responded adequately to topical therapies or UVB, and those in whom the disease effects at least 20% of the body surface. PUVA is highly effective, inducing remision for approximately one year compared with the six months typically seen after broad-band UVB. In more than 85% of patients, skin lesions disappear after 20 to 30 photochemotherapy treatments.

PUVA therapy is usually administered two to three times per week. Maintenance therapy is less rigorous, often involving only one treatment every two to four weeks, with eventual discontinuation of treatment.

The short-term side effects of PUVA include nausea in 15% of patients. Burning or severe pruritus may problems and depend on the cumulative UVA dose. In one3 study, one or more squamous cell carcinoma developed in 8% of patients who received 2,000 to 4,0000 joules and in 15% of those who received 4,000 joules0. There are no data regarding the number of PUVA treatments at which the risk of melanoma begins toincrease substantially. To reduce the risk of genital skin cancer in men, it is important to shield unaffected parts of the genitalia during treatment and to minimize UVA exposure to the affected areas. After 150 PUVA treatments, patients should be switched to oral therapy.

Bath PUVA therapy has been suggested as a potentially safer alternative to conventional PUVA. In this method, a lotion or emulsion containing trimethylpsoralen or 8-methoxypsoralen is applied to the skin five minutes to two hours before UVA radiation. The treatment protocol is otherwise similar to conventional PUVA. Bath PUVA may avoid the nausea associated with systemic psoralen; it is preferred for localized psoriasis, especially on the palms and soles. Disadvantages include the risk of se4vere local phototoxic reactions and patchy pigmentation.

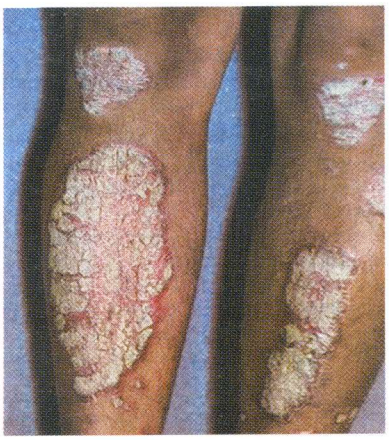

Figure II: Wide pustules or silvery scales a typical psoritic patient

Retinoids, vitamin A metabolites have proven themselves in the treatment of psoriasis. Acitretin has become the retinoid of choice. Acitretin has more favorable pharmacokinetic properties, including a significantly shorter elimination half-life. The optimal dose range for monotherapy is 25 to 50 mg a day, starting at 10 to 25 mg a day and escalating as needed to enhance efficacy. The overall rate of complete remission is genreally less than 50%. Higher doses (50 to 75 mg /day) result in more rapid and possibly more complete responses but are associated with significantly more frequent side effects.

Acitretin monotherapy is most effective for pustular and erythrodermic psoriasis. Combination regimens with other systemic agents or UV radiation are generally preferred for plaque psoriasis; in these cases, it is even more advantageous to start with lower doses of acitretin (10-25 mg/day).

Oral retinoids are highly teratogenic. Contraception is mandatory for all women of chiildbearing potential for one month beginning acitrefin therapy, during therapy, and three years after therapy. Other potential side effects of acitretin include hair loss, pyogenic granuloma formation, thin nail plates, onychomadesis, rhinitis and cheilitis, photosensitivity reaction, xerophthalmia,

Methotrexate. dermatologists have used methotrexate in the

treatment of severe cases of plaque, erythrodermic, and pustular psoriasis for more than 30 years. Methotrexate inhibits the enzyme dihydrofolate reduclase, which is necessary for nucleotide and amino acid synthesis. Thus, the drug decreases DNA synthesis and so inhibits mitosis and cell prolifereation in rapidly dividing cells. It also affecs the immune system by altering lymphocyte and monocyte activity cytokine production, and neutrophil function.

Careful patient selection and close follow-up are essential for optimal results with methotrexate. Patients with alcoholism, diabetes, obesity, or liver disease may not be appropriate candidates, and all patients are at risk for side effects ranging from nausea to malignancy. Recommended pretreatment laboratory tests include complete blood and platelet counts, liver function tests, and measurement of serum creatinine and blood urea nitrogen levels. Some investigators recommend obtaining baseline folic acid levels, especially in older patients. Blood counts should be obtained weekly during the first few months of therapy. When the methotrexate dosage has been stabilized, the interval between monitoring may be increased. In patients with no hepatic risk factors, liver biopsies should be performed after a cumulative dosage of 1.5 gm. Repeat liver biopsies should be performed after every additional 1 to 1.5 gm of methotrexate.

Every patient should receive a test does of methotrexate prior initiation of treatment in order to assess tolerability. The recommended starting dose is 7.5 mg given as a single dose once a week or divided into three doses to minimize gastrointestinal side effects. Some authors recommend supplemental folic acid (1 mg/day) to minimize both gastrointestinal and hematologic side effects.

Cyclosporine is a fairly recent addition to the psoriabc armamentarium. The immunosuppressant inhibits interleukin-2 production, thereby suppressing T cell-mediated immunity. Clearing of lesions begins as early as two weeks after the start of treatment at a dosage of 2.5 to 4 mg/kg/day given in two divided doses, and considerable improvement occurs in most patients by week 12. The patient should be kept on the 2.5 mg / kg / day at two-week intervals based on clinical response and tolerability.

Baseline monitoring should include a complete history, physical examination (including two measurements of blood pressure), chemistry screening, complete blood count, and two measurements of the serum creatinine level. Follow-up monitoring is performed every two weeks for the first two to three months of therapy, then monthly thereafter. The dosage should be reduced if the serum creatinine increases 30% above the baseline level.

In addition to nephrotoxicty, major side effects of cyclosporine include hypertension, hirsutism, and gingival hyperplasia. The development of lymphoma has been reported. Patients should not be treated with cyclosporine for more than one year at a time. Intermittent short courses of cyclosporine are safe and effective for clearing moderate to severe psoriasis and may induce prlonged remission in some patients.

Tacrolimus (FK-506) has a mechanism of action similar to that of cyclosporine. In a double blind, placebo-controlled European multicenter trial, oral tacrolimus was effective in the treatment of reclacitrant plaque psoriasis at a daily dose of 0.1 to 0.15 mg/kg. The most common side effects were paresthesias and diarrhea. The same monitoring guidelines used for cyclosporine apply. Topical tacrolimus is not effective for psoriasis.

Hyoxyurea, although of limited benefit as monotherapy, hydroxyurea may provide enhanced efficacy when used in combination with retinoids or phototherapy. Its major dose-limiting side effect is bone marrow suppression.

Thioguanine. The antimetabolite 6-thioguanine has reported to be efficacious in patients with severe psoriasis. Because of the risk of myelosuppression, a complete blood and platelet count should be obtained every two weeks, and every week when the dose is increased. The drug should be discontinued if the platelet count falls below 125,000 /pL or the white blood cell count below 4,000/mm3.

Combined Systemic Therapy
Some patients eventually require combination therapy with various agents to maintain adequate clearing of their psoriasis. Several combinations have proved effective in such cases.

Combination Systemic Treatments for Psoriasis
Methotrexate + Phototherapy (PUVA or UVA)
Methotrexate + Topical Corticosterroids
Methotrexate + Acitretin
Acitretin + Phototherapy (PUVA or UVA)
Hydrothrotrexate + Acitretin + Phototherapy (PUVA or UVB)

Unusual treatment : Antimicrobials sometimes help in remission of psoriasis:
Surgery : Tonsillectomy my help in guttale pseriasis of children.
Electrogasulation, Gyotherapy and Laser also may help.

Mentioned, there is evidence that sterptococcal antigens can trigger an immune cascade that leads to the development of psoriasis. Consequently, a prospective, controlled study is being conducted to determine the efficacy of oral clindamycin for the treatment of the disease. The increased expression of angiogenesis factors in psoriatic lesions has led to the investigation of angiogenesis-blocking therapy with shark cartlage extract. The treatment has shown only modest results.

Several new biotechnological therapies that target the immune system are currently being investigated for psoriasis. These include fusion proteins monoclonal antibodies, cytokines, T-cell receptor vaccines, and gene therapy:
Fusion Proteins. The fusion protein DAB 391L-2consists of interleukin-2 attached to diphtheria toxin. DAB 391L -2 binds specifically to high-affinity receptors on activated T cells. After binding it enters the cell and the toxin detaches, resulting in cell death. LFA3TIP, a fusion of the protein LFA-3 and Fc fragment of a human lgG antibody, blocks CD2 receptors on the surface of T cells, thereby preventing the co stimulatory signals necessary for T-cell activation. The fusion protein CTLA4-lg also inhibits costimulatory signals but acts at CD28 receptors on T-celfs. Monoclonal Antibodies. A preliminary study indicates that a monoclonal antibody directed against T cells, anti-CD1 1 a, may be useful for psoriasis. Monoclonal antibodies that block activation of C 134 T cells are also being developed.

Cytokines
Various cytokines involved in the regulation of the immune process are being targeted as potential treatment for psoriasis.

Gene Therapy
Chromosomes involved in psoriasis have already been mapped, and more genes involved in the expression of psoriasis are being identified. Gene therapy promises to be one of the most important areas of treatment of psoriasi f th new millennium.

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Intra-articularinjection therapy in frozen shoulder : An Urban Study

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The Orion 2003 ; 15: 89-90

Summary

157 patients of frozen shoulder were treated with 80 mg of methyl prednisolone(2 vial of Depo Medrol) mixed with 2 cc of 2% Xylocain 2 sessions in 4 to 6 weeks interval in Brahmanbaria sadar Hospital and in private chamber between the period of January 1991to July 2001 who were followed up included in this series. 7 patients absconded from the follow up and total 150 patients were included in this study, among which 84(56%) cases were male. Mean age of the patients was 57.5 years. 83 cases (55.33%)had left shoulder involvement and 37 (24.6%) cases had diabetes mellitus.

Satisfactory results (excellent and good) were found in 142 (94.67%) cases and unsatisfactory (fair and poor) results were found in 8 (5.33%) patients within 6 to 8 months of treatment. Nocturnal exacerbation of pain with difficulty in lying on affected side more marked in all cases. In early cases, there was found restriction of internal rotation and late cases all movements were almost equally affected.[1]

All patients were assessed clinically and improvements in the particular variables eg. pain score and range of various shoulder movements. No remarkable side effects were found in any of the cases. All patients were treated with analgesic (tablet tramadol hydrochloride 50 mg) twice daily & antiemetic coverage (tab promethazine hydrochloride 5 mg) twice daily for 3 to 4 weeks. Some patients who reported adverse effects with tramadol hydrochloride were treated with NSAIDS (tab naproxen 500 mg) twice daily with ranitidine coverage. The findings of the results are very much rewarding.

Introduction

Frozen shoulder or Adhesive Causalities is an inflammatory lesion of the Gleno-humeral joint capsule that leads to thickening and contraction with consequent loss of joint volume. Clinically it is well defined disorder of spontaneous onset with progressive shoulder pain of uncertain aetiology, accompanied by limitation of active and passive range of all shoulder movements, [2,4]. Codman in 1934 used the term frozen shoulder.[5] other names are adhesive causalities. Periarthrosis of shoulder.[3,4,6] It is most common and disabling disorder of shoulder joint [5]. There still exists confusion over the natural history and response of treatment[7]. It has been suggested that this is an autoimmune response to the products of local tissue breakdown1. Reflex sympathetic dystrophy is thought to be pathognomotic factor [8,9].

Clinically diagnostic of capsulitis is more reliable. Insidious onset of the shoulder pain and stiffness without joint involvement is characteristic.Pain persists both on rest and movements particularly at night[2,4]. Symptoms resolve spontaneously after12 to 18 months[1].

Treatment is basically conservative, which aims in relieving pain and preventing furtherstiffness while recovery is awaited. Analgesic and anti inflammatory is used to reassure the patients that recovery is certain. Heat, UST has some soothing effects. Modernization and regularity of pendular exercise have definite role in recovery.

But intra-articular injections of long acting corticosteroid mixed with local anesthetic in two 2 sessions at 4 to 6 weeks interval hasten recovery within 6 to 8 months instead of 12 to 18 months.

Patients and Methods

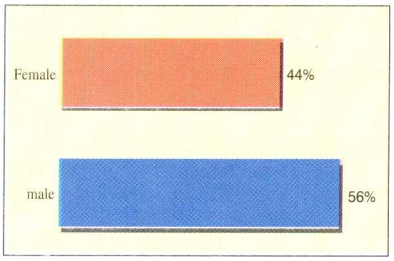
This study was performed in Sadar Hosital. B. Baria and in private chamber between the period January, 1999 to July. 2001. 157 patients were randomly selected. 7 patients absconded from the follow up and total 150 patients were taken into consideration for the study. All patients were evaluated by through history and full clinical examination. Laboratory investigations like random blood sugar and X-ray of the affected shoulder to exclude other pathology. Diagnosis was made by characteristic pain, active and passive restrictions of all shoulder movements, no history of trauma and exclusion other diseases.

After confirmation of diagnosis clinically, under strict aseptic precautions 2c.c. of Injection Depo-Medrol (80 mg methyl prednisolone into 5 c.c. disposable syringe was injected into sub acromial bursa twice in 4 to 6 weeks interval, taking care that drug was not infiltrated into the muscle, cap. tramadol hydrochloride 50 mg. given 12 hourly along with tab. promethazine hydrochloride 5 mg 12 hourly before meal. Some patients showed adverse reactions like vomiting, constipation, sweating and sense of unwell being treated with tab. naproxane 12 hourly after meal with ranitidine as coverage treatment of NSAID. All patients were encouraged for regular moderate shoulder mobilization exercises.

Observation and Results:

Out of 150 cases of frozen shoulder 84 (56%) were male and 66 (44%) were female (chart I).

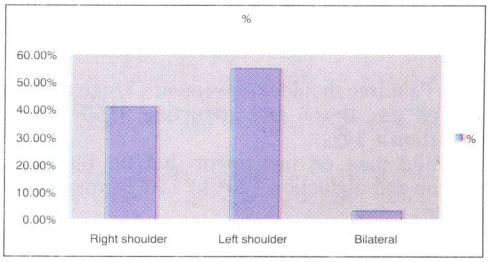
Chart I: Sex distribution of Patients



(Male: Female 1.27: 1) P> 0.05

Right shoulder involved in 62 (41.34%), left in 83 (53.33%) and bilateral in 5 (3.33%) cases respectively (chart II).

Chart II: Percentage of distribution by site of involvements



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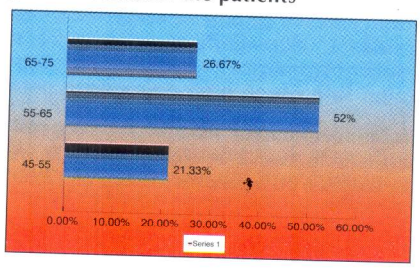
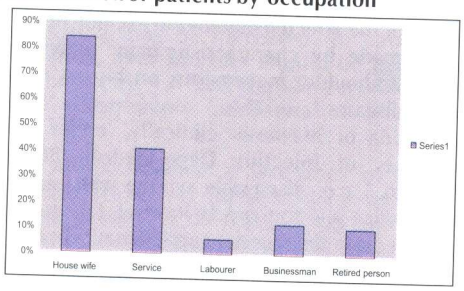
Age range of the patients was 45 to 75 years. Mean age 57.5 years. Most of cases (52%) were in 55 to 65 years age groups (Chart III)

Chart III: Age distribution of the patients



Most of the female patients were housewives 46 (30.67%) and 18 (12%) patients were service holder and businessman respectively (Chart IV).

Chart IV: Distribution of patients by occupation



Among 150 cases, 37 (24.67%) cases were diabetic, 41 (27.33%) had history of trivial trauma over the shoulder before the onset of the disease, 13 (8.67%) were suffered from CVD and 33 (22%) were suffered from hypertension. 26 (17.33 %) cases were found no association with any diseases (Table I)

Table I: Percentage of patients suffering from different diseases

Type of disease	No. of patients	Percentage
Diabetes	37	24.67
Trivial trauma over the shoulder	41	8.67
CVD	13	8.67
Hypertension	26	17.33
No diseases	26	17.33

Pain was insidious in onset in 142 (44.67), maximum at night in 133 (88.67%). aggravated on movement 143 (96%) and radiated to arm or chest in 102(68%) cases. 67% patient complained of rest pain (Table II).

Table II: Percentage of type of pain

Type of pain	No. of patients	Percentage
Insidious	142	44.67
Maximum at night	133	88.67
Aggravated on movement	143	96
Radiated to chest or arm	102	68

The results were analyzed on the basis of patient's statements regarding the relief of pair and clinical findings and arbitrarily categorized as excellent, good, fair and poor after 6 to 8 months of treatment.

i. Excellent: Pain free shoulder movements, range of movements full or almost full e.g. flexon and abduction $>150^0$; extension and internal rotation $> 50^0$.

ii. Good: Mild pain on movements but no rest pain, range of motion-flexon and abduction 120^0 to 150^0; extension and internal rotation $> 50^0$.

iii. Fair: Moderate pain on movement with mild nocturnal rest pain, range of motion flexon and abduction 100^0 to 120^0; extension and internal rotation 20^0 to 30^0.

iv. Poor: Moderate to severe pair on movements, moderate nocturnal rest pain, range of motion-flexon and abduction $<100^0$; extension and internal rotation $<20^0$.

126 (84%) patients were rated as excellent. They regained excellent range of pain free motion. 16 patients (10.67%) rated as good. Though they complained mild tolerable pain with reasonable good range of movements. 6 patients (4%) experienced moderate pain on movements and mild nocturnal rest pain with mild restriction of all movements categorized as fair. 2 patients (1.33%) were under the category of poor. They had the moderate to severe nocturnal rest pain with see disturbances and moderate restrictions of all movements (Table III).

Table III: Overall results after 6 to 8 months of treatment

Category	No. Of patients	%
Excellent	126	84%
Good	16	10.67%
Fair	6	4%
Poor	2	1.33%
Total	150	100%

Discussion

Frozen shoulder is a common disorder usually occurs during 5th to 6th decades[10]. In the present study, majority of the patients (52%) belonged to 55 to 65 years. Mean age of the patients was 57.5 years which is slightly higher than a study by KHAN[11] which was 51.06 years. Male: female ratio in our series was 1.27:1 which is different from a series of HSU and CHAN[12], which was 0.56:1 and statistically significant which is due to takin of more treatment facility in male domination society in our country. Out of 150 patients, 9 (6%) were labourer which reflects that frozen shoulder is less common among manual workers. 37 (24.67%) cases had mellitus. HSU and CHAN[12] found diabetes in 11 (16.7%) patients ($P < 0.05$). Characteristics of pain in Frozen shoulder were similar to standard book picture [1,8].

Satisfactory results (excellent and good) were found in 142 (96.67%) cases and unsatisfactory results (fair and poor) were found in 8 (5.33%) patients within 6 to 8 months of treatment with intra-particular long anesthetic in 2 sessions in 4 to 6 weeks interval. The time of recovery is much earlier and treatment is cheaper than long standing treatment with NSAIDS and physiotherapeutic devices, which require 12 to 18 months[1]. This is probably due to suppression to immunologic process by steroid to local tissue product[1].

Conclusion

Frozen shoulder is a common problem, which can be diagnosed easily from history and physical examination. Recovery in relation to relief of pain and progress of shoulder movements can be hastened by intra-articular long acting steroid with local anesthetic along with analgesic and active exercise regularly within 6 to 8 months rather them application of physiotherapeutic devices e.g. UST or SWD in respect to cost, convenience and time of recovery.

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Febrile Seizure

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The Orion 2003; 15 : 91

Summary

Commonly occur in 3% of all children. Usually occur between 6 months and 5 years of age. Rare after 5 years of age. Seizure is usually at onset of febrile illness and takes a T-C form. Febrile Seizure recurs in 30-50% of children. Complex Febrile Seizure: duration greater than 30 minutes; focal features; recurs within 24 hours. No particular infection can be incriminated.Prognosis excellent; risk of continuing epilepsy small. Prognosis worse if age of onset < 13 months, in the presence of prior neurological abnormalities, complex seizure. 3% of epileptic patients suffer from febrile seizure. 3% febrile seizures turn into true epilepsy.

Definition

Febrile seizures are epileptic seizures that are provoked by fever of extracranial infective origin and occur 3% of children aged between 6 months and 5 years[1,2].

Classification of febrile seizures

Simple febrile seizures

Febrile seizures are called simple when they are single, are generalized, and last less than 15 minutes. 80-90% of all seizures are simple.

Complex febrile seizures

Complex febrile seizures are defined as having any focal seizures, lasting longer than 15 minutes, having more than one seizure in 24 hours, or showing new postictal neurological signs. Less than 5% of seizures last longer than 15 minutes.

Aetiopathogenesis

Febrile seizures occur in 2-5% of all children, making them the most common form of seizures in children[3]. Many people with epilepsy may have their first seizure during a fever, but the epidemiological study indicates that febrile seizures are a distinct and benign disorder[4,5].

The causes of febrile seizure can be divided into three components[6]

a) The genetic background - The mode of inheritance of febrile seizure is not definitely established but is generally believed to be autosomal dominant. Febrile seizures are 2-3 times more likely in family members of affected children than in the general population, whereas no clear association exists between febrile seizures and family history of febrile seizures. (b) The neurological development before the first convulsion. (c) The precipitating event in association with the fever -1. Maternal ill health, 2. Parental subfertility, 3. Bleeding during first and second trimester, (4) Delivery other than vertex, 5. Low birth weight and (6) Low serum zinc.

Clinical features

90% of first febrile seizures occur between 6 months and 3 years, but may range from 1 month to 10 years. The diagnosis of febrile seizure requires excluding all underlying causes other than fever. 80% of febrile seizures occur during the first day of fever, often before the parents are aware of the fever. The long-held belief that the triggering mechanism is related to the temperature curve has never been established. An alternative hypothesis that seizures are prolonged by different temperature levels in different children is supported by the observation that the risk of recurrence decreased with increasing temperature at first presentation. Approximately 1/3rd of children with febrile seizure will have recurrence but less than 10% have 3 or more.

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The risk of recurrentseizure increases when the first febrile seizures occur before the age of 12-18 months, duration of fever is short, the temperature elevation is low; and other family members have febrile seizures. Complex febrile seizures increase the risk of later epilepsy, but it is not established that they increase the risk of febrile seizure recurrence.

Investigations

Diagnostically it is important to exclude infection of CNS.
An otherwise well-child, who recovers quickly from the seizure, does not have meningitis; lumber puncture and imaging studies are not needed.
The source of infection should be sought.

Management

The usual standards of management apply for the child who presents with active seizure.
The source of infection should be sought and treated.
Hospitalization is not usually required for a febrile seizure[7].
The prophylactic management of febrile seizure has been divided into two categories:

Intermittentprophylaxis

More than 90% of children with febrile seizure can be successfully managed with intermittentprophylactic therapy using paracetamol and diazepam 0.33mg/kg body weight (per rectal or oral) during fever episodes.

Continuous prophylaxis

Children who have frequent or prolonged febrile seizure, especially if associated with development delay and/or neurologic dysfunction and epileptiform discharge in the EEG may need continuous prophyaxis with either sodium valproate or phenobarbitone. Generally sodium valproate is preferreddue to the adverse effect of phenobarbitone on cognition and learning. Generally children need prophylaxis till 5 years of age, since they have a theoretical chance of seizures till that age. However, epidemiological studies have shown that the vast majority of febrile seizures occur during the first 3 years. So prophylaxis till 2 years of continuous seizure free interval and then start tapering the medication is justified[8].

Prognosis

The prognosis is excellent. Children who were neurologically normal before the seizures, even several febrile seizure, develop normally afterwards. Factors that increase the risk of later afebrile seizure are: 1. Neurological or development abnormally before the febrile seizure, 2. Family history of febrile seizure and 3. a complex febrile seizure.
The presence of one of these factors does not increase the risk of epilepsy, but the concurrence of the two factors increases the risk to 2% and three factors increases the risk to 10%[7].

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Telepathology in the diagnosis of Carcinoma of breast : A case report.

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The Orion 2003 ; 15 : 92

Introduction

Telepathology is the practice of pathology at a remote site using images (macroscopic, microscopic) transmitted by a variety of telecommunication system. Many countries have an acute shortage of specialist cytopathologists both for diagnostic service and for educational service. There are also many busy overcommitted pathologists who try to cope with Cytopathology, working in isolation in large traffic clogged cities, in remote inaccessible hospitals and in remote rural areas, who would benefit from regular contact with colleagues for confirmation of diagnoses, for second opinions, for discussion of difficult cases and for continuing education.

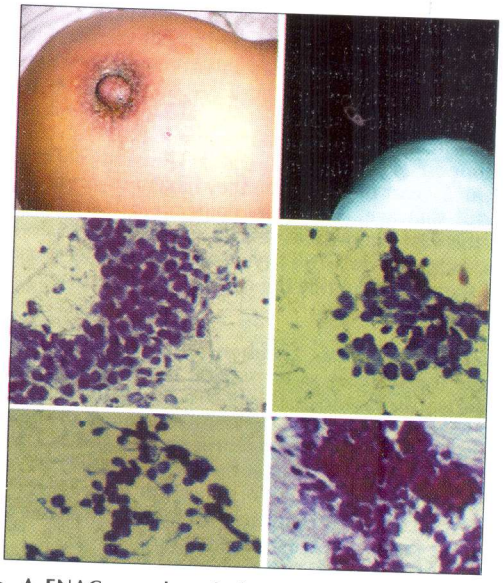
E -mail connections have facilitated the convenient and inexpensive transfer of digital images around the globe.

Sending images by e-mail attachment is easy and inexpensive. Their reception in most areas of the globe in very good, the quality and resolution of the images is surprisingly sharp with low, medium and high magnification.

We are reporting here a case where telepathology played a vital role in the diagnosis of breast carcinoma.

Material and Method

A 33 year old single female presented with a left sided 6 cm firm breast lump. The overlying skin is fixed with the lump. The naked eye appearance suggests a tumour with pagetoid involvement of the



nipple. A FNAC was done before by a competent pathologist and reported as traumatic fat necrosis. FNAC is done for second time by one of the authors (MGM). The features are presented below.

Pathology findings:

The material is hypercellular with a good number of atypical cells arranged in tight clusters and loose groups but the single malignant tumour cells are not present in the background. The cellular atypia are not sufficient enough to qualify it as malignant but there is obvious abnormality.Moreover, considering the clinical appearance of the breast the lesion was reported as suspicious malignant lesion but a confident diagnosis of breast carcinoma could not be made. The case was processed for telepathology consultation. Digital images are prepared from the cytology slides and also clinical images are prepared. All the images are sent to the participating pathologists by email with the above mentioned clinical history. Within 72 hours, five pathologists of Europe opined the case as duct cell carcinoma. The information was passed to the patient and also to the Surgeon. Accordingly, the patient was given chemotherapy and surgery was done. The surgical specimen came out as infiltratingductal carcinoma, NOS, moderately differentiated.Again the case was sent to the same groups of Pathologists and everybody opined the same.

Discussion

Telepathology can play an important role in the diagnosis of patient particularly for second opinion. It can also play an important role in the education of Pathologists. In the present case the lesion was schirrous type and the tumour cells were small. Diagnosis of small cell type of breast cancer is very difficult and requires much experience. The practice of telepathology definitely helps the Surgeon in proper management of patients. At the same time it helps in the training of local Pathologists and thus increasing capabilities of local experts.

Reference:

1. Mostafa MG, Learmonth GM. Telepathology in Bagladesh. The Orion 2003; 14: 49.

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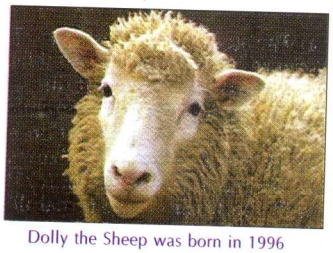
Dolly the cloned sheep dies



Dolly the Sheep was born in 1996

Dolly the sheep, who became famous as the first animal to be cloned from an adult cell, has died. The news was confirmed by the Roslin Institute, the Scottish research centre which created her, on Friday. A decision was taken to "euthanase" six-year-old Dolly after a veterinary examination showed she had a progressive lung disease, the institute said in a statement. Dolly became the first cloned mammal after being born on 5 July, 1996 at the research institute in Scotland.

Post mortem

She was revealed to the public following year. Dr Harry Griffin, from the institute, said: "Sheep can live to 11 or 12 years of age and lung infections are common in older sheep, particularly those housed inside. "A full post-mortem is being conducted and we will report any significant findings" Dolly was a sheep created totally by design - even her name was picked specifically to be appealing. It came about during the latter stages of labour when Dolly was born. Stockmen involved in the delivery thought of the fact that the cell used came from a mammary gland and arrived at Dolly Parton, the country and western singer. Cloning row Her birth was only announced seven months later and was heralded as one of the most significant scientific breakthroughs of the decade. But it also prompted a long-running argument over the ethics of cloning, reaching further levels with the latest allegations of human cloning. Dolly, a Finn Dorset, bred normally on two occasions with a Welsh mountain ram called David. She first gave birth to Bonnie in April 1998 and then to three more lambs in 1999. But in January last year her condition caused concern when she was diagnosed with a form of arthritis.

bbc.com/health

Launching of New Products.

Orion Laboratories Ltd. has recently introduced the following eight new products in the market.

Maximox

Moxifloxacin INN 400mg.

Feel better faster

Maximox(Moxifloxacin) is a 4th generation synthetic fluoroquinolone antibacterial agent. It is indicated in the treatment of acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community acquired pneumonia. Rapid onset of action, excellent tissue penetration & low Mic lever are the prime characteristic of Maximox. Maximox is presented in the form of 400mg tablet. MRP. TK. 100.00/tab.

Fenocap

Fenofibrate BP 200mg

The super lipid regulator

Fenocap (Fenofibrate) is a fibric acid derivative approved by FDA.It is indicated as adjunct to diet for the treatment of adults with hyper- triglyceridemia (types IV and V hyperlipidemia) who have not responded adequately to diet therapy.It is also indicated in mixed hyperlipidemia (types-II hyperlipidemia). Fenocap is presented in the form of 200mg capsule. MRP. TK. 7.00/cap.

Ralox

Raloxifene HCL INN 60mg

Magic therapy for post -menopausal osteoporosis.

Ralox (Raloxifene)is a selective estrogen receptor modular . It is indicated for the prevention and treatment of osteoporosis in postmenopausal women. Ralox effectively prevents bone loss and protects fracture . Ralox is presented in the form of 60mg tablet.
Price: MRP TK. 10.00/tab.

Flegnil

Carbocisteine BP

The first and only expectorant suspension in Bangladesh

Flegnil (Carbocisteine) is a mucoregulator- mucolytic. It is indicated for the treatment of chronic respiratory conditions like bronchitis, bronchial obstruction as in asthma, bronchiectasis, upper respiratory tract congestion, glue ear, otitis media, cattarrah, rhinopharyngitis. Flegnil is presented in the form of suspension 125mg/5ml. MRP. Tk .30.00/phial.

Tamlosin

Tamsulosin Hydrochloride INN 0.4mg

Drug of first choice for the management of BPH

Tamlosin (Tamsulosin), a supper selective $\propto_{1A}$- adrenergic blocking agent is indicated for the management of Benign Prostatic Hyperplasia. Tamlosin significantly improves the urinary flow rate of BPH patient. Tamlosin is safest among all a blockers. Tamlosin improves the AUA symptom score within seven days. Tamlosin is presented in the form of 0.4mg tablet. MRP. TK.15.00 / tab.

Glucart

Glucoseamine HCl INN 500mg

Natural healing drug for Osteoarthritis

Glucart (Glucoseamine HCl) is a natural substance found in cartilage,tendons and ligament tissues. It is indicated for the treatment of Osteoarthritis.Glucart accelerates cartilage repair , minimizes narrowing of joint space and improves joint function and relieves pain. Glucart is presented in the form of 500mg tablet. MRP. Tk 2.50/tab.

Axet

Cefuroxime Axetil USP

Decisive Assault Against Pathogens.

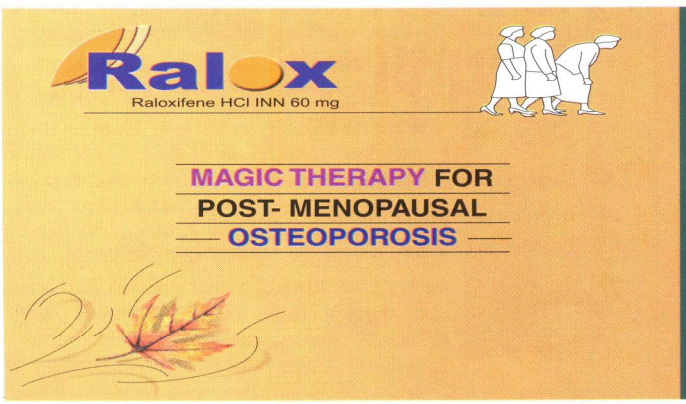
Axet (Cefuroxime Axetil) is a prodrug of cefuroxime, a semisynthetic analog of cephalosporin, which is active against a wide range of gram - positive and gram- negative bacteria. It is indicated for the treatment of upper respiratory tract infections, lower respiratory tract infections, uncomplicated skin and skin structure infections, uncomplicated gonorrhoea, genito-urinary tract infections. Axet is presented in the form of 125mg and 250mg tablet. MRP. Axet 125 -TK. 15.00/tab, Axet 250 Tk.-25.00/tab.

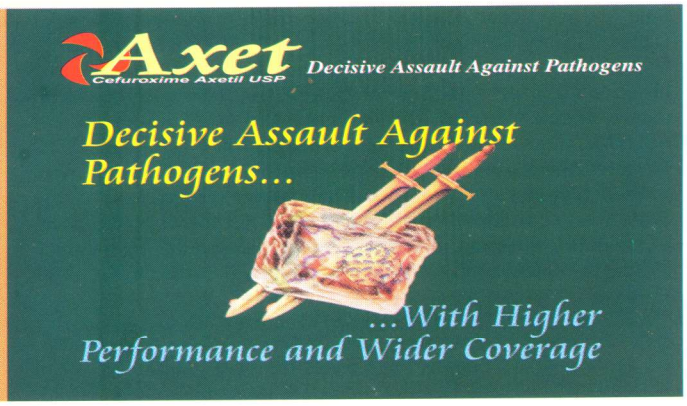
Venlaf

Venlafaxine 25mg

FDA approved 1st line therapy for Depression and Generalized Anxiety Disorders (GAD)

Venlaf 25mg has been launched which is the brand extension venlaf 75 mg. MRP. Tk. 4.00/tab.





MSD NEWS

MSD personnel of ORION Laboratories Limited spent a busy schedule in the last quarter of 2003, in arranging seminars in different topic as a part of Continued Medical Education Program.

Seminar on Management of Depression

Venue: Dr. Milon Auditorium of BSMMU, Dhaka

A scientific seminar on Management of Depression: Pharmacological Aspect's was arranged by Orion Laboratories Ltd. on 31st December 2002 at Dr. Milon Auditorium of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka. Prof. M. A. Sobhan, (Chairman of Psychiatry Department of BSMMU), chaired the session and Prof. M.A. Tahir(Pro -Vice Chancellor of BSMMU), Prof. M.A. Mannan Miah(Pro-Vice Chancellor of BSMMU), Prof. A.K.M.N. Chowdhury(Professor of Psychiatry - Retired), Prof. Hidayetul Islam(Professor of Psychiatry -retired), Prof. Anisul Haque (Chairman of Neuromedicine Department of BSMMU) and Assoc. Prof. Dr. Shah Alam (Head of Psychiatry Department ,DMCH) were also discussed their valuable opinion as a pannel member on the occasion.

From left to right: Assoc. Prof. Dr. Shah Alam, Prof. Anisul Haque, Prof. Hidayetul Islam, Prof. M A Sobhan, Prof. AKMN Chowdhury, Prof. M A Tahir, Prof. M A Mannan Miah

Venue: Pabna Mental Hospital, Pabna.

A Scientific seminar was arranged by Orion Laboratories Ltd. on 'Venlaf- A new approach for the treatment of depression' on 29th January 2003 at Sagotom Chinese Restaurant,Pabna . Prof. Dr. Md. Nazmul Ahsan , Director of Pabna Mental Hospital, Pabna was present as the chairperson of the seminar.

Venue: Monorog clinic, Mirpur, Dhaka

A Scientific seminar was arranged by Orion Laboratories limited on - A new approach for the treatment of Depression on 20th February 2003 at Monorog clinic, Mirpur, Dhaka. Eminent Prof .Hidayetul Islam (Professor. of Psychiatry -retired) was present as the chairperson of the seminar. Prof. M.A. Sobhan Chairman of Psychiatry Department, BSMMU & Prof A.K.M.N Chowdhury (Professor of Psychiatry -retired) was also presented their scientific papers on "Overview on Depression" and "Management of Depression" respectably.

Seminar on Management of Congestive Heart Failure

Venue: Lecture Gallery of Faridpur Medical College

A Scientific seminar was arranged by Orion Laboratories Ltd. on Role of Diuretics in Clinical Practice on 23rd February 2003 at Lecture Gallery, Faridpur Medical College (FMC), Faridpur. Dr.Md. Enamul Karim, Principal of FMC chaired the session and presented his scientific papers on "Role of Diuretics in hypertension and up date in diuretics therapy".Dr. Sk. Yunus Ali , Asstt. prof.of cardiology, FMC and Dr. Md. Abdus Salam, Asstt. prof.of cardiology, FMC delivered their scientific paperson Pharmacology of diuretics and Role of diuretics in Congestive heart failure respectively. all the Professors, consultanta, doctors of FMCH & general practitioners of Faridpur expresssed their opinion on Frulac as thev right choice for the treatment of Congestive heart failure.

Venue: Thana Health Complex, Charfession, Bhola

A Scientific seminar was arranged by Orion Laboratories limited. on Frulac- Right Choice for Congestive heart failure on 22nd March 2003 at Thana Health Complex, Charfession, Bhola.. Dr. M. A. Rashid, THO, Charfession was present as the chairperson and expressed his valuable opinion on Diuretics.

Venue: Sadar Hospital, Bhola

A Scientific seminar was arranged by Orion Laboratories Ltd. on Frulac- Right Choice for Congestive Heart failure on 23rd March 2003 at Sadar Hospital, Bhola. Dr. Md. Kabiruzzaman, Consultant (Orthopaedic), Civil Surgeon (in charge)of Bhola ,chaired the session and expressed his view on Diuretics .

Seminar on allergy management

Venue: Auditorium of Nuclear Medicine Centre, SSMCH, Dhaka

A seminar was arranged by Orion Laboratories Ltd on January 29th 2003 at Auditorium of Nuclear Medicine Centre SSMCH on Management of Psoriasis - An overview & A Newer H1 blocker - Deslor. Prof. Md. Shahidullah (Prof. & Head of the Department of skin & VD) was present as Chairperson of the seminar.

Venue: Islamia Eye Hospital, Dhaka

A seminar was arranged by Orion Laboratories Ltd. on 9th February 2003 on 3rd Generation Antihistamine-Deslor - A break through in allergy management at Hall room of Islamia eye hospital, Dhaka. The seminar was chaired by Prof. M A Manzur, Director of Islamia Eye Hospital, Dhaka. Dr. S A Hasan presented his scientific paper on the occasion.

Medi News

The Top 10 anti cancer foods

The most powerful anti-cancer food of all is, of course, a daily helping of seafood - for the complete range of the 72+ natural trace elements, without which we cannot help but sicken - and worse.

Tomatoes. Besides loads of vitamin C, tomatoes are one of the richest sources of the flavenoid lycopene - which gives them their red colour - which has shown to defend, in study after study, against cancers of the lungs, cervix, prostate and mouth. Tomatoes are also one of the chief ingredients of "the Mediterranean diet", now well known for the many important health benefits it conveys.

Blueberries. In addition to plenty of flavenoids - the rich pigment of the berries - which has repeatedly shown to protect against several cancers, blueberries may also hold "the secret of youth". In a study published in Journal of Neuroscience, investigators found that elderly rats fed the human equivalent of at least 1/2 cup of blueberries per day, improved in balance, coordination and short term memory. A normal serving consists of one cup. Like other fruits and vegetables - and particularly so the 'dark' ones - blueberries contain chemicals that act as antioxidants, now believed by scientists to protect the body against "oxidative stress," one of several biological processes that cause aging.

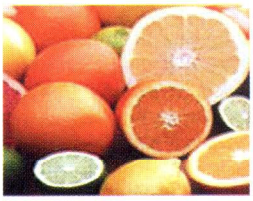
Red Cabbage, Red Beets. All cabbages - including their kin broccoli, cauliflower, kale, brussel sprouts bok choy, and so forth - are not only rich in calcium, but recent research has shown that they are also extremely rich in cancer-fighting flavenoids, the source of the purple colour of the red cabbages. But the red cabbage tops them all; it is the richest source of all vegetables, besides red beets. Red beets have so much of these flavenoids that it can alarm people who are not used to them, because it turns urine red. But there is no reason to panic, it's just the abundance of the potent flavenoids in red beets.

Spinach. Also one of the "dark" vegetables, spinach is also a rich source of vitamin C, beta-carotene - both are potent antioxidants - and folic acid, now discovered to be so vital to our health that the US Dept. of Health is considering adding it to flour. In several studies (University of Minnesota, Environmental Health Services, and others), it has been found that people who include two or more servings of spinach per week in their nutrition have considerably lower lung and breast cancer rates.

Garlic. Studies focused on garlic have shown, again and again, that this pungent onion kin lives up to its age-old reputation of being a powerful all-around health promoting food. The sulphur compounds that give it its strong flavour have now been shown to protect against cancer by neutralizing carcinogens and slowing tumor growth. In a recent Iowa Women's Health study, investigators found that women who consume garlic at least once a week also have a 32% lower incidence of breast cancer. Garlic is, of course, also a major ingredient in the now well known "Mediterranean diet".

Whole Wheat. In a recent study at the University of Iowa, scientist found that the more whole grain there is in a woman's diet, the lower her risk of breast cancer, as well as heart disease. In this study, as well as an analysis of 40 other studies on 20 kinds of cancer, investigators established that consumers of whole wheat products (bread, pasta, cereals) have a 33% lower risk of these diseases than those who do not eat whole wheat products.

Oranges. Already well known for their high vitamin C content, much recent research in the food sciences has shown that oranges are also rich in many other potent cancer-fighting compounds. Investigators have now found that oranges contain more than 170 photochemical, including more than 20 from the potent carotenoid family alone. In addition, compounds called limonoids - which give citrus fruit their slightly bitter taste - appear to be highly active cancer fighters as well. Regular consumption of oranges is associated with significantly lower lung and stomach cancers.



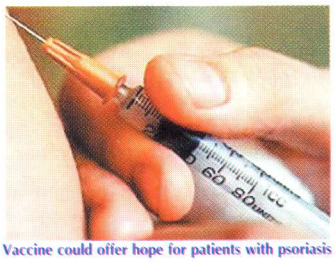
Strawberries. In a study tracking the diet and health of 1.271 people, researchers at the Harvard School of Health found that people who love strawberries have a 70% lower incidence of cancer. But, and as many other studies have shown, the same holds true for all other colourful and deeply coloured berries, such as cranberries, raspberries, blackberries, blueberries, red and purple grapes, and so forth.

Beans. Much recent research in the food sciences has established that all kinds of beans are loaded with protease inhibitors, compounds that make it hard for cancer cells to invade adjacent tissue. Fava beans contain much herein, which has shown to block carcinogens in the digestive tract. And soy beans are especially rich in isoflavones, which appears to reduce the risk of breast cancer by blocking the tumor-growing influence of estrogen. Lentils also belong to the bean family, and are one of the tastiest, most versatile, and easiest to prepare beans.

General Remarks. In addition to the above, all 'colorful' and deeply coloured fruit and vegetables - and the deeper the colour the better - including carrots, strawberries, red and purple grapes, and so forth - are rich in cancer-fighting flavenoids and anti-oxidants. And if you can get them as organically grown - without agricultural poisons - that much the better. This will also eliminate these poison residues from your nutrition. As the example of the whole grains demonstrates, try to stay as close to natural food - as Nature has made it - as possible in your choice of foods. Much that is important, even vital to our health is lost in the 'refining' of food.

CNN.com/health

Vaccine 'switches off' psoriasis


Vaccine could offer hope for patients with psoriasis

A vaccine which "switches off" part of the immune system - could provide a treatment for a debilitating skin condition. In tests, psoriasis disappeared in a quarter of cases and half saw an improvement. Benefits lasted for 18 months. Psoriasis is a disfiguring genetic condition, which affects at least one in 50 people in the UK, making it as common as rheumatoid arthritis and diabetes. It is thought to be caused by a malfunctioning of the immune system, which causes accelerated growth of skin cells. These cells pile up on the surface of the skin when the body cannot shed them fast enough, leading to unsightly patches of raised red skin covered by a flaky white build-up. The condition tends to affect people first in their twenties, though people can carry the gene and not suffer from the condition.

Treatment can currently either be with a drugs or with a cream.

Psoriasis is rarely fatal, but the psychological damage people can suffer because of the disfigurement can have a devastating effect on their lives. It can flare up because of stress or severe throat infections.

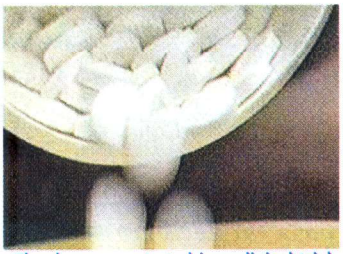
Vaccine hope

The vaccine, developed in New Zealand appears to "turn off" part of the immune system. The researchers say that a single shot can offer long-lasting protection. The vaccine was tested on 24 patients with psoriasis. Larger trials are now being carried out. Researchers carried out the trial after tests of an anti-leprosy virus in India had failed to cure leprosy, but had cleared up one patient's psoriasis.

That vaccine contained microscopic organisms called Myobacterium vaccae which had been killed using heat treatment. The New Zealand team used the same preparation in their vaccine. Dr James Watson, the Auckland researcher who led the trial, said most research concentrated on trying to find the proteins which trigger the disease. Instead his team had concentrated on changing the response of the immune system. Dr Watson said though the vaccine worked, they did not know why it had been successful in treating psoriasis. "Somehow the vaccine reprograms the immune system, turning off cells that attack the skin". He added that trials on animals had shown that the vaccine could be modified to be effective against other autoimmune diseases such as cardiovascular disease and diabetes.

Swift cholesterol drug'stops strokes'

Thousands of lives are being saved every year because doctors are prescribing more cholesterol-lowering drugs, government figures are expected to show.


The drugs were tested in a clinical trial

Radical improvements in combating heart disease over the last three years are due to be revealed in Department of Health statistics due out on Monday. But the Conservatives claim the cost of prescribing the cholesterol-lowering drugs, known as statins, is forcing local trusts to cut budgets for other treatments. Shorter waiting times for heart operations and quicker life-saving treatment for Britain's number one killer are also expected to be unveiled.

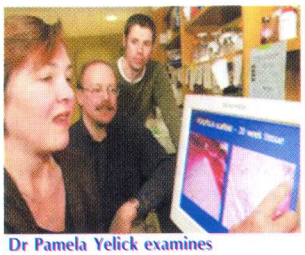
Risk lowered

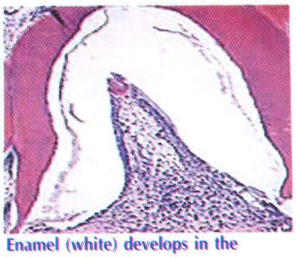
Statins work by reducing the level of cholesterol in the blood of patients with heart disease. About 6,000 lives in England alone may have been saved by the use of the drug, the DoH is expected to say.

Studies have highlighted the benefits of taking statins. Doctors have argued starting on anti-cholesterol drugs within days of having a heart attack might halve the risk of going on to suffer a stroke.

A study of more than 3,000 patients, carried out in California, reported in the journal Circulation last year suggested if the statins were given early, then the benefits could be greater. But some concern has been raised elsewhere by experts in the US that there may be an increase in deaths as a result of the success in keeping people with weakened hearts alive for many more years. Last week a survey found the UK still has one of the highest death rates for heart disease in western Europe, topping the table with Ireland and Finland, although rates are falling. The number of coronary artery bypass grafts has doubled over the last 10 years, and the number of angioplasties has risen by around 40% in the past year, the survey by the European Society of Cardiology (ESC) found.

Scientists grow teeth in lab


Dr Pamela Yelick examines tooth development


Enamel (white) develops in the implants after 30 weeks

Scientists have successfully used tissue engineering techniques to grow almost fully formed teeth. "It points the way for biologic repair in dental disease"- Dr Joseph Vacanti. They believe the breakthrough could eventually lead to a biological tooth substitute to replace human teeth. The researchers made a suspension of individual cells from a young tooth reorganise into a tooth crown containing both enamel and dentin. Dr Pamela Yelick told BBC News Online that it might be possible one day to grow human teeth of a particular size and shape. She predicted that within five years, we would know whether dental stem cells could be manipulated to bioengineer teeth. To generate a human tooth might take an additional five to 10 years.

Zinc cuts diarrhoea deaths

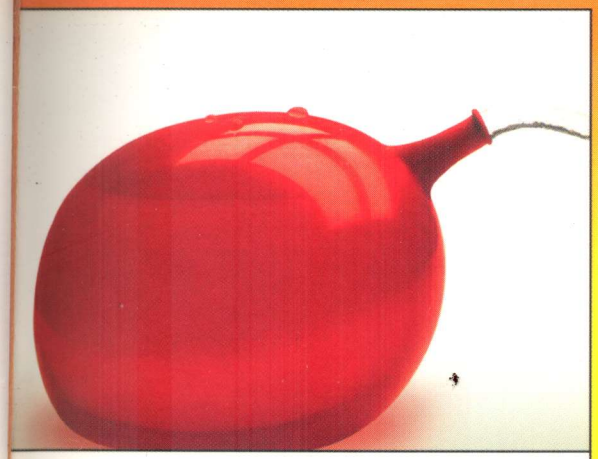

Zinc was tested on Bangladeshi children

An international study has found that zinc supplementation during diarrhoea reduces illness and death from the disease in Bangladeshi children. Researchers, led by Abdullah Baqui, associate professor at the John Hopkins Bloomberg School of Public Health, examined the impact of combining zinc therapy with an oral rehydration solution (ORS) in a study of more than 8,000 children who had diarrhoea. They found the combination significantly cut rates of death, illness and hospitalisation among the children. Despite medical advances, diarrhoeal diseases and the resulting dehydration are still responsible for about two million child deaths every year across the world. Most cases occur in developing, resource-poor countries where children suffer from malnutrition and access to clean water, safe sanitation and health facilities are limited. The children in the zinc areas received 20 mg zinc daily for seven days during each episode of diarrhoea in addition to ORS.

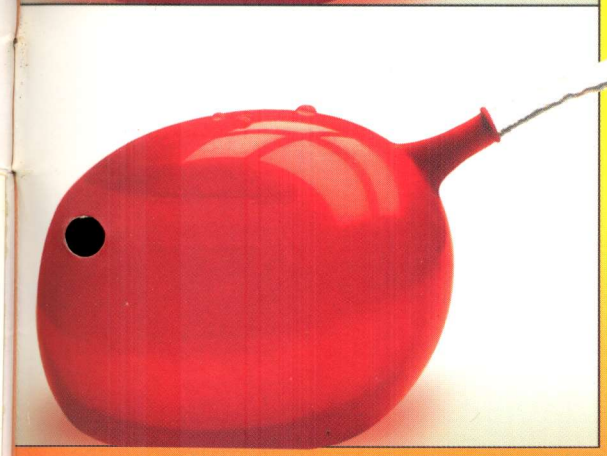
Antibiotics cut

Not only did zinc therapy help the children, its use led to a signficant cut in the use of antibiotics. Lead researcher Dr Abdullah Baqui, a Bangladeshi scientist, said: "The lower rates of child morbidity and mortality with zinc therapy represent substantial benefits from a simple and inexpensive intervention that can be incorporated within existing diarrhoeal disease control efforts and which should significantly improve child health and survival."

bbc.com/health



When advancing age signals BPH



Nothing works like

Tamlosin

Tamsulosin 0.4 mg

First time in Bangladesh

FenoCap

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The Super Lipid Regulator

First time in Bangladesh

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