

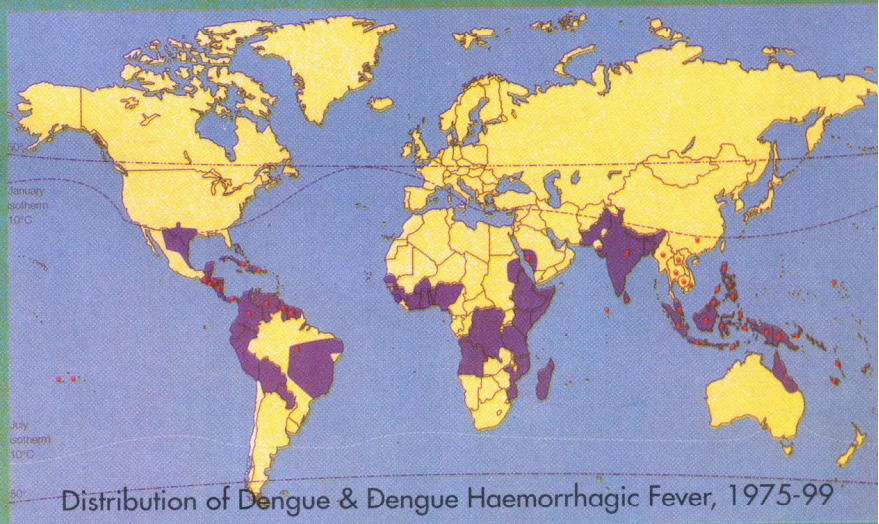
The ORION

Medical Journal

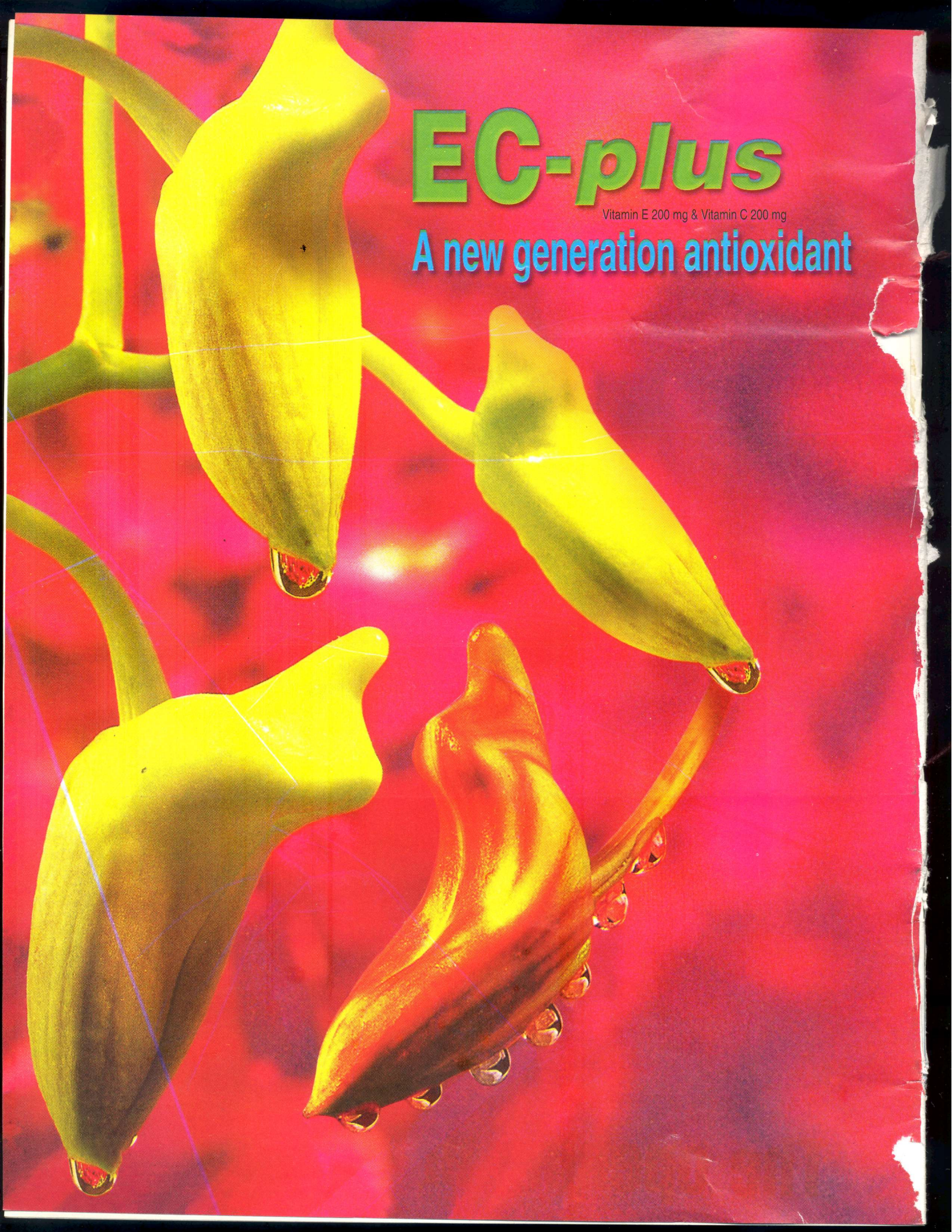
MULTI
DISCIPLINE
Vol. 6, May 2000

Situation of Neonatal Health in Bangladesh

Dengue and Dengue Haemorrhagic Fever in Bangladesh



ORION LABORATORIES LIMITED

A vibrant advertisement featuring four yellow bell peppers against a deep red background. The peppers are arranged in a cluster, with several clear water droplets clinging to their surfaces, particularly on the lower peppers. The lighting creates bright highlights and shadows, emphasizing the smooth texture of the peppers. The overall composition is dynamic and visually appealing.

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Cover Illustration : A pictorial depiction of the child health status in Bangladesh and geographical distribution of dengue and dengue haemorrhagic fever.

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Editorial

We offer our thankful gratitude to the esteemed readers of "The ORION" for their continuous patronization, leading suggestions and inspirations, and all these encouraged us to present this 6th volume of "The ORION".

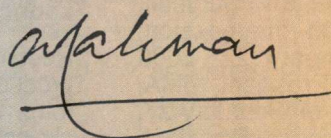
From this volume in view of the suggestions by our valued readers, we decided to cover all the disciplines of Medical Science (e.g. Medicine, Surgery, Gynae & Obs. and other specialities). We hope this form of presentation will be appreciated by you, as it will be more attractive for the doctors community.

"Zinc Therapy"-the much discussed topic among the medical professionals, was the theme of our last issue. Your overwhelming responses on this topic assured us - we are moving right towards "**our goal**", that is upgrading and updating the knowledge of medical science among the professionals.

Bangladesh is a small country with vast population of 120 million people. Half of this population is under 15 years of age of which 18.77% are below 5 years. Not only with population boom, we are also besieged with high Neonatal Mortality Rate(NMR) and Infant Mortality Rate(IMR). The prime causes of such high NMR & IMR are- neonatal jaundice, lack of proper pre and post-natal care, low birth weight(LBW), intrauterine growth retardation(IUGR), perinatal asphyxia, septicaemia etc. The situation is clearly alarming and requires urgent attention. For your better assessment we are highlighting the situation.

Infectious diseases remain the leading cause of death in Bangladesh and emerging infections contribute significantly to this ongoing burden by increasing the health care cost and days of disability. Among the emerging infectious diseases, Dengue & Dengue haemorrhagic fever is the common one. Noble laureate Dr. Joshua Lederberg has stated that "the microbe that felled one child in distant continent yesterday can reach yours today and seed a global pandemic tomorrow." As geographically, Bangladesh is situated in the dengue affected area, Dr. Joshua's statement may come into reality. For this, we are also enlightening Dengue and Dengue haemorrhagic fever in Bangladesh.

We expect our efforts will be very much helpful for all concerned. Suggestions and recommendations from our dignified readers will be most welcome.



Dr. ATM Azizur Rahman
Chief Editor, "The Orion"
and
Manager, Medical Services Department.



MSD News

In the first quarter of the new Millennium, the Medical Services Department (MSD) of Orion Laboratories Ltd. (OLL) once again spent a busy work schedule. As a part of its activities, MSD further arranged a number of Seminars and completed two important Clinical Trials. First one is the Efficacy Trial on Maprocin™ (Ciprofloxacin) and Nidazyl™ (Metronidazole) both intravenous and oral forms at the Department of Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka under the direct supervision of Professor A. N. M. Atai Rabbi, FCPS, FICS, Chairman and Head of the Department of Surgery, BSMMU. The excellent result of the Efficacy Trial prove the unparalleled merits of the brand which will definitely win the confidence of the medical professionals. The complete report of the trial will follow later on.

Second completed Clinical Trial is on Ortac™ (Ranitidine), Orixly™ (Amoxicillin) and Nidazyl™ (Metronidazole) as a regimen of triple therapy in eradication of *Helicobacter Pylori*, at the Department of Medicine, Dhaka Medical College Hospital, Dhaka, under the supervision of Professor Ferdous Ara J. Janan MBBS (Dhaka), MD (U.S.A), FCPS (M), FRCP (Edin), FIBA (U.K), Professor and Head of the Department of Medicine, DMCH. It is the most economic regimen (among all others regimen) which shows the highest cure rate (92.30%) against *H. Pylori*. The complete paper of the trial will be published in the next issue of "The ORION".

Seminars

a) *In Search of Ideal Antioxidant To Combat Cardiovascular Disease*

As a part of regular activities, MSD has arranged a number of Seminars on "In Search of Ideal Antioxidant To Combat Cardiovascular Disease". Dr. Md. Mamtaz Hossain, Associate Professor and Head of the Department of Cardiology, Dhaka Medical College Hospital, delivered speech on the topic as Keynote speaker in most of the following venues:

Khulna Medical College Hospital (KMCH) on January 21, 2000 chaired by Professor Dr. Md. Abu Bakkar, Professor, Department of Medicine, KMCH; Naogaon Sadar Hospital on January 24, 2000 chaired by Dr. Habibur Rahman, President, BMA, Naogaon & Dr. L. K. Sanyal, Civil Surgeon, Naogaon was the chief guest of the seminar; Bogra Medical College Hospital (BMCH) on January 26, 2000 chaired by Professor Dr. Abdus Shakur, Head of the Department of Paediatrics, BMCH; Gaibandha Sadar Hospital on February 20, 2000 chaired by Dr. Shah Aminul Islam & Dr. Eusuf Ali, Civil Surgeon, Gaibandha was the chief guest of the session; Nilphamary Sadar Hospital on February 22, 2000 chaired by Dr. Md. Alam Sufi, Vice President, BMA, Nilphamary; Gopalganj Sadar Hospital on February 27, 2000 chaired by Dr. Shah Nerod Chandra, President, BMA, Gopalganj; Kushtia Sadar Hospital on March 23, 2000 chaired by Dr. M. A. Quasem, President, BMA, Kushtia & Dr. Sardar Badar Uddin Civil Surgeon, Kushtia was the chief guest; Chuadanga Sadar Hospital on April 17, 2000 chaired by Dr. Zinnatul Ara, Secretary, BMA,

Chuadanga & Dr. Md. Abdur Razzak, Consultant of Surgery was the chief guest; Jhenidha Sadar Hospital on April 18, 2000 chaired by Dr. Azizur Rahman, President, BMA, Jhenidha & Dr. Moya Uddin Ahmed, Civil Surgeon, Jhenidha was the chief guest; Comilla Medical College Hospital on April 20, 2000 chaired by Prof. Jamal Nizam Uddin Ahmed, Head of the Department of Eye and Chairman, Scientific Committee, CoMC & Prof. Abdul Hoque, Principal (in charge) and Head of the Department of Surgery and Chairman, Course Committee, CoMC was the chief guest of session.

b) *Importance of Zinc for Health*

MSD also arranged a number of clinical sessions in the following venue to bring into focus the Significance of Zinc for Maternal and Child Health:

Khulna Medical College Hospital (KMCH) on January 21, 2000 chaired by Professor Dr. Md. Abu Bakkar, Professor, Department of Medicine, KMCH. Naogaon Sadar Hospital on January 24, 2000 chaired by Dr. Habibur Rahman, President, BMA, Naogaon & Dr. L. K. Sanyal, Civil Surgeon, Naogaon was the chief guest of the Seminar. Dr. Younus Ali, Civil Surgeon, Gaibandha was the chief guest of the session. Nilphamary Sadar Hospital on February 22, 2000 chaired by Dr. Md. Alam Sufi, Vice President, BMA, Nilphamary. Jameson Red Crescent Maternity Hospital (JRCMH), Chittagong on February 24, 2000 chaired by Dr. Shahana Begum, Chief Medical Officer, JRCMH. Gopalganj Sadar Hospital on February 27, 2000 chaired by Dr. Shah Nerod Chandra, President, BMA, Gopalganj. Kushtia Sadar Hospital on March 23, 2000 chaired by Dr. Quasem, President, BMA, Kushtia & Dr. Sardar Badar Uddin, Civil Surgeon, Kushtia was the chief guest of the Seminar; Chuadanga Sadar Hospital on April 17, 2000 chaired by Dr. Zinnatul Ara, Secretary, BMA, Chuadanga & Dr. Md. Abdur Razzak, Consultant, Surgery was the chief guest; Jhenidha Sadar Hospital on April 18, 2000 chaired by Dr. Azizur Rahman, President, BMA, Jhenidha & Dr. Moya Uddin Ahmed, Civil Surgeon, Jhenidha was the chief guest; Comilla Medical College Hospital on April 20, 2000 chaired by Prof. Jamal Nizam Uddin Ahmed, Head of the Department of Eye and Chairman, Scientific Committee, CoMC & Prof. Abdul Hoque, Principal (in charge) and Head of the Department of Surgery and Chairman, Course Committee, CoMC was the chief guest of session.

Launching of New Products

Recently Orion Laboratories Ltd (OLL) has launched a new product Eril (Enalapril Maleate) in both 5 mg & 10 mg doses form. This is the ideal product that will provide highly effective clinical application and ensure better compliance specially in Hypertensive and Congestive Cardiac Failure patients.

Orion Laboratories Ltd (OLL) is also going to introduce "EC-plus", (vitamin E 200mg & vitamin C 200mg) a new generation antioxidant, specially ideal for the patients with cardiovascular disease as well as for patients with other diseases.

Situation of Neonatal Health in Bangladesh

M. N. Islam

Introduction

Bangladesh is a small country of 147,570 Square Kilometers with a vast population of 120 million. Remarkable is that about half of the population is under 15 years of age, of which 18.77% are below 5 years. Greater portions of our children are besieged with poverty, diseases and illiteracy. Infant mortality rate is very high (81/1000 live births) in this country. More than two third of this high infant mortality rate accounts for deaths within 1 month of age (Neonatal mortality rate, 58/1000 live births). Total neonatal death 152,000/ year in Bangladesh. Compared to the neonatal deaths of the other countries, it is one of the highest (Japan: NMR 5/1000 live births). Neonatal morbidity is also among the highest in the world (Table 1).

Disease Profile

The disease profile among the neonates in Bangladesh is not exactly known as very few data are available from rural Bangladesh. The figures available are mainly hospital based. The commonest illness for which a newborn is admitted in the neonatal ward is neonatal jaundice (30.71%). This includes physiological jaundice, jaundice of prematurity and other conditions like Rh incompatibility, ABO incompatibility & jaundice due to septicaemia. Other causes of neonatal admission include perinatal asphyxia (21.98%), low birth weight (13.25%), septicaemia (9.06%), very severe pneumonia, infant of diabetic mother, haemorrhagic disease of the newborn, meconium aspiration syndrome, congenital abnormalities etc. (Table 2). Prenatal asphyxia which is a major neonatal health problem in Bangladesh and in this subcontinent is more common in rural areas. About 95% of rural birth and 65% of urban births are attended by untrained personnel. 12 out of 1000 newborns die within few hours of birth. Perinatal asphyxia is common in rural area because antenatal risk factors are not identified. This is because the pregnant mothers are not motivated to attend antenatal care. Therefore hypertension, diabetes, and other maternal illness are not diagnosed in time. Care to overcome the maternal malnutrition during pregnancy is not given.

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Mothers in rural areas work very hard during pregnancy which also results in IUGR. When these deliveries are conducted at home by untrained personnel- results into perinatal asphyxia in most of the situations.

Low birth weight is a major neonatal health problem. Incidence of LBW is about 30-50% in Bangladesh. This is common due to the same reasons like maternal malnutrition, overwork during pregnancy, uncontrolled hypertension, prolonged UTI & other maternal illness. These babies die because of hypothermia, hypoglycemia and infections.

Septicaemia is the third common cause of neonatal morbidity and mortality which accounts for 13-18% of neonatal death. Common cause for this is poor unsafe delivery, prolonged rupture of membrane and poor hygiene. Septicaemia if not treated in time and adequately will result in high mortality.

Congenital abnormality, birth injuries & other causes account for 13-18% of neonatal death. Important social factors for such high neonatal morbidity & mortality are illiteracy, ignorance, poverty, superstition and religious belief.

Causes of Neonatal Deaths

The most important cause of neonatal deaths in Bangladesh is perinatal asphyxia (39%). Other important causes include preterm, low birth weight and IUGR (21%), septicaemia (16%) (Table 3). This figure is obtained from hospital admission.

But the situation in rural community is different. Studies from Matlab, a rural area in Bangladesh shows that the majority of the newborn die due to complications of small size at birth (59%). Pneumonia, diarrhoea, birth trauma are other causes of death (table 4).

Existing Facilities

The existing facilities which are available in Bangladesh for care of newborn is not adequate. This is available mainly in tertiary care hospitals and some of the district hospitals. As such the facilities available are giving service to the urban and peri urban areas. As the vast majority (90%) of population are living in rural areas and most of the deliveries (95%) occurring in rural areas by untrained persons (Table 5), the real break through in neonatal care and reduction in neonatal mortality rate will occur only when neonatal care is provided in rural areas.

Grade III (Level III) and Grade II (Level II) facilities are available only in city hospitals. Grade III facility provides

care to very sick newborns that is ELBW, extreme preterm baby, severe perinatal asphyxia and severe respiratory depression due to other causes. The facilities include ventilators, central oxygen supply, closed and open incubators, blood gas analyzer, syringe pump phototherapy unit and arrangement to control room temperature. This facility are available in Dhaka Shishu Hospital (DSH) and BIRDEM Hospital (both are autonomous).

Grade II facilities provide all care except ventilator care. This means these units provide care to perinatal asphyxia, LBW, preterm babies, babies with hyperbilirubinemia and septicemic babies. These facilities are available in Bangabandhu Sheikh Mujib Medical University (BSMMU) all Medical College Hospitals (13 Govt. and 7 Private), some District Hospitals, Institute of child and Mother Health (ICMH), and some Private Hospitals and Clinics in major cities. Besides the expansion of neonatal care facilities in

Government Hospitals, some Private Hospitals and Clinics are also developing neonatal health care facilities now-a-days, which includes both Level-III and Level II care.

As a matter of satisfaction, it is worth mentioning that the Govt. of Bangladesh is introducing HPSP (Health and Population Sector Programme) and under this programme the facilities are being extended in the rural areas.

The Essential Service Package (ESP) under the HPSP for neonatal care includes-

- I) Training of Manpower-Doctors, Nurses, Paramedics, FWV, TBA etc.
- II) Services in the community at thana, union and village level. Each Community clinic situated in the village will serve 6000 population in the area.

This programme is planned as follows :

The ESP operational Plan of the Government's HPSP has the following components in relation to newborn care:

No	Level	Service Provider	Skills required
A	community outreach/satellite = "community clinic"	A. HA B. FWA C. Community midwives D. Community volunteers	1. Umbilical cord care 2. Health education for mothers on cleanliness 3. Resuscitation of asphyxiated newborn 4. Prevention of hypothermia Initiation of exclusive breast feeding.
B	Union level	1. FWV 2. MA 3. MO 4. AHI 5. FPI	1. Umbilical cord care 2. Health education for mothers on cleanliness 3. Resuscitation of asphyxiated newborn 4. Prevention of hypothermia 5. Initiation of exclusive breast feeding 6. Special care of preterm and LBW babies through ❖ nasogastric tube feeding of expressed breast milk ❖ maintenance of warmth ❖ barrier nursing ❖ hand washing before handling each baby
C	THC/ First Referral level Service provider:	1. FWV 2. MA 3. MO 4. AHI 5. FPI	1. Umbilical cord care 2. Health education for mothers on cleanliness on cleanliness 3. Resuscitation of asphyxiated newborn 4. Prevention of hypothermia 5. Initiation of exclusive breast feeding 6. Special care of preterm and LBW babies through ❖ nasogastric tube feeding of expressed breast milk ❖ maintenance of warmth ❖ barrier nursing ❖ hand washing before handling each baby

Professional Bodies

Besides the activities of the Government sectors, some professional bodies like Bangladesh Pediatric Association (BPA), Bangladesh Perinatal Society (BPS) and Bangladesh Neonatal Forum (BNF) are working conceitedly to develop manual on "essential care of the newborn" to incorporate this in the Essential Service Package (ESP) of HPSP. This manual is nearly ready for adoption by the Government. These societies have already conducted few training programme on "Resuscitation of the newborn" and have organized few seminars and workshops on perinatal care and neonatal care.

Future of Neonatal Care :

Future programme for care of newborn in tertiary, secondary and primary levels is expected to be improved. The Ministry of health and FW, Govt. of Bangladesh along with the assistance of WHO, UNICEF and other giving organization is planning to provide level -III care in all Medical. College Hospitals and post graduate institutes including BSMMU. The HPSP programme is expanding the services of neonatal care up to the community level through community health centers and Union sub-centers. Professional bodies like BPA, BPS, BNF, are also trying to form strategies for training man power and helping Govt. Programme in the HPSP.

Conclusion :

The present situation about neonatal care in Bangladesh indicates that much more has to be done to improve the situation. This includes-

- Increased antenatal care especially for the rural population.
- Safe delivery in hospitals and clinics so that death of the newborn babies due to obstetric causes reduced.
- Immediate care of the newborn babies like clearing of the mouth cavity, keeping the baby warm by warping with warm clothes, care of the eyes, breast feeding immediately afterbirth for the full term babies and special care for feeding low birth wt. and preterm babies, transferring the risk babies to hospitals where Level -II and Level -III facilities are available.

Cooperation and combined efforts between the countries of the South East Asian region will help each other to improve the over all situation in the region. In this respect the experiences of some of the countries who have improved neonatal care to satisfactory level will help other countries of the region. SriLanka which is very near to India and Bangladesh can be taken as a model of development in child health and neonatal health.

Table I
Country Data-Bangladesh

Total Area	: 147,570 Sq. Km
Population	: 120 Million
Children below 16 years	: 47 %
Population below 5 years	: 18. 77%
Infant mortality rate	: 81/1000
Neonatal mortality rate	: 58/1000
Total Neonatal death	: 152, 000/ yr

Table II
Disease Profile with Death in Neonatal Unit

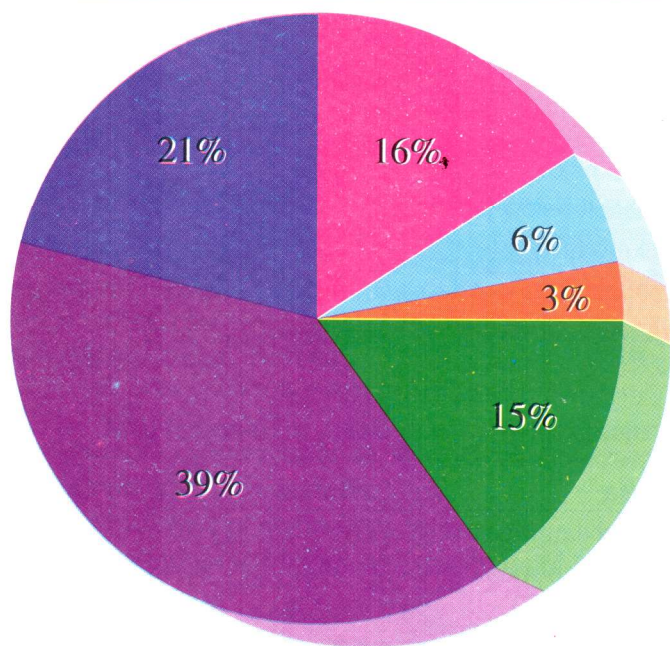
Disease	Total admission	Total death
Neonatal Jaundice	278 (30. 71 %)	*10 (6.49%)
Perinatal asphyxia	199 (21.98%)	60 (38.96%)
Low birth weight	120 (13.25 %)	32 (20.77%)
Septicaemia	42 (9.06%)	25 (16.23%)
Convulsion	49(5.45%)	4(2.5%)
Very severe pneumonia	20 (2.20%)	5(3.24%)
Infant of diabetic mother	19 (2.0%)	-
Haemorrhagic disease	16 (1.7%)	-
Meconium aspiration syndrome	15 (1.65%)	-
Congenital malformation	15 (1.65%)	-
Intrauterine growth retardation	10 (1.105%)	-
Others	82(9.06%)	18(11.64%)

* Mortality associated with infection & low birth weight

Table III
Causes of Neonatal Mortality

Perinatal Asphyxia	39%
Preterm / LBW/ IUGR	21 %
Septicaemia	16%
Neonatal Jaundice	6%
Very severe pneumonia	3%
Others	15%

Important Causes of Neonatal Mortality



- Perinatal Asphyxia -39%
- Septicaemia -16%
- Very Severe Pneumonia-3%
- Preterm /LBW/IUGR-21%
- Neonatal Jaundice -6%
- Others -15%

MORTALITY RATES: PER THOUSAND LIVE BIRTH

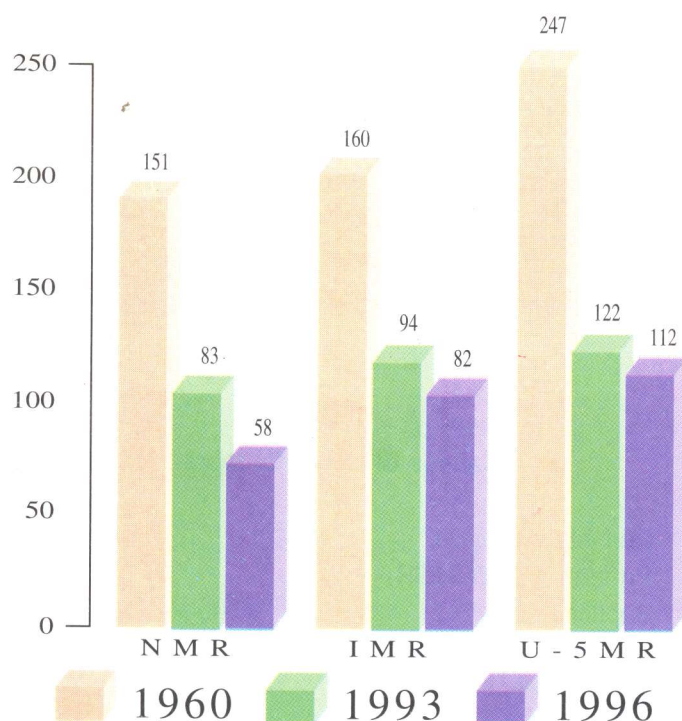


Table IV
Causes of Neonatal Death in the Community

Cause of Death	%
Complications of small size at birth	59
Neonatal pneumonia	9
Birth trauma	8
Diarrhoea	2
Neonatal tetanus	1
Other infections	3
Other disorders	6
Impossible to specify	12

Table V
Person Providing Assistance During Delivery in Rural Areas

Person	%
Untrained TBAs	57
Relatives/Others	25.7
Trained TBAs	7.5
Doctors	5.2
Nurse/trained midwife	2.8

References

1. Bangladesh Bureau of Statistics (BBS)
2. State of World Children; 1999:UNICEF
3. HPSP Manual; Ministry of Health and Family Welfare: Govt. of Bangladesh.
4. Progotir patha; 1999: UNICEF



The exhibition 'Body World' which opened on February 11, 2000 in Cologne, consists of anatomical specimens made from plastic. It attracted controversy when it was previously shown in Mannheim and Basle, with critics claiming that it dehumanised people.

Dengue & Dengue Haemorrhagic Fever in Bangladesh

M. N. Alam

Dengue (pronounced as 'Dhen Gey') is a mosquito borne febrile viral illness. Since its first recognition during the last quarter of eighteenth century, periodic outbreak has been reported from both developed and developing countries with Asia always remaining the area of highest endemicity^{1,2}. Until the middle of 20th century dengue was regarded as self-limited, non-fatal febrile illness with occasional hemorrhagic manifestations that only rarely resulted in severe or fatal outcome. Epidemic dengue with severe hemorrhagic manifestations was first reported in the Philippines in 1956^{3,4}. Since then epidemics which came to be known as dengue hemorrhagic fever (DHF)⁵ have occurred periodically in other South-East Asian countries^{4,6} and term dengue shock syndrome (DSS) was subsequently coined to describe cases of dengue associated with increased vascular permeability leading to intravascular hypovolemia and shock^{7,8}.

Although the disease has not been reported in detail from this country, serologic studies and virus isolation conducted on 25 cases during the outbreak of a febrile illness popularly known as "Dacca Fever" that occurred during the summer of 1964 revealed that the condition was due to dengue viral infection⁹. The associated severe hemorrhagic manifestations took a heavy toll during the outbreak. Another epidemic fever with features closely mimicking that of DHF occurred again in 1968 in areas of Bangladesh bordering Myanmar¹⁰.

Since that time sporadic cases and small outbreaks clinically suggestive of Dengue and DHF were seen from time to time by clinicians of the country but these cases remained unreported although entomologic and serologic study reports indicate that the mosquito vector and the dengue virus both existed during this period in Bangladesh¹¹⁻¹⁴.

An outbreak of an acute febrile illness that started in summer 1999 is currently spreading rapidly in and around the Dhaka city¹⁵⁻¹⁷. The illness, occurring in all age groups of both sexes, is often associated with hemorrhagic manifestations and other features suggestive of DHF/DSS and a positive serologic evidence of the condition in the majority of the cases.

This communication, which is based on the currently available literature on the disease, intends to provide answer to the various queries that are likely to occur in the minds of the clinicians on encountering cases of suspected dengue^{18,21}. Hopefully, these information will create an awareness that would be helpful in the detection, management and prevention of the condition in clinical practice.

What exactly is Dengue?

Dengue is a febrile viral illness common throughout the tropical regions of the world. In humans, dengue infection causes a spectrum of illness ranging from relatively mild, nonspecific viral syndrome known as dengue fever to severe hemorrhagic disease and death. The severe hemorrhagic form of disease is called dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

What are the different varieties of Dengue virus?

This virus has four serotypes- DEN-1, DEN-2, DEN-3 and DEN-4. Infection with one serotype does not offer protection against other serotypes; in fact, a second dengue infection leads to an even worse infection. This manifests as either DHF or DSS which can be fatal. All four serotypes can cause DHF/DSS, but severe disease appears to be more commonly associated with DEN-2 and DEN-3.

What are the vectors for Dengue?

Dengue viruses are transmitted in nature by day-biting Aedes mosquitoes. The most important mosquito vector is the highly domesticated urban species, *Aedes aegypti*.

How is it transmitted?

Dengue viruses are not contagious and person-to-person transmission does not occur. Transmission requires an infective mosquito (with infected salivary glands) to probe an individual in search of a blood meal. Multiple feedings or probing by an infective mosquito may result in transmission to multiple persons in the same household or building, all having onset of illness within a few days of each other.

Mosquitoes may become infected when they take a blood meal from a viremic person. Viremia is present for about 24 hours prior to onset and for an average of 5 days after onset of illness, usually coinciding with the period of fever. The infected mosquitoes require a period of incubation (the extrinsic incubation period) of about 8 to 12 days, before they can transmit dengue viruses to another person. During this time the virus grows within the midgut and infects a number of tissues in the mosquito, including the salivary glands.

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How long is the incubation period?

The average incubation period is 4 to 6 days but this can be as short as 3 days and as long as 14 days.

How long a patient will remain infectious to others after onset of symptoms?

An infected individual is never infectious to other persons, but remains infectious for mosquitoes for an average of about 6 days.

Can a survivor transmit Dengue to others after she or he has fully recovered?

No. Recovery is complete and there is no relapse or recrudescence of disease.

What is the natural reservoir for Dengue?

The most important reservoir hosts for dengue viruses are *Aedes* mosquitoes and humans.

All four virus serotypes are maintained in an *Aedes aegypti*-human-*Aedes aegypti* cycle in most urban centers of the tropics, where no other reservoir hosts are present or needed. It is this pool of viruses that played an important role in the current global resurgence of epidemic dengue in recent years, primarily by airplane travelers.

What is the geographical distribution of Dengue?

Dengue fever occurs in most tropical areas of the world and has a distribution that is similar to that of the principal mosquito vector, *Aedes aegypti*. The geographic distribution of DHF/DSS has been expanding in recent years and now occurs in tropical areas of Asia, the Pacific and the Americas (Figure-1).

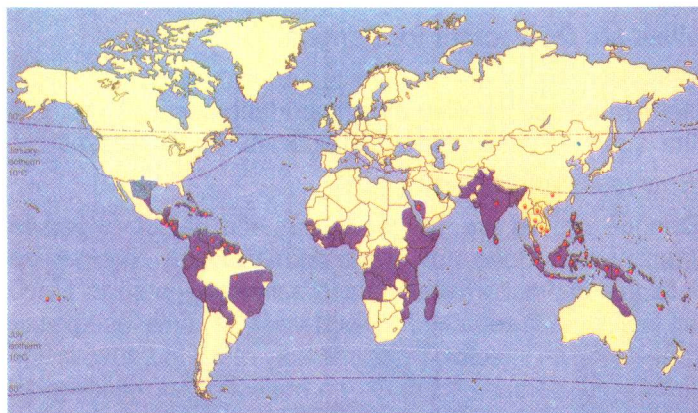


Figure 1: Geographical distribution of Dengue & Dengue Haemorrhagic fever.

What has caused Dengue epidemics to end in the past?

Emergency mosquito control measures have been used but these are generally not very effective and most epidemics end because of increased herd immunity. The end of an epidemic does not necessarily mean that the virus has disappeared from the area. During interepidemic periods, dengue viruses are maintained endemically in a mosquito-human-mosquito cycle in most large urban centers of the tropics.

What are the conditions that would lead to an increased epidemic activity?

Aedes mosquitoes like to breed, especially after rains, in standing water such as may be found in flower pots, cans, water jars, artificial ponds, nonbiodegradable plastic or cellophane bags and used automobile tires that are discarded in the environment. These are quite common in tropical urban areas, even around hotels.

The factors that have been implicated in the current increase of dengue include, urbanization, overpopulation, crowding, poverty, and a weakened public health infrastructure. Increased international air travel provide the ideal mechanism for the rapid movement of dengue viruses including new strains between populations.

Where exactly in the body the dengue virus replicates?

The primary site of dengue virus replication appears to be cells of mononuclear phagocyte but infection of the megakaryocytes in the bone marrow has also been proposed. The Viruses produce a viremia and virus can be isolated from the blood during the acute phase of illness.

In DHF/DSS cases, there is generally liver involvement. In fulminant hemorrhagic disease, which is not as common, viral particle or antigen have been detected in monocytes in most of the major organ systems including liver, lung, kidney, spleen, lymph nodes and heart. There is, some evidence that dengue viruses can infect the central nervous system.

How do I avoid catching it?

The best way to avoid dengue infection is to avoid *Aedes aegypti* mosquito bites.

The mosquito vectors of dengue are day-biters, with peak feeding activity in the morning for several hours after daybreak and in the late afternoon for several hours before dark. However, these mosquitoes may feed throughout the day in the shade, indoors, or on overcast days.

To avoid mosquito bites, persons should be aware of the above feeding behavior and use repellents containing less than 30% DEET on exposed skin at appropriate times and places. DEET, especially in high concentrations, can cause serious side effects, particularly in children; therefore, precautions should be taken. Mosquito coils are also useful repellents.

How the Dengue fever is manifested?

The dengue fever typically begins with sudden onset of high fever, severe headache-mostly frontal or retroorbital, weakness, malaise, depression, skin rash, and backache, deep muscle, bone & joint pains. The disease is known as 'breakbone fever' for these last symptoms. Taste aberrations, anorexia, nausea, vomiting and abdominal pain are other presenting features. The rash usually

appears 3-4 days after the start of the symptoms as diffuse flushing, mottling or pinpoint eruptions that begins on the trunk, spreading out to the face, arms and legs. Conjunctivitis may also be present.

There is often a relative or paradoxical bradycardia in the face of increased temperature.

Lymphadenopathy and hepatomegaly may occur but splenomegaly is infrequent.

Fever and associated symptoms may subside after 3 to 4 days and the patient may recover completely.

Alternatively, the decline in the fever may be followed 1 to 3 days later by a resurgence of fever and symptoms (biphasic), giving a "saddleback" appearance to the temperature curve.

A second rash, varying in form from scarlatiniform and maculopapular to petechial and occasionally purpuric, may appear with the initial decline of the fever.

Severe itching, especially of the hands and feet, may accompany this rash, which is sometimes followed by desquamation. The symptoms persist for 1 to 3 days more and then subside with the fever.

Mild hemorrhagic manifestations, such as epistaxis, petechiae, gingival bleeding and menorrhagia, are accepted as part of the clinical picture of classic dengue.

Most cases of dengue are benign, ending after about 7 days.

How can the DHF/DSS can clinically be suspected?

Patients who develop DHF/DSS generally have an onset of illness similar to that seen in "classical" dengue fever.

The critical stage of DHF/DSS occurs as the fever begins to drop around Day 3 to 5 of the illness.

Usually from 24 hours before to 24 hours after the temperature fall to or below normal, hemorrhagic manifestations may occur, and more importantly, circulatory instability may develop with signs of decreased peripheral perfusion leading to shock. The liver may become enlarged and pleural effusions may develop, usually beginning on the right side.

Disseminated intravascular coagulation and severe gastrointestinal hemorrhage and hematuria may also occur.

Manifestations of severe dengue (DHF/DSS) include severe hemorrhage leading to shock through blood loss, sudden increased vascular permeability acute effusion in serous cavities leading to shock with or without hemorrhage and severe hepatitis with encephalopathy. Encephalitis with convulsions and/or coma has recently been described with dengue infection.

How is it detected in the laboratory?

Diagnosis of dengue infection is best accomplished by obtaining an acute serum sample within 5 days after the

onset of illness for virus isolation and antibody testing and a convalescent serum sample 14 to 21 days after illness onset for detecting a rise in IgG antibody titer and/or the presence of antidengue IgM.

Most serologic screening for dengue infection is now done with an IgM ELISA. With appropriately timed samples, the sensitivity and specificity of this test in diagnosing dengue infection appear to be high. For single serum samples high (40 units or higher) antidengue IgM or for a paired sample at least a double rise in antidengue IgM (from below 15 units to more than 30 units) is considered as evidence of recent acute dengue infection. A high IgG > 100 units with low IgM (< 40 units) indicates recent secondary dengue infection. The IgM : IgG ratios as determined by ELISA may help in distinguishing primary from secondary infections. IgM / IgG ratios of 1.8 : 1 or more is considered to be indicative of primary dengue infection.

Specific diagnosis of dengue infection is made by isolating the virus from the patient's blood. Virus isolation can be made by mosquito inoculation, and by using C6/36 mosquito cell cultures. Virus is detected and identified by immunofluorescence using serotype specific monoclonal antibodies. Virus may also be detected from serum by amplifying dengue viral RNA by PCR technology.

What is the treatment of dengue fever?

Treatment for classic dengue fever is supportive. Patients should be encouraged to drink plenty of fluids.

Paracetamol may be taken to control fever and aching if necessary. Aspirin is contraindicated both because of its antiplatelet effects and the increased risk of developing Reye syndrome.

What is the treatment of DHF/DSS?

Suspected DHF/DSS cases should preferably be hospitalized, since shock may develop in about one-third of the patients. Patients should be carefully watched for any signs of clinical deterioration or warning signs of shock which usually occur on or after the third day of illness. The rather constant finding that a decrease in platelet count usually precedes the rise in hematocrit is of great diagnostic and prognostic value. In order to be able to recognize the evidence of a capillary leak syndrome & early signs of shock and thus take preventive action, platelet count and hematocrit value should be estimated daily.

Patients with mild DHF can usually be rehydrated orally and an antipyretic drug may be all that is needed. Salicylates should be avoided.

Patients should be treated immediately by intravenous fluids if there are any signs or symptoms of shock, a sudden rise in hematocrit or continuously elevated hematocrit. The fluid used for volume replacement should be isotonic solution with an electrolyte composition similar

to plasma. Administration of crystalloid solutions (Ringer's lactate or 0.9% w/v "normal" saline) to patients with shock is usually effective in restoring circulating blood volume, but large volumes are often required. More refractory cases may require use of colloid (Dextran 70 or the protein digest gelafundin 35,000). The administration of colloids containing molecules that escape slowly from the circulation may overcome shock more quickly and may be beneficial in preventing recurrence of shock and reducing the requirement for large volume of intravenous fluid and thus the risk of fluid overload. Fluid replacement must be stopped when the hematocrit and vital signs return to normal and diuresis ensues; otherwise, pulmonary oedema will occur when the extravasated plasma is reabsorbed.

Blood transfusions are contraindicated in patients with severe plasma leakage in the absence of hemorrhage, and if given, many cause pulmonary edema. Blood transfusions are indicated for patients with significant clinical bleeding. It may be difficult to recognize internal bleeding in the presence of hemoconcentration. A drop in hematocrit of 10% with no clinical improvement despite adequate fluid administration may indicate significant internal hemorrhage. Fresh whole blood is preferable and fresh frozen plasma and/or concentrated platelets may be indicated in some cases when consumptive coagulopathy causes massive bleeding.

Use of steroids is controversial, and the general consensus is that they have no beneficial effect in treatment of severe DHF/DSS.

Frequent recording of vital signs, platelet count and hematocrit determinations and monitoring urine output are important in evaluating the results of treatment. Prognosis depends on early recognition of shock based on careful monitoring, and proper management.

Can Dengue recur in a survivor? Does survival confer subsequent immunity?

Survival of infection with one virus serotype confers lifelong immunity to reinfection with that serotype, but not to the other three serotypes. Persons can have as many as four dengue infections in their lifetime, one with each serotype.

Is isolation required for the patient?

Isolation of the DHF patient is not required because there is no person-to-person transmission. It is recommended, however, that suspected DHF patients be housed in mosquito free facilities, i.e., closed buildings with air conditioning which are located in *Aedes aegypti* free grounds.

Is quarantine required as a preventive measure?

Quarantine is not required for Dengue.

How can Dengue be controlled?

Prevention and control of dengue can only be accomplished at the present time by mosquito control. This

can be achieved by the use of an integrated approach of environmental sanitation, insecticides and biological control, utilizing both government and community resources.

Is there any vaccine for dengue?

A live attenuated tetravalent dengue vaccine has been developed and is undergoing phase II studies but vaccine is not currently available for clinical use.

The ongoing outbreak of dengue in Bangladesh is likely to continue for some time and will perhaps take a heavy toll unless clinical cases are quickly recognized and a proper management is instituted promptly. Until an effective and safe tetravalent dengue vaccine is available for public health use, adequate measures to control the vector is warranted for quick containment and prevention of further spread of the condition.

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Neonatal Jaundice- A Practical Approach

M.A.K. Azad Chowdhury

Recognisable jaundice appears in about 60% of newborns in their first week of life. More than 90% of them are simple physiological jaundice, almost disappears by 3rd week of life and needs no intervention. But in these cases parents and relatives may have undue anxieties like- is it dangerous? infectious? transmitted from mother? and so forth. So, we need to have very clear idea about distinguishing physiological or benign jaundice from pathological or harmful jaundice. Failure of which still result in undue prolonged morbidity, mortality and very delayed referral.

Very careful history taking, physical examination and simple tests, if available can solve this problem.

Pathophysiology of Physiological Jaundice in the Newborn

In utero the foetus has to derive its total nutrition and oxygen from maternal blood perfusing the placental villae. This blood is about 60-70% saturated with oxygen, that is it contains less oxygen than that we inhale in our lungs. So to maintain proper oxygenation of the very rapidly growing tissues of the foetus the foetal blood has special characteristics to extract as much as possible oxygen from the maternal blood.

Foetal haemoglobin is different from adult haemoglobin and has higher affinity for oxygen and also the amount of haemoglobin in the foetus is about 60% more (18-20 gms /dl of blood) than in adult.

After birth, when the newborn starts breathing and receives oxygen directly from the air through his/her lungs, he/she no more requires those especially designed and excess haemoglobin to maintain oxygenation and metabolism of his/her tissues. At this time the redundant haemoglobin tends to rapidly breakdown and be cleared from the circulation. The life span of foetal R.B.C. is also less (80-90 days) than that of adult R.B.C.s so they breakdown rapidly and in large amounts. During this period the bone marrow finding no necessity to produce much R.B.C.s, takes some rest and functions minimally for several weeks.

The breakdown of this excess red cells & their haemoglobin produces excessive amounts of bilirubin pigments (35 mgm of bilirubin is liberated from 1 gm of haemoglobin) and is presented to the yet to fully mature

liver (structurally and enzymatically) to handle this bilirubin load for conjugation and excretion.

As the load of bilirubin gradually increases to beyond capacity of the liver to conjugate, clinically apparent jaundice appears.

In a normal full term baby by day 7 to 10 there is usually balance between production and excretion of bilirubin and the jaundice gradually disappears.

In a pre-term baby this process of maturity takes some longer time and the jaundice usually disappears between 15-20 days of life unless some other complication arises.

So, Physiological Jaundice will have following Features

- Will clinically be evident after 2-3 days of birth.
- The jaundice will gradually increase for 4-5 days.
- Will gradually decline spontaneously after one week of age and be almost unnoticeable after 2 weeks of age.
- Stool colour of the baby will be normal (yellowish).
- The baby's activity including sucking, swallowing will remain normal.

But if the features are otherwise as stated below, investigations are indicated

Pathological Jaundice

About ten percent of the clinically apparent neonatal jaundice may be outside the physiological domain and require investigations and active management.

The principal reasons for this abnormal neonatal jaundice are-

- 1) Excessive haemolysis, eg. Blood group incompatibility (Rh incompatibility, ABO, incompatibility, Minor group incompatibility)
- 2) Enzyme deficiencies, eg. G6PD deficiency
- 3) Haemoglobinopathies, eg. α -thalassaemia
- 4) From sequestered blood, eg. Cephalhaematoma, Multiple bruises.
- b. Infections like septicaemia.
- c. Impaired enterohepatic circulation, eg. Intestinal obstruction, hypertrophic pyloric stenosis.
- d. Obstruction to biliary flow.
- e. Immaturity/ congenital absence of enzymes.

Features of Pathological Jaundice include

- Jaundice appearing within day one or two of birth.
- Increases very rapidly.

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- c. The Jaundice appears to be very high at any time (the lower limbs and soles being prominently yellow)
- d. The jaundice don't start decreasing clinically after 7-10 days of age.
- e. The baby is sick otherwise with less activity - poor feeding, fever, vomiting, unhealthy umbilicus etc.
- f. The stool colour of the baby is pale.

Before sending blood for investigations the baby should be very carefully examined for signs of infection, injury, haematoma, hepatosplenomegaly, rashes, etc.

Following simple investigations will give clue to the diagnosis in more than ninety percent cases of neonatal jaundice.

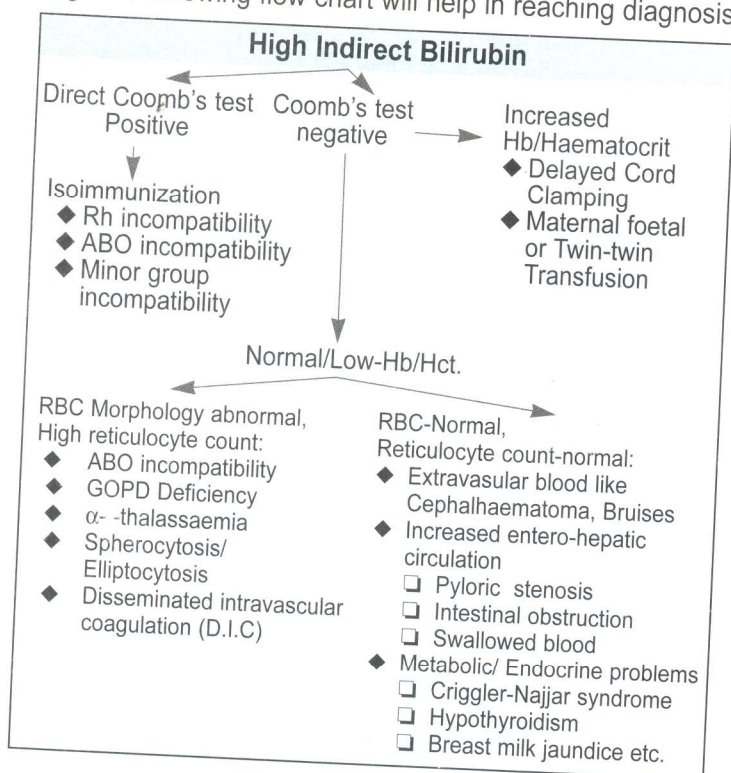
- * Mother's Blood group.
- * Baby's Blood group, Hb%,
- * Direct Coomb's test
- * Peripheral film, Reticulocyte count.
- * S. bilirubin

Total (Direct and indirect)

If the direct bilirubin is predominantly high the following possibilities need to be considered-

- ☐ Sepsis ☐ Hepatitis ☐ Biliary atresia ☐ Choledochal cyst.
- ☐ Transplacental infections, congenital - Rubella, Toxoplasma, CMV. ☐ α -antitrypsin deficiency.
- ☐ Congenital metabolic problem like galactosaemia etc.

If the indirect or unconjugated bilirubin is predominantly high the following flow chart will help in reaching diagnosis



After the initial tests further investigations should be done depending on the possibility, e.g. for suspected biliary atresia-ultrasonogram of hepatobiliary system and HIDA scan, for congenital infection-TORCH screening etc.

Clinical Assessment

So, whenever a neonate is brought with jaundice we should carefully take the history including the day it was first noticed, other associated features, mother's blood group, and very careful examination of the baby from head to toe. Clinical Assessment of jaundice should be made in open daylight. Gentle pressure over the skin of face, trunk, limbs will give idea about the degree of jaundice. If the jaundice is mainly limited to the face, chest and abdomen- it is likely to be mild to moderate (bilirubin usually below 10-12 mgm/dl). If the lower limbs soles and palms are prominently yellow it is usually moderate to high jaundice (bilirubin usually above 15mgm/dl). Our clinical experience correlates with this observation. So at places where serum bilirubin estimation is not easily available, this guideline may be used to decide whether a neonate with jaundice should be referred to a centre where proper investigations and management are available.

If there is strong suspicion of biliary atresia on the basis of high direct bilirubinaemia, pale stools, the baby should urgently be referred to a place where surgical intervention is possible. Because early diagnosis and surgery has high degree of success and good prognosis and delay of only six to eight weeks will cause irreversible damage to the liver.

Management

Physiological jaundice-requires reassurance to parents, encouragement for frequent breast feeding to avoid dehydration.

Early morning sun-bath for 15-30 minutes will accelerate the disappearance of jaundice and parents may like to do this but is not essential.

Phototherapy

Special blue light of wave length spectrum 420-470 nm. has been shown to make the indirect bilirubin water soluble by isomerization and photooxidation. Exposure of the baby's skin to this light hastens bilirubin elimination.

All cases of indirect hyperbilirubinaemia will benefit from this bili-light therapy.

The eyes and gonadal areas of the baby should be covered during therapy to avoid possible damage from ultraviolet light.

Use of ordinary light bulb for phototherapy is crude and only a fraction of this light has that specific wave lengths, so the effectiveness is less than the specially prepared

bulbs for phototherapy (bili-light bulbs). These bulbs are now available in our country.

It has been observed that intermittent phototherapy works almost as good as continuous phototherapy. So it is advised to give some rests, usually during and a while after feeding.

It should not be prescribed with hard fast rule of 45 minutes exposure and 15 minutes rest- it is just a guide line. During initial exposure baby quickly becomes irritable and cannot withstand the light more than only a few minutes but gradually he/she becomes accustomed. So the therapy period may need to be gradually increased and also, if the baby is found sleeping under the light, it is illogical to awaken him and bring out of therapy. Both sides of the body should be exposed to light by turning him/her from time to time.

Baby's temperature should be noted as frequently as possible to avoid hypo or hyperthermia. Some 20-30 ml per Kg body weight extra fluid will be needed during the course of phototherapy. Some loose stools and macular rash are acceptable minor side-effects.

If a jaundiced baby has some fever, feeding difficulty, vomiting, abdominal distention etc. infection should be highly suspected and looked for by doing a W.B.C. count, blood C/S and antibiotic should be started.

Exchange Transfusion

If a full term baby is found to have indirect bilirubin of more than 25 mg/dl or a pre-term baby with indirect bilirubin of 20mg/dl or more, he/she should be urgently referred to a place where exchange transfusion can be done. Baby of Rh negative mother with rapidly increasing jaundice should also be referred for early exchange transfusion.

Breast Milk Jaundice

Some mother's milk contain excessive amount of a progestational hormone (β -pregnendiol) which competes with bilirubin in the hepatocellular conjugation process, so indirect bilirubin remains high for prolonged period. The baby is otherwise healthy, sucks well and grows well. Blood investigations will show no abnormality. If one highly suspects breast milk jaundice and wishes to confirm it for parents satisfaction, estimation of S. bilirubin before and after temporary withholding of breast milk for about 24 hours will show a significant decline in bilirubin level. Management is only explanation and reassurance to parents. Breast feeding should never be stopped for this.

Explanation of the disease to the parents is very very important and should never be ignored.

So, simple but stepwise judicious approach to a case of neonatal jaundice is, what is required for its proper and effective management.



"Water baby" by Henry Korda.

Pelvic Inflammatory Disease (PID)

Sultana Zahan¹, Afsana Karim²

Introduction

In our daily practice the incidence of PID is very high approximately 1 in 5 patients. So it is very important to diagnose a case of PID and treat her appropriately. And we know that PID is a disease of the women which makes her life hazardous miserable. For the suffering of the women, who is the candle of the whole family, all the members of the family suffers most.

Risk Factors of PID

In some study it was assessed that the risk factors of PID are namely, use of intrauterine device, sexual activity with multiple partners, history of previous PID, history of minor gynecological operation, after age at menarche (≥ 14 years), history of stillbirth and no previous pregnancy, history of tuberculosis, history of previous laparoscopy.

Incidence of PID is increased three to nine fold in IUD users compared to non-users. More recent studies indicate that PID among IUD users is strongly related to the insertion process and to background risk of STD.

Pathogenesis of PID

Multiple microorganisms can cause PID but the most important causative organisms are *Chlamydia trachomatis*, *Neisseria gonorrhea*, and microorganisms associated with bacterial vaginosis. PID results most frequently from the ascent of these infections from cervix to the upper genital tract. The importance of cervical chlamydial infection in the pathogenesis of PID is well recognized.

Clinical Spectrum of PID

The clinical spectrum of PID ranges from subclinical endometritis to severe salpingitis, pyosalpinx, tubo-ovarian abscess, pelvic peritonitis, and peri-hepatitis. Diagnostic difficulties are compound by the wide variety of clinical presentations and insensitivity and poor specificity of laboratory tests. Better recognition of mild and atypical

disease needs a high index of suspicion whenever young, sexually active women present with gynecological symptoms. Statistics suggest that adolescents have a significantly higher rate of PID than does any other age group. Even symptomatic and minimally symptomatic PID can lead to adhesion, infertility and ectopic pregnancy. So clinicians should maintain a high index of suspicion when evaluating female adolescents with lower abdominal pain.

Estrogen-Progestogen contraception (OC) is significantly associated with the high prevalence of chlamydia trachomatis in the lower genital tracts of young women. In contrast PID is frequent and is associated with milder pelvic lesions in OC users than in non-users. A recent study suggests that OC use can be associated with silent endometritis and salpingitis. Thus OC masks symptoms of Chlamydial PID.

Diagnosis of PID

Clinical diagnosis of PID has limitations. The clinical diagnostic criteria are insensitive and nonspecific. False-positive and false-negative diagnosis is common; however, direct visual diagnosis is not always feasible, requires general anesthesia, and is costly.

For detection of microorganism, high vaginal swabs or aspiration from pouch of Douglas can be done. Laparoscopy and Trans vaginal sonography is done. Uterine sonographic findings may demonstrate free fluid in the cul-de-sac, ovarian enlargement, tubular adnexal structure or it may presents a complex nature. C-reactive protein concentrations and ESR values correlated positively with the sonologically determined volumes of pyosalpinx /pyoovaries, cul-de-sac fluid and ovaries.

Management of PID

A study demonstrated that clinical cure rate was 97% in the clindamycin and ciprofloxacin group and 95% in the ceftriaxone and doxycycline group in the treatment of mild to moderate PID. Side effects were similar in both groups. Triple-antibiotic therapy with ampicillin plus clindamycin plus gentamycin is the treatment of choice in women with tubo-ovarian abscess. Partner notification is an essential

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part of management if the PID is due to the infection of sexually transmitted organism.

In resistant and chronic cases where the medical treatment fail the surgical treatment is the answer. That is total abdominal hysterectomy and, bilateral salphingo-oophorectomy and removal of parametrial tissue as far as practicable.

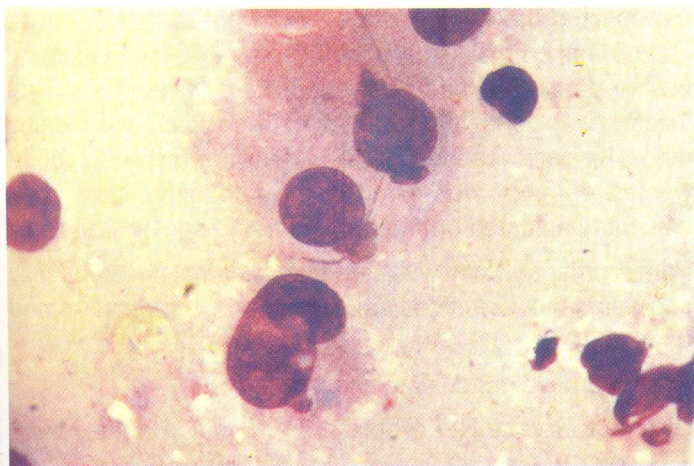
Here it is to be noted that the ovaries if healthy to be preserved when the patient is young (<40 years). The idea is to preserve the hormonal function of the ovaries. In other cases after operation, Hormone Replacement Therapy to be prescribed.

Prevention of PID

Certain reproductive behaviors could be targeted for public health attention and risk reduction interventions to reduce the incidence of PID. These include, limiting number of sexual partners and, encouraging the use of barrier methods of contraception for STD prevention. Another thing is that it is probably best to avoid sexual intercourse during menstruation.

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Chlamydial infection : Microscopic View.

(Abdominal Pregnancy - Continued from page no. 16) Discussion

Ectopic pregnancy is one of the leading cause of pregnancy death during the first trimester of pregnancy. It is a major problem in Obs. & Gynae because of its difficulties in diagnosis.

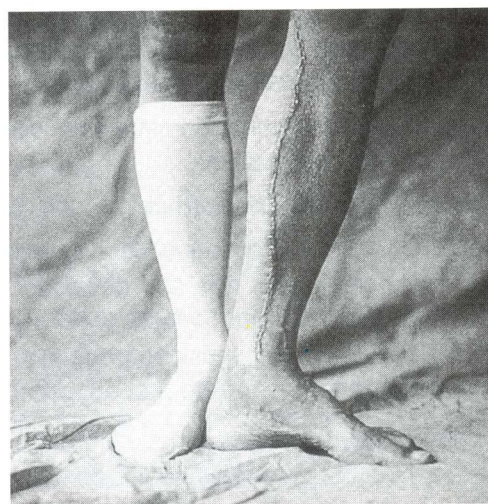
Abdominal pregnancy is one of the rarest variety of ectopic pregnancy, 1.5 of all ectopic is abdominal pregnancy. Abdominal pregnancy can be primary which is extremely rare. Second is secondary abdominal pregnancy. Primary abdominal pregnancy occur when fertilisation & implantation everything occur from the beginning in the abdominal cavity. secondary abdominal pregnancy occur when fertilisation occur in the fallopian tube-secondarily implanted in the abdominal cavity either after abortion or expulsion from the tube when blood supply to the pregnancy sac remain intact

Site of implantation may be in the omentum, liver, wall of the intestine, Secondary abdominal pregnancy can continue till term. Though it is rare but we have literature where abdominal pregnancy continue till term & living baby delivered by laparotomy.

Our case is one of the secondary abdominal pregnancy where primary fertilisation occurred in the fallopian tube & secondarily implanted on the omentum. Patient had typical symptoms of ectopic pregnancy but suspicion of abdominal pregnancy was not done though diagnosed as ectopic pregnancy .

In this case if careful searching was not done it could be missed. So suspicion in mind for the rarest variety should be kept. Only then the diagnosis can be done and patient will be benefited.

The Dance of Life



Kevin Robinson(a professional photographer) took this photograph of his father's legs 5 days after triple bypass surgery at St Vincent's Medical Center, Connecticut, USA.

Abdominal Pregnancy

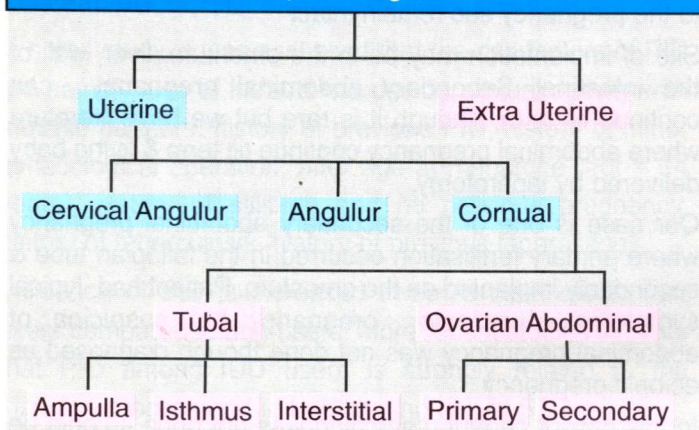
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Introduction

Ectopic Pregnancy is one in which a fertilized ovum implants in an area other than the uterine cavity.

The incidence in United Kingdom is 1:300 pregnancy. But the incidence varies from place to place & from country to country. In West Indies the incidence is 1:28 of pregnancy. The incidence is increasing due to the assisted reproductive techniques since 1972.

Sites of Ectopic Pregnancies are



95% of ectopic pregnancy occurs in fallopian tube. 1.5% abdominal, 0.5% ovarian, 0.03% cervical.

One of the rarest variety is our case-The abdominal pregnancy.

Case History

A 32 years old lady was admitted in OBS/Gyn department under G.U - I in BIRDEM with the chief complains of-

- 1) Occasional severe lower abdominal pain with fainting attack more than one month.
- 2) H/O MR for 6 weeks, amenorrhoea 1 month back.

She had M. R. On 13th September 1999 at Comilla Health Complex. 1 (one) week after MR she developed sudden severe lower abdominal pain which was spasmodic, persisted for 5-10 minute and subsided gradually. She had fainting attack during the pain. She had recurrent episode

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of similar pain with fainting attack every 2-3 days interval. According to advice by a doctor she had ultrasonogram of lower abdomen and report was given as a ectopic pregnancy and she was referred to BIRDEM for proper management.

She was married for 14 years, mother of two child and had one MR. She had irregular menstrual cycle and was taking injectable contraceptive last 5 years. She did not take her last due dose which was due on May 1999. Her LMP 28.07.1999.

On admission she was anxious, moderately anaemic with tachycardia of 112 pulse/per minute, BP 120/80 mm of Hg, other CVS+RTS was ok. On per abdominal examination, abdomen slightly distended, soft, no muscle guard, moderate tenderness on palpation, rebound tenderness +ve, BS+ve. On pervaginal examination, uterus was normal size, retroverted & mobile. Cervical excitation test was +ve. No fullness in pouch of Douglas or any fornices. No definite lump felt.

Provisional Diagnosis was Ectopic pregnancy.

Investigation was done. Her blood group B-ve, Hb%-8.5 gm/dl. Ultrasonogram of whole abdomen revealed single living ectopic pregnancy in right tubo-ovarian region about 10 weeks pregnancy size. Peritoneal collection suggestive of haemoperitoneum. Patient was managed with I/V fluid, blood transfusion and prepared for diagnostic Laparoscopy.

Diagnostic Laparoscopy done on 17.10. 1999 and diagnosed as a ectopic pregnancy.

Laparotomy proceeded-

On opening the abdomen- free blood in peritoneal cavity. Uterus was normal size. Right fallopian tube was lacerated but no pregnancy sac was found there. When peritoneal toileting was done, huge amount of fresh blood was coming out. After careful searching, a male living foetus about 12 week pregnancy was found in the abdominal cavity with placenta implanted on the omentum and sac ruptured.

Partial omentectomy with removal of complete pregnancy sac was done. Left sided tubectomy done, abdomen closed as usual.

Post operative period was uneventful.

Histopath Report: Rt-Fallopian tube-Ectopic Pregnancy.

Final diagnoses: Secondary Abdominal Pregnancy.

(Continued to page no. 15)

Tropical Pancreatitis

Motior Rahman

Tropical pancreatitis is a syndrome characterised by abdominal pain, diabetes mellitus and pancreatic calculi occurring in non alcoholic individuals in the tropics and subtropical regions. The disease is synonymous with tropical calcific pancreatitis, juvenile tropical pancreatitis, nutritional pancreatitis and chronic pancreatitis of the tropics.

The earliest report of this condition was described by Kini in 1937. Mahadevan reported his experience with 17 cases of pancreatic lithiasis in 1959. He treated several patients by external drainage of the pancreatic duct followed by washout of stones for as long as three months. In many of his patients long term pain relief was obtained for about 14 years. The largest series of cases was reported by Professor Gee Varghese in 1966 from Kerala. The disease occur in endemic form in this state of India.

Prevalence

The highest incidence in the world of tropical pancreatitis is in Kerala where 12 to 16% of the diabetics admitted to hospital had pancreatic calcification. A survey amongst newly detected diabetes mellitus under 30 years was carried out at BIRDEM which showed incidence of tropical pancreatitis (TP) is about 6 percent. An average of 40 new cases are diagnosed every year in our Centre.

Aetiology

The aetiology of TP is unknown. The following factors have been implicated:

Malnutrition

Protein calorie malnutrition has been regarded as a likely cause because of the following reasons: a) malnutrition cause suppression of pancreatic function and render it more susceptible to damage by toxins b) TP is mostly reported from developing countries where malnutrition is quite common.

Food Toxin

Cassava a tuber has been implicated as a possible cause. Cyanogenic glycosides and methyl linamarin is present in Cassava. This tuber has been the simple food of a large section in Kerala. Few people consume cassava in Bangladesh.

Prof. Motior Rahman,
MBBS, FRCS, FACS, FICS.
Senior Consultant Surgeon, BIRDEM.

Other Factors

Micronutrient deficiency (Selenium, copper and vitamin A) has been implicated as a potential cause. Genetic factors may also play a part and this may account for development of disease in migrant of Kerala who live in the West. Immunologic causes have also been postulated.

Pathology

The pancreas appears small, firm. Changes may be local or diffuse. In advanced stage of disease two types can be recognised: a fibrotic type and an adipose type. A study of the composition of the pancreatic juice in TP revealed a) decrease in volume of pancreatic juice b) normal concentration of bicarbonate and c) high concentration of calcium.

Microscopic features include acinar atrophy with replacement by fibrosis. Islets are spared even in advanced stage of the disease.

Clinical Features

The main symptoms are abdominal pain (70%), diabetes mellitus (55%), weight loss (65%) and obstructive jaundice in 2%. Rarely patient may present with abdominal mass, ascitis or gastrointestinal bleeding. Steatorrhoea was not seen in our series.

Gee Varghese in 1968 described the features of TP as "recurrent abdominal pain in childhood, diabetes at puberty and death at the prime of life." This pattern of presentation has changed after 30 years. The male and female ratio was 1.71 and 1.18.

Complications

- Cysts
- Malignancy
- Pancreatic ascitis
- Pancreatic pleural effusion
- Gastro-intestinal bleeding
- Biliary obstruction.

Diagnosis

TP can be diagnosed with certainty if the patient does not consume alcohol and two of the following criteria are positive :

1. Pancreatic calculi on plain X-ray of abdomen
2. Ultrasound evidence of dilatation of the main pancreatic duct
3. Endoscopic retrograde cholangiopancreatography (ERCP) evidence of changes of chronic pancreatitis. These features help in diagnosing patients with acalculous disease and those with normal sized ducts.

Management

Pain is the commonest symptom which leads to surgery. Many patients get relief from pain for long periods with anti-spasmodics, NSAIDs and narcotic analgesics.

Indications for Surgery

1. Intractable pain.
2. Pancreatic pseudocysts.
3. Carcinoma, proven or unproven.
4. Gastro intestinal bleeding
5. Pancreatic ascites or pleural effusion.
6. Biliary or duodenal obstruction.

Operative Procedures described in TP

Drainage Operations

Lateral pancreatico jejunostomy (LPJ)

Pancreatico gastrostomy (PG)

Transduodenal pancreatic sphincteroplasty (TDPS)

Resections

Whipple resection

Distal resection (40-95%)

Total pancreatectomy

Denervation Procedures

Splanchnicectomy

Post coeliac neurectomy

Lateral pancreatico-jejunostomy is the most common operation performed in patients with TP. This allows drainage of the ducts from head to the tail; cysts can also be drained.

Management of TP in BIRDEM

125 TP patients were admitted under our care from 1987 to 1999. Number of operations were 114; Male 69 & female 45.

Average age ranged from 12-64 with a mean of 32.

Lateral pancreatico jejunostomy (LPJ) was performed in 94 subjects. Transduodenal sphincteroplasty in 3 in addition to LPJ.

Pancreatico gastrostomy in 1. Distal pancreaticectomy in 9 subjects. Carcinoma of pancreas was present in 110.

Internal drainage of pancreatic cyst with LPJ in 3. LPJ and resection of segment of ileum in association with crohn's in one. LPJ & right hemicolectomy for carcinoma of caecum in one.

Non Operative Methods

Endoscopic pancreatic stenting in TP in 67. Sphincteroplasty and removal of stones in 60.

Results of Surgery

Owing to improvement in perioperative and postoperative management of diabetes, mortality rates has been very low in our series - only 1% over a median follow up of about 3 years (longest follow up of about 10 years). Pain relief was observed in 75% of cases. Re operation were required in 3%.: indications included failure to carry the ductotomy well into the head and tail region, persistent head disease, bowel adhesions and chronic duodenal ulcer. Our aim is to perform a wide ductotomy extending from the tail to within 0.5 to 1 cm of the medial border of the duodenum and obtain complete clearance of the main duct. Formal head resection may be necessary in patients with severe head involvement or biliary and duodenal obstruction.

Future Goals

Many aspects of the disease remain to be understood. Aetiology of the disease remains unclear and multiple factors may be responsible. Most patients (90%) have calculi at presentation, it is apparent that a precalculus stage exist. TP is premalignant. The predisposition to cancer may be genetically determined and not dependent upon stones and chronic inflammations.

Future goals in TP should be prevention of the disease by identification of causative factors, Judicious use of non operative and operative methods for the relief of pain, and early identification of carcinoma.

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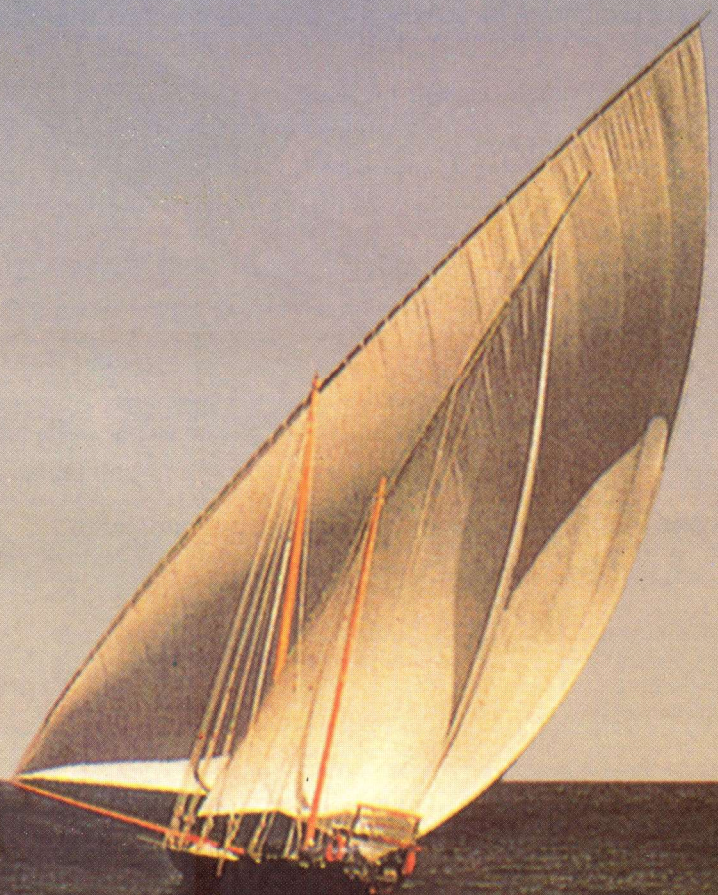
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Drug Distribution in Human Milk

Introduction

Assessing the safety of breast feeding during maternal drug therapy is an individualised risk:benefit analysis. An infant's exposure depends on drug transfer to milk, daily milk intake and the bioavailability of the drug in the infant. Exposure and the potential for adverse effects is greatest in premature neonates and decreases over the first few months of life as the infant's clearance mechanisms mature. Risk should be assessed in the light of the inherent toxicity of the drug and any published data on milk transfer and infant exposure. When maternal drug therapy is necessary, the breast-fed infant should be regularly assessed for adverse effects such as sedation, failure to thrive and achievement of developmental milestones. Laboratory measurement of drug transfer into the milk and the infant's blood should be used, where possible, to confirm suspected adverse effects.

T a b l e 1

Distribution of analgesics into human milk, calculated infant dose interpretation of data

<i>Drug/Group</i>	<i>M/P ratio</i>	<i>Infant dose(%)</i>	<i>Comments and recommendations for breast feeding</i>
Aspirin	0.06	3.2	Possible association with Reye's syndrome. Avoid.
Codeine	ND	ND	Trace amounts in milk, Considered safe.
Ibuprofen	-	-	Non-detectable in milk. Considered safe.
Indomethacin	0.37	0.18	One case of seizure, but causality questionable. No. adverse effects in infants. considered safe.
Methadone	0.45	2.6	Symptoms of withdrawal occur in the first week for 60% of infants born to mothers on methadone maintenance. Considered safe.
Naproxen	ND	2.8	Low concentrations in milk. Exposure is approximately 3.6% of paediatric dose. Probably safe, but more data needed.
Paracetamol	1.0	4.2	No adverse effects. Dose in milk is about 4.5% of therapeutic paediatric dose. Considered safe.
Sumatriptan	4.1-5.7	0.3-6.7	Probably safe. Actual dose received probably diminished by low oral bioavailability of drug. Expressing milk for 8 hours will completely avoid exposure from a single 6 mg subcutaneous maternal dose.

Infant dose infant dose in mg/kg as percent maternal dose in mg/kg. Data from selected studies

ND no data available **MP** Milk to plasma concentration ratio

T a b l e 2

Distribution of anticonvulsants into human milk, calculated infant dose and interpretation of data

<i>Drug/Group</i>	<i>M/P ratio</i>	<i>Infant dose(%)</i>	<i>Comments and recommendations for breast feeding.</i>
Carbamazepine	0.24-0.69	3.6-4.1	Considered safe; observe infant for undue tiredness and poor suckling
Clonazepam	0.33	ND	Considered safe; observe infant for CNS depression and apnoea, particularly after in utero exposure.
Phenobarbitone	0.4-0.6	48.2-93.6	Infant exposure too high. Sedation observed in some infants. Avoid.
Phenytoin	0.18-0.54	0.5-4.8	Considered safe. One report of methaemoglobinaemia, drowsiness and poor suckling.
Sodium valproate	0.01-0.05	1.2	No adverse effects reported in infants. Considered safe at low dose rates. Use with caution at high doses when there is a risk of hepatitis and haemorrhagic pancreatitis.

Self Assessment

Invasion of the Fleshy Papules

A 33-year-old woman was admitted to the hospital because of left lower lobe pneumonia. She had no significant findings in her personal or family history. Other than crackles at the base of the left lung, examination revealed only raised, coalesced, flat-topped, flesh-colored papules on the lower eyelids and upper cheeks. The patient reported that the papules had been present for many years and were asymptomatic, although the number had increased over time. The presence of a lipid disorder was suspected.



**What
is
your
diagnosis?
Turn
the
page
for
the
answer.**

M i s c e l l a n e o u s M e d i c a

Septic shock hope

Macrophage migration inhibitory factor (MIF) is a "critical mediator of septic shock", report researchers. Antibodies against MIF protected mice against lethal peritonitis induced by caecal ligation and puncture and by *Escherichia coli*. Co-injection of MIF and *E Coli* increased the lethality of the infection. The scientists also found high plasma concentrations of MIF in patients with septic shock. They suggest that MIF may be a target for therapeutic intervention (*Nat med* 2000;6: 164-70).

Megamineral therapy death

A report in *Pediatrics* (www.pediatrics.or/cgi/content/full/105/2/e18) warns paediatricians to keep an eye open for the use of alternative therapies in their patients. A 28-month-old mentally retarded boy who was given high doses of magnesium oxide as part of an unsupervised megavitamin and megamineral regimen died of fatal hypermagnesaemia, an uncommon side-effect of the use magnesium-containing compounds.

Medline falls short

Medline is the best known medical bibliographic database, but it is not all-inclusive. A study in *Health Libraries Review* (1999;16:151-6) that used Ulrich's International Periodicals Directory (which indexes 150 000 serials from 80 000 publishers in 200 countries) as a gold standard showed that a Medline search in psychiatry would retrieve only half of the relevant journals. Cross searching four databases-psychlit, Medline, Biosis, and Embase-retrieved 90% of electronically indexed papers, but (obviously) none of the 96 journals categorised by Ulrich's as academic but not indexed by any service.

Imaging has role for hernia

Most hernias are still diagnosed accurately using clinical means, but a review in the *British Journal of Surgery* (1999;86:1243-50) suggests that cross sectional imaging may have a role in some cases. The increasing quality of both computed tomography and magnetic resonance imaging over the past decade provides increasingly accurate assessment of the neck of the sac and its contents, enhancing diagnostic accuracy in obese patients with intestinal obstruction.

The answer : Syringomas**Discussion :**

These benign tumors of the sweat glands occur more often in women than in men, and onset is usually at puberty. They are found primarily on or around the eyelids, axilla, umbilicus, and pubic area. Although usually bilateral in distribution, they may be unilateral. The papules are flesh-toned or slightly yellow, firm, and 1 to 3 mm in diameter.

A variant called eruptive syringoma or eruptive hidradenoma of Darier and Jaquet first manifests during the first decade of life and presents with numerous lesions on the neck, chest, and abdomen.

The eyelids may or may not be involved. The lesions either remain unchanged for years or resolve spontaneously. A familial variant has also been described.

Diagnosis

Syringoma must be distinguished from another sweat gland tumor, eccrine hidrocystoma. In this condition, a single lesion on the face is typical, but occasionally several occur. The cysts are 1 to 3 mm in diameter and often translucent. However, they may have a yellowish or bluish hue. The lesions tend to enlarge when the patient perspires, because they result from occlusion of the intradermal portions of the sweat ducts. They are, therefore, more obvious in summer than in winter.

Two other lesions may resemble syringoma: xanthoma palpebrarum and molluscum contagiosum.

Xanthoma palpebrarum appears as flat, raised, yellow-hued plaques on the eyelids, primarily the medial aspects.

Despite popular belief, the majority of patients with these lesions do not have an identifiable disorder of lipid metabolism. However, some affected patients do have such a disorder, and therefore a search for a dyslipidemia is warranted. In general, xanthomas may be classified as either "normolipidemic" or dyslipidemic," depending on whether they are associated with a lipid disorder.

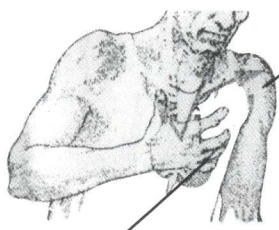
Molluscum contagiosum is a skin infection with the molluscum contagiosum virus, a member of the *Poxviridae* family. The characteristic lesion is a papule 1 to 2 mm in diameter, often with a central umbilication, that may contain a white, cheesy material. Small numbers of lesions are usually seen, except in immunocompromised patients, who may have multiple papules. The lesions tend to occur in young persons and favour the face, although they may occur on the genitals in adults when transmitted through sexual contact. Transmission usually occurs through skin contact with an infected individual; however, transmission by fomites has been described.

Treatment

Because syringomas have no malignant potential, treatment is not necessary; however, it is often requested for cosmetic reasons. This can be accomplished by electrodesiccation and curettage or by elevating individual lesions with a small-gauge needle and excising the base with a small, curved scissors or scalpel blade. The skin defect is then allowed to heal by second intention.

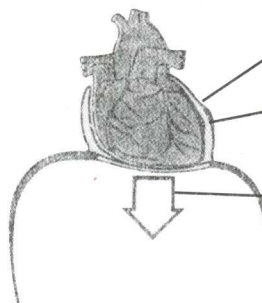
Clinical Highlights

CLINICAL FEATURES OF PAIN IN PERICARDITIS.



Pain in pericarditis radiates to the left shoulder, upper back and neck

Pain maybe sustained, crushing, Localized in the precordial area, simulation myocardial infarction (may be relived by squatting or leaning forward)



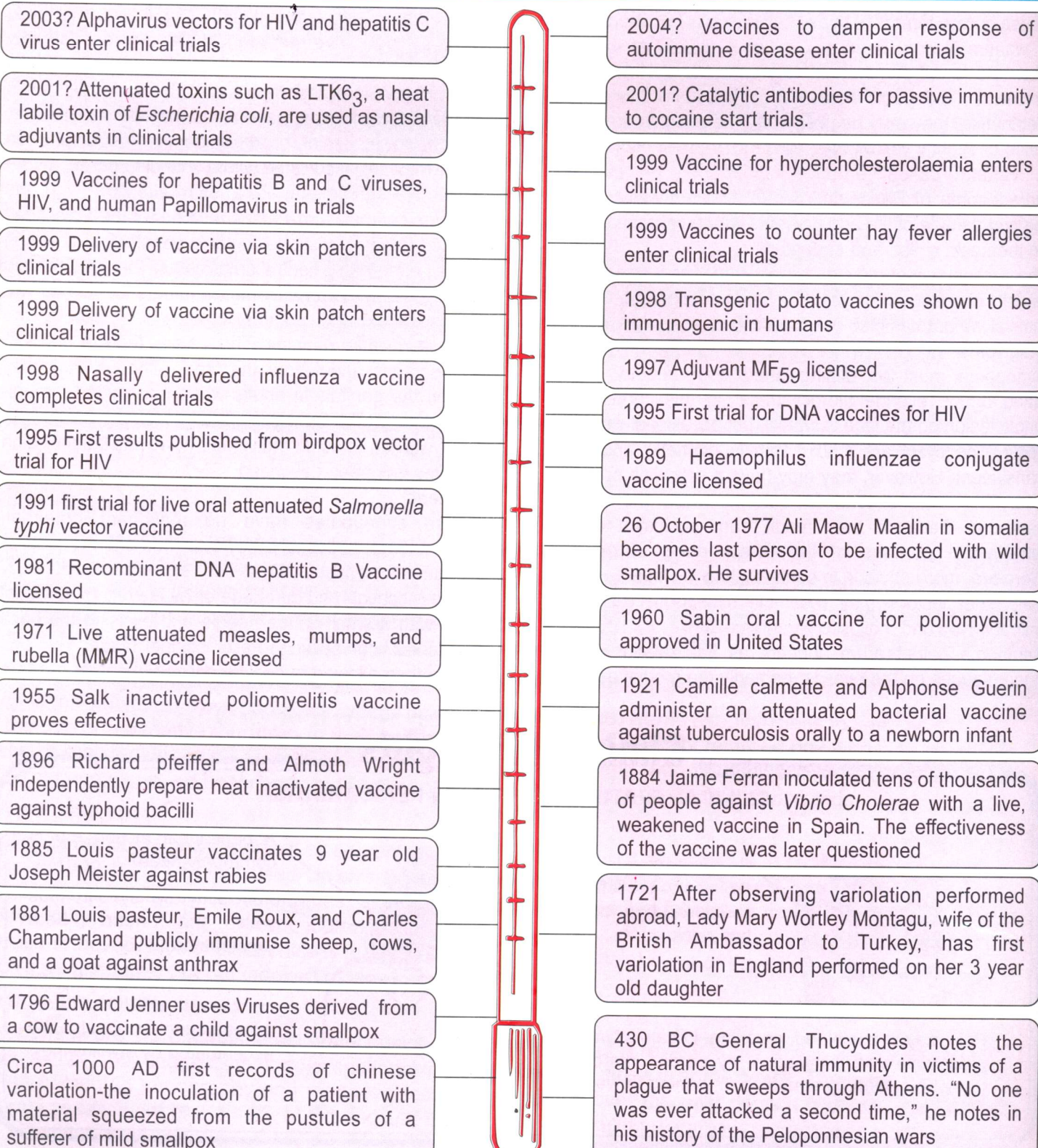
A pericardial friction rub is commonly heard

Pain amy be synchronous with the heart beat (uncommon)

There is frequently a pleuritic component with inspiratory accentuation (may also be accentuated by swallowing)

Vaccine Timeline

The History of Vaccines and Immunisation



Medi Tips

P R A C T I C E T I P S

Rice sock for pain and stress

Soothing the discomfort of arthritis pain is difficult, but moist heat applied with a "rice sock" is quite effective for this task. It also works for everyday stress and for muscle strain and spasm. Have the patient fill an old tube sock with uncooked rice, tie it off at the top, and place it in the microwave for about 3 minutes. The sock holds heat for up to an hour, and it conforms to almost any body part.

Patients seem to love the sock and they don't have to worry about heating pad burns. However, care must be taken not to get the sock wet; cooked rice does not convey heat.

Preserving healthy skin

When podophyllin or other caustic agents are applied to skin lesions, the surrounding healthy tissue may become irritated. A good approach to this problem is to use a cotton swab to "Paint" the healthy tissue around a lesion with antibiotic ointment before treatment. This helps preserve skin integrity while promoting effective, pain-free therapy.

Hidden bronchial asthma in children

When children with asthma do not have obvious shortness of breath or wheezing, a misdiagnosis of bronchitis, bronchiolitis, or pneumonia may be made when symptoms do occur. As a result, the child may be given antibiotics over and over and never receive help for the asthma. It is important to recognize the condition to prevent difficulties in school work and social interactions.

Clues to hidden asthma include so-called respiratory infections that last for weeks and often recur, chest tightness and pain, dry cough, inability to run and keep up with other children, irritability, and chronic fatigue. Subtle symptoms may seem normal to parents, but a child who cannot keep up with other children feels different and left out. Parents are often surprised at how well the child feels when taking asthma medication.

Caution with antiulcer medication

Be cautious when you prescribe antiulcer medications in patients who are taking warfarin. Prothrombin times may dramatically increase when these agents are being used.

Stopping nosebleed

Epistaxis is usually diffuse in patients who have a coagulation disorder or who use certain medications (eg, aspirin, coumarin, heparin). Even minor manipulation of the nose in these patients may aggravate the condition, and the goal is to stop the bleeding with as little trauma as possible.

Dissolvable materials, such as Avitene and Surgicel, used along with an antimicrobial ointment, induce coagulation with local pressure, and the packing material does not have to be removed. After it has been in place for 24 to 48 hours, saline spray is applied to hasten dissolution.

Preventing blood spills

Blood is often spilled when an intravenous line is started or changed. This can be prevented as follows: Once the catheter is in the vein, the arm is slightly elevated with the tourniquet released (ask the patient to point upward). The intravenous lines can then be connected and taped in place with no spillage.

A numbing occasion

Lidocaine jelly can be used to make immunizations and suture removal less painful in both children and adults. This is a small matter for physicians, but it is very important to patients.

Superglue for fissures and lacerations

If a patient has painful fissures adjacent to the fingernails or a well-apposed superficial laceration, superglue can be used for treatment. After application, the patient should not touch any thing until the glue is thoroughly dry. This takes about 5 minutes.

Apical examination for left ventricular enlargement

Precordial examination is often considered less important than an electrocardiogram (ECG) or a chest film in the evaluation of left ventricular size and volume. However, an impulse of more than 3 cm in diameter during palpation of the apex with the patient in the left lateral decubitus position is 92% as sensitive and 91% as specific as an echocardiogram in indicating left ventricular enlargement and is far superior to the ECG and chest film for this purpose. The normal apical impulse covers an area of about 1 cm. If the area is more than that of your stethoscope (about 3 cm), you can be fairly sure that the patient has an enlarged left ventricle:

Medi News

From Internet / Journals

The Relationship of Arsenic Levels in Drinking Water and the Prevalence Rate of Skin lesions in Bangladesh

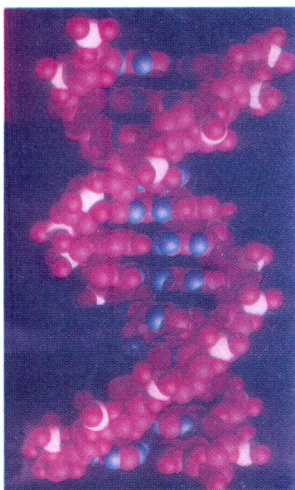
To determine the relationship of arsenic-associated skin lesions and degree of arsenic exposure, a cross-sectional study was conducted in Bangladesh, where a large part of the population is exposed through drinking water. Four villages in Bangladesh were identified as mainly dependent on wells contaminated with arsenic. Martin Tondel and colleagues (Department of Health and environment, Faculty of Health Sciences, Linköping University, Sweden) interviewed and examined 1,481 subjects >30 years of age in these villages. A total of 430 subjects had skin lesions (keratosis, hyperpigmentation, or hypopigmentation). Individual exposure assessment could only be estimated by present levels and in terms of a dose index, i. e. arsenic levels divided by individual body weight. Arsenic water concentrations ranged from 10 to 2,040 µg/L, and the crude overall prevalence rate for skin lesions was 29/100. After age adjustment to the world population the prevalence rate was 30.1/100 and 26.5/100 for males and females, respectively. There was a significant trend for the prevalence rate both in relation to exposure levels and to dose index ($p < 0.05$), regardless of sex. This study shows a higher prevalence rate of arsenic skin lesions in males than females, with clear dose-response relationship. The overall high prevalence rate in the studied villages is an alarming sign of arsenic exposure and requires an urgent remedy.

Environmental health Perspectives

Stem cell therapy for and neurodegenerative diseases

Having the ability to restore damaged brain tissue could open the door to treatment for a wide range of neurodegenerative diseases such as Alzheimer's and Parkinson's disease and stroke. This therapeutic idea has recently become more of a realizable goal because, contrary to medical dogma, the brain has shown its ability to generate new nerve cells. Since that recent discovery, scientists have been trying to isolate the source cells of this neurogenesis.

Based on knowledge that such cells are likely to be located in the region of the brain known as the hippocampus, Steven Goldman



Stem cell therapy- hope for neurodegenerative diseases.

and colleagues at Cornell Medical Center have developed a method to identify and isolate cells from the adult human dentate gyrus section of the hippocampus and shown them to be neurogenic progenitor cells-meaning that they mature into neurons in culture. Thus, the adult hippocampus harbors neurogenic stem cells that can be isolated, and may be useful in re-populating damaged or degenerated brain tissue.

www.nature medicine.com

A vaccine for kidney cancer

Cancer vaccine strategies are based on the concept that human tumors possess tumor-specific proteins (antigens) that can be targeted by the immune system. One approach involves 'pulsing' immune cells known as dendritic cells with peptides from tumor antigens, causing the cells to stimulate an immune attack against the tumor. In fact, dendritic cell-based vaccines are one of the most promising strategies for treatment of metastatic cancer, due to their tumor specificity and low level of toxicity.

In March 4, 2000 issue of Nature Medicine, Alexander Kugler and colleagues at the University of Göttingen, Germany, report the success of a therapeutic vaccine for metastatic renal cell cancer, created through the electrical fusion of dendritic cells with tumor cells from the same patient. Seven of 17 patients responded to the vaccine; four achieved complete regression of their cancer and have had no evidence of recurrence for periods of up to 21 months, two had prolonged disease stabilization. These data are promising, as the response rates for treatment of metastatic renal cell cancer with the usual chemotherapeutic or hormonal agents are less than 10%.

Donald Kufe of the Dana-Farber Cancer Institute writes, in an accompanying article, "If confirmed, the results of this study represent an unprecedented advance in the selective and non-toxic immunotherapy of a disseminated and lethal carcinoma."

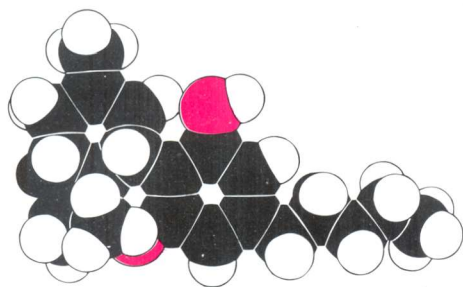
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Cannabis could be effective against brain tumors

Interest in investigating the potential medical properties of the cannabinoid, marijuana, is increasing because of the drug's suspected pain and nausea relieving effects in patients with cancer, HIV and multiple sclerosis. Now, scientists at Complutense University, Spain, have discovered that compounds acting at cannabinoid receptors eradicate brain tumors (gliomas) in one third of rats treated, and prolong the survival of another third.

In vitro experiments lead Manuel Guzman and colleagues to suggest that cannabinoids kill glioma cells by inducing apoptosis (programmed cell death) via a second messenger protein called ceramid and an intracellular signaling cascade.

These findings suggest a new therapeutic approach for glial tumors, which are known to be peculiarly resistant to



Tetrahydrocannabinol : the active component of cannabis effective against brain tumors?

traditional therapy. In the context of the aggressive treatment currently available for glioma and its median survival rate of 40-50 weeks, "This bleak scenario alone should provides sufficient motivation to continue [these cannabinoid] studies." writes Daniele Piomelli from the University of California, Irvine.

www.nature-medicine.com

New treatment proposed for chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease, which occurs in 15-20% of heavy, long-term cigarette smokers - is the fifth leading cause of death in western countries. Yet it remains an unresolved medical problem. So far, there is no way to slow the disease's natural progression other than stopping smoking, and even that does not halt the disease in all patients.

James Hogg (St Paul's Hospital, Vancouver, Canada) believes that, in patients with COPD, latent adenoviral infection might amplify the inflammation that cigarettes trigger in all smokers. His team has detected large amounts of an adenoviral protein in lung samples from patents with COPD, localised to areas of inflammation and emphysema.

Bill MacNee (University of Edinburgh, UK) presented evidence of ongoing oxidative stress in people with active disease. Each puff on a cigarette delivers 10^{17} oxidant molecules straight to the lung, he said "Apart from the direct injury that these could produce, oxidative stress is a fundamental process in inflammation. Thus, antioxidants could become the new anti-inflammatory treatment."

Antioxidants such as vitamins and N-acetyl-cysteine have shown promising results in placebo-controlled trials of chronic bronchitis, but lack potency. Inhalation of small, aerosolised

molecules with superoxide dismutase activity may have better therapeutic potential, suggested Mc Nee.

Corticosteroids are ineffective in COPD, explained peter Barnes (Imperial College, London, UK), so "to treat COPD, we need new nonsteroidal anti-inflammatory drugs". From the range of options currently in the pipeline, Barnes is confident that a new drug class - phospho-diesterase-4 inhibitors-will deliver the best results. In early clinical trials, one such drug improved lung function and quality of life in patents with severe COPD. Phospho-diesterase-4 inhibitors arrest neutrophil activity and stop macrophages releasing chemotactic factors, which contribute to the acute inflammation in patients' airways, explained Barnes.

But the "Holy Grail" of COPD therapy is to find a drug that repairs damaged lungs, rather than merely halts disease progression. Gloria and Donald Massaro (Georgetown University School of Medicine, Washington DC, USA) reported that retinoic acid stimulates the regrowth of alveoli and reverses permanent damage in rats with emphysema. "It is a very stimulating finding," says Hogg. "We don't know yet if it will work in people, but it's a start."

The LANCET. Vol 355. Feb 5. 2000

PAR2 antagonists - the next generation of anti-inflammatories?

New understanding of how sensory nerve cells transmit their, signals to the central nervous system has been reached by researchers at the University of California in San Francisco.

Nigel Bunnett, professor of surgery and physiology, and his team have shown that tryptase-a degradatory enzyme known to be involved in triggering the inflammatory process-works by activating a new class of receptor called PAR2 (proteinase activated 2 receptors).

Professor Bunnett's work suggests that substances that block these receptors could make good candidates for new anti-inflammatory drugs (Nature Medicine 2000;6:151-8).

When sensory nerve cells are activated, calcium levels inside these cells rise and the neuropeptides, such as substance P and calcitonin gene related peptide (CGRP) are released. Both of these are important in the formation of inflammatory oedema.

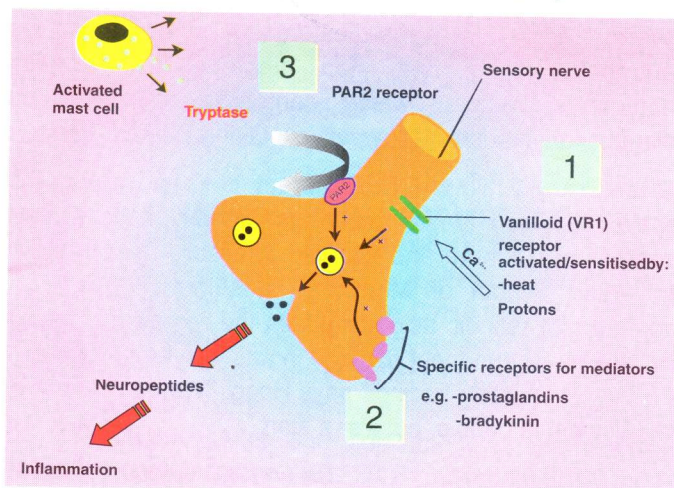
Mast cells sit in the vicinity of sensory nerve endings in both animals and humans. When mast cells degranulate they release tryptase, in addition to histamine and prostaglandins. It has been shown that tryptase activates PAR2 receptors, which are located on sensory neurons.

Professor Bunnett and his colleagues wanted to find out if the release of neuropeptides from neurons is mediated by tryptase activated PAR2 receptors. "We wanted to establish

whether the mast cells were 'talking' to neurons via tryptase," explained professor Bunnett.

They first examined rat sensory nerves to see if they expressed PAR2 receptors and found that 63% of them did. Up to 40% of them also expressed substance P and CGRP.

The researchers then cultured sensory nerve cells and measured the level of intracellular calcium, as a measure of nerve cell excitation. When they introduced pure human



A nerve cell releases neuropeptides, triggered by tryptase activated PAR2 receptor

tryptase and trypsin (a PAR2 agonist), the intracellular calcium level went up, indicating excitation had occurred.

"We then wanted to see whether tryptase stimulated the release of substance P and CGRP from nerves," said Professor Bunnett. They did this by taking pieces of rat tissue, perfusing them with buffer, and adding tryptase and specific PAR2 agonists. Both substance P and CGRP were released.

In the final experiment, the team took a single rat paw and injected a PAR2 agonist into the pad. After six hours the paw had become swollen, and the amount of oedema was measured.

The team repeated this procedure in animals that had been pretreated with antagonists of the substance P and CGRP receptors or with capsaicin—a neurotoxin that ablates sensory nerves. When the researchers then introduced PAR2 agonists, very little oedema was produced.

"This confirmed to us that PAR2 receptors on sensory nerves are critical to the inflammatory process," said professor Bunnett, "and substances that specifically block PAR2 receptors should make good anti-inflammatory agents."

www.bmj.com

Surgery is the best medicine after a heart attack

Surgery to restore the normal flow of blood after a heart attack has better long-term results than drug therapy.

Nearly 400 patients with acute myocardial infarction (MI) were assigned to undergo primary angioplasty or treatment with the fibrinolytic drug streptokinase.

In a study designed to compare the two treatments, Dutch researchers then followed them for five years.

In spite of the risks associated with the procedure, angioplasty came out resoundingly on top. During follow-up, 13% of those who had angioplasty died compared with 24% of those treated with streptokinase.



Surgical solution : a blood clot inside a coronary artery

Patients who were treated with angioplasty after their first MI also less likely to have another heart attack. Only 6% had a second infarction compared with 22% of those in the streptokinase group.

Surgery also reduced the incidence of heart failure and ischaemia among patients and the need for hospital admission because of them.

Although angioplasty is initially more expensive than thrombolytic therapy, the surgical procedure saves money in the long term, the authors say, mainly by reducing hospital costs.

NEJM; 314: 19, 1413-1419

Aspirin underused

According to a US survey of nearly 11 000 physician visits between 1980 and 1996, aspirin use by people with coronary heart disease increased from 5% in 1980 to 26.2% in 1996. The author of the article argues that aspirin use is still suboptimal among these patients and that more should be done to "Translate clinical recommendations into practice."

Circulation 2000; 101: 1097-101.

Orixyl 500



The opening of a new Horizon