

The **ORION**

Medical Journal

Importance of
Zinc for Health
Millennium Issue
Vol. 5 January 2000



**Vitality and Multifold Functions
of Zinc in Human Health**

**Role Of Zinc In Pregnancy
and Foetal Development**



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Editorial

We offer our best compliments to the esteemed readers through this Millennium issue of "THE ORION" with New Year Greetings and Eid Mubarak. Encouraged by constant appreciations, supports, suggestions and comments of respected readers we are presenting 5th volume of our medical journal. We hope that our previous issue on "Ideal Antioxidant" which is a subject of wide discussion in doctors forum, is tremendously beneficial to realise the dream of human society to remain active and sound even before last heart beat.

In this issue, considering the vitality and multifold functions of zinc in the development of normal human body, we have decided to focus on "Importance of Zinc for health".

Zinc is one of nineteen nutritionally important trace elements. It's involvement almost in all fundamental activities accounts for the essentiality of Zinc for humans.

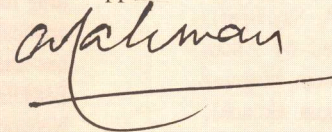
The global health and social costs of nutritional disorders are apparent and have been amply documented. In Bangladesh, deficiencies of macro nutrients as well as micro nutrients have an enormous impact on health and productivity due to primary effects as well as their effects as critical co-factors in a variety of conditions including gastrointestinal and other infections, low birth-weight, psychomotor and cognitive development, immune dysfunctions, congenital maleformations, among others.

Unlike other essential trace elements zinc demands some special attention as through out pregnancy even in the presence of optimal Zinc nutrition there is a decline of plasma zinc and requirement of Zinc during lactation is greater than that of during pregnancy. Body stores zinc are not readily mobilized and ingested Zinc excretes from the body within 24 hrs. and so regular exogenous supplementation of Zinc will be required in deficient conditions. It also possibly helps in potentiation of vaccine through activation of immune system directly.

Zinc may play an important role in strategic plan to the year 2000 regarding women's reproductive health, safe motherhood and child survival, prevention of respiratory tract infections and diarrhoeal diseases. In seminars arranged by MSD, Orion Laboratories Ltd. through out the country, eminent professors, public health experts and nutritionists expressed that considering the importance of Zinc in human health it should be included in primary health care to have highest attainable level of achievement with Zinc therapy. Government, Donors, Private sectors should have scientifically designed nutrition research as one unified team towards better health and well being of our people.

We hope creating awareness about Zinc through publications like 'The Orion', mass media, seminars will ultimately inspire future researchers, policy makers and programme planners in their important goal to ease the burden of malnutrition and to achieve the success of national programme "Health for All in year 2000" in Bangladesh.

We expect that our attempt in enlightening this topic will be very much helpful for all concerned. Suggestions and recommendations from our dignified readers will be most appreciable.



Dr ATM Azizur Rahman

Chief Editor

and

Manager

Medical Services Department

MSD News

In the last quarter of 1999, the Medical Services Department (MSD) of Orion Laboratories Ltd. (OLL) has arranged a large numbers of programmes throughout the country. These include Seminars in different Institutions, Hospitals and Health Centres in different districts of Bangladesh, conducted Efficacy Trial on Maprocin (Ciprofloxacin) & Nidazyl (Metronidazole) both parenteral and oral forms at Surgery Unit-IA, BSMMU; Clinical Trial on Ortac (Ranitidine), Orixyl (Amoxicillin) and Nidazyl (Metronidazole) at Medicine Unit-IA, DMCH in the eradication of *Helicobacter Pylori* as a regimen of tripple therapy and several other activities to serve the needs of Medical Professionals.

Efficacy Trial on Maprocin & Nidazyl

MSD has successfully completed the Efficacy Trial on **Maprocin & Nidazyl** both Intravenous and oral forms among post operative patients under direct supervision of Professor A.N.M Atai Rabbi, FCPS, FICS, Chairperson & Head of the Department General Surgery, BSMMU at Surgery Unit-IA, BSMMU. The results of the trial show, the infection rate is about 00% among post operative patients and the success rate of the Efficacy Trial on **Maprocin & Nidazyl** is almost 100%. It is a tremendous achievement of the brand and this results will definitely win the confidence of the Medical Professionals. The complete report of the trial will be published in the next volume of "The ORION".

Seminars

a) In Search of Ideal Antioxidant To Combat Cardiovascular Disease

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

Dhaka National Medical College Hospital (DNMCH), on August 26, 1999 chaired by Professor Mahmud Rahman (Principal & Head of the Department of Medicine, DNMCH); Jahurul Islam Medical College and Hospital (JIMCH), Bhagalpur, Bajitpur, Kishoregonj on September 11, 1999 chaired by Professor Azizur Rahman (Principal, Jahurul Islam Medical College); Sayedpur Sader Hospital, Sayedpur on September 16, 1999 chaired by Dr. M. A. Hanif (President, BMA, Sayedpur); Sadar Hospital, Magura on October 08, 1999 chaired by Alhaz Professor Dr. M. S. Akbar (Honourable Member of Parliament, Magura-I, Renound Paediatrician & President of BMA, Magura Branch); BIRDEM on October 10, 1999 chaired by Major General Dr. A. R. Khan (Chief Consultant, BIRDEM); Diabetic Hospital, Comilla on October 16, 1999 chaired by Dr. Zobaida Hannan (Founder of Diabetic Hospital, Comilla); Rajshahi Medical College Hospital (RMCH), on October 18, 1999 chaired by Professor M.A. Azhar (Head of the Department of Medicine, RMCH); Lalmonirhat Sader Hospital, on

October 24, 1999 chaired by Dr. Md. Rafiqul Islam (Civil Surgeon, Lalmonirhat); Christian Missionary Hospital, Rajshahi (CMH), on November 16, 1999 chaired by Dr. S. K. Haldar (Medical Superintendent, C.M.H. Rajshahi); Natore Sader Hospital, on November 17, 1999 chaired by Dr. Mizanur Rahman (Director Health, Rajshahi Division).

b) Antioxidant & the Prevention of Coronary Heart Disease

MSD also arranged a Seminar on a new topic "Antioxidant & the Prevention of Coronary Heart Disease" on October 29, 1999 at National Institute of Cardiovascular Diseases (NICVD), Dhaka. Professor Nazrul Islam, Professor of Cardiology, NICVD was the Keynote Speaker of the Seminar. The Seminar was chaired by Professor M. Zaman, Director Cum Professor, NICVD. All the Professors, Consultants and Doctors of NICVD were presented at the Seminar.

c) Importance of Zinc for Health

MSD also arranged Seminars on "Importance of Zinc for Health" in the following venues:

Institute of Child & Mother Health (ICMH), Matuail, Dhaka on August 29, 1999 chaired by Professor M. Q. K. Talukder (Director, ICMH); Sayedpur Sader Hospital, Sayedpur on September 16, 1999 chaired by Dr. M. A. Hanif (President, BMA, Sayedpur); Sadar Hospital, Magura on October 08, 1999 chaired by Alhaz Professor Dr. M. S. Akbar (Honourable Member of Parliament, Magura-I, Renound Paediatrician & President of BMA, Magura Branch); Diabetic Hospital, Comilla on October 16, 1999 chaired by Dr. Zobaida Hannan (Founder of Diabetic Hospital, Comilla); Rajshahi Medical College Hospital (RMCH), on October 19, 1999 chaired by Professor Merina Khanam (Head of the Department of Obs. & Gynae., RMCH); Lalmonirhat Sader Hospital, on October 24, 1999 chaired by Dr. Md. Rafiqul Islam (Civil Surgeon, Lalmonirhat); Christian Missionary Hospital, Rajshahi (CMH), on November 16, 1999 chaired by Dr. S. K. Haldar (Medical Superintendent, C.M.H. Rajshahi); Natore Sader Hospital, on November 17, 1999 chaired by Dr. Mizanur Rahman (Director Health, Rajshahi Division).

Lunching of New Products

Orion Laboratories Ltd. recently launched a new product named **Oclazid** (Glyclazide) from October 09, 1999 which is the outstanding drug for NIDDM patients. This product will provide effective clinical application and ensure better patient's compliance. In this respect, MSD has arranged a number of launching programmes with the doctors of BIRDEM, Diabetic Hospitals and branches of National Diabetic Network (NDN) all over Bangladesh.

Another two products were introduced by Orion Lab. Ltd. named **Erythromycin Dry Syrup** on November 01, 1999 and **Tab. Tocopherol** (Vitamin-E) on November 15, 1999 with a view to provide better options for physicians to prescribe and also to provide better patient complaints.

Vitality and Multifold Functions of Zinc in Human Health.

Khursheed Jahan¹ ATM Azizur Rahman²

Introduction : Recent years there have been advance in the knowledge of the significance of trace elements in human health and diseases. New trace elements have been discovered and sophisticated analytic techniques have developed. The global health and social costs of nutritional disorders are apparent and documented. Deficiencies of macronutrients as well as micronutrients have an enormous impact on health and productivity due to primary effects and their co- factors in a variety of conditions including gastro intestinal tract and other infections, low birth-weight, psychomotor and cognitive development etc.

A number of workshops and seminars were organized by International Agencies in response to these developments in a fast changing field, and the need to review and update recommendations for intake of trace elements.

For last two and half decades in our country discussion about the utility of Zinc becomes popular and several research works were done in academic institutions like International Centre for Diarrhoeal Disease Research, Bangladesh, Bangladesh Institute for Research of Diabetic and Endocrine Medicine and Dhaka University. The advent of modern techniques which were developed during last 20 years such as atomic absorption spectrometry, microwave excitation emission and atomic fluorescence quantitation of very minute amount of Zinc is possible. It is, therefore, no wonder that most of the informations of Zinc only recent origin though hints for its role were obtained more than a hundred year ago.

Zinc is probably the most ubiquitous element in nature and absolutely essential for metabolic function in the bodies of animal kingdom. More than 90 metalloenzymes contain Zinc. Minute variation of Zinc can impair and subsequently increase or decrease the activities of these enzymes. It also acts as co-factor for more than 200 enzymes. Zinc plays vital role in the functioning of metalloenzymes including carbonic anhydrous, peptidases alkaline phosphates, dehydrogenases, Polymerases, thymidine kinase, delta-

ALA dehydratase, pyruvate carboxylase and thermolysin. Apart from these Zinc is associated with many other substances, the so called Zinc Bound Ligands (ZBL), (e.g Protein, DNA RNA, ADP, ATP, Insulin, collagen to name only a few) and it is always located only at the active site with participation in the actual catalytic process.

By virtue of its essentiality and involvement in a large number of enzymes as a stabilizer of the molecular structure constituents and membranes reflects its vital role in human body.

Zinc participates in the synthesis & degradation of carbohydrates, lipids, proteins and nucleic acids. It's involvement in such basic activities probably accounts for the vitality of Zinc for humans and all other life forms, and thus its status in nutrition has become a subject of tremendous interest.

Physiological Aspect of Zinc : Zinc is present in all the tissues and fluid of the body. The total body content has been estimated to be approximately 2-3 gm. whole blood contains about 900µcg/ 100 ml, of which 85% in RBC, 12% in plasma and 3% in leukocytes and 70% plasma Zinc is bound to albumin which is the transport form of blood Zinc.

Zinc concentration in human tissues
(mg per kg dry weight.)

TISSUE	AMOUNT
LIVER	141-245
KIDNEY	184-230
LUNG	67-86
MUSCLE	197-226
PANCREAS	175-135
HEART	100
BONE	218
PROSTATE	520
EYE	RETINA-571 CHOROID-562 CILARY BODY-288

Zinc is not accumulated in any tissue, so there is no store of Zinc in the body. In contrast to iron, body stores of Zinc are not readily mobilized and a regular exogenous supply is necessary. It has a rapid turn over, regulated by metalothionein and its level appears to be under close homostatic control. Studies showed that

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most of the ingested Zinc disappears from blood within 24 hours. It has been observed that, typically, after ingestion of 4-8 gm of Zinc common manifestations like nausea, vomiting, diarrhoea, fever and lethargy has been occurred. Bioavailability of inorganic Zinc solution approaches 70% but that from dietary sources is much less, approximately 10% due to presence of antagonists and phytates.

Dietary Sources and Daily Requirement of Zinc

Dietary Sources in Bangladeshi Foods

Mg/100 gm

1	Cereals & Cereals Products	0.79-2.65
2	Pulses & legume	2.31-3.67 (mosur)
3	Poultry & meat	0.77-3.25 (beef)
4	Liver	2.51 (goat), 2.85 (beef)
5	Egg Yolk (not white)	3.97 (hen), 3.78 (Duck)
6	Fishes	0.38-4.10 (tengra)
7	Leafy vegetables	0.24-1.48 (pui shak)
8	Fruits	0.08-0.54
9	Milk	0.56 (liquid), 2.84 (powder), 3.91 (cheese)
10	Ground nut	3.38
11	Coconut	1.00
12	Spices	0.42-4.33 (coriander)

Other sources : Oysters, wheat bran, oatmeal, sardines.

The daily requirement varies with age and growth state. The approximate figure is.

1. At one month of age	800 µg/ day
2. Between 1-10 years	3-10 mg /day
3. In normal adults	10-15mg/ day
4. During pregnancy (for growing foetus)	20-25mg/ day
5. Deficient state in general	30-50mg/ day

Pathophysiology of Deficiency and some

Important Clinical states: Restricted or less intake or living in a place of zinc deficient soil caused decrease in levels of zinc in plasma, erythrocytes and leukocytes with an adverse effect on total protein, total collagen, DNA, RNA and deoxythymidine kinase activity in the sponge connective tissue. It influences almost all the systems of the body and its deficiencies caused a large number of diseases including weight loss, growth retardation, embryonic malformation, diarrhoea, night blindness, diabetes mellitus, immunological dysfunctions etc.

Growth Retardation: Growth retardation is a common manifestation in zinc deficiency in man, as it is directly relates to loss of appetite and decrease food intake. It is observed that adverse effects on thymidine kinase which is essential for DNA synthesis in all cell division. The activity of RNAase increased what is responsible for protein synthesis. Thus zinc deficient cells fail to divide and differentiate, with consequent impairment

Diarrhoea: Zinc deficiency increases the incidence of diarrhoea and its supplementation reduces the prevalence. The role of zinc in diarrhoea may be mediated through several mechanisms, which include membrane stabilization, mucosal integrity, electrolyte transport, water transport, immuno-competence, protein and essential enzyme synthesis.

The maintenance of integrity of mucosal cell membranes, repair of mucosal injury by increased protein synthesis, multiplication of epithelial cells, and improvement of sodium and water transport are likely to reduce fluid loss during diarrhoea. Repair of mucosal paracellular tight junctions would allow better absorption of water. The improvement in immunological function especially on secretory IgA and T-lymphocytes would be expected to limit the growth and multiplication of diarrhoeal pathogens within the intestinal lumen. Thus the physiological, ultrastructural and immunological role of zinc mentioned above offers a set of mechanisms which explain why there is a reduction in diarrhoeal severity and duration.

Immunological Dysfunction: Zinc is essential for the formation and function of the immune system. with zinc deprivation, the thymus atrophies and viable thymocytes are not formed. The function of macrophages and T-cells are impaired and lymphocyte concentration decreased -the result is an inability to respond to antigens or defend the organism against infections. Zinc also may help in potentiation vaccine through activation of immune system directly as it is essential for the formation and function of immune system. studies are also going on this respect and obstetricians are prescribing zinc to their patients with aim to enhance immune system in the neonates to overcome future complications.

Vitamin A, Zinc and Night Blindness

Mobilization of vit-A requires a specific protein called retinol-binding protein (RBP). Zinc deficiency induces the reduction of retinol binding protein (RBP) in plasma and liver leading to poor mobilization

hepatic vitamin A. Recent studies show that zinc directly involved in the process of vitamin A absorption from intestine and also in its metabolism. It also influences the oxidation-reduction of vitamin A in the retina. Reduced level of plasma Zinc-vitamin A interaction causes impaired dark adaptation leading to night blindness and interestingly it has been shown to be improved on zinc therapy.

Relation with insulin and diabetes mellitus:

One of the most exiting and hotly discussed examples of ZBLs is insulin. The story began in 1934 first reported that crystalline insulin contain a considerable amount of zinc (about 0.5%) and amorphous insulin also did not crystallize without the presence of zinc. Later it was found that pancreatic islets contain zinc and many studies elucidate exact role of zinc in the function and metabolism of the hormone and its relationship with diabetes mellitus. The role of zinc in insulin biosynthesis lies in the fact that proinsulin monomer binds the metal during its polymerization. It has been demonstrated that molecular organization in zinc proinsulin hexamer is maintained through all the subsequent steps in insulin biosynthesis. Zinc is believed to be involved in insulin biosynthesis, hexamer formation and retention of its activity under storage condition and during mobilization. So if zinc deficiency occurs, it will reduce insulin's effect, gradually plateauing from the initial high level and finally diminishing to the base position. The reduced level of blood insulin activity, aggravated by high blood sugar and fat concentration, onsets adult or maturity diabetes (type II) in obese subjects having history of hereditary predisposition and metabolic dysfunctions, occasionally leading to functional failure of the islet cells and pancreatic cyst formation.

Role of zinc as antioxidant: Zinc is an antioxidant, protecting from the damaging effects of oxygen radicals generated during immune activation. Zinc also regulates the expression in lymphocytes of metallothionein and metallothionein like proteins with antioxidant activity. Membrane zinc concentrations are strongly influenced by dietary zinc deficiency and supplementation. Zinc concentrations in cell membranes to be important in preserving their integrity through poorly defined mechanisms involving binding to thiolate groups. It is noteworthy that zinc release from thiolate bonds can prevent lipid peroxidation. In addition, nitric oxide induces zinc release from metallothionein, the primary zinc binding and transport protein in the body, which may limit free radical membrane damage during inflammation.

Conclusion : Several studies were done by Bangladesh Agriculture Research Council on soil and plant zinc content and extent of zinc deficiencies. A range of zinc deficiencies varied from 37% -65% in the 9 districts (Dinajpur, Rangpur, Bogra, Rajshahi, Pabna, Noakhali, Barishal, Chittagong & Chittagong Hill Tracts) was reported in soil by 0. IN HCL method of extraction. Thus soil zinc deficiencies has widely been identified in Bangladesh and it is natural that the people of Bangladesh will be in the deficient state of Zinc. More over main food of Bangladeshi people is rice which contains least amount of Zinc. So a large number of Zinc deficiency disorders or diseases may be at random and prevail among our people. Previously probably many diseases which were considered to be idiopathic or unknown origin may be due to zinc deficiency. For example, after research it is now evident that zinc has a great role in the etiology and management of paediatric diarrhoeas, and gynaecologists, obstetricians and paediatricians are now convinced that complications of pregnancy, labour and of neonates may be due to zinc deficiency. Doctors community was not aware previously about such important trace element Zinc as studies, researches, discussions and seminars on this element are recent. Zinc therapy is important for doctors of all discipline. Zinc may play an important role in strategic plan to the year 2000 regarding women's reproductive health, safe motherhood and child survival, prevention of respiratory tract infections, diarrhoeal diseases, diabetes mellitus and even for reduction of incidence of falciparum malaria.

Creating awareness about zinc through publications like 'The Orion', mass media, seminars will ultimately inspire future researchers, policy makers and programme planners in their important goal to ease the burden of malnutrition and to achieve the success of national programme "Health for All in year 2000" in Bangladesh.

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Role Of Zinc In Pregnancy and Foetal Development

T. A. Chowdhury¹, Habiba Khatun²

Introduction :

Zinc is an element which is widely distributed in nature. It is present in nature as five stable isotopes but in biological system it is always in the divalent state. Zinc readily complexes with amino acids, proteins and nucleotides.

Importance of Zinc in the biological system of animals have been demonstrated since early thirties. It was found that deficiency of Zinc can produce endemic hypogonadism and dwarfism. Zinc is now well recognized as a very important trace element for intrauterine growth of the foetus, and for growth and development in later life. Zinc deficiency also reduces the effectiveness of the immune system.

Over two hundred Zinc containing enzymes have been identified in the biological system. Zinc is a component of the bio-membranes and is thought to be necessary for DNA, RNA and ribosome stabilization. Hence its deficiency may explain some of the developmental defects associated with zinc deficiency.

Metabolism of zinc :

Zinc containing foods are widely distributed in nature. Meat, liver, eggs and seafood are considered to be good sources of dietary Zinc. Other sources include legumes, whole grains, nuts and cheese.

Zinc is absorbed all along the small intestine but mostly from the jejunum. It is absorbed both by carrier-mediated mechanism as well as by diffusion across the brush borders of the cells of the small intestine. Absorbed Zinc is carried by the portal vein to the liver where it is largely albumin bound. Excess fibers and phytate decrease Zinc absorption whereas glucose, amino acids and peptides increase its absorption. Large amounts of calcium and iron in food decrease Zinc absorption. Folic acid may interfere with Zn absorption when the Zinc intake is low but not when it is high.

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About 3 gm of Zinc is normally circulating in the plasma at any given time. This Zinc is partitioned between albumin (57%), α -2 macroglobulin (40%) and amino acids (3%).

Daily Requirement of Zinc :

Daily requirement of Zinc varies with age and the growth state. Approximate recommended figures are as follows (Harrison) :

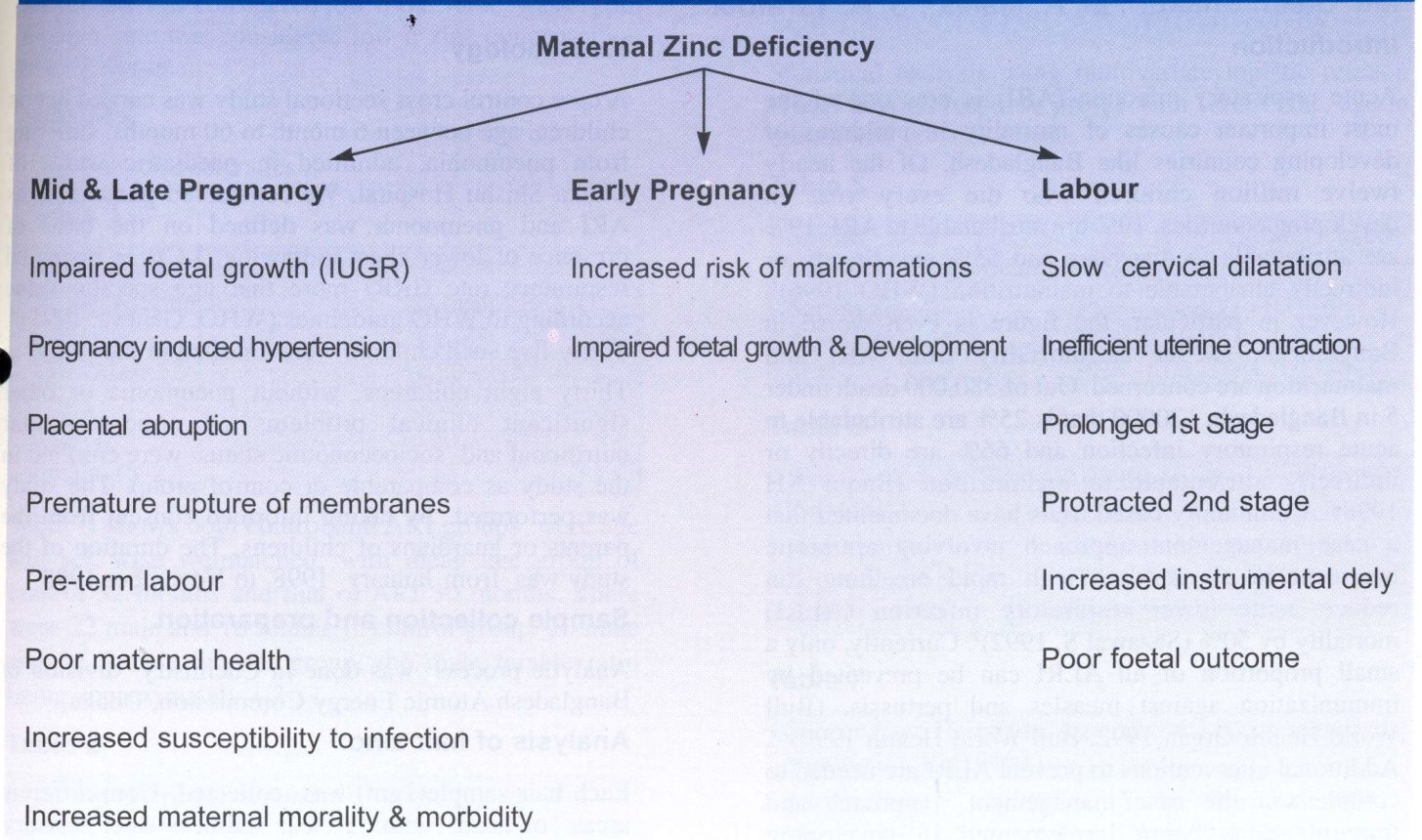
At the age of one month	800 μ gm/day
Between 1-10 years	3-10 mg/ day
Normal adults	10-15 gms/day
During pregnancy	20-25 mg/ day

Consequence of Zinc Deficiency :

- Growth Retardation** : Zn deficient cells may fail to divide and differentiate properly with consequent growth retardation.
- Congenital Malformation** : Zinc is essential for normal embryonic development. Deficiency may result in malformations of the brain, eyes, bones, heart and other organs. The survival of the embryo may be at risk even when there is Zinc deprivation even for a short period of time during the first trimester of pregnancy.
- Impaired Spermatogenesis** : Testicular Zinc content is critical for normal spermatogenesis and for the normal physiological function of the spermatozoa. It preserves the genomic integrity of the sperm and stabilizes the attachment of the sperm head to the tail.
- Immunological Dysfunction** : Zinc is essential for the formation and function of the immune system. With its deprivation, the thymus atrophies and viable thymocytes are not formed. The function of the macrophages and T-cells are impaired ; the result is inability to defend against infection or to respond fully immunologically to an antigen stimulus.

A large number of risk factors as a consequence of Zn-deficiency during pregnancy has been postulated which can be schematically shown as follows :

Possible Consequences of Maternal Zinc Deeciciency



The Winter Garden

Original Article

Zinc Status of Bangladeshi Children Suffering from Acute Respiratory Infection.

Md. Salim Shakur¹, M. A. Malek², S. A. Tarafder³

Introduction

Acute respiratory infection (ARI) is now one of the most important causes of mortality in childrens of developing countries like Bangladesh. Of the nearly twelve million children who die every year in developing countries, 19% are attributable to ARI, 19% are attributable to diarrhoea and 55% are directly or indirectly attributable to malnutrition (WHO 1996)¹. However in particular, the figure is even worse in Bangladesh, as far as mortality from ARI and malnutrition are concerned. Out of 380,000 death under 5 in Bangladesh, 120000 that is 25% are attributable to acute respiratory infection and 66% are directly or indirectly attributable to malnutrition (Baqui AH 1998)². Community based trials have documented that a case management approach involving antibiotic treatment to all children with rapid breathing can reduce acute lower respiratory infection (ALRI) mortality by 50% (Sazawal S. 1992)³. Currently, only a small proportion of all ALRI can be prevented by immunization against measles and pertussis. (Bull World Health Organ 1992, Bull World Health 1990)^{4,5}. Additional interventions to prevent ALRI are needed to complement the case management approach and immunizations being implemented in developing countries (WHO 1984, WHO 1990)^{6,7}. The increased susceptibility to infections particularly pneumonia is postulated to be due to reduction in immunological capacity, specially in cellular immunity. The reduced immunological competence may be attributable to zinc deficiency, because this is associated with improved cellular immune response. (Fraker PJ 1987, Schofield 1979)^{8,9}. On the basis of the background mentioned, a study was carried out to assess zinc status in children suffering from Pneumonia, by simultaneous estimation of serum and hair zinc.

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2. **Prof. M. A. Malek**,
Professor, INFS, Dhaka University.
3. **Dr. S. A. Tarafder**,
Chief Scientific Officer, Chemistry Division,
Bangladesh Atomic Energy Commission, Dhaka.

Methodology

A case control cross sectional study was carried out on children, age between 6 month to 60 months, suffering from pneumonia, admitted in paediatric wards of Dhaka Shishu Hospital. We considered pneumonia as ARI and pneumonia was defined on the basis of presence of lower chest indrawing (LCI) or increased respiratory rate (IRR) more than age specific value according to WHO guidelines (WHO, Geneva, 1991)¹⁰. Thirty five such children were enrolled in the study.

Thirty eight childrens, without pneumonia or other significant clinical problems of almost similar nutritional and socioeconomic status were enrolled in the study as comparable or control group. The study was performed by taking informed consent from the parents or guardians of childrens. The duration of the study was from January 1998 to November 1998.

Sample collection and preparation

Analytic process was done in Chemistry division of Bangladesh Atomic Energy Commission, Dhaka.

Analysis of hair zinc:

Each hair sample (1gm) was collected from different areas of head with a clear stainless steel scissors. They were kept in small polythene envelop with proper labeling of the patients until sent for analysis. According to recognized procedures (Report IAEA)¹¹, the samples were properly washed and dried. From dried hair, samples were prepared by wet ashing method of analysis (Perkin elmer 1982)¹², by treating with HNO₃ and digesting with HClO₄ and then heating at 200°C, until solution became water clear, which was then transferred to 5ml volumetric flask where it was further diluted to 1: 10 dilution. The solution was preserved in a dessicator for analysis.

Analysis of serum zinc:

For serum zinc, 5ml of venous blood was collected in deionized vials, using a deionized syringe, centrifuged and serum was stored at 20°C until ready for analysis. The serum was diluted with deionized water, mixed with 10% glycerol and then treated with spectroscopic graded salts of the element and suprapure acid (2 ml of 65% nitric acid). The predigested samples were then heated at 110°C for 6 hours and at 150°C until ashing procedure was completed.

The zinc concentration in hair and serum after proper processing and preparation were measured by flame atomic absorption spectrophotometry(AASP) using Perkin Elmer model 3110, using wave length of 213.9 nm. Results were expressed in parts per million(ppm). Serum zinc was considered low if the value was <1ppm and hair zinc was considered low if zinc concentration was <150ppm.

Results

Baseline characteristics

Table 1

Age and sex distribution	
Group A(control)	Group B(ARI)
n-38	n-35
Age- 32±6.52	30± 6.54
Sex	
male-22	20
female-16	15

Table -1 shows both control and ARI groups were age and sex wise welmatched; with mean age group of control 32 months and that of ARI 30 months. There were 22 male and 16 female in control group, 20 male and 15 female in ARI group, the male female ratio being approximately 1.3 : 1.

Table 2

Anthropometric measurement			
	Weight for age	Weight for height	Height for age
Group A(control)	98.6 ±10.54	92.92 ± 8.35	96. 38 ± 9.90
Group B(ARI)	94.63 ± 8.62	90.52 ± 8.29	95.35 ± 9.35

Table 2 showing both groups had similar anthropometric measurement, and they are well nourished, with no underweight according to weight for age, no wasting according to weight for height and no stunting according to height for age.

Table 3

Serum zinc in ppm	
	Serum zinc<1ppm
Group A(control)n 38	1.76± 0.98 5(13%)
Group B(ARI)n 35	0.90 ± 0.51 18(54%)
OR 6, 95%CI of OR(1.83,19.62), p<0.05	

OR= odds ratio, CI= Confidence interval,

To convert ppm to µmol/L, multiply by 15.3, 1.76 ppm=26.92 µmol/L

Table 4

	Hair zinc (in µgm/gm)	Hair zinc<150 ppm
Group A (control) n 38	249 ± 154	8 (21%)
group B (ARI) n 35	158 ± 48	16 (46%)
OR 3, 95% CI of OR(1.457, 10.044), p<0.05		

Statistical analysis using multivariate logistic relation model in ARI, response profile with serum zinc, age in month and sex as variable.

Table 5

Serum zinc, age, sex in ARI (Model used statistically significant, P=0.0001)	
Serum zinc	PE= -3.6640(P=0.0139)*
Age in month	PE= -0.1935(P= 0.05)*
Sex	PE= -1.0671(P= 0.934 NS)

Table 6

Hair Zinc, Age, Sex in ARI(model used significant, P=0.0001)	
Hair zinc	PE=-0.00600(P=0.1282 NS)
Serum zinc	PE= -0.0569(P=0.022)*
Age in month	PE=-0.9117(P=0.042)*

Table 7

Serum Zinc, Hair Zinc, Age, Sex in ARI (model used significant, P=0.0001)	
Serum Zinc	PE = - 5.4503 (P=0.247) NS
Hair Zinc	PE = -0 0.0923 (P=0.2741) NS
Age in month	PE = - 0.4240 (P=0.0482)*
Sex	PE = -3.0854 (P=0.2173 NS)

PE=Parameter Estimates

NS = Not Significant

* Significant

Table 3, shows, mean serum zinc was found significantly lower in ARI patients than control (0.90±0.51 Vs 1.76±0.98 P < 0.05) and statistically serum zinc was found 6 times lower in ARI children than control children.

Hair zinc (Table 4) also showing zinc concentrations significantly lower in children suffering from ARI than control. (158±48 Vs 249±154, P < 0.05) and hair zinc concentration was found statistically three times lower than hair zinc concentration of control.

Statistical analysis by multivariate logistic relation model shows negative, association of serum and hair zinc with ARI; that is low zinc status is associated with ARI. It also shows negative association of ARI with age and sex; that is lower age, and female children are more associated with ARI.

Discussion

The result showed significantly low association zinc status with ARI children. The assessment of zinc with simultaneous estimation of serum and hair zinc, both showing significantly low association of zinc with ARI and multivariate analysis by logistic relation model showing negative association of both serum and hair zinc with ARI in well-matched age and sex in both control and ARI strongly supports that the results are less likely to be erroneous and not likely to be affected by selection bias and therefore expected to be widely acceptable. The reported literature on relationship of zinc and respiratory morbidity in children is limited. Three studies reported a higher respiratory morbidity in zinc deficient children, identified in two studies by low hair zinc (Lombeck I 1988, Van Wouwe JP 1986)^{12,13} and in a third by low plasma zinc (Bondestam M 1985)¹⁴.

Although until now the best way to demonstrate zinc deficiency, is to observe clinical response with zinc supplement in specific conditions with appropriate control, a beneficial effect of zinc supplement is observed only in the presence of preexisting biochemical zinc deficiency (Sanstead HH 1970)¹⁵. Therefore, zinc deficient ARI children as found from the study, are expected to be benefited by routine zinc supplement and will be less likely to be affected by ARI in terms of frequency and severity. Very recently Sazawal S et. al. found a significant reduction in the incidence of acute lower respiratory infection in zinc supplemented children in India (Sazawal S 1998)¹⁶. A possible mechanism for the effects of zinc on ALRI is enhanced immune status through adequate zinc status, preventing establishment of infection or improving the clearance of infectious agents (Singh KP 1992, Drissen C 1994)^{17,18}. Another possible mechanism of zinc is a direct anti viral effect (Al Nakib W 1987, Potter YS 1993)^{19,20}.

On the basis of the result, further interventional study with zinc supplement may be undertaken by nutrition researchers in Bangladesh to find the effect of zinc supplement in reducing frequency and morbidity from ARI in Bangladesh. The result of the study may help policy makers and programme managers in Bangladesh to undertake intervention policy by providing routine zinc supplement to Bangladeshi children, particularly to vulnerable groups like malnourished children of Bangladesh. However the study is a hospital based and a more broad based population studies are required in this field by non government or government organisation like Bangladesh bureau of statistics, ministry of planning, by conducting child nutrition survey (CNS) to help adopt national intervention policy to provide routine zinc

supplement to Bangladeshi children in order to reduce incidence, morbidity and mortality from pneumonia.

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Zinc and Rehabilitation from Severe Protein Energy Malnutrition; Higher Dosages Regime Associated with Increased Mortality.

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Abstract

A randomized double blind prospective trial was carried out to investigate catch up growth in severe protein energy malnutrition, with particular reference to linear growth and the effect of Zinc supplementation. 141 Children between the ages of 6 months to 3 years were recruited after admission to a Nutritional Rehabilitation Unit in Dhaka Shishu Hospital and randomized to receive either 1.5 mg/kg for 15 days, 6 mg/kg for 15 days, or 6 mg/kg for 30 days of elemental Zinc and then followed for a total of 90 days. Anthropometric outcome variables included change in height for age z score, change in knee/heel length as measured by knemometer, change in weight for age and weight for height z scores and change in mid upper arm circumference as well as change in skinfold subscapular/triceps thickness. No anthropometric variable demonstrated a significant improvement with increased Zinc dosage and in addition mortality was significantly increased in these subjects exposed to high dose Zinc (6 mg/kg) as opposed to those exposed to low dose zinc supplementation (1.5 mg/kg) with a yates corrected chi square p value of 0.033 and a risk ratio of 4.55 (95% confidence limits : 1.09 <RR<18.8) We conclude that there is no benefit from employing higher dose zinc supplementation regimes and indeed that they may contribute to increased mortality in the severely malnourished child.

This topic has already been published in 'American Journal of Clinical Nutrition' Vol. 68, 748. It was a prospective randomized double blind trial of three zinc regimes. Our hypothesis was 'increased doses and long time supplementation of zinc is associated with increased weight and linear growth in severely malnourished children'. This study has been carried out at Dhaka Shishu Hospital over a period of 13 months from November 1995 to November 1996. 141 children from the ages of 6 months to 3 years were recruited from severely malnourished admitted patients of the Nutritional Rehabilitation Unit of this hospital.

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Children were randomised to receive either of three regimens:

- (1) 1.5 mg/kg/ day (elemental zinc per kg body weight) for 15 days followed by placebo for 15 days.

Or

- (2) 6.0 mg / kg / day (elemental zinc per kg body weight) for 15 days followed by placebo for 15 days.
- (3) 6.0 mg / kg / day (elemental zinc per kg body weight) for 30 days.

Baseline characteristics of these 141 children are depicted in table 1. The average age was 15 months old and with severely wasted and stunted.

Table 1 : Characteristics of children Z scores expressed as mean (S.D.)

	1.5/ Placebo	6.0/Placebo	6.0/6.0
Number	49	49	43
Age (months)	15.5 (8.7)	15.0 (9.0)	16.3(8.6)
Weight for Age Z score	-4.47(0.91)	-4.56 (0.98)	-4.66 (0.86)
Weight for Height Z score	-2.56 (0.97)	-2.73 (0.90)	-2.71 (0.93)
Height for Age Z score	-3.89 (1.3)	-3.79 (1.4)	-3.98 (1.45)
Marasmus	29	27	26
Marasmic Kwashiorkor	15	14	11
Kwanshlorhor	5	7	6
Completed protocol	43	38	25

All the recruited children got appropriate treatment for their infection or other illness. They also got appropriate food, which was duly regulated and supervised by qualified Nutritionist and also received health education and nursing care.

Whilst in-patients weights were recorded daily. Knemometry (Heel-knee length) was taken on alternate days. Height and skin fold thickness were recorded on days 1, 8 and 15. Then after discharge all these patients were followed up on days 21, 30, 45, 60, 75 and 90 when morbidity and anthropometric data was collected and health education was re-enforced.

After completion of the study it was seen that there were no significant differences in changes of any anthropometric variables between these three regimens, neither higher dose nor longer duration Zinc supplementation regimens had any appreciable anthropometric benefit over the lower dose regimen over the 90 day of the study. On average, good weight gain and catch up growth was achieved within all 3 groups.

The most striking finding of this study was the increase in mortality associated with initial high dose regimen (6.0 mg elemental zinc/kg/day) as opposed to the lower zinc regimen (1.5 mg elemental zinc / kg/ day). The inpatient death rate of those recruited to the higher dose zinc regimen was 12% whereas that for the lower dose zinc group was 4%; this compared with the unit in-patient death rate of 18% just before starting this trial.

Most of these deaths were sepsis related and occurred during the in-patient phase of rehabilitation and therefore the effect of supplemental zinc on the immune system of these malnourished children might be considered.

There are many studies showed that zinc deficiency is associated with poor immune function particularly cellular immunity and zinc supplementation of malnourished children improves immune function, contrarily zinc supplementation in the presence of ongoing sepsis may not be necessarily beneficial. High dose inhibits copper absorption, which is associated with reduced phagocytic and fungicidal activity.

In conclusion, we would say that our study did not support our hypothes; neither the use of a higher dose of zinc initially nor prolongation of the period of supplementation resulted in a significant anthropometric benefit in severely malnourished children, and indeed the high dose was associated with increased mortality. We recommend therefore that low dose (1.5 mg elemental zinc/kg/day for 15 days) can be prescribed in protein energy malnutrition with out sepsis but caution be used with high dose (6 mg elemental zinc /kg/day) zinc supplementation. Further studies are needed to define the relation between zinc and the immune responses, determine how best to assess zinc status, determine the optimal concentration of zinc supplementation and determine when it is best to administer zinc.

Zinc and Malaria

The Papua New Guinea trial (Medi News, p-27) also examined the impact of prophylactic Zinc supplements on malaria, and found a 40% reduction in clinic attendances related to falciparum malaria. A previous trial in Gambia found a similar (30%) reduction, although the Gambian result was not statistically significant ($P=0.09$).

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Dermatological Changes Related to Zinc Deficiency

A. Z. M. Maidul Islam,¹ Md. Mahmud Hasan.²

Introduction

Although human deficiency of Zinc was not clearly established before 1969, since then it has been emerging as a nutrient of clinical importance through clinical trials and studies [1]. Zinc belongs to the group of essential trace elements [which at present comprise Zinc, Iron, Copper, Manganese, Nickel, Cobalt, Molybdenum, Selenium, Chromium, Iodine, Fluorine, Tin, Silicon, Vanadium and Arsenic] which are extremely vital for maintaining normal health [2]. As the metal component of more than 200 important enzymes such as alkaline phosphatase, alcohol dehydrogenase and several dehydrogenase and digestive enzymes it is involved in the synthesis and degradation of protein, lipid, carbohydrates and nucleic acids. It has recently been found to play an essential role in polynucleotide transcription and translation and thus in the processes of genetic expression. It's involvement in such fundamental activities probably accounts for the essentially of zinc for human and all other life forms [3].

High concentrations of Zinc are present in shellfish, legume, nuts, whole grain and green leafy vegetables, whereas fruits usually contain insignificant levels [4]. The Zinc supply depends largely on the protein content of the food and so protein under nourishment will lead to an insufficient Zinc supply. Phytate interferes with Zinc absorption and a high fibre content of the food also tends to decrease the bioavailability of the element [6.c]

The daily oral intake of Zinc should average 3 mg in infants less than 6 months, 5 mg in infants 0.5- 1 yr. old, 10 mg in children 1-7 yr. old and 16 mg from the eleventh year and onwards. Pregnant and lactating women should receive 20-25 mg zinc daily[5].

Zinc deficiency

Zinc deficiency may be caused by a specific absorptive defect present in acrodermatitis enteropathica or by insufficient nutrition as reported from the Middle East and Turkey. These causes of Zinc deficiency are referred to as **Primary**. Zinc deficiency may also be consequent upon diseases of the gastrointestinal tract causing diarrhoea and malabsorption. Such cases are called **Conditional** or **Secondary Zinc deficiency**.

In general common causes of Zinc deficiency are chronic liver disease, chronic alcoholism, cancer chemotherapy, intestinal disease, collagen disease, nephrotic syndrome, haemodialysis, burn, trauma, use of oral contraceptives and diabetes mellitus. Whatever the cause of Zinc deficiency is, it definitely causes a series of disorders as described in the following Table-1 [6].

Primary zinc deficiency [7].

Acrodermatitis enteropathica: The disease was recognized in 1936 by the Swedish dermatologist Thore Brandt. His findings were corroborated and further investigated by Danbolt and Closs who coined the name of the disease. It is the only known inherited Zinc deficiency disease in man, transmitted as an autosomal recessive trait.

Clinical features: The disease typically starts 4-6 weeks after weaning or earlier if the infant is not weaned. The child turns peevish, withdrawn and photophobic, develops a vesiculobullous dermatitis on hands, feet and peri-orificial areas and scalp hair is lost. Diarrhoea is often present. Growth is stunted and there is a decreased resistance to infections. Wound healing is poor.

Without proper management the prognosis is usually fatal and in the past a lethal outcome without therapy has been described in most cases [8].

Treatment: Zinc sulphate supplementation is found to be the only treatment for acrodermatitis enteropathica and was first introduced in 1973-1974 [9, 10] Oral Zinc in a dose of 2 mg/kg daily was found to cure all clinical manifestations related to the Zinc deficiency within a few weeks. Prolonged therapy at least up to adult age is necessary to prevent recurrence of Zinc deficiency.

Secondary (conditioned) Zinc Deficiency

Zinc depletion syndrome: Adults who receive 0.2 mg Zinc daily, which is 1.3% of the recommended allowance, become clinically Zinc deficient within three months [11]. Where there is disturbed bowel function the Zinc loss is increased, and if combined with a

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TABLE - 1

Zinc Deficiency May Cause The Following Disorders : [2, 3, 6, 22]

GROWTH RETARDATION	Zinc deficient cells fail to divide and differentiate, with consequent growth impairment .
IMPAIRED SPERMATOGENESIS	Testicular zinc is critical for normal spermatogenesis and for sperm physiology; it preserves genomic integrity in the sperm and stabilizes attachment of sperm head to tail.
HYPOGONADISM AND SUPPRESSION OF SECONDARY SEXUAL CHARACTERISTICS	The development of primary and secondary sex organs in male, and all phases of the reproductive process in the female from estrous to parturition and lactation, can be adversely affected in zinc deficiency. Zinc deficiency results in a reduced gonadotrophin output and consequent fall in androgen production which in turn results in hypogonadism with suppression of secondary sexual characteristics.
CONGENITAL MALFORMATION	Zinc is essential for normal embryonic development. Deficiency results in malformation of brain, eyes, bones, heart, and other organs. Zinc deficiency significantly reduces the activity of thymidine kinase, an enzyme vital to DNA synthesis- results in congenital malformation.
IMMUNOLOGICAL DYSFUNCTION	Zinc is essential for the formation and function of the immune system. With zinc deprivation, the thymus atrophies and viable thymocytes are not formed. The function of macrophages and T-cells are impaired and lymphocyte concentration decreased-the ultimately result is an inability to respond to antigens or to defend the organism against infections.
RESPIRATORY TRACT INFECTION	In recent studies, it is evident that zinc deficiency increases the incidence of respiratory tract infection in children.
DERMATOLOGICAL DYSFUNCTION	Zinc deficiency causes a wide variety of dermatological dysfunction includes of hyperkeratosis, parakeratosis and alopecia.
DIARRHOEA	Zinc deficiency increases the incidence of diarrhoea and its supplementation reduces the prevalence. The role of zinc in diarrhoea may be mediated through several mechanisms, which include 1)membrane stabilization,2) mucosal integrity, 3)electrolyte transport and)water transport,4) immune competence, 5)protein and essential enzyme synthesis.
LOSS OF APPETITE AND ANOREXIA	Desensitization of the taste buds in zinc deficiency causes loss of appetite and anorexia
OTHERS	Night blindness, Abnormal hair growth, Deformed bone formation

decreased absorption and low dietary Zinc intake- Zinc depletion will develop. The Zinc depletion syndrome was originally identified because of the acrodermatitis enteropathica-like skin lesions of patients who received prolonged total parenteral nutrition for inflammatory bowel diseases and chronic diarrhoea. The cause of the depletion is often triple: pre-existing latent Zinc deficiency, prolonged total parenteral nutrition with a low Zinc content and a sudden weight gain provoked by high calorie supply with the parenteral nutrition. In most cases reported the parenteral nutrition was given for 2-3 months before signs of Zinc deficiency occurred. The serum Zinc level is significantly decreased, often less than 20 mg/100 ml(normal about 70-12 mg/100 ml. equivalent to 11-19 mmol/L).

Zinc depletion observed in infants on total parenteral nutrition [12]. Premature infants are particularly at risk of developing such a state because they are born with negligible Zinc stores and undergo rapid growth within their first months of life. Apart from cutaneous lesions of zinc deficiency they may show gastric retention and paralytic ileus [13] which resolves promptly following

Zinc therapy. Chronic Zinc deficiency may develop in patients suffering from malabsorption-malnutrition associated with alcohol liver cirrhosis and alcoholic pancreatitis. It may also develop following bypass surgery.

Skin changes related to Zinc deficiency [14]

Systemic Zinc deficiency causes lesions including alterations in nail and hair growth. The findings are similar whether the cause is primary or secondary.

Acute Zinc deficiency: General symptoms include septicaemia, photophobia and mental depression. There is an acute eczematous eruption on hands and feet, in the anogenital regions and around the body openings. The volar aspects of the fingers show characteristic flat bullous lesions on the flexural creases. There are various degrees of paronychia inflammation on fingers and toes. Oozing lesions may be seen on the heels of bedridden patients. Some lesions are black and necrotic and burn-like skin changes may be seen. There is angular stomatitis with perioral lesions sparing the vermillion border.

Chronic Zinc deficiency: Chronic Zinc deficiency lesions are typically seen on skin areas subject to pressure and minor trauma such as elbows, knees, knuckles and malleolar regions of the ankles. The lesions are sharply demarcated, thickened and of a red-drawn colour. Lichenification is present as an important clue to distinguish it from psoriasis. Seborrhoeic dermatitis-like changes may be seen on the face of adult patients. Pre-existing acne vulgaris tends to flare. A severe reticulate non-itchy scaly dermatitis on the trunk has been described in chronic Zinc deficiency of alcoholics [15]. It remains unresponsive to topical steroid treatment but clears rapidly with oral Zinc.

Hair and nail changes related to Zinc deficiency[16]

In acute Zinc deficiency diffuse thinning of the scalp hair becomes progressive and eventually leads to total alopecia. In chronic Zinc deficiency the hair growth is poor and sparse. Structural changes of the hair may be observed with the microscope, e.g. broken spearhead-like endings, transverse striation of the shaft, pseudomonilethrix, longitudinal spits and bayonet hairs. Severe Zinc deficiency usually leaves deep transverse depressions (Beau's lines) on the finger nails. White transverse bands may be seen alone or in association with the depressions [17].

Pathology: In acute vesiculobullos acrodermatitis-light microscopy reveals pronounced epidermal extracellular oedema with formation of suprabasal cysts and clefts. The horny layer is often separated or lost. Necrosis of the outer epidermis may be seen [18], simulating migratory necrolytic erythema. In chronic Zinc deficiency there is psoriasis-like acanthosis of the epidermis. In the dermis a slight perivascular infiltrate of lymphocytes, neutrophils and a few histiocytes is present. Electron microscopy of acute lesions shows degenerate basal cells with slender cytoplasmic protrusions and an intact basal lamina with multiple invaginations [14.a].

Diagnosis: Severe Zinc deficiency is usually suspected from the clinical findings and the history. The serum Zinc and alkaline phosphatase levels are low [14,19] but rise promptly during Zinc administration. The parallel indices of the two parameters can be used for diagnosis and for control of the treatment [14,20]. It is important always to consider the level of plasma albumin which binds 60-70% of circulating Zinc. Severe hypoalbuminaemia therefore is generally associated with low serum Zinc values which do not reflect a state of Zinc deficiency.

In suspect cases a therapeutic trial with oral or parenteral Zinc should be undertaken. If no clinical improvement occurs within 4-5 days and the serum alkaline phosphatase remains unaltered or even

decreases despite a rise in serum Zinc the patient is not deficient in Zinc.

Treatment: In adult patients oral Zinc sulphate 0.2g are given two to three times daily (about 2 mg Zinc/kg). Similar doses on a kilogram basis are given to children. Parenterally 0.2-0.3 mg Zinc/kg daily (about 10-20 mg daily in adult patients) is sufficient in severe cases of acute Zinc deficiency. For prophylactic purposes total parenteral nutrition should supply no less than 70-80 µg Zinc/ kg. daily. Infants and premature babies on parenteral nutrition should receive a prophylactic dose of 0.1 - 0.3 mg/kg daily [21].

Conclusions

Considering the decreasing level of Zinc in our soil and food grains, a patient having clinical features resembling Zinc deficiency, should be investigated and treated accordingly.

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Special Article

Congenital Dislocation Of The Hip

A. F. M. Ruhul Haque

Introduction

Hip dislocation is not uncommon but the congenital variety i.e. by birth is a more serious variety. If the baby is not seen carefully then this dislocation goes undetected and is only apparent when the child starts to walk with a limp. Quiet often this is also ignored for a long time and presented to us around 12-15 years of age.

It is to be understood that if diagnosed at an early age preferably immediately after birth then the dislocated hip can be corrected fully. The later the presentation the more difficult is the treatment. *The treatment varies from Double Nappy, Abduction Splint, Traction, Plaster or Surgery to put the head of the femur back into the acetabulum.* The method of treatment chosen depends on the severity and age of the patient. The whole range of treatment is available now in Bangladesh. *The most important factor is to identify the problem hip immediately after birth.* Before coming to the ways of diagnosis of diseased hip I will point out a few points to remember.

Causes

a) Genetic- Familial incidence especially where inter-marriage is common. Two separate genetic factors are involved, 1) Joint Laxity (of dominant inheritance) which account for most cases diagnosed in first week of life. 2) Acetabular dysplasia (polygenic inheritance) usually diagnosed later. 75% of the lax joints which are dislocatable recover spontaneously within 6 weeks.

b) Hormonal or environmental- 1) at the time of delivery mother secretes ligament relaxing hormone. If this crosses the placental barrier any tendency to joint laxity is enhanced. This accounts for the variety of dislocations of premature babies and possibly for the relative infrequency in boys (male hormone counteracts the female hormone). 2) Intrauterine malposition- Breech presentation with extended legs favour dislocations linked with the high incidence of first born babies where spontaneous versions is often less. 3) Racial customs where babies are dressed tightly with legs extended and hips together eg, North America, HongKong Chinese, Africa, etc. where dislocations are common.

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Pathology

The acetabular roof is shallow and underdeveloped. After walking starts the false acetabulum develops above the original fossa. The nucleus of the femoral head appears late, femoral head is shorter and usually antverted. The dislocation is always posterior. The capsule remains intact. In time it becomes hour glass in shape crossed by psoas muscle. The labrum is large and infolded often. The ligamentum teres is unduly thick and with time muscles arising from pelvis becomes shorter.

How Do We Diagnose Early?

Asymmetry of hips with extra skin folds in thigh and clicking sound in moving (abduction & adduction) of hips. Difficulty in putting napkin with limited abduction of hip. Late walking not a usual feature although commonly believed. After walking asymmetry and limp becomes more apparent. This is for one-sided dislocations. Bilateral dislocations are not uncommon and asymmetry is not present and the waddling gait is often taken as normal for a baby.

Premature delivery, breech presentation, female child, first baby and left hip with limited abduction should raise the clinician's suspicion of Congenital Dislocation of hip.

Moving the hip in flexion by holding the thigh between thumb and fingers in abduction and adduction often a click sound is elicited.

When hip is reduced (Ortolani's test) or head of femur moved out of acetabulum (Barlow's test) gives the diagnosis of dysplasia of hip joint or dislocatable hip.



Figure : 1

X-Ray

In older children X-Ray is helpful and dislocation is obvious but before the appearance of the nucleus diagnosis is facilitated by drawing two lines one through triradrate cartilage (Horizontal) & outer edge of acetabulum (verticals). Normal position of head is medial to vertical & below the horizontal line. There

are other lines to measure acetabular angle & shaft of femur to acetabular angle. Arthrogram (putting dye into the hip joint & taking X-Ray) gives the best diagnosis.

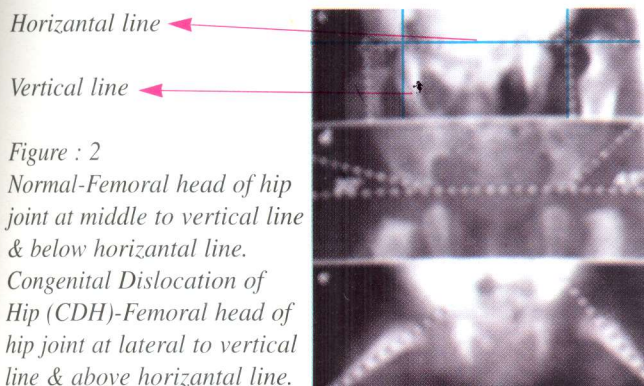


Figure : 2
Normal-Femoral head of hip joint at middle to vertical line & below horizontal line.
Congenital Dislocation of Hip (CDH)-Femoral head of hip joint at lateral to vertical line & above horizontal line.

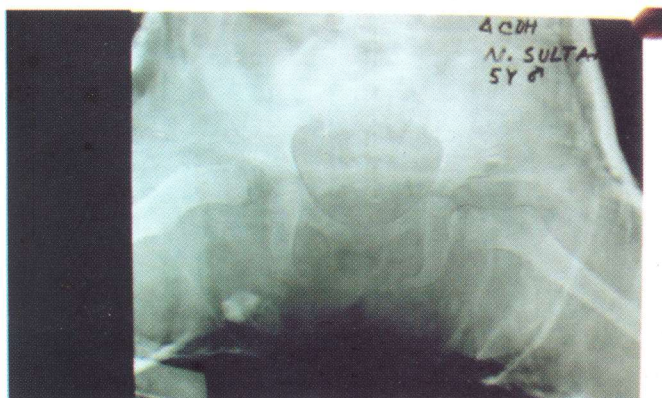
Other Causes of Dislocation:

Post Septic Arthritis Dislocation
Spina Bifida
Cerebral Palsy, Etc.

Radiograph of a five year aged female child named Sultana with Bilateral Congenital Dislocation of Hip showed below:



Treatment Bilateral Congenital Dislocation of Hip: Pre-operative.



Bilateral Congenital Dislocation of Hip: Post operative-after both operatory.

Early stage the treatment is simple before the child starts crawling (This puts weight through hip) - The hips are to be kept abducted. This can be done by putting thick Nappy (Double) or small pillow between legs or by splint (Von- Rosen splint) for few months. In older children after weight bearing has started treatment becomes difficult but basic principle remains same -

The hip must be reduced and held reduced until stable.

- Closed Reduction by traction, in both legs and gradual abduction, - if hip is reduced then plaster hip spica is given.
- Open Reduction -If closed method fails then Surgery has to be done to put the hip into acetabulum . Before this procedure an Arthrogram might show infolding of limbus.

If reduction fails then surgery is needed, failure may be due to (1) limbus (2) Hour-glass constriction of capsule (3) Tight psoas, long thick ligamentum teres.

There is nothing to be afraid about the surgical procedure, this is well documented and much literature is available on the subject, the procedure can be managed in our situation with proper training on this subject.

In our situation the patients present in older age group up to 10 year or older with dislocation. Common teaching is to leave alone children above 5 years with dislocation of hip.

I think no reason to believe this as I have successfully treated many children above that age. Of course the ideal time to treat the dislocations is the early age. Since in our situation we do face older age group with congenital hip dislocations we should study this in more detail to find out the ideal age for the treatment.

Here are some of the patients treated-

A seven years old female child named Habiba with series of pictures of surgical procedure showed below:



Figure A: Unilateral Congenital Dislocation of Hip(left):Pre-operative.

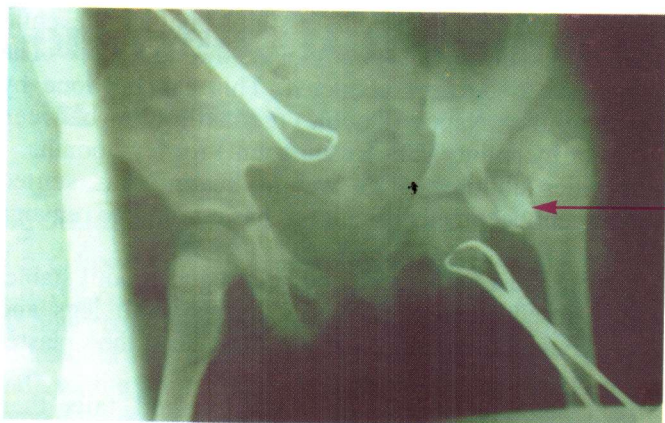


Figure B: At operation: Arthrogram.



Figure C: At operation: After reduction and check X-ray.

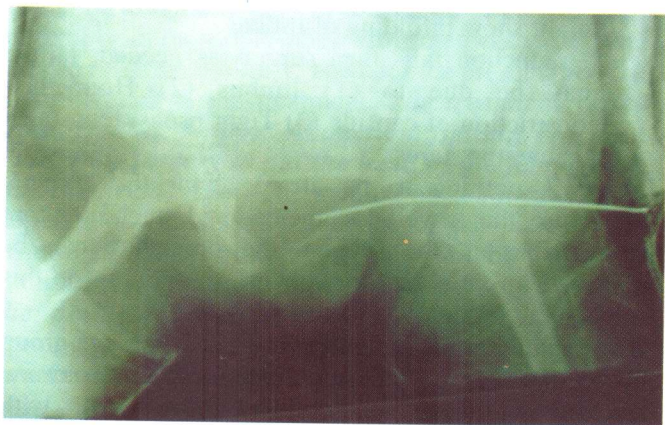
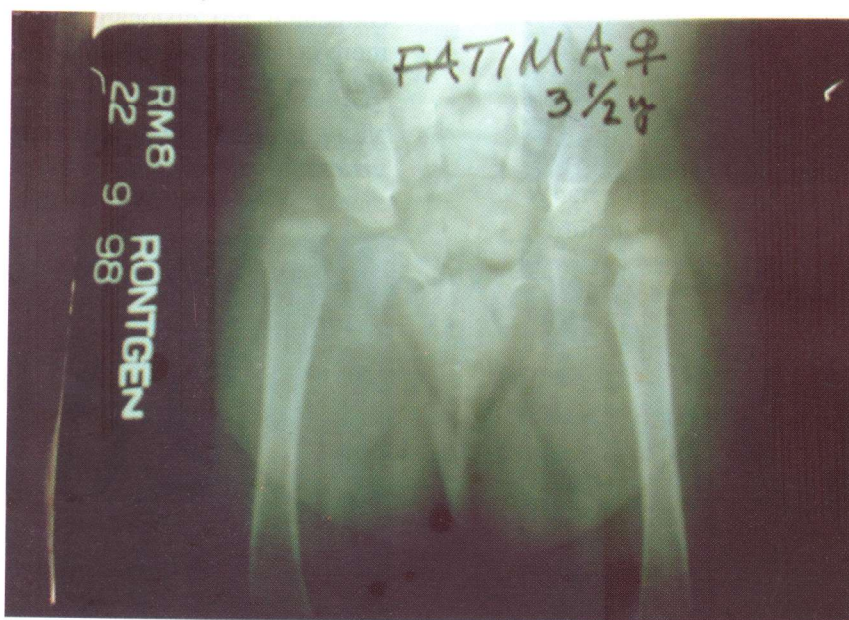


Figure D: Immediately after operation with Hip Spica.



Figure E: Six weeks after Open Reduction and De-rotation osteotomy.

Radiograph of Bilateral Congenital Dislocation of Hip of a three & half years old female child named Fatema showed below:



Bilateral Congenital Dislocation of Hip- Waiting for Surgery.

Orixyl 500

Amoxycillin 500 mg



A Convenient Approach for
Effective Clinical Application

Daily Nutritional Requirement

Minerals																						
Water-Soluble Vitamins																						
Fat-Soluble Vitamins																						
Category	Age (Years) or Condition	Weight (kg)	Height (cm)	Protein (g)	Vita- min A (mg RE)	Vita- min D (mg)	Vita- min E (mg)	Vita- min K (mg)	Vita- min C (mg)	Thia- mine (gm)	Ribo- flavin (mg)	Niacin (mg NE)	Vita- min B ₆ (mg)	Folate (μg)	Vita- min B ₁₂ (mg)	Cal- cium (mg)	Phos- phorus (mg)	Mag- nesium (mg)	Iron (mg)	Zinc (mg)	Iodine (μg)	Sele- nium (μg)
Males	15-18	66	145	176	69	59	1,000	10	65	60	1.5	1.8	20	2.0	200	1200	1200	400	12	15	150	50
	19-24	72	160	177	70	58	1,000	10	70	60	1.5	1.7	19	2.0	200	1200	1200	350	10	15	150	70
	25-50	79	174	176	70	63	1,000	5	80	60	1.5	1.7	19	2.0	200	800	800	350	10	15	150	70
	51+	77	170	173	68	63	1,000	5	80	60	1.2	1.4	15	2.0	200	800	800	350	10	15	150	70
Females	15-18	55	120	163	64	44	800	10	55	60	1.1	1.3	15	1.5	180	1200	1200	300	15	12	150	50
	19-24	58	128	164	65	46	800	10	60	60	1.1	1.3	15	1.6	180	1200	1200	280	15	12	150	55
	25-50	63	138	163	64	50	800	5	65	60	1.1	1.3	15	1.6	180	800	800	280	15	12	150	55
	51+	65	143	160	63	50	800	5	65	60	1.0	1.2	13	1.6	180	800	800	280	10	12	150	55
Pregnant					60	800	10	65	70	1.5	1.6	17	2.2	400	1200	1200	320	30	15	175	65	
Lactating	1st 6 months				65	13,00	10	12	65	95	1.6	1.8	20	2.1	280	1200	1200	355	15	19	200	75
	2nd 6 months				62	12,00	10	11	65	90	1.6	1.7	20	2.1	260	1200	1200	340	15	16	200	75

Source : National Research Council : Recommended Dietary Allowance, 10th ed.

Drug Induced Side Effects

Effect of drugs on nutrient absorption and metabolism.

DRUG EFFECT

Analgesics and anti-inflammatories

Salicylates	Decrease serum ascorbic acid; increase urinary loss of acid, potassium, and amino acids.
Sulfasalazine	Impairs folate absorption and antagonizes folate supplementation.

Antacids

Aluminum antacids	Decrease absorption of phosphate and vitamin A.
H ₂ Blockers	Decrease iron and vitamin B ₁₂ absorption.
Octreotide acetate	Hypo- and hyperglycemia; decreases fat and carotene absorption.

Anticonvulsants

Phenobarbital	Decreases serum folate; increases vitamin D and Vitamin K turnover and may cause deficiency.
Phenytoin	Decreases serum folate; increases vitamin D and Vitamin K turnover and may cause deficiency.
Primidone	Decreases serum folate and vitamins B ₆ , B ₁₂ ; decreases calcium absorption; increases vitamin D and vitamin K turnover and may cause deficiency.

Antimicrobials

Neomycin	Binds bile acids and decreases absorption of fat, carotene; of vitamins A, D, K, and B ₁₂ ; and of potassium, sodium, calcium, nitrogen.
Amphotericin B	Decreases serum magnesium and potassium
Aminosalicic acid	Increases absorption of folate, Vitamin B ₁₂ , iron, cholesterol, fat.
Chloramphenicol	Increases need for vitamins B ₂ , B ₆ , B ₁₂ ; increases serum iron.
Penicillin	Hypokalemia; renal potassium wasting.
Tetracycline	Calcium, iron, magnesium inhibit drug absorption; decreases vitamin K synthesis.
Cycloserine	May decrease absorption of calcium, magnesium; may decrease serum folate and vitamins B ₆ , B ₁₂ ; decreases protein synthesis.
Isoniazid	Vitamin B ₆ antagonist; may cause deficiency.
Sulfonamides	Decrease absorption of folate; decrease serum folate, iron.
Nitrofurantoin	Decreases serum folate.
Pyrimethamine	Decreases serum B ₁₂ and folate.

Antimitotic

Methotrexate	Decreases activation of folate.
Colchicine	Decreases absorption of vitamin B ₁₂ , carotene, fat sodium, cholesterol, lactose, nitrogen.

Cathartics

Phenolphthalein	Malabsorption, hypokalemia; deficiency of vitamin D, calcium.
Mineral oil	Malabsorption; decreased absorption of vitamins A, D, K

Diuretics

Some cause hypokalemia, hypomagnesemia; may increase urinary excretion of vitamins B₁, B₆; calcium, magnesium, potassium.

Hypocholesterolemics

Cholestyramine	Binds bile acids; decreases absorption of fat, carotene; vitamins A, D, K, B ₁₂ ; folate, iron
Clofibrate	Decreases absorption of carotene, vitamin B ₁₂ , iron, glucose.

Hypotensives

Hydralazine	Vitamin B ₆ deficiency.
Captopril	May cause hyponatremia, hyperkalemia; decreases taste acuity.

Oral contraceptives

Vitamin B₆, folate deficiency; may increase the need for other nutrients.

Current Medical Diagnosis & Treatment

Self Assessment

A bullous dilemma

A 66-year-old man presented to the emergency department because of multiple fluid-filled lesions on his face, buccal mucosa, upper body, and genitalia. A few days earlier he had been seen for mouth ulcerations, which at that time were thought to be the result of improper use of inhaled corticosteroids. His medical history included hypertension, type 2 diabetes mellitus, and asthma.

Treatment with topical and oral antibiotics and an oral antiviral agent was unsuccessful. The persistent bullae were tense and noninflammatory but were not painful or pruritic. Nikolsky's sign (separation of the epidermis in response to manual pressure) was absent. The condition responded to a short course of systemic corticosteroids, but a subsequent flare produced additional lesions.



Bullae and lesions after corticosteroids treatment.

**WHAT IS
YOUR
DIAGNOSIS?**

**LOOK AT
THE NEXT
PAGE FOR**

THE ANSWER

Miscellaneous Medica

WHO gives southeast Asia a health warning

HIV/AIDS, malaria, and tuberculosis are the most formidable challenges for southeast Asia and account for more than 40% of the global communicable disease burden, according to WHO's 52nd Regional Committee Meeting (Dhaka, India; Sept 6-11, 1999).

Between July, 1997, and March 1999, southeast Asia reported a 40% increase in AIDS cases with Thailand, Myanmar, and India accounting for more than 95% of cases. "It is estimated that less than 25% of the total AIDS cases have been reported", writes WHO regional director Uton Muchtar Rafei in his biennial report.

Tuberculosis still has the highest mortality in the region. The annual number of new smear positive cases has increased from 18 000 to 70 000—a 2.5% increase. The region also accounts for 80% of global leprosy cases but is expected to achieve the target prevalence rate of less than 1 in 10 000 by 2002, albeit 2 years later than planned.

THE LANCET. Vol 354. Sept 18, 1999

The First American Civilian Saved by Penicillin

The first U. S. civilian whose life was saved by penicillin died in June 1999 at the age of 90 years. In March 1942, a 33-year old woman was hospitalized for a month with a life-threatening streptococcal infection at a New Haven, Connecticut hospital. She was delirious, and her temperature reached almost 107°F (41.6°C). Treatments with sulfa drugs, blood transfusions, and surgery had no effect.

As a last resort, her doctors injected her with a tiny amount of an obscure experimental drug called penicillin. Her hospital chart, now at the Smithsonian Institution, indicates a sharp overnight drop in temperature; by the next day she was no longer delirious. She survived to marry, raise a family, and meet Sir Alexander Fleming, the scientist who discovered penicillin. In 1945, Fleming was awarded the Nobel Prize in physiology and Medicine, along with Ernst Chain and Howard Florey, who helped develop penicillin into a widely available medical product.

JAMA Sept. 8, 1999. Vol. 282 No. 10



The answer : Epidermolysis bullosa acquisita

Discussion :

Epidermolysis bullosa acquisita is a rare subepidermal, blistering, autoimmune skin disease that occurs one tenth as often as bullous pemphigoid. The disease is now believed to be caused by an autoantibody to type VII collagen located in anchoring fibrils of squamous epithelium in the basement membrane. Although epidermolysis bullosa acquisita can present with variable clinical features common to any subepidermal bullous disease, it follows a chronic course of remissions and exacerbations that may result in scarring or other, more ominous morbid complications (eg, sepsis, ocular or laryngeal involvement).

As its name suggests, epidermolysis bullosa acquisita is an acquired form of the disease. There are also three major types of inherited epidermolysis bullosa: simplex, junctional, and dystrophic. The types are classified on the basis of electron-microscopic and immunofluorescent data and more than 20 phenotypes have been reported. Unlike the acquired form, which is most common in middle-aged and older adults, inherited epidermolysis bullosa presents within the first few years of life.

The lesions of epidermolysis bullosa acquisita must be distinguished from those of numerous other subepidermal blistering diseases, including pemphigus vulgaris, drug-induced pemphigus, paraneoplastic pemphigus, bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, bullous eruptions of systemic lupus erythematosus or diabetes, linear IgA bullous dermatoses, porphyria cutanea tarda, and pseudoporphyria. Definitive diagnosis can be made only on histologic evaluation of skin biopsy specimens obtained with the salt split-skin technique and on results of direct and indirect immunofluorescent studies. The autoantibodies in epidermolysis bullosa acquisita bind exclusively to the dermal portion of the dermoepidermal junction, and studies have shown that all affected patients have linear deposition of IgG at the basement membrane zone.

Treatment :

Treatment of epidermolysis bullosa acquisita involves long-term therapy with corticosteroids and other immunosuppressive medications (eg, dapason). The disease can be quite refractory, which is often frustrating for both the patient and the physician.

VOL 105/ NO 6/1999/PGM

Risk of type 2 diabetes reduced by regular brisk walking

Greater physical activity is associated with a decreased risk of developing type 2 diabetes, according to data from the Nurses' Health Study. The reduced risk correlated not only with intense exercise, but also with exercise of moderate duration and intensity, including walking.



Get a move on for health

Frank Hu (Harvard School of public Health, Boston, MA, USA) and colleagues looked at 70102 women in the Nurses' Health study who were free from diagnosed diabetes, cardiovascular disease, and cancer in 1986, and who completed questionnaires on physical activity in that year. Weekly physical activity in metabolic equivalent taskhours (MET-hours) was quantified. 1419 women developed type 2 diabetes during 8 years of follow-up.

After adjustment for covariates such as smoking and hypertension, each quintile of increased weekly physical activity showed a reduction in relative risk. Women in the highest quintile of activity had a relative risk of 0.54 ($p < 0.001$) compared with the least active women.

The team then analysed the correlation between MET hours expended each week by walking and risk of type 2 diabetes in the subset of women who did not do vigorous exercise. "Previous studies have focused on men and didn't look at moderate activity versus intense exercise", explains Hu. As with total physical activity there was a step-wise decrease in relative risk with increasing energy expended by walking: the relative risk for the top quintile of walkers compared with the bottom quintile was 0.58 ($p < 0.001$). In addition, walking pace correlated with reduction of risk : brisk walkers (more than 3 miles per hour) had a relative risk of 0.41 compared with those walking at less than 2 miles per hour.

These findings are reassuring, write the authors, "since walking is a physical activity that is highly accessible readily adopted, and rarely associated with physical-activity- related injury"

THE LANCET. VOL. 354. 1999

Medi Tips

PRACTICE TIPS

Easy Application of eyedrops in children

Use of eyedrops in infants and small children is extremely difficult because of their reaction to the liquid. This problem can be avoided rather easily by putting the drops in while the child is asleep. The trauma is over before the child realizes what has happened, and there is no crying with tears to wash out the drops.

Glue for split skin

Split skin at the ends of fingers may be a problem in winter when the air is dry. Prevention with a moisturizer is recommended, but for the occasional split, superglue can be used to decrease pain and prevent enlargement of the split. It should be tried only if the split is superficial and there is no bleeding. Also be sure to caution your patients not to put their fingers together or to touch their eyes before the glue dries. The glue can also be used to mend a torn fingernail by applying a small amount over the tear and allowing it to dry.

Another option for split skin is to apply zinc oxide ointment and cover it with an adhesive bandage. This will promote healing and decrease discomfort.

New-onset insomnia and BPH

Whenever an elderly man comes in complaining of new-onset insomnia, we must inquire about nocturia. Men with benign prostatic hypertrophy (BPH) often present first with insomnia. The latter re-solves when BPH is treated.

Persistent hiccups

When a patient has had hiccups for several hours or days and has tried all pharmacologic options as well as the Valsalva maneuver unsuccessfully, the following procedure may resolve the problem.

Insert a nasogastric tube as far as the stomach and immediately remove. The hiccups should stop at once. If not, try a second time. The mechanism is irritation of the posterior nasal mucous membrane and lower esophageal sphincter.

Stained contact lenses

When rifampin is being used in combination therapy for group A streptococcal tonsillopharyngeal infections patients should be advised that the drug produces orange discolouration of urine and tears. This is a harmless side effect, but it may cause permanent staining of contact lenses.

Sip helps locate the thyroid gland

While checking out a lump in a patient's neck, it is sometimes difficult to delineate the thyroid gland. Having the patient swallow a sip of water is often helpful in locating the thyroid gland and defining the anatomy more precisely.

Difficult venipuncture

When venipuncture of small veins of the extremities is difficult, apply a blood pressure cuff and manometer and then pump the pressure above diastolic but not near or over systolic levels. Because the blood escapes through the arteries but is inhibited through the veins, the latter become distended, more prominent, and accessible.

Warts and calluses

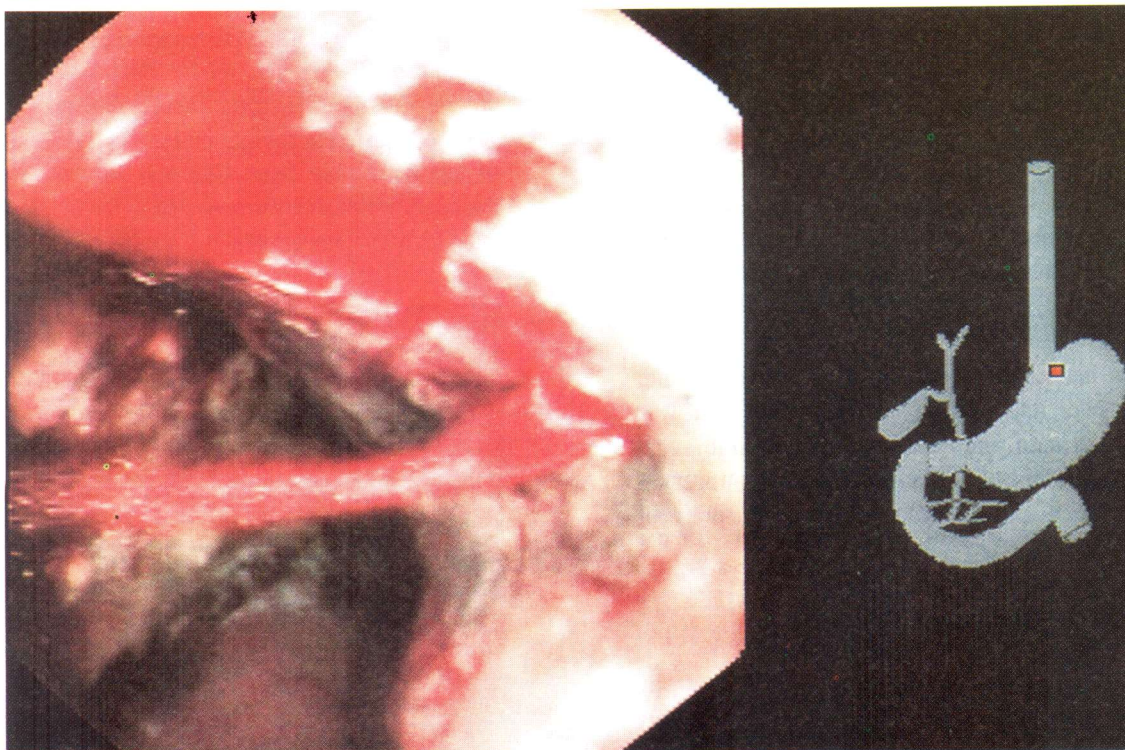
Often a plantar callus is difficult to distinguish clinically from a plantar verruca. Both may look like hyperkeratotic lesions and are painful on ambulation.

It is possible to tell the two apart by palpation. A plantar callus is painful on direct palpation, while a verruca is usually painful on lateral (side-to-side) palpation. Treatment is more likely to be successful if the lesions are differentiated.

SOURCE : Post Graduate Medicine

Medi Image

IMAGES IN CLINICAL PRACTICE



Briskly Bleeding Gastric Ulcer

A 67-year-old woman was evaluated for a one-week history of mild epigastric pain and black stools. On the day of admission she had two episodes of hematemesis. Physical examination revealed a pulse of 92 per minute, blood pressure of 120/67 mm Hg, and pallor with minimal epigastric tenderness. Hypochromic microcytic anemia was found, with a hematocrit of 25 percent. The patient was not taking aspirin or other nonsteroidal antiinflammatory drugs. She had quit smoking a few years earlier, after she was found to have ischemic heart disease.

Upper endoscopy showed a large gastric ulcer at the cardia, which began bleeding during the procedure. The bleeding was arterial in character and filled the stomach with blood in less than five minutes. Attempts to inject the bleeding site with epinephrine and thermocoagulation were unsuccessful. The patient underwent an emergency subtotal gastrectomy, which revealed a large benign gastric ulcer with a large feeding artery. She recovered completely and was discharged within a week after surgery.

NEJM. Vol. 338 No 12

And a assay for heart disease?

Scientists have developed a prototype assay for the evaluation of complex genetic risks in coronary heart disease. Probes for 35 biallelic sites within 15 genes implicated in the development of atherosclerosis were attached to nylon strips. 27 targets from test genomic DNAs were amplified by PCR and the binding pattern of the amplified DNAs to the panel of probes measured. In an analysis of DNA from 142 patients with atherosclerosis, several potentially interesting associations were found. Evaluation of these associations will require "analysis of an independent and larger cohort", say the authors, who add that the assay format could eventually be developed into a diagnostic test.

THE LANCET. VOL. 354. October 23, 1999.

Resident Round

Pregnant, vomiting and going blind

A 21-year-old woman consulted an obstetrician 9 weeks into her third pregnancy with progressive nausea and vomiting. A diagnosis of hyperemesis gravidarum was made. She was a non-smoker and did not drink alcohol. She discharged herself from hospital after 2 days, before her symptoms resolved. She consulted obstetricians at 11, 13, and 15 weeks of pregnancy with the same complaints. On each occasion, she took her own discharge from the hospital within a couple of days of admission. At 17 weeks, she rapidly developed visual loss over 10 days. She was seen in the ophthalmological outpatient department when her visual symptoms began but no definite diagnosis was made. She became virtually blind and was admitted to a medical ward. She was a little confused, with some impairment of concentration. She was unable to count fingers at 1 m. There was restriction of conjugate gaze in all directions but especially on right lateral gaze. Visual fields could not be evaluated accurately owing to the visual loss. Horizontal and vertical nystagmus was present. There was bilateral disc swelling with retinal haemorrhages in both eyes, but the retinal arteries and veins appeared normal (figure). Other cranial nerves were intact and there were no cerebellar signs or ataxia. All her reflexes were absent, even with reinforcement, although her muscle power was full and there was no sensory deficit in her limbs. Initial investigations showed hypokalaemia (potassium 2.7 mmol/L), normal thyroid function tests, and a normal magnetic resonance imaging scan of her brain excluded a pituitary tumour causing chiasmal compression. Ultrasound scan of her abdomen showed a non-viable fetus.

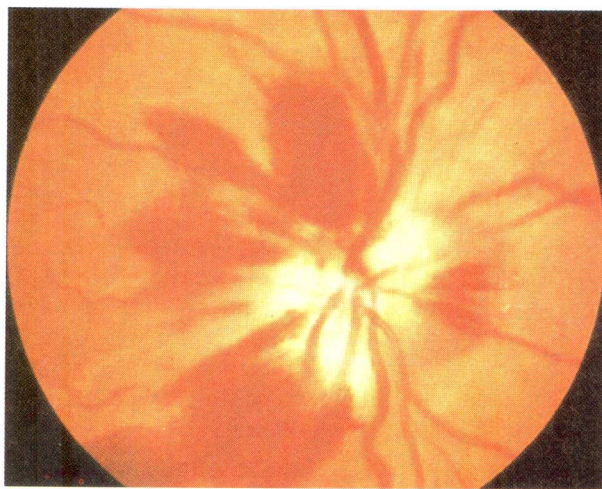
10 days after the onset of her visual loss, the diagnosis was still not clear; then a family member pointed out that she had not eaten solid food, managing only to take fluids, since the third week of her pregnancy because of her nausea and vomiting. **Wernicke's encephalopathy** was then considered the most likely diagnosis and she was started on intravenous thiamine and oral multivitamins. Her vision improved within a few hours, and she was able to read 12 hr. later. 24 hr. later her visual acuity had improved to 6/6 right eye and 6/9 left eye, and there was only residual horizontal and vertical nystagmus. Visual fields were

now full. Her mental state also improved over 48 hr. After 3 days of intravenous thiamine, all her deep tendon reflexes became present with reinforcement. These improvements continued and she was transferred back to obstetric care to have an evacuation of her non-viable fetus. She was discharged home on oral thiamine. When she was reviewed in the medical clinic 3 weeks later, her visual impairment had almost completely resolved with only residual slight horizontal nystagmus. Her retinal haemorrhages also almost cleared.

Although Wernicke's encephalopathy is known to occur in association with hyperemesis gravidarum, the diagnosis is not often apparent early. The patient reported here appeared well nourished with a weight of 71 kg. It only became apparent later that she was overweight before pregnancy, and had lost 12 kg

during her pregnancy. Impairment of vision in Wernicke's encephalopathy is unusual. In a large series only 2.6% of patients had this symptom. Most patients have central or centrocaecal scotomata, complete blindness being extremely rare. In a recent report of Wernicke's encephalopathy presenting with complete blindness, the optic discs were normal; blindness was believed to be due to tobacco-alcohol amblyopia. The pathological mechanisms by which thiamine deficiency causes brain lesions is not yet fully understood. Since thiamine is a cofactor for several important enzymes including pyruvate

dehydrogenase and transketolase, its deficiency leads to a decrease in use of cerebral glucose, which may contribute to neuronal dysfunction. Necropsy studies have shown that the damage usually involves the central nervous system only and is characterised by neuronal loss, gliosis, and vascular damage in regions surrounding the third and fourth ventricles and cerebral aqueduct. It was suggested that any patient presenting with a history suggestive of inadequate nutritional intake associated with visual impairment should be suspected to have Wernicke's encephalopathy and be treated promptly with thiamine. Women with hyperemesis gravidarum should be given thiamine supplements.



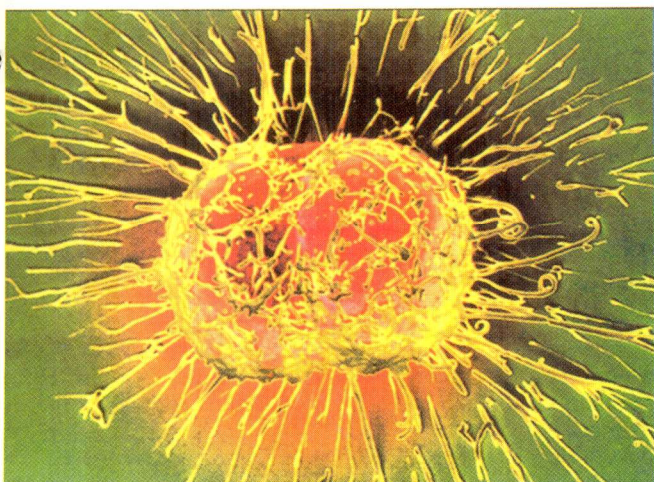
Right fundus of the patient before treatment

Medi News

From Internet/Journals

Scientists create human cancer cells

Scientists have succeeded in genetically transforming normal human cells into cancer cells, a feat that eluded the research community for years. The work yields fresh insights into the process of carcinogenesis and may lead to new anticancer treatments (*Nature* 1999;400:401-2). Although researchers have converted normal human cells into cancer cells before, this is the first time that a precise molecular recipe has been applied to cause that transformation.



Cervical cancer cells: research throws new light on carcinogenesis

In the past, cancer cell lines were created through transfection with a virus or via physical and chemical manipulation, such as exposure to carcinogens and irradiation. These processes were random and equivalent to a sledgehammer approach, inducing so many changes in the cells that it was impossible to determine which ones were necessary to cause cancer.

The new research, led by Drs William Hahn and Robert Weinberg of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, relied on the observation that rodent cell lines are easily converted to cancer cells with the introduction of a few oncogenes. In contrast, human cells are relatively resistant to this change. Further investigation led to the realisation that most mouse cells express the enzyme telomerase whereas most human cells do not.

Telomerase is the enzyme responsible for maintaining the telomere, the sequence of DNA that caps each chromosome. The telomere serves as an internal time clock, shortening with successive replications and cell divisions.

Commenting on the work, Dr Hahn said; "One important conclusion from this study is that there are not an infinite number of cellular changes separating cancer cells from normal cells but that tumor development is a finite process." The experiment raises several lines of continuing research. For example, assays for telomerase as a marker of malignant transformation may be developed. Telomerase inhibitors may be produced that might serve as an anticancer agent.

www.bmj.com.

VEGF linked with new Vessels

The secret to some patients' ability to form coronary artery collateral beds may lie in the amount of vascular endothelial growth factor (VEGF) they produce during hypoxia.

In a study of 51 patients with 70% or greater blockage in at least one coronary artery, Israeli researchers performed diagnostic angiography to determine the extent of each patient's collateral blood supply. Patients were separated into three groups according to collateral beds, and their VEGF levels were tested. Researchers found no difference in VEGF production when heart muscle cells received sufficient oxygen.

However, they found that patients who produced the most VEGF during hypoxia had the most extensive collateral blood supply. The correlation between VEGF production and collateral blood vessel growth remained when the researchers controlled for age, sex, hypertension, blood cholesterol levels, smoking, diabetes, and previous attempts to increase blood flow in the heart through bypass surgery or balloon angioplasty.

The research team has developed a simple laboratory test to determine levels of VEGF production during hypoxia. The investigators are conducting further research that may lead to development of a drug to increase VEGF production in patients with low levels, said lead author Andrew Levy, MD, PhD, of Technion-Israel Institute of Technology. The study appeared August 3 in *Circulation: Journal of the American Heart Association*.

JAMA, Sept. 8, 1999—Vol. 282 No. 10

Vitamin A and Malaria

Researchers in Papua New Guinea and the United States have teamed up to try to determine if vitamin A supplementation may reduce complications from malaria in children.

In the July 17 *Lancet*, researchers at the Papua New Guinea Institute of Medical Research and Johns Hopkins University School of Public Health and Hygiene reported on 480 children aged 6 to 60 months who received high dose vitamin A or a Placebo every 3 months for 13 months. The children were from an area of Papua New Guinea where *plasmodium falciparum* is endemic. They were evaluated at regular intervals as part of the study and at community based surveillance programs where they could seek treatment.

At the end of the study period, episodes of *P falciparum* fever were 30% lower in children who received vitamin A than in the control group. Younger children reaped greater benefits from the supplements. Those aged 12 to 36 months had 35% fewer bouts of fever, 26% fewer enlarged spleens, and 68% lower parasite density than older children in the study. All of the children who took vitamin A had fewer enlarged spleens and lower parasite density, but those findings were not significant.

The researchers concluded that vitamin A could be an effective low cost way to reduce complications from malaria in young children.

JAMA, August 11, 1999—Vol. 282 No. 6

Vagus-nerve stimulation of benefit in epilepsy, say us neurologists

Vagus-nerve stimulation is a "safe, effective" way to treat refractory epilepsy in patients with partial seizures who are not candidates for potentially curative brain surgery, according to an American Academy of Neurology (AAN) consensus assessment published on Sept 11 (Neurology 1999; 53 666-69). "It's well-tolerated, and its efficacy is comparable to that seen with a new antiepileptic medication", says Adrian Handforth (Veterans Administration of the Greater Los Angeles Health Care System, CA, USA), co-author of the report. "Some uncontrolled follow-up evidence shows that efficacy seems to go up over time, so a year or so later, it looks even more favourable."

Handforth, co-author Robert Fisher (Barrow Neurological Institute, Phoenix, AZ, USA), and members of the AAN Therapeutics and Technology Assessment Sub-committee reviewed all clinical studies of the vagus-nerve stimulator—an implanted device which electrically stimulates the left vagus nerve. The review included two large, randomized, controlled trials involving 310 patients who had a 25-30% reduction in seizures with the device. "Most patients don't become seizure-free, but more than half say their quality of life has improved because the number or the intensity of the seizures has gone down", says Handforth.

Vagus-nerve stimulation should be considered "whether the issue is seizures or incapacitating side-effects of medications", emphasises Epilepsy Foundation spokesperson Steven Schachter. "I don't think we pay as much attention to the latter as we should, maybe because we really haven't had non-pharmacological options until now." Drug side-effects, he notes, "can be worse than seizures". And although implanting the device has risks because it involves surgery, untreated seizures also pose risks, says Schachter. "Many of my patients have scars from falls, burns, and other injuries they sustained during seizures, so two small incisions from the surgeon are no big deal." The main side-effect—hoarseness during stimulation—is lessening now that neurosurgeons have gained experience with the implant, adds Handforth.

For now, the stimulator is indicated for patients older than 12 years. But studies in children are underway, and "It may not be long" before results are reported, says Philip Sheridan (US National Institute of Neurological Disorders and Stroke, Bethesda, MD, USA). Because other antiepileptics that work in adults work in children, it is possible that the same will be true of the stimulator, he says, and the findings with device are also important because they "point the way to future epilepsy therapies that may be even more effective, such as deep brain stimulation."

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Ovarian transplant raises hope for women facing cancer treatment.

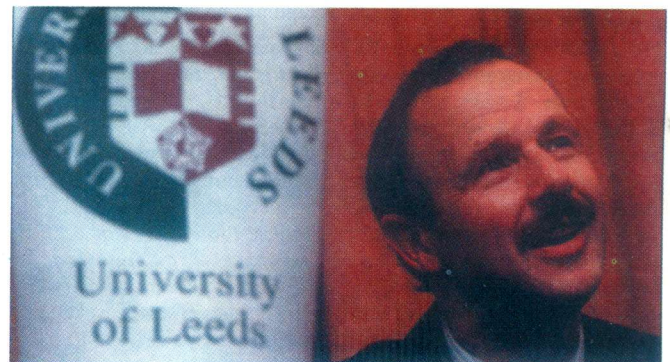
Scientists have successfully transplanted ovarian tissue back into a 30 year old woman who had the tissue removed and cryopreserved a year earlier.

The technique, pioneered by Professor Roger Gosden at the University of Leeds and carried out at New York Methodist Hospital by Dr Kutluk Oktay, offers hope of some degree of

fertility to women who have ovarian tissue removed and banked prior to chemotherapy.

But fertility specialists urged caution after widespread popular speculation that the success of the operation could mean the end of the menopause and herald the arrival of fertility at any age, as well as preventing ageing and replacing hormone replacement therapy.

The patient who underwent the procedure, 30 year old American Margaret Lloyd-Hart, had lost one ovary when she was a teenager because of cysts, and had the other removed last year because of an undisclosed hormonal problem. Before the second bout of surgery, she had decided to have tissue preserved at a unit that provides cryopreservation at the University of Arizona.



Professor Roger Gosden of Leeds University, who has pioneered the transplantation of ovarian tissue

After the operation she began to experience menopausal symptoms and sought out professor Gosden, who has performed ovarian grafts on sheep. His work was focused on the possibilities of banking ovarian tissue for women about to undergo chemotherapy to protect it from sterilisation, but an obstacle to working on humans was the risk of transferring cancer cells with the tissue. With Ms Lloyd-Hart there was no such risk, and the operation went ahead.

"This is proof of the principle that ovary grafts could be used to rescue fertility. There is no reason why ovaries could not be stored for decades," said professor Gosden.

In the aftermath of the success, there has been extensive speculation about the long term implications, but fertility specialists are more cautious.

"Biologically, it is a very important development because it shows that ovarian function can be restored to some extent. But when it comes to clinical practice, people have to understand that its use is very limited and the ideas of longevity are grossly exaggerated," said Professor Michael Hull, Professor of reproductive medicine at the University of Bristol.

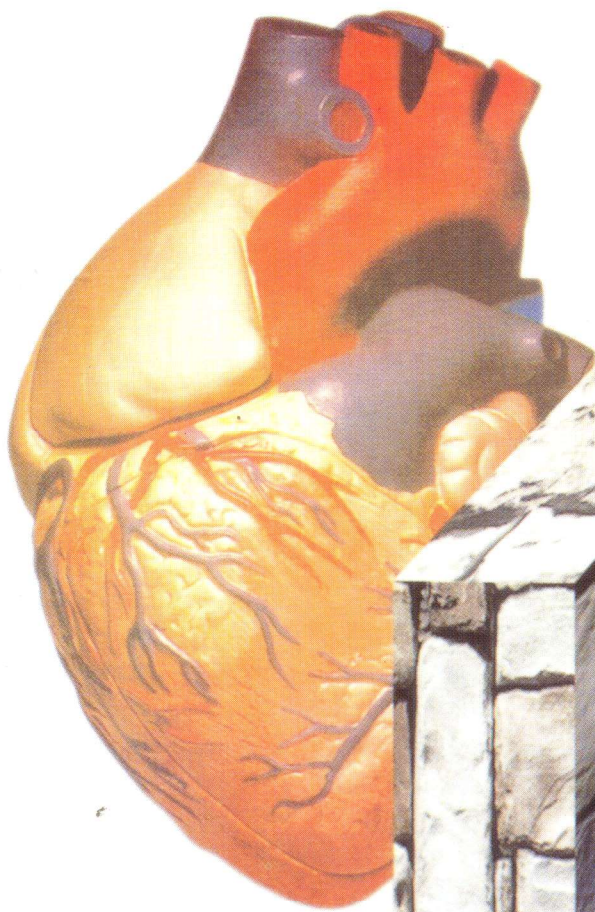
"The only real place for this kind of technique is to preserve the eggs in a woman whose eggs are likely to be destroyed in cancer therapy, and with the specific purpose of achieving temporary fertility at some time in the future," he continued. "It is particularly important for the increasing number of girls and young women who are successfully treated for cancer and who could lead a normal healthy life but who are caught by the double whammy of infertility."

He added, "There is no way anyone can say that the menopause can be put off and that women will be feminine for ever. That is a non-starter; it is ridiculous."

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