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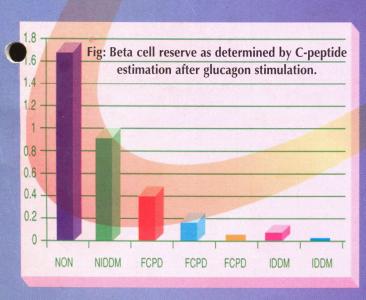
# The ORION

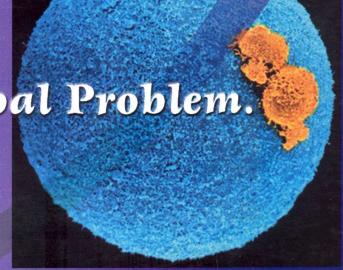
Medical Journal



Antioxidant and Eye Diseases.

Infertility: A Global Problem.





First day of Fertilization.

Fibrocalculous Pancreatic Diabetes.

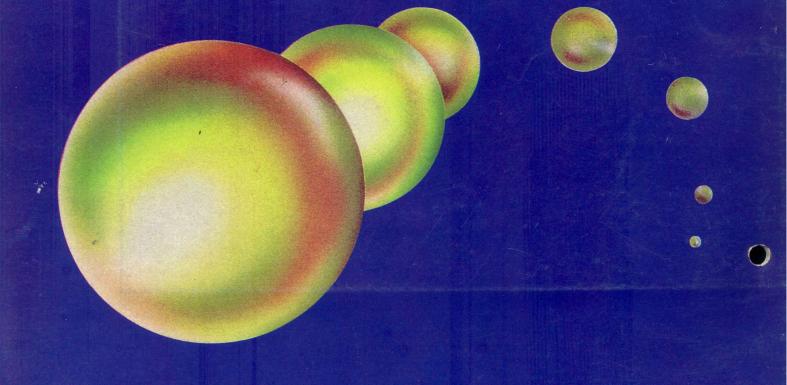


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Medi Image and Medi Tips

MSD News and Information for Authors

Pictorial depiction of Role of Antioxidant in Prevention of Eye Diseases, Infertility: A Global Problem and Fibrocalculous Pancreatic Diabetes (FCPD) by the picture of eye, first day of fertilization and bar chart consecutively with disease spectrum in the background.

### COVER

Dr. Md. Mahmud Hasan (Shuvro)

### **PUBLISHER'S NOTE**

We acknowledge to quote different authors regarding their original contributions in the text books, journals and manuals etc. We reiterate that these deliberations are not of commercial uses and values. The views expressed in this publication do not necessarily reflect those of its editors or of Orion Laboratories Ltd.

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# **Editorial**

Your enormous responses on the topics published in previous issues reflect the image and recognition of our efforts and attempts in Continued Medical Education (CME) by updating the knowledge of recent developments in Medical Science among the professionals.

We are moving towards our goal in achieving high standard services to the professionals nationally and internationally through guidance, endorsement and counsel of the honourable members of the Advisory and Review Board.

We are very much thankful to the valued readers of "The ORION" for continuous inspiration, suggestion and patronization. All these encouraged us to publish 9th volume of "The ORION".

In this issue we have focused *Eye Diseases* by the topic "Antioxidant and Eye Diseases", *Infertility* by the topic "Infertility: A Global Problem", and *Diabetes* by the topic "Fibrocalculous Pancreatic Diabetes (FCPD)".

There are about 4.5 million blind people world-wide. Though there is no statistical data available in Bangladesh, it is claimed that about 1.2 million people are blind and 60% of blindness is due to cataract. World Health Organization already has launched a project "Vision in 2020" to eliminate preventable blindness by 2020. It is only possible if appropriate measures are taken in right time.

Though infertility is not a physically debilitating disease, yet the strongest desire that people experience is to have a child. No wonder that among life's greatest stresses, infertility is ranked similar in intensity of having a life threatening illness.

Diabetes is one of major health disorders. It may occur in any age group. Usually many other serious diseases such as Hypertension, Ischaemic Heart Diseases, Cataract, Retinopathy, Nephropathy, Neuropathy etc. may arise as complications of diabetes mallitus. So this burning medical problem demands extensive research. Mass awareness through health education for prevention and treatment is necessary to ease the burden of the people and to increase the productivity of the nation as a whole.

We are hopeful that our attempts in highlighting these topics will be helpful for all concerned. Views and opinions from our respected readers will be most welcome to enrich our publication.

May all our readers be in the best of health and spirit.

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Dr. ATM Azizur Rahman

Chief Editor

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Manager

Medical Services Department.

## **MSD News**

The overwhelming acclaim received by our trial at BSMMU on "Efficacy of Maprocin™ (ciprofloxacin) and Nidazyl™ (metronidazole) both parenteral and oral forms in management of post operative infections" has inspired us to put our effort in conducting a full flagged clinical trial at DMCH on "Eradication of Helicobacter pylori by Triple Regimen" and we have completed it successfully. As recognition to our efforts, the paper on the trial "Eradication of Helicobacter pylori (in Peptic ulcer patients) with a metronidazole containing regimen, in a metronidazole abusing population" was published in the Indian Journal of Gastroenterology, Vol. 20, No. 1, Jan-Feb 2001. We acknowledge to all concerned for such a precious achievement.

We believe, seminars, symposiums and round tables are the essential components of CME. That is why, MSD personnel again spent a busy schedule in arranging these events at different venues in the first quarter of 2001.

#### **SEMINARS**

### Seminar at Jessore

A seminar on "Micronutrients" was held on January 20, 2001 at the Rose Garden Chinese Restaurant, Jessore. The seminar was chaired by Dr. Lt. Col.(Retd.) AKM Azizur Rahman, President, BPMPA, Jessore and Dr. AKM Mesba-ur-Rahman, Secretary, BPMPA, Jessore was the Co-Chairperson. All doctors of BPMPA, Jessore attended the seminar.

### Seminar at BIRDEM

MSD also arranged a seminar on "Role of Zinc in Child Health" on March 10, 2001 at the Department of Paediatrics, BIRDEM. The seminar was chaired by Prof. Dr. Kishwar Azad, Head of the Deptt. of Paediatrics. Dr. Shahida Akhter, Assistant Professor, Deptt. of Paediatrics, BIRDEM was the Key-note speaker on the occasion. All doctors of the Department of Paediatrics, BIRDEM attended the seminar.

#### Seminar at Cox's Bazar

A seminar on "Micronutrients" was held on March 21, 2001 at the Conference Room, Cox's Bazar Sadar Hospital. The seminar was chaired by Dr. M. A. Hai, Civil Surgeon, Cox's Bazar and Dr. Habibur Rahman, Consultant, Medicine,

Cox's Bazar Sadar Hospital was the Key-note speaker on the occasion. All doctors of Cox's Bazar attended the seminar.

#### Seminar at Chittagong

A seminar on "Importance of Zinc in Maternal & Child Health" was held on March 24, 2001 at the Conference Room, City Corporation, Chittagong. The seminar was chaired by Prof. Sayeda Nurjahan Bhuiyan, Health Advisor, City Corporation, Chittagong and Dr. Rezaul Karim Chowdhury, Chief Medical Officer, City Corporation, Chittagong was the Co-Chairperson. Dr. Babli Mallink, Paediatrician, Memon Hospital, Chittagong were the Key-note speakers on the occasion. All doctors of Hospitals and Health Centres under City Corporation, Chittagong attended the seminar.

### Seminar at Comilla

MSD also arranged a seminar on "Ideal Antioxidant" on April 07, 2001 at the Conference Room, Diabetic Hospital, Comilla. The seminar was chaired by Dr. Zobaida Hannan, Vice-President and Treasurer, Diabetic Hospital, Comilla. All doctors of Diabetic Hospital, Comilla attended the seminar.

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## Information for Authors

"The ORION" considers only original work that has not been published previously in print or electronic media. We especially welcome review articles that help our audience of busy primary care physicians solving common clinical problems. Because of our primary care focus, at least one of the authors must be a physician. The author (s) must have no financial interest in or connection with any product mentioned in the article or any competitive product. Material submitted must not be under consideration for publication elsewhere.

The text of clinical articles should not exceed 1,000 words (for double-spaced pages). Suggested order of presentation is cover page, text, summary reference list, tables, figure legends and author affiliation (s).

The journal style is to use generic names for drugs. All elements of the article must be presented in the same type font, and manuscript should be printed in a letter-quality typeface. The right margin should not be justified. Number pages consecutively, starting with the cover page.

On the cover page, indicate the article title and designate a corresponding author, for each author, list full name, highest pertinent academic degree, title of current position, address, office phone and fax numbers. For the corresponding author, provide this information plus e-mail address and home phone number.

Send the original and four copies. <u>If you used a computer to prepare your manuscript</u>, send a disk along with the hard copies. Note the type of software on the disk label.

### REFERENCE

Key sources must be properly credited and referenced. References should be current (past 5 years) and must not exceed 20. They should be cited in the text in numerically consecutive order. With the first page of each article referenced. Format reference as shown in this examples:

 Prisant LM, Houghton JL, Bottini PB, et al. Unstable angina: Pharmaceutical versus Invasive therapy, Post grad Med 1994;96 (1): 88-95.

### **TABLES**

Tables should not duplicate the information in the text. Each should have a title and should be numbered consecutively according to its citation in the text. If a table has been published previously, include the complete reference as well as a letter granting permission from the previous publisher.

### **ILLUSTRATIONS AND PHOTOS**

Illustrations and photos are welcome. All graphics must be numbered consecutively according to their citation in the text and must include short descriptive legends. For photos and x-ray films, submit glossy prints in duplicate. On the back, label the top and include the author(s) name and the figure number. Include a reference and permission letter if the figure has been published before. A signed release from the patient is needed for photos that show identifying features. Original illustrations are returned after publication if required.

### **AUTHOR PHOTOS**

A photo of the author (s) in a clinical or office setting is welcome for publication with the article. Send a group shot for an article by more than one author.

### REVIEW PROCESS

Authors are notified of receipt of their article. Each article goes through a careful peer-review process. Decisions about acceptance may take 6 weeks.

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Articles accepted for publication are edited to conform to the journal's style and format. An edited copy of the manuscript is sent to the corresponding author for approval. The author is responsible for all changes in the manuscript, including those of the manuscript editor.

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# Antioxidant and Eye Diseases.

### Mustafizur Rahman

It is my personal privilege to present the paper on "Role of Antioxidants in Prevention of Blindness" organized by a joint venture of M.A.I Institute of ophthalmology, Islamia Eye Hospital and Medical Services Department, Orion Laboratories Ltd.

Of all the causes of blindness, cataract is claimed to be the number one cause of reversible blindness world-wide and age-related macular degeneration is another leading cause of irreversible blindness. Cataract is a disease where crystalline lens inside the eye becomes gradually opaque and light can not pass into the retina, sentient layer of the eye and the patient becomes gradually blind. Age-related macular degeneration (AMD) is a disease where most important part of retina i.e. macula undergo some pathological changes and the patient becomes gradually blind.

There are about 45 million blind people world-wide. Though there is no statistical data available in Bangladesh, it is claimed that about 1.2 million people are blind and 60% of blindness is due to cataract.

The Aim of "VISION in 2020", a project of the World Health Organization (WHO) is to eliminate preventable blinds by 2020. It is only possible if appropriate measures are taken in right time.

A patient with cataract in an otherwise healthy eye can get back his full sight if operated in time with success. But due to illiteracy, poverty and ignorance many patients in Bangladesh with cataract do not get treatment in time. They become blind and remain blind longer than in any developed country.

Age-related cataract is a sequence of aging process in old age. Other cataract due to genetic defect, complications of eyes and systemic diseases could probably be prevented by taking appropriate measures such as genetic counselling, treating systemic and eye diseases in time.

But the age-related cataract- the so called senile cataract and agerelated macular degeneration (AMD) could probably be much delayed by some agents which are known as antioxidants.

Investigators observed through various researches that in our normal physiological process in the body some free radicals are released which attack the cells and damage them. Biomedical researchers found some agents which can combat these attacks from which the term antioxidant come.

### Prof. Mustafizur Rahman

D.O, FRCS (I), FRCS (E), FRC Ophth (E), FCPS. Director, M.A.I. Institute of Ophthalmology and Chief Consultant, Islamia Eye Hospital; Ophthalmologist, Bangladesh Armed Forces.

From where does this idea of oxidation and antioxidants con About a century ago<sup>2</sup> it was observed that some organic compour such as rubber looses its life time when they come in contact watmospheric oxygen.

The contact of oxygen with lipid materials is known as au oxidation<sup>3</sup>. The auto-oxidation can be divided into

- A. Initiation reaction: Where single oxygen when mixed will lipid material releases hydroperoxide radical.
- B. Propagation reaction: Where lipid radicals mix with oxygen molecule release hydroperoxide.
- C. Termination reaction: Where two radicals combine a produce a stable product.

Auto-oxidation of lipid radical produces toxic radicals who destroy the vital elements of cell in the absence of antioxidants. Antioxidants are microingradients present in all foods and presentation of lipid material in our body. These are vitamin A, C Selenium, Zinc, Folic acid, Lecithin etc.

### ANTIOXIDANTS ARE OF TWO TYPES

## A. Primary or chain-breaking antioxidants

They react with lipid radicals and convert them to more staperoducts. Primary antioxidant is a molecule that is able to don hydrogen atom to lipid radical.  $\beta$ -carotene at low oxygen press in human tissue act as antioxidant by preventing formation hydroperoxide.

### B. Secondary antioxidants

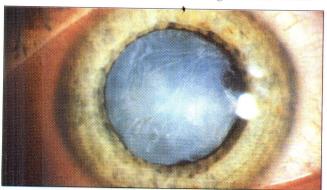
Compound that retard the rate of auto-oxidation of lipid and there converting free radicals to more stable specimen in presence of metal ions and reducing agents such as ascorbical are known as secondary antioxidants. Oxygen is essential for libut complex oxidation reaction that occur in human tissue produces to the control of the con

Tocopherols (vitamin E), ascorbic acid (vitamin C) and carotent react with free radicals notably peroxyl radicals and with six molecular oxygen which is the basis for their function antioxidants. A more broad definition of all antioxidant is a substance that, when present at low concentrations compared withose of an oxidisable substrate, significantly delays or inhaboxidation of that substrate.

Antioxidant functions are associated with lower D.N.A dama diminished lipid peroxidation or inhibited malignant transformation vitro. Epidemiological studies show that they lower the incider of certain types of cancer and degenerative diseases such ischaemic heart disease, cataract, and age-related manadegeneration (AMD).

5

There are studies by various authors on the role of antioxidants such as vitamin C and trace minerals which suggest that they have the properties that prevent the onset and progress of cataract and age related macular degeneration<sup>9,10</sup>. In POLA study group<sup>4</sup> done by Delcourt-C et al published in Arch-ophthalmol., Oct.1999, suggest that vitamin E may provide protection against age-related macular degeneration. No association were found with plasma retinol and ascorbic acid levels or with red blood cells glutathione values.



Picture shows hypermature stage of age-related cataract.

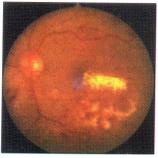
In another study by POLA group published in Ophthalmology February, 1999 issue suggest that there is a strong association of high levels of plasma glutathione peroxidase (PLGX) with age related macular degeneration and high levels of erythrocyte superoxide dismutase (SOD) were also associated with increase risk of nuclear cataract. So it is evident that antioxidant has some role in the prevention of AMD and nuclear cataract.

Christen-WG<sup>5</sup>, suggest that oxidative mechanisms may play an important role in the pathogenesis of cataract and age-related macular degeneration, the two most important causes of visual impairment in elderly age group. These findings raise the possibility that vitamins and trace minerals with antioxidant properties can be of benefit in preventing age-related macular degeneration and cataract.

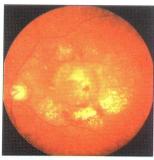
According to the study by Lyle et al<sup>6,8</sup> serum level of carotenoids and copherols and their link with the incidence of age-related nuclear cataract were compatible with the possibility that nuclear cataract may be linked inversely to plasma concentration of vitamin E. But neither strongly supported nor rejected the hypothesis of inverse association of nuclear cataract with serum carotenoids.

Another study by Xue-AN et al published in Biomed-Environ. Sci.1996 September<sup>7</sup> on the antioxidant status in persons with and without senile lens changes. The result suggest that appropriate amount of antioxidant nutrients might be helpful to prevent or retard the process of lens changes. Although potentially important benefit of vitamin supplementation in eye diseases will emerge mainly from well designed large scale, randomized trials.

Combination of vit-E and C were found to inhabit glycation at physiological concentration and more effective than either vitamin, suggesting that synergistic antioxidant effect of these two nutrients may have contributed to the inhibition of glycation in diabetes mellitus. Thus this combination is helpful in the prevention of diabetic retinopathy<sup>11</sup> which is also an important cause of blindness world wide.



Picture shows very advanced background diabetic retionopathy with large plaque of hard exudate involving macula.



Picture shows advance exudative agerelated macular degeneration (AMD).

In the body, highest amount of Zinc is present in the retina. It is directly involved in absorption, metabolism and mobilization of vit-A. Zinc also influences the Oxidation-Reduction of Vit-A in the retina. Thus Zinc deficiency causes impaired dark adaptation leading to night blindness. Zinc is also an strong antioxidant. As a part of it's anti-degenerative process, it has a protective mechanism in the prevention of age-related macular degeneration (AMD)<sup>12,13</sup> of retina.

Antioxidant is gaining popularity like burgers have gained the popularity world wide. The role of antioxidant in eye till now is mainly focused to cataract, diabetic retinopathy and age-related macular degeneration (AMD). We predict, in future, antioxidant may play an important role in prevention of many other eye diseases. From the studies of different authors, it can be concluded that vitamins such as vitamin E, C and also some trace minerals with their antioxidant properties have some positive role in preventing the onset and progress of cataract, age-related macular degeneration (AMD) and diabetic retinopathy, the three important causes of reversible and irreversible blindness.

"The ORION" Medical Journal is undoubtedly playing an important role in bringing this issue to the doctors community-who can play a vital role by implementing this knowledge at the community level thereby preventing at least three major causes of blindness in Bangladesh.

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# Infertility: A Global Problem.

## T. A. Chowdhury<sup>1</sup>, Nusrat Mahmud<sup>2</sup>

The simple union of man & wife
in love creates A brand new life.
A child to cherish, play with, and be
their link with immortality.
What bless and joy they anticipate.
Unless infertility become their fate
and buries dream that die within
as they mourn their child whom might have been.

(J. Assisted Reproduction & Genetics, Vol-4, No-14, 1997).

### **INTRODUCTION**

Infertility is not a physically debilitating disease. However, the desire to have a child is the strongest that people experience, and no wonder that infertility is ranked among life's greatest stresses, similar in intensity of having a life threatening illness. It also effects the psychological harmony of sexual life and social function, even in those countries where the family planing and birth control is their special policy and social vogue. Unfortunately, because infertility involves the loss of something that has never been, it goes unnoticed. Perhaps that is why infertile couples have been called the most neglected silent minority.

### **INCIDENCE**

According to data provided by United Nations Population Division, the world population in 1991 was about 5.3 billion and half of the worlds residents are women. About 20% of female are in the reproductive age and the mean incidence of infertility throughout the globe would be approximately 90 million.

In rural population of Bangladesh, 3.2 percent of married women of reproductive age has primary infertility and 3.0 percent has secondary infertility. Majority of infertile women i.e. more than 40 percent believed this to be their fate and about 33 percent accused themselves for infertility.

### **DEFINITION**

Normal fertility means achievement of pregnancy by a couple within two years by regular coital exposure. Those couples who do not achieve a pregnancy within two years include sterile members of the population, for whom there is no possibility of natural

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Lithe ORION AVOI 9 A May 2001

pregnancy and the reminder are those who are sub fertile. Together they comprise the infertile population. The term sterile may refer to either the male or female whereas the term sub-fertile refer to the couple.

### **Definition of infertility**

Infertility is usually defined as the inability to conceive after 1 year of regular unprotected coitus. Infertility is said to be *primary* when that couple has not previously initiated a pregnancy and *secondary* when they have been successful on at least one previous occasion.

# MANAGEMENT OF INFERTILITY AT PRIMARY CARE LEVEL Male Factor (Incidence)

- 1) Male factor is important cause in approximately 40% of infertile couples.
- 2) In 15%-30% of cases both partners have detectable abnormalities.
- 3) Thus male factor play a significant role in about 50% of infertile couples.

### Asses the opportunities for conception

H/O Duration of fertility and past fertility.

H/O Smoking and alcohol consumption.

H/O Mumps, orchitis or other infection.

H/O Sexual function- frequency/adequacy of erection and use of lubricants.

### Medical history of significance

Bronchitis, Diabetes Mellitus, Recent pyrexial illness, Thyroidisorder.

### Surgery of significance

Herniorraphy, Vasectomy, Hydrocele repair, Varicocele Prostatectomy.

### Drug history of significance

- Sulphasalazine
   Reduces concentration and motility of sperm
- Nitrofurantoin –Can cause spermatogenic arrest.
- Tetracycline- Interferes with sperm motility.Cemetidine-Seminal abnormalities, gynecomastia, impotence
- Ketoconazole Impotence, loss of libido, gynecomastia.
- Colchicine and Allopurinol Defects of fertilization.
- α-adrenargec blockers/MAO inhibitors/Trycyclic antidepressant drugs–Ejaculatory defect.
  - Chemotherapeutic agents-Chromosomal abnormalities.
  - Cannabis/Anabolic steroid-Affects sperm morphology ar motility i.e. more abnormal forms of sperm.



### Female (Investigations at Primary care level )

History and examination: Following points should be remembered

- Female rubella status
- \* Plasma folic acid level
- If BMI >30, advice weight loss \* Drug history
- Occupational history
- Cervical smear history

### Consider early referral to the specialized clinics if history suggestive of

- 1. Female age > 35 yrs 2. Amenorrhoea/ Oligomenorrhoea
- 3. Previous abdominal / pelvic surgery 4. Previous PID/ STD
- 5. Abnormal findings in pelvic examination.

### Investigation

Mid luteal progesterone level should be done to confirm ovulation. Serum progesterone should be measured 7 days before expected period in all women. Interpret after next period starts.

- If correctly timed and found to be < 16 nmol/L-Repeat in
  </p> another cycle. If consistently low refer to specialist.
- If > 16 nmol/L but < 30 nmol/L repeat in another cycle. If the same or lower, may be indication for controlled ovarian stimulation. So needs referral to specialist.
- If serum progesterone > 30 nmol/L-consider as proof of adequate ovulation.

### MANAGEMENT AT PRIMARY CARE LEVEL

If husband's semen analysis is normal and wife's menstrual cycle is regular and there is no positive factor in the history, coital function and physical findings are normal:

Consider waiting before doing any invasive procedure. Many patients will conceive spontaneously if sufficient time is given, provided they are not waiting for too long period and are not in the advanced age group.

### Reassure the couple regarding their normality and give advice regarding

- 1. Timing and Frequency of coitus,
- 2. Reduction of body weight if obese,
- 3. Avoiding smoking by the husband.

### Unnecessary investigations or procedures are not advisable at this stage

Do not do a D&C without anaesthesia. This does not enhance the possibility of conception, rather can reduce the chances of subsequent successful pregnancy.

- Not recommended to do VDRL or prostatic smear at this stage.
- Ovulation inducing drugs can be prescribed if there is knowledge and experience regarding the use of these drugs.
- If semen analysis is abnormal, repeat the analysis at an interval of 3-4 weeks, two times.
- Many male partners complain of imaginary sexual problems. Asses these problems correctly by taking a detailed history and reassure if they are of not much consequence regarding fertility. Administration of androgens for sexual problems may lead to a deterioration in

the quality of semen.

- Duration of sexual intercourse and orgasm has no relationship with fertility.
- It is natural for a part of the seminal plasma to come out of the vagina after intercourse. Patients are often worried. It is of no consequence. Reassurance should be given.
- If the patient has been examined and found to have a retroverted uterus do not tell the patient that retroversion is the cause of infertility, because it has not been shown to be so.
- A good ultrasonography can give informations which can be elicited from a vaginal examination. Consider advising an ultrasonic scan where vaginal examination is not possible or refused.
- If abnormality is found in any partner or if the couple do not conceive within a reasonable time, refer to secondary care level.

### MANAGEMENT OF MALE INFERTILITY AT SECONDARY LEVEL

Men with persistent poor semen quality should have-

- Hormone assays, particularly FSH, LH, Prolactin, TSH, Testosterone, blood sugar should be done and the results should be properly interpreted.
- Semen and prostatic smear for bacteriology should be done and treatment should be given accordingly.
- In case of Azoospermia or severe Oligo /Asthenozoospermia refer the patient to specialized clinic.
- Empirical therapy with hormone, vitamins etc. has no proven
- Change in life style may have some beneficial effects.
- Couple should be informed about the poor result of male
- Option for ICSI (Intracytoplasumic sperm injection) and IVF (Invitro fertilization) and their success rate should be discussed with patient.

### MANAGEMENT OF FEMALE INFERTILITY AT SECONDARY LEVEL

### A. For ovulation disorders

- 1. Anovulation should be established, if ovulation induction is given as or repeated.
- 2. Clomiphene is a safe drug for use, but should not be used for more than 12 cycles. Ovarian ultrasound facilities will be an added advantage in such circumstances.
  - FSH and LH can be used but only if the consultant has expertise and facilities for monitoring is available. Risk should be explained to the patient.
  - Bromocriptine is an effective treatment for hyperprolactinaemia, but the diagnosis must be established accurately. The level should be three times normal or should be sustained on at least more than one occasion to initiate treatment. Skull X- ray and C-T scan is essential in proven cases. Treatment should be continued for 6 months to one year with standard dose.
  - Laparoscopic ovarian drilling can be done in genuine polycystic ovary cases if the
- consultant is experienced in this technique. 6) Blood sugar, Thyroid function test, Post coital test can be done if facilities are available.





### B. Tubo – peritoneal factors

- 1. Hystero- salphigography can be an effective investigation for finding tubo-peritoneal factors, but should be done by the consultant himself under proper aseptic condition.
- 2. Diagnostic laparoscopy can be very useful investigation at this level.
- 3. Tubal surgery should be performed only by micro-surgical technique, otherwise it may cause more harm than doing good.
- 4. Endometriosis should not be diagnosed only on the basis of clinical feature and/or ultrasonography; laparoscopic assessment is essential, as treatment is prolonged, expensive and complicated.
- 5. Medical treatment of mild, moderate or severe endometriosis do not significantly improve fertility.
- 6. Surgical management of endometriosis by laparoscopy or laparotomy often improve fertility provided it is done with proper care by a trained person.
- 7. All attempts should be made to do salphingostomy rather than a salphingectomy in the management of tubal pregnancy.
- 8. Pelvic inflammatory disease should be treated aggressively to prevent future infertility.

### OTHER CONSIDERATION

- 1. Empirical D&C is not the proper treatment of infertility. It does not improve fertility.
- 2. It's main role is in endometrial sampling.
- 3. Tubal insufflation is unreliable as diagnostic procedure and carries considerable risk of air embolism.
- Hydrotubation may have some beneficial effect in selected cases, but must be done under full aseptic condition.
- 5. Myomectomy is not the first line of treatment of infertility in women with uterine fibroids until all other causes of infertility has been excluded. Done unnecessarily or improperly, it may make infertility permanent and irreversible.
- Ovarian cysts found incidentally during surgery for other reasons should be dealt with caution. They are often functional cysts and attempt at their removal may cause more harm than good.
- 7. Correct handling of tissues without trauma, prevention of dehydration and proper haemostasis should be the standard

practice during surgery in and around the genital tract if preservation of future fertility is important.

### CONCLUSION

- 1. Treatment of infertility is demanding and requires time and patience. It can also be very rewarding.
- 2. Treatment should be rational to provide the patient with best chances of success.
- 3. Management of infertility requires development of certain skills which should be acquired if someone is interested in the management of infertility.
- 4. Cases should be referred to specilized centres where expertise is available in the management of such cases.
- 5. Empirical treatment should be avoided.
- 6. Premature intervention should be discouraged.
- 7. Proper counselling is essential to prevent severe psychological and financial strain on the family.
- 8. Always maintain an optimistic attitude. Pregnancy can sometimes occur under most unusual circumstances.
- 9. Try to preserve the integrity of the family as far as possible and do not put the blame solely on person if the other partner also have same problem.
- 10. Newer treatments are becoming available. Couple may have better chances later.

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## Assisted Reproductive Technologies

### In Vitro Fertilization (IVF)

laboratory dish

1. Eggs are combined with sperm in a

Gamete Intrafallopian Transfer (GIFT)





1. Eggs and sperm are collected in a syringe.



Zygote Intrafallopian Transfer (ZIFT)

Intracytoplasumic Sperm Injection (ICSI)





- 2. Fertilization occurs and embryo made 2. Unfertilized eggs and sperm are transferred to Fallopian tube.
- 2. Fertilization occurs and a single-celled embryo, called a zygote, is removed.
- 2. The single sperm is injected into an egg in a Laboratory dish.



of two to four cells is removed.

- Fertilization occurs naturally in Fallopian tube. Embryo travels to woman's uterus.
- 3. Zygote is transferred to Fallopian tube, where it grows normally and travels to woman's uterus.
- 3. The fertilized egg is transferred to woman's uterus.

In these methods used to treat infertility, in the three methods shown (IVF, ZIFT, and ICSI) artificially induce the union of sperm and egg in the Laboratory before implanting the fertilized egg inside the female reproductive system. The forth method (GIFT) mixes unfertilised eggs and sperm in the Laboratory before transferring them to the Source : Encarta. fallopian tube, where fertilization takes place naturally.





# Fibrocalculous Pancreatic Diabetes (FCPD).

### Khwaja Nazim Uddin<sup>1</sup>, A.R. Khan<sup>2</sup>

### INTRODUCTION

According to WHO and American Diabetic Association Classification (ADA) in 1985, etiologically, Diabetes Mellitus is of five types-1. Insulin dependent diabetes mellitus (IDDM). 2. Non-Insulin dependent diabetes mellitus (NIDDM), 3. Malnutrition related diabetes mellitus (MRDM) 4. Gestational diabetes mellitus (GDM) and 5. Diabetes associated with other conditions and syndromes<sup>5</sup>.

MRDM has again been subdivided into two groups: Fibrocalculous pancreatic diabetes (FCPD) and Protein deficient diabetes mellitus (PDDM). In recent (1997) classification WHO and ADA expressed that FCPD is a straight forward secondary diabetes. Experts in this region of the world contradict this opinion. Their reasoning are based on findings viz

- (i) Pancreatic diabetes, Tropical calcified pancreatic diabetes (TCPD) present at the older age group than FCPD patients.
- (ii) The socioeconomic status, BMI, Glucose and C-peptide values (both basal and stimulated states) of TCPD and FCPD patients are sharply demarcated'.
- (iii) There is a lack of straight line relationship of the degree of duct damage and exocrine state and endocrine pancreatic function and
- (iv) Many FCPD patients has shown SPINKI/PSTI mutation (marker of idiopathic chronic pancreatic).

### **DEFINITION**

In a tropical country ketosis resistant, insulin requiring diabetes mellitus occurring in young lean (body mass index below 19) individual showing evidence of malnutrition and pancreatic calculi and/or fibrosis with occasional abdominal pain may be said to be suffering from fibrocalculous pancreatic diabetes (FCPD) provided that alcoholism and biliary diseases are excluded.

### **EPIDEMIOLOGY**

### **Geographical Distribution**

FCPD has a worldwide distribution and is located on both sides of the equator and is restricted to the tropical countries between 23° north and 23° south (between tropics of cancer and tropics of capricorn). Countries involved are-Bangladesh, Brazil, India, Indonesia, Jamaica, Kenya, Madagaskar, Malwi, Nigeria, SriLanka, Thailand, Uganda, Zaire, Zambia etc.

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### Prevalence of FCPD

The precise prevalence of FCPD is not known, because detailed population survey for this condition is not available. The only one paper available is that of Balaji² which shows a prevalence of 0.09%. Most of the data for prevalence is clinic based which shows percentage of FCPD cases among the diabetic patients attending those clinics. The clinics give the percentage of diabetic cases from the figures of diabetics below the age of 30. Thus Ramachandaran et al³ showed that FCPD was present in 4% cases in their under 30 patients. In Nigeria prevalence has been reported to be 8.6%, in Thailand 5%, in Orissa-India it has been reported to be 24.3%⁴. In BIRDEM (unpublished paper) it has been found to be 19%. If we consider percentage of FCPD amongst the diabetics of all ages it becomes lower still. Thus in the studies of Ramachandaran percentage of FCPD was 1% while IDDM was 2% and NIDDM 96% and others 1%³.

### **ETIOPATHOGENESIS**

Etiopathogenesis of FCPD is relatively unexplained. The cause for tropical distribution of the diseases is far from clear. A number of hypothesis have been put forward. It is possible that they may act as a complement to each other rather than a single factor being responsible.

### a) Malnutrition

Evidence of malnutrition either at present or stigmata of malnutrition in the past has been suggested to be one of the criteria in the diagnosis of FCPD. Whether the malnutrition is the cause or effect of diabetes is debatable. It has been suggested that malnutrition particularly protein energy malnutrition in combination with other factors (Casava/cyanide) may be causative factors of this disease. SH radicals of sulphur containing amino acids are needed for detoxication of cyanides. In their absence cyanides accumulate in the body and damage pancreas. Prolonged starvation may lead to blockage of pancreatic duct by inspissate mucus plug and can cause pancreatitis. Subclinical malnutrition may cause micronutrient deficiency particularly that of Zn, Cu and may cause tissue damage. Malnutrition may also enhance infection and can cause tissue damage. In a study in children, it has been shown that protein energy malnutrition (PEM) cause glucose intolerance; in severe cases associated with diminished immunoreactive insulin response to glucose and may enhance growth hormone production<sup>17</sup>.

### b) Casava hypothesis

Casava is a plant whose root or tuber is used as a food in the tropical African countries. It is very cheap and contains only 0.4% protein and 95% starch. More than 400 million people residing in 80



countries use this food either as powder (tapoica) which is used to make various preparation of foods or it can be sliced and taken as such or fried. Some variety of casava mainly tapoica manihot is known to contain cyanogenic glycoside-Linamarin. On hydrolysis of the root hydrocyanic acid is liberated. Liberated cyanide is detoxicated in the body by conversion into thiocyanates which is excreted in urine. This detoxication requires sulphur of SH group which is provided by the sulphur containing amino acidsmethionine and cystine. In absence of these amino acids as in case of protein energy malnutrition, cyanides cannot be detoxicated and thus accumulates in the body. Accumulated cyanides then damage the pancreas. Macmillan and Geeverghese<sup>7</sup> has shown that experimental rats can survive after regular ingestion of cyanides provided that their protein nutrition is maintained. In these cases cyanides are regularly passed in the urine. However if they are deprived of protein particularly in growing age their thiocyanate excretion in urine is diminished and there was evidence of hyperglycemia and cyanosis. Other arguments in favour of casava hypothesis is epidemiological studies, FCPD occurs in some geographical areas where casava is grown. Casava hypothesis is an attractive one but it does not apply to all cases of FCPD. Thus there are some countries where there are large number of FCPD casesthough no cassava is grown or taken e.g. Madras, Orissa, Tripura in India and Bangladesh. This suggest that there must be some other factors which alone or in combination are capable of producing FCPD.

### c) Food toxins

In non casava areas foods like Sorgan, Ragi, Gwar, variety of peas may contain cyanide which need SH radicals of sulphur containing amino acids for their detoxication<sup>16</sup>. Cerfruits may also contain cyanogenic glycosides.

### d) Oxidant stress hypothesis of Braganze<sup>17</sup>

Heightened oxidant stress along with deficiency of antioxidants has been proposed as a possible pathogenic mechanism of FCPD. Braganze had shown that chronic pancreatitis could be caused by heightened oxidative detoxification reaction conducted by cytochrome P450-1 within the pancreas. Theophyllin clearance was taken as standard of measurement of cytochrome P 450-1 activity. It has been proposed that similar mechanism can also occur in FCPD where theophyllin clearance was found to be high.

### e) Xenobiotics

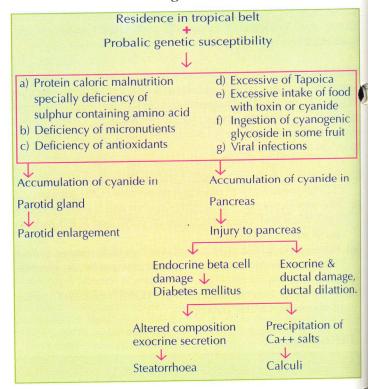
It is suggested that various xenobiotics (cigarettes, alcohol, occupational chemicals, corn oil etc) may induce cytochrome P-450 and that relative deficiency of antioxidants (ascorbic acid, micronutrients, fat soluble antioxidants) could set stage for free radicals to damage the pancreas.

### f) Genetic factor

Genetic factors has largely been thought to be unimportant although familial clustering of FCPD cases have occurred. It has been found, FCPD shares susceptibility genes in common with NIDDM and IDDM patients (HLA DQB)<sup>6</sup>.

Summarising the etiopathogenesis-one can say that residence in the tropical belt along with probable genetic influence to develop diabetes when exposed to the combination of dietary intake of casava or other food toxins including cyanides and associated with protein energy malnutrition may lead to extensive accumulation of cyanides in the pancreas and other tissues leading to damage of pancreatic  $\beta$  cells which result in diabetes mellitus. Destruction of acinar cells lead to fibrosis of pancreas, dilatation of pancreatic ducts, result in initial lesion is an exocrine pancreatic dysfunction resulting in impaired secretion of watery bicarbonate rich alkaline pancreatic juice. Subsequent stagnation and accumulation of viscid acidic material in the duct causes, further impediment to the flow of pancreatic secretion providing a nidus for stone formation  $^{16}$ . These facts are depicted in the figure-1.

### Figure-1



### **PATHOLOGY**

### a) Pancreas

Pancreatic calculi is the hall mark of FCPD and affect upto 90% of the patients. Calculi are located inside the ducts- mainly in the major ducts in head of the pancreas-but may also be located inside the tributaries of the pancreatic ducts. Calculi are composed mainly of calcium carbonate but also contains protein, phosphate, oxalate, iron and nickel. Grossly pancreas becomes small, atropic and fibrosed. The ducts are dilated and have irregular calibre. Microscopically, there is evidence of extensive fibrosis of the pancreas with little or no inflammatory cells, cellular architecture is lost with disorganisation of acinar tissue. Islet cells may be normal but may be damaged partially or completely. α cells may also be destroyed and this may also explain absence of ketosis<sup>8</sup>.

### b) Parotid glands

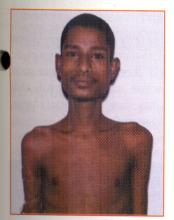
Parotid glands are occasionally enlarged on both sides. Microscopically, they show hypertrophy of acini initially, subsequently they may show evidence of periductal fibrosis and finally atrophy.

### c) Liver

Initially there is mild to moderate enlargement of liver with microscopical evidence of fatty change, sequentially there may be evidence of cirrhosis.

### **CLINICAL FEATURES**

A patient usually below thirty years of age in a tropical country may present with symptoms of diabetes mellitus with polyuria, polydypsia, extreme weightloss etc. He/she may also present with recurrent episodes of mild abdominal pain which may be very severe and not being relieved by antacids or antispasmodics; pain may be relieved on stooping down and on lying prone. Sometimes the pain persists in spite of all efforts. Some of the cases may present with history of passage of bulky, aluminium coloured stool.





Patients with FCPD Showing grossly emaciation, bilateral parotid swelling, thin hair with discolouration and polyneurophthy and mature cataract.

Physical examinations reveal that the patient is grossly emaciated and underweight (BMI usually less than 19 in case of male and less than 18 in females). Hair may be thin and discoloured, lips may have a peculiar cyanotic tinge, there may be angular stomatitis with raw glazed magenta coloured tongue-indicating vitamin B complex deficiency. There may be evidence of dry conjunctiva, corneal opacity, dry rough skin with follicular hyperkeratosis suggesting Vitamin A deficiency. Bilateral parotid swelling may be striking in an emaciated facies. Liver may be found to be moderately enlarged. Abdomen is protuberant. Cases with complication may show clinical signs of polyneuropathy. However the most striking one is the presence of mature cataract in a patient in his/her teens. Scabies and skin infections are common.

### LABORATORY INVESTIGATIONS

Glucose tolerance test will confirm diagnosis of diabetes mellitus according to WHO criteria. Urine will show glycosuria but no ketonuria. Blood haemoglobin may be low. Blood sugar is usually moderately high.

### SPECIAL INVESTIGATIONS

### a) Plain X-ray abdomen

Plain X-ray abdomen may show presence of pancreatic calculi which can usually be found on the right side of the vertebral column or overlapping it, but in long standing cases calculi may be present in the body and tail of the pancreas.

### b) Ultrasonogram abdomen

This non invasive investigation is very useful in the diagnosis of FCPD. Not only it can show up the presence or absence of pancreatic calculus, it can also show the volume of pancreas, so that one can have a clue about fibrosis and shrinkage of the pancreas. It can also show the ductal dilatation.

### c) CT scan abdomen (MRI abdomen)

This can clearly show up in pancreatic calculi, ductal dilatation and shrinkage of pancreas, but because they are expensive they cannot used as routine investigation.

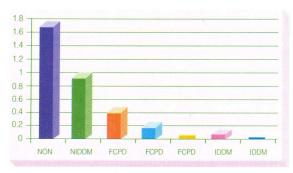
### d) ERCP

It is another tool for the investigation of FCPD where calculi can be diagnosed by showing ductal dilatation and fibrosis of pancreas and other signs of chronic pancreatitis.

### e) Exocrine pancreatic function tests

- 1. Secretion Pancreozymin test, D-xylose absorption test, N-BT PABA tests are used for this purpose<sup>15</sup>. In the later test after ingestion of N-BT PABA (N-Benz-oyl-a-Tyrosil P-amino benzoic acid) urinary para amino benzoic acid is estimated. In cases of FCPD, PABA excretion is impaired because it is not absorbed from the intestine. This test has 97% sensitivity and 81% specificity.
- 2. Fecal chemotrypsin test-Fecal chemotrypsin less than 6U/gm is diagnostic<sup>14</sup>. It has 90% sensitivity and has 87% specificity.
- f) Endocrine pancreatic function tests (C-peptide estimation) In FCPD, C-peptide level is higher than IDDM but lower than non-diabetics and NIDDM<sup>9</sup>. (Fig. 2)

**Fig - 2**: Beta cell reserve as determined by C-peptide estimation after glucagon stimulation (Ref. 1-modified)



Non Diabetic	1.7	NIDDM	0.98
FCPD Controlled OHA	0.48	FCPD Insulin Required	0.23
FCPD Insulin Dependent	0.09	IDDM Early	0.13
EDDM Late	0.02		

### **DIAGNOSIS OF FCPD**

Criteria for diagnosis of FCPD slightly varies according to various authors though the basic principle remain same. There are four schools of thoughts as follows

### a) Bajaj point score system

In this system he has given separate marks for each item. Total marks are fifteen in number; of these a score of 10 or above is diagnostic of MRDM, between 7 to 9 is a probable MRDM<sup>16</sup>. Any case with diagnosis of MRDM who have pancreatic calculi or pancreatic fibrosis or ductal dilatation or deficient pancreatic exocrine function should be diagnosed FCPD<sup>16</sup>. See table -1.



### b) Ahujas criteria for diagnosis 10, 11, 12

### Absolute

- 1. Geographical location: On both sides of equator between N-23° to S-23°.
- 2. Evidence of chronic consumption of low protein diet (less than 30 gm per day) and/or other cereals and other foods containing anogens.
- 3. Subclinical or overt undernutrition as indicated by bodymass index below 19 kg per sq meter.
- 4. Onset during adolescence below 30 yrs of age.
- 5. Moderate to severe hyperglycemia with blood glucose concentration greater than 200 mg/dl.
- No demonstrable evidence of serum acetone above 5mg/dl after subcutaneous injection of epinephrine in a dose of 0.01mg/kg body weight or clinically no ketonuria after withdrawal of insulin for two weeks.
- 7. Insulin dependency requiring more than 1.5U per kg in 24 hour.

### Relative (for diagnosis of FCPD only)

- 1. Recurrent abdominal pain suggesting pancreatitis.
- 2. Radiological evidence of pancreatic calcification.
- 3. Exocrine pancreatic deficiency.
- 4. Ultrasonographic demonstration of small size of pancreas and dilatation of pancreatic duct or ductal stones.
- 5. Residual  $\beta$  cell function evidenced by intermediate values-basal C-peptide as well as C-peptide after glucose stimulation.

### Absent

- 1. Biliary disease or alcohol consumption.
- 2. Genetic markers like HLA are not yet identified.
- 3. Pancreatic autoantibodies are absent.
- 4. Lymphocytic infiltration in pancreas to suggest insulinitis or systemic autoimmune disorders.
- 5. Therapeutic response to sulphonylureas.

### C) Surabaya - Kobe criteria (1986)<sup>13</sup>

### A. Suggestive of MRDM

- \* Diabetes mellitus-WHO 1985 criterias
- \* Malnutrition-Relative body weight 80%
- \* Age mostly around 15-40
- \* Insulin resistance
- \* Ketosis resistance
- \* Pancreatic calcification may or may not be present

### B. Definite MRDM

All the above plus NBT-PABA excretion in urine less than 60%.

### D) Mohan's criteria for diagnosis of FCPD<sup>8</sup>.

- A) Diabetes must be present according to National Diabetic Data group or WHO study group series.
- B) There must be evidence of chronic pancreatitis: for this-
  - 1. Either there should be presence of pancreatic calcification on plain x-ray abdomen or

- 2. At least three of the following are present
- (a) Presence of structural pathology in the pancreas as fibrosis, ductal dilatation etc. as evidenced by ultrasonogram, CT scan, ERCP or histopathology.
- (b) History of recurrent abdominal pain since childhood.
- (c) History of Steatorrhoea.
- (d) Abnormal exocrine pancreatic function-by PABA or fecal chymotrypsin test.

### E) Other causes of chronic pancreatitis are excluded

There are some helpful clinical points which are not diagnostic as follows: Onset at young age, leanness-body mass index below 19, insulin requiring diabetes often large quantity is required but does not become ketosis on withdrawal of insulin and present or past evidence of protein energy malnutrition.

**N.B.** Mohan<sup>20</sup> has pointed the heterogeneity of FCPD where clinical features are variable; patient may be asymptomatic or symptomatic normoglycemic, frank diabetic or IGT.  $\beta$  cell reserve may be good, poor or negligible. Exocrine function may be normal, mild steatorrhoea. Pancreatic pathology may show mild ductal change, gross ductal change, no stone or one or multiple stones.

### **COMPLICATION OF FCPD**

### Ketosis

By definition these cases are ketosis resistant. The explanation suggested for this is-

(a) Low body fat-Body can't utilise fat to convert to them into energy. It has been found that when these cases are well fed and when they gain weight they may develop kenosis. Experimental infusion of intralipid may cause ketosis

(b) Inability of hepatic production of ketosis.

(c) Diminished production of glucagon Damage to the pancreas may lead to damage to α cells which produce glucagon. Though, by definition these cases are ketosis resistant, under special circumstances particularly after stress e.g. infection, trauma etc. ketosis can develop.

### Microvascular complications

Diabetic Nephropathy, diabetic neuropathy and diabetic retinopathy occur as frequently as it occurs in other forms of diabetes mellitus.

### Macrovascular complications

Coronary heart disease, cerebrovascular disorder and peripheral vascular diseases and other forms of macroangiopathy are less frequent than other forms of diabetes mellitus.

# Infection and other forms of complications including hypoglycemia

They are found in similar proportion as in other forms of diabetes. Special mention is to be made to diabetic cataract which is striking, when one finds that patient in his teens have bilateral mature cataract.

### MANAGEMENT

Management of FCPD cases are similar to the principle of management of all diabetes. However the following points are worth mentioning-

#### A) Diet

- 1. Because these patients are underweight, there should be no calorie restriction, rather high calorie should be given with high protein content.
- 2. If steatorrhoea is present fatty food may be restricted.
- 3. Vitamin supplements should be given preferably parenteral.

### B) Drugs

Oral hypoglycaemic agents are usually not helpful. Most of the cases (80%) will need insulin therapy often in large doses 1.5 or 2 units/kg body weight. Some cases can be treated by oral agents or diet alone. Steatorrhoea can be treated by giving pancreatic enzymes. Pain should be treated with analgesic, antispasmotics and antacid preparations. If no improvement, the problem should be discussed with surgeons for operative treatment of total or partial pancreatectomy and/or removal of pancreatic stones.

### PREVENTION OF FCPD

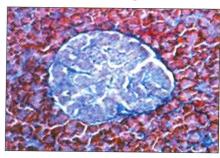
Steps should be taken to improve nutritional intake during pregnancy and infancy, specially at the time of weaning<sup>21</sup>. Since cyanoglycoside in casava has been implicated, diminishing it's level in food to within safe limit (less than 50 mg of such glucoside per kg of freshly greeted casava) constitute an important health strategy. A large portion of cyanogenic glucoside can be eliminated by pealing and washing the tuber, sun drying tapoica slices and cooking and frying foods prepared from casava. Mixing casava with wheat or ground nut flour may also help. Hoticulture research of developing varieties of casava rich in protein and low in cyanide glycoside should be encouraged. Research should be made to find out other food staff which contain cyanogen, so that they can be avoided. It is rational to prescribe anti-oxidant drugs-Vit E, Vit C etc. to neutralise food toxins which has been incriminated to be causative factor.

### **SUMMARY**

Fibrocalculous pancreatic diabetes, subclass of malnutrition related diabetes mellitus occurs in the tropical countries located between the tropics of the Cancer and Capricorn. Casava intake or intake of some other food containing HCN or some other food toxins in association with protein energy malnutrition has been incriminated for the production of this disease. Diagnostic criteria for this condition are residence in this specified geographical areas, presence of calculous in pancreas or evidence of exocrine pancreatic dysfunction and presence of diabetes mellitus. Supportive evidence are onset at an young age of diabetes, history of malnutrition or presence of stigmata of malnutrition, resistance to ketosis in the absence of insulin therapy, requirement of high dose of insulin for diabetes control, association of bilateral parotid enlargement. This form of diabetes may have all the complications found in other types of diabetes though macrovascular complications are less common. About 80% of cases do need insulin for their diabetes control, insulin dose required often is high, more than 1.5 or 2U/kg body weight. Cases with intractable abdominal pain may have to be treated surgically for removal of their pancreatic calculi. Prevention includes improvement of nutritional status of the whole population, avoiding foods-containing cyanogens and taking anti-oxidant drugs.

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Section of human pancreas shows one of the islets of Langerhans, (Centre). The blue and white lines in the islets of Langerhans are blood vessels that carry insulin to the rest of the body.

# A SHORT HISTORY OF MEDICINE: "Doctor, I have an ear ache."

2000 B.C - " Here, eat this root."

1000 B.C. - "That root is heathen, say this prayer."

1850 A.D. - "That prayer is superstition, drink this potion."

1940 A.D. - "That potion is snake oil, swallow this pill."

1985 A.D. - "That pill is ineffective, take this antibiotic." 2000 A.D. - "That antibiotic is artificial. Here, eat this root!"



# An Aetiological Study of Hepatosplenomegaly in Adults.

Md. Zilan Miah Sarker<sup>1</sup>, Md. Rezaul Karim Khan<sup>2</sup>, Md. Tahir<sup>3</sup>

### ABSTRACT

A total of fifty cases of hepatosplenomegaly were randomly selected from medical units of three hospitals in Dhaka. The causative diseases found in the study are blood disorders, infections and liver diseases in descending order.

### **OBJECTIVE**

Hepatosplenomegaly is a feature of a number of diseases encountered in clinical practice. The study is conducted with a view to finding out the common diseases responsible so as to give emphasis on preventive and therapeutic measures.

### **METHODS**

A total of fifty cases admitted in medical units of IPGMR (BSMMU), DMCH and SSMC and Milford Hospital, Dhaka were included in the study from July/87 to December/87. Selection of cases were random from both sexes, all above the age of 12 years. All cases were subjected to clinical history, physical examinations and investigations available and when indicated. All these features were recorded in a format - one for each patient.

### RESULTS

Results are shown in tables. The study shows blood disorders, infections and cirrhosis of liver are the leading causes.

### CONCLUSION

Malignant disorders of haemopoietic tissue are at the top of the list of causes while infections except Kala-azar contribute the least. Kala-azar shows a dreadful increase in incidence with a reflection of resurgence of the disease.

### **KEY WORDS**

Hepatosplenomegaly, adults, and aetiology.

### **SUMMARY**

This is a randomized hospital-based study of fifty cases from either sex-all above the age of twelve years. There were 41(82%) male and 9 (18%) female patients. 52% of cases belong to low income group and 48% hail from middle class. Occupations of the patients were cultivation (26%), service (24%), studentship (20%), housewife (14%) and business (10%). The study shows malignant disorders of haemopoietic tissue as the prime cause while infections excluding Kala-azar contribute the least. Leukemia and lymphoma constitute 13 (46%) cases. Of these, chronic granulocytic leukemia (CGL)

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constitutes 12 (24%) cases, Hodgkin's Lymphoma comprises 5(10%) cases, acute lymphoblastic leukemia (ALL) comprises 4(8%) cases and there was one (2%) case of chronic lymphocytic leukemia (CLL) and one (2%) case of acute myeloblastic leukemia (AML). Kala-azar shows a dreadful increase in incidence with a reflection of resurgence of the disease. Kala-azar constitutes 10(20%) cases, chronic liver disease comprises 10(20%) cases followed by thalassaemia and haemoglobinopathy comprising 5(10%) cases. There was one (2%) case of hepatosplenomegaly due to typhoid fever and another case (2%) was due to congestive cardiac failure (CCF) with mitral valve disease.

### **INTRODUCTION**

Hepatosplenomegaly is a feature of a number of diseases encountered in clinical practice. The study is aimed to find out the common causes of hepatosplenomegaly in hospitalized patients so as to give emphasis on necessary preventive and therapeutic measures. Though it may not reflect the exact picture applicable for the community but may be regarded as a modest attempt to review the problem.

### **MATERIALS AND METHODS**

A total of fifty cases admitted in medical units of IPGMR (BSMMU), DMCH and SSMC and Mitford Hospital, Dhaka were included in the study from July/87 to December/87. The cases were selected randomly from both sexes, all above the age of twelve years. All cases were subjected to clinical history and physical examination. Hepatomegaly and splenomegaly were measured by recommended clinical methods. Laboratory investigations like-blood for TC, DC, Hb%, ESR, urine and stool for routine microscopic examination (RME), blood sugar, blood urea, serum creatinine, X-ray of chest P/A view, ultrasonography of abdomen, ECG, platelet count, comment on peripheral blood film (PBF), ALT (Aldehyde lest), CFT for Kalaazar, SGPT, SGOT, Alkaline phosphatase, prothrombin time, HBsAg, total serum proteins, Hb-electrophoresis, bone-marrow examination, lymph node biopsy, liver biopsy were done where indicated. All these features were recorded in a format-one for each patient.

### **RESULTS**

Results are shown in tabulated forms.

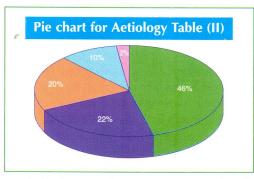
Table-1 shows break-up of fifty (n=50) cases. Table - II shows the aetiology of hepatosplenomegaly under broad headings.

Table-I. Break up of fifty (n=50) cases

No.	Diseases	Number	Percent (%)
1	Chronic granulocytic leukemia	12	24
2.	Chronic Kala-azar	10	20
3.	Cirrhosis of liver	10	20
4.	Lymphoma	5	10
5.	Thalassaemia and	5	10
	hemoglobin -E disease		
6.	Acute lymphoblastic leukemia (ALL)	4	8
7.	Chronic lymphocytic leukemia (CLL)	1	2
8.	Acute myeloblastic leukemia (AML)	1	2
9.	Congestive cardiac failure (CCF)	1	2
10.	Typhoid fever	1	2

Table-II. shows the aetiology under broad headings. (n=50)

No.	Diseases	Number	Percent (%)
1	Haemopoietic tissue malignancy	23	46
2.	Infections	11	22
3.	Liver disease	10	20
4.	Haemoglobinopathy	5	10
5.	Other	1	2



The haemopoietic tissue malignancies account for the highest number of 23(46%) cases followed by infective causes of 11(22%) cases. There were 41(82%) male and 9(18%) female patients. Occupation of the patients were respectively cultivation (26%), service (24%) studentship (20%), house-wife (14%) and business (10%). Socio-economically 52% of cases belong to low income group and 48% from middle class.

Table -III. shows the presenting symptoms. Fever (30%), swelling of abdomen (24%), mass in abdomen (18%) and yellow coloration of urine and eye (8%) were the main symptoms.

Table-III. Shows the presenting symptoms (n=50).

No.	Diseases	Number	Percent (%)
1	Fever	15	30
2.	Swelling of abdomen	14	28
3.	Mass in abdomen	9	18
4.	Yellow coloration of urine and eye	4	8
5.	Gradual swelling of neck, axilla and inguinal region	3	6
6.	Pain in joints and bones	3	6
7.	Weakness	1	2
8.	Gradual loss of weight	1	2

The associated clinical findings are anaemia (100%) lymphadenopathy (28%), ankle oedema (26%), ascites (26%), jaundice (20%), darkening of body (14%), pruritis (10%), raised jugular venous pressure (JVP) (10%), engorged veins on abdomen (4%) and clubbing of fingers (4%).

### **DISCUSSION**

Chronic granulocytic leukemia (CGL) comprises the highest number of cases. There were 12(24%) cases of CGL showing conformity with other study' and differs from the finding by Kushwaha et al<sup>2</sup>. 83.34% cases of CGL were male and 16.66% of cases were female which are inconsistent with other study' and equal sex incidence was described by some author3. All cases of CGL were anaemic in varying degree like other study<sup>2</sup>. Typhoid fever constitutes single case. Low infective causes found in the study may be related to improved health care in the rural areas. Among infections, Kala-azar comprises 20% of cases showing a reflection of resurgence of visceral leishmaniasis. 40% of cases in the study belong to age group of 41-50 years in contrast to other studies<sup>4,5</sup>, where age group of 5-10 years and young adults and teenagers were the main victims. Fever was irregular in 80% of cases and irregular with double rise was found in 10% of cases in contrast to other study. Cirrhosis of liver constitutes 20% of cases in the present study which is higher then other study<sup>7</sup>. Lymphomas -all are Non-Hodgkin's type constitute 10% of cases of hepatosplenomegaly in the study. Both acute and chronic leukemia were found in 12% of cases. 10% of cases of hepatosplenomegaly in the series was constituted by thalassaemia and haemoglobinopathies. Thalassaemia -Hb-E disease was found in 6% of cases. Thalassaemia major in 2% of cases and Hb-E disease in 2% of cases-similar to that found by other study<sup>8</sup>.

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What is a double-blind study?
Two orthopaedists reading an electrocardiogram!!!



# Reconstruction of Neglected Patellar Tendon Injury by Double Breasting of Tendon, Augmented with Quadricep Apponeurosis.

A. K. M. Eshaque

### ABSTRACT

10 cases of neglected cut injury of patellar tendon have been treated by double breasting of patellar tendon without disturbing its fibrous union. It is then re-strengthened by Quadricep-Apponeurosis. Tension-wire have been given in 4 cases to give early mobilization of knee joint. All cases are adult and has history of assault. They have received initial treatment at local hospitals. Soft tissues have been sutured without touching the tendon. Age of injury varies from 2 to 3 months. Mean age is 2.19 months. 3 cases have developed post-operative infection. Staphylococcus aureus is the causative organism. Infection has been controlled within 7 to 10 days except one which took 5wks to control.

Two years is the minimum and five years is the maximum follow up. All cases have good knee movement with normal muscle power.

### **INTRODUCTION**

Normal activity of life needs healthy extensor apparatus of knee joint. Disruption at any level of it will hamper its normal activity and cause disturbance in normal weight bearing walking. Degenerative rapture of patellar tendon is seen. So its management is well described by many authors. But neglected complete cut injury of patellar tendon is very very rare. So available text books and Journals provide inadequate information regarding it and thus management of these neglected cases become difficult. Author treated these 10 neglected cases by a new technique. This procedure is easy.

**Aim of this study** is to see the clinical result and to establish a new approach in the management of neglected cut injury of patellar tendon.

### PATIENTS AND METHODS

10 patients of neglected cut injury (complete) of patellar tendon have been treated by reconstructive procedure at Mitford hospital and private clinics, Dhaka from Jan. 1992 to Dec. 1997. All patients are young and their mean age is 24.03 years. 6 cases have right sided and 4 cases have left sided involvement. All cases have been treated at local hospitals by simple repair of soft tissues only. Tendon has been kept intact. They have history of assault and wound healed by first intention. Since then, they cannot walk properly in uneven surface and cannot straight the leg. With these complains they have been admitted at hospital within 2 to 3 months. Thorough clinical examination has been done. Tendon is not taught when leg is extended against resistance. In all cases patella is in higher position. Palpable gap is present bellow the patella and can be pulled down to anatomical position.

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Knee joint has passive full range of motion but has lag of extension is about 20° to 25°. Wasting of muscle at thigh is about  $\frac{1}{4}$ " -  $\frac{1}{2}$ ". Routine investigations are done. Plain x-ray of patella is done at 45° flexion of knee joint to see position of patella. With all aseptic precautions a long lazy 'S' shaped incision is given on anterior aspect of knee joint, starting from 7cm. above the upper pole of patella to 2cm. bellow the tibial tuberosity. Quadricep tendon, patella and patellar tendon are exposed. Movement of patella has been tested. In all cases patella is mobile and it can be pulled down easily. Movement of knee joint has also been tested. In all cases joint has full range of motion. Joint is not opened. Patellar tendon is examined. It is healed but lengthened by fibrous tissue. Tendon is completely isolated from underlying structures. Patella is pulled downwards to anatomical position and its tendon is overlapped like long lazy 'S'. Now tendon length is measured. It's length will be the same as longitudinal length of patella. It is then sutured all round by 'Vicryl 3.0'. Movement of the joint and that of patella are tested. A strip of quadricep apponeurosis with some tendinous fibers (7cm. x 3cm.x5cm. i.e. twice the length of patella+2cm.) is taken keeping it's patellar attachment. It is placed over patella and wrapped round the newly constructed patellar tendon. Interrupted sutures have been given. Movement has been again tested. In 4 cases it is restrengthen by tension wire through patella to tibial tubersosity. It is an added support to patella to keep it in position, to immobilise the tendon and to give early movement of knee joint, without disturbing it's healing process. Wound is closed in layer. Long leg well padded plaster cast has been given. Sutures has been removed at 12th postoperative period. Isotonic quad-exercise has been advocated for 3 wks. Cast is removed and joint is again tested. Long leg pop slab is given for another 3 wks and isometric quad-exercise has been advocated. Patient is allowed to walk with full weight when he can actively raise his lower limb. Tension wire is removed after 3 months. 3 cases developed post-operative infection. Pus showed Staphylococcus Aureus. Infection has been controlled after giving proper antibiotic depending on C/S report within 7 to 10 days except one which took 5 wks to control.

Follow up is done in every 6 wks interval. One case is lost from follow-up after 3 months (Lately controlled infected case). It again came for follow up after 5 years with good functional result. 9 cases have achieved full range of motion of knee joint and patellar movement within 2-5 months. Rest one took 7 months to achieve full range of motion. Full muscle power has been achieved within 12-16 months. Minimum followup is 2 years and maximum follow up is 5 years.

### RESULT

A new technique described above has been used in 10 neglected cases of complete cut injury of patellar tendon to reconstruct the tendon. Double breasting of lengthened patellar tendon has been done. Quad-apponeurosis is used. Tension-wire is used to give early movement of knee joint, to avoid stiffness in 4 cases. 3 cases developed post operative infection. Infection has been controlled by antibiotic. *Staphylococcus Aureus* is the causative organism. Tension wire is helpful for early mobilization without disturbing healing process. All cases achieved full range of motion within 2-7 months. Mean period is 3 months 5 days. They have gained full muscle power within 12-16 months. Mean period is 13 months 20 days. Long follow-up showed good functional result and maintain normal, healthy life.

Table -I. Shows age distribution with duration of rupture.

No. Pt.	Age of Pt.	Mean age.	No. of Pt.	Duration of rapture	Mean duration
1. 2. 1. 3 1 1	20 yrs. 25 Yrs. 21 yrs 5mth. 26 yrs. 24 yrs 6mth. 16 yrs. 5mth. 30 yrs.	24.03 yrs.	4 2 1 2 1	60 days. 70 days 80 days 68 days 63 days	2.19 months

Table - II. Shows duration of achievement of full motion of knee joint.

No. of pt	. Durati	on: Months	Mean Mont	ns. Days.	
4 2 2 1 1		4 4 5 3 7	0 15 0 0	3	5

Table - III.
Shows duration of gaining full muscle power.

No. of pt.	Duration of gaining full muscle power. Months - Days.	Mean duration. Months - Days.
4	12 0	13 20
1	15 12	
3	14 3	
1	15 5	
1	16 0	

### **DISCUSSION**

Fresh rupture as well as degenerative rupture of patellar tendon are often seen in day to day practice. Neglected rupture of patellar tendon is very rare. So management of neglected case is difficult.

Ecker, Lotke and Glazer² used gracilis or semitendinosus for reconstruction of patellar tendon. They also used tension wire for pulling down of patella. The new technique described by the author uses quad-apponeurosis for augmentation of newly constructed patellar tendon. Patellar tendon is constructed by double breasting lengthened tendon. In new technique tension wire is used for early mobilization of joint. Author managed 10 cases but Ecker, Lotke and Glazer² treated 4 neglected cases. In both series results are rewarding. The aim of surgery is to reconstruct the neglected cut injury of patellar tendon and to achieve full motor power of knee joint.





Full flexion of operated limb.

Shows muscle power of operated limb.

This new technique is easy and not necessary to sacrifice the other active tendon.

### **CONCLUSION**

Ten neglected complete cut injury of patellar tendon have been treated by double breasting of patellar tendon, augmented with Quad-apponeurosis. Post-operative results and follow-up results are good. The author consider that this procedure should have place for treatment of neglected rupture or cut injury of patellar tendon.

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- 1. If you understand it and can prove it, then send it to "The ORION" Medical journal.
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- 4. If you can neither understand it nor prove it, then send it to a psychology journal.
- 5. If it attempts to make something important out of something trival, then send it to a journal of education.
- 6. If it attempts to make something trivial out of some-thing important, send it to a journal of metaphysics.



# Appendicitis-Clinical Judgement and Operative Findings.

# S.M Amjad Hossain<sup>1</sup>, AKM Mujibur Rahman<sup>2</sup>, Khairun Nahar<sup>3</sup>, Jawharlal Sen<sup>4</sup>, Ferdous Mahal<sup>5</sup>, Sharmin Rahman<sup>6</sup>, Proddut Kumar Shaha<sup>7</sup>

### **ABSTRACT**

Appendicitis is a common intra-abdominal disorder that requires emergency surgery to prevent mortality and long term morbidity. In the past few decades, despite improvement in diagnostic facilities, it remains a diagnostic dilemma as the presentation may be atypical especially in the young and elderly patients. Recent literature report rates of negative appendectomy ranges from 9% - 40% which is not different from earlier reports of 15%-35%.

The present study was carried out to evaluate clinical performance of physicians and surgeons in the diagnosis of appendicitis and the factors related to subsequent complications.

412 consecutive appendectomy cases were involved in the present study. 270 were male and 142 were female with a mean age of 24.8±14.2 years. 22 patients had surgical digestive tract disorder and 17 had surgical gynaecological conditions. Negative appendectomy cases were 46(11.16%). Complications were related to longer delay before operation. Ultrasonography remains a good diagnostic tool as well as to rule out differential diagnosis. If properly performed, its sensitivity is about 93% and specificity about 70%. In conclusion, the diagnosis of appendicitis still remains a clinical entity despite many advances in diagnostic modalities.

### INTRODUCTION

Appendicitis is the most common intra-abdominal disorder that requires emergency surgery, with a 6% lifetime risk. At the end of  $20^{\text{th}}$  Century, appendicitis still remains a clinical entity and an ongoing diagnostic dilemma as the presentation may be atypical '.

Recent literature reports rates of normal appendix removal ranging from 9% to 40%. These results are not different from earlier reports of negative appendix removal between 15% to 35%<sup>1,2</sup>. In these cases signs of acute inflammation are absent. Some researchers suggest that inflammatory reactions, which might also involve epithelial cells and neuroproliferation, may cause chronic or repeated attacks of acute pain. Furthermore some classes of neuropeptides, such as Substance P (SP) and Vasoactive Intestinal Peptide (VIP) are involved in pain generation <sup>2</sup>.

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Perforation rates range from 11% to 32%. Delay in diagnosis and treatment is associated with more advanced stages of disease. However, delay in patient consultation leads to perforation, whereas physician-related delay has little or no influence on the incidence of complicated appendicitis. Despite new adjuncts in the evaluation the patients with a suspected diagnosis of appendicitis, (Ultrasonography, Complete Blood Count and Urinalysis) there is no difference in perforation or negative appendectomy rates <sup>3</sup>.

### **AIMS AND OBJECTIVES**

In the present study we tried to evaluate (1) The clinical performance of Physician and Surgeons (With limited adjunctive diagnostic modalities) with histological findings in relation to suspected appendicitis and (2) The factors associated with complicated appendicitis.

### **MATERIALS AND METHODS**

412 consecutive appendectomy cases with suspected appendicitis, were reviewed from March 1997 to December 1999, from Department of Surgery, Medicine, Gynaecology as well as from General practice. Demographic data (Age, Gender), Symptoms (Fever, Nausea, Vomiting, Anorexia, Diarrhoea, Constipation, Dysuria), Clinical signs (Temperature, Pulse, Rebound tenderness, Peristalsis) and white blood cell count were collected. The results of ultrasonography, if done, was obtained. The delays were categorised as: (a) Delay occurring before first physician consultation, (b) Delay between consultation and surgical intervention.

The status of appendix at the time of operation was obtained from operation note and later-on from biopsy report. It was divided into Noncomplicated (Inflamed, gangrenous without perforation), Complicated (Perforation, abscess, peritonitis) and Normal. Other diagnosis were surgical-gynaecological conditions. Analysis with ANOVA method was carried out to identify which factors could predict the presence of complicated appendicitis.

### **RESULTS**

There were 270 (65.51%) males and 142 (34.49%) females with a mean age of 28.4±14.2 years. 22(5.33%) patients had surgical digestive tract disorder, and 17(4.13%) had surgical gynaecological conditions. In the remaining 373 (90.53%) cases, there were 209(50.73%) cases with noncomplicated appendicitis, 118(29.64%) cases with complicated appendicitis and 46 (11.16%) cases with normal appendix. After exclusion of cases with other surgical disorder, the percentage of noncomplicated appendicitis, complicated appendicitis and normal appendix removal represents 56.03%, 31.64% and 12.33% respectively.

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Anorexia, the most frequent complaint, was present in over 90% of cases. Rebound tenderness, the most important clinical sign, was present in over 80% of cases in each group. The mean temperature was 100.4±0.8° F in noncomplicated appendicitis,102.1±0.9° F in complicated appendicitis 99.7±1.2° F in normal appendix and 100.5±1.2° F in other surgical conditions. The mean white blood cell count was 12.7±4.7 mm³ in noncomplicated appendicitis, 16.6±4.5 mm³ in complicated appendicitis, 3.4±4.9 mm³ in normal appendix, 14.9±4.5 mm³ in other surgical conditions. An ultrasound was obtained in 188(89.95%) of noncomplicated appendicitis, 101(85.59%) of complicated appendicitis, 37 (80.43%) cases of negative exploration and 28 (71.79%) in other conditions. Results of ultrasonography are shown in Table-1.

Table-I. Results of Ultrasonography.

	N1/0/ \	D '(' -/0/)	D L45-1(0/)	Magativa (9/)
Туре	N(%)	Positive(%)	Doubtful(%)	Negative(%)
Noncomplicated (N=209)	188(89.95%)	63(30.14%)	130(62.20%)	16(7.65%)
Complicated(N=118)	101(85.59%)	55(46.61%)	41(34.75%)	5(0.04%)
Normal(N=46)	37(80.43)	11(23.91%)	14(30.43%)	12(26.08%)
Other diseases $(N = 39)$	39(71.79%)	5(12.82%)	6(15.38%)	17(43.59%)

The different delays are presented in Table - II. Delay between appearance of symptoms and first consultation was significantly longer in cases of complicated appendicitis (3.5 days) and negative exploration (5 Days) versus cases of noncomplicated appendicitis (1.5 days. P <0.001). The decision to operate was immediate in 84.5% of noncomplicated cases, 69% of complicated cases, 42.4% of negative cases and 45.7% of cases with miscellaneous surgical condition.

Table- II. Delay before surgery in different groups of appendicitis patients.

Delay	Noncomplicated	d Complicated N	<mark>egative explorati</mark> o	on Other diseases
	N = 209	N = 118	N = 46	N = 39
Before first consultation (da	1.5 ays)	3.5	5.2	6.8
Before surgical intervention (c	2.1	4.2	6.4	5.7

Appendectomy was carried out by "Grid-Iron" incision in all case. No case of mortality was observed in different groups. Complications are listed in Table-III.

Table-III. Complications observed in different groups.

Groups of patients	Types of complication (N)
Noncomplicated appendicitis (N=209)	- Wound infection-7; Cardiac arrhythmia(2)
Complicated appendicitis (N=118)	- Wound infection-11; Ileus-7
Negative exploration (N=46)	-Wound infection-3
Other surgical condition (N=39)	-Wound infection-3; Pneumonia-2

7 patients (3.35%) had wound infection in the group with noncomplicated appendicitis, 11 patients (9.32%) in the group with complicated appendicitis, 3 patients (6.52%) in the group with negative laparotomy and 5 patients (12.82%) in the group with other surgical diseases.

Hospital stay was  $3.5\pm1.7$  days in the group with noncomplicated appendicitis,  $6.2\pm2.9$  days in the group with complicated

appendicitis, 4.1±2.8 days in the group with negative exploration, 7.6±2.4 days in the group with other surgical conditions.

### **DISCUSSION**

Clinical judgement still remains the most important diagnostic tool for acute appendicitis. A negative exploration rate of 11.17 % in this study represents a good clinical judgement.

No symptoms or signs accurately differentiated among normal, noncomplicated, complicated appendicitis or even other surgical condition. Complicated appendicitis was associated with increased delay before treatment.

It was believed that perforation rate was inversely proportional to negative appendectomy rate<sup>4</sup>. However, the rate of perforation and the rate of negative appendectomy are two independent phenomena<sup>5,6</sup>. Perforation is primarily due to factors related to the patients. In our study, delay before first medical consultation was significantly longer in complicated appendicitis versus noncomplicated cases (6.2 versus 3.5 days, P <0.001, Table -II). It was also longer (4.1 days) in the group with negative exploration. Delay before surgical consultation and delay before decision to operate were not significantly different in each group. Immediate decision to operate was more frequent in the group with noncomplicated appendicitis.

Ultrasonography was done in 354 (85.92%) cases for diagnosis of noncomplicated and complicated appendicitis as well as to rule out other differential diagnosis. Sonographic evaluation of suspected appendicitis is based on "Graded Compression Technique"<sup>7,8</sup>. This method was first described by Puylaret in 1986 and is based on the observation that normal appendix can be compressed with moderate pressure, but the inflamed appendix can not be compressed. The US criteria for diagnosis of acute noncomplicated appendicitis include (1) Noncompressibility of appendix. (2) Enlargement of appendix with wall thickening (Axial diameter exceeding 6 mm). (3) Presence of faecolith in the lumen.

The criteria for diagnosis of perforated appendicitis include-

- (1) Altered echogenicity of the surrounding fat.
- (2) Disruption of submucosal wall.
- (3) Presence of loculated fluid<sup>9,10</sup>.

Laparoscopy remains a good diagnostic modality, but because of its invasive nature, we did not use it as a preferred diagnostic tool.

### CONCLUSION

The diagnosis of appendicitis still remains clinical entity despite many advances in diagnostic modalities 12,15. Complicated appendicitis was primarily associated with a longer delay before the first medical consultation was made. Most of the patients remained symptom-free after operation, even though the appendix appeared normal at histological examination. In most series, the histologically normal appendicectomy specimens is around 20%. This may be due to increased immunoreactivity of peptidergic innervation of appendix for Substance P(SP) and Vasoactive Intestinal Peptide (VIP). A large scale clinical as well as immunohistochemical study is required to find-out the way in which nervous system and immune cells interact, producing neuroimmune in histologically normal appendicitis, which may be regarded as distinct clinical entity.



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### **CONTINUED FROM PAGE NO. 22** (Cervical Factors in Infertility)

### **Treatment of Antisperm antibody**

Therapy for anti sperm antibodies in the female is complicated by their multiple potential site and modes of action, and by our incomplete understanding of their clinical significance. Thus if anti sperm antibody present in the serum as well as in cervical mucus, their effects are unlikely to be overcome by IUI with washed sperm. Pregnancy rate is about 20-30% of patient who complete at least 3 cycle and alternatively by GIFT (gamete intrafallopian transfer).

In male with sperm-bound antibodies, immunosuppressive therapy given in the absence of contraindication to corticosteroid using a cyclical regime of prednisolon 40 mg/day taken from  $D_1$  to  $D_{10}$  of the female partner cycle (Hendry et al 1986). Treatment continued for at least 9 months to achieve result and should be monitored from time to time with repeating antibody test on semen. When there is contraindication to corticosteroid a non steroidal anti-inflammatory agent such as naproxen 50 mg twice daily may lower the antibody levels. Sperm washing and IUI have proved ineffective, but IVF, GIFT and ICSI provide good result.

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### **FERTILITY TREATMENT STATISTICS**

About one in four attempts at *in-vitro* fertilization results in a successful birth, according to the Fourth Annual Assisted Reproductive Technology ([ART] Report, published by the Centres for Disease Control and Prevention. For women using their own eggs, age plays a pivotal role in success: those under 35 years fare best, with a 32% success rate, while women aged 40 and older successfully carried a fertilization attempt to term just 8% of the time. For women who opt for a donor egg, a much smaller group, the success rate is about 40%, regardless of age.

The report, meant to aid women and couples considering assisted fertilization, surveyed 360 fertilization clinics in the United States and covers virtually all of the *in-vitro* pregnancy attempts made in 1998. Of 80,600 attempts reported that year, about 30% resulted in pregnancy, culminating in some 28,000 live births.

While ART offers infertile couples the chance to have children, it bears a downside: increased risk for multiple births. Nearly 31% of all ART deliveries in 1998 were multiple births, more than 10 times the rate in the general population. Multiple births carry increased risk of possibly serious complications for infants, such as preterm delivery, low birth weight, and long-term disabilities.

The report includes data on procedures in which eggs are removed and implanted in the uterus or fallopian tubes and does not include statistics on artificial insemination.

Source: Fertinet



# Cervical Factors in Infertility.

### Nilufar Sultana<sup>1</sup>, Kohinoor Begum<sup>2</sup>

The cervix is very important in the process of reproduction. The spermatozoa must travel through it's canal to fertilize the ovum in the fallopian tubes. Millions of sperm must be deposited in a receptive cervical canal to ensure that hundreds will get to the tubes. Cervix also functions as a biological vulve, this is in the sense, that in the proliferative phase, it permits the entry of sperm and in the secretory phase, hinders their penetration. So, dysfunction at this level should be carefully evaluated.

In infertility, cervical factors account for 5%. Whether the real cause is unexplained or "Cervical" infertility, the treatment of choice is super ovulation/IUI, followed by IVF if the previous one fails.

Abnormalities of the cervix or it's endocervical secretion can cause infertility. It is unfortunate that the cervix often neglected in an infertility investigation. So during infertility investigation, proper evaluation of cervical factors should be done by a) Physical Examination of cervix, b) Properly and timed post coital test (PCT).

# THE FOLLOWING ANATOMICAL AND PHYSIOLOGICAL FACTORS PLAY IMPORTANT ROLE IN NORMAL FERTILITY:

The cervix usually pointed towards the posterior fornics, so that following ejaculation, the external OS is immersed in the seminal pool.

Cyclical alteration occur in the diameter of the external OS, cervical canal and isthmus, being widest at ovulation time for passage of spermatozoa.

Cyclical changes of the secretion of endocervical glands which under estrogenic influence in the pre-ovulatory phase produce favorable mucus for sperm penetration and survival, and under progesterone influence in the post ovulation phase produce inhibitory effects.

Properly and timed post coital test is most important for the evaluation of cervical factors. It has been traditionally employed to asses sperm survival in cervical mucus, characteristic of cervical mucus and the ovarian function by examining the cervical mucus under high power microscope, because altered cervical mucus and increased immunogenicity is mostly responsible for infertility. The characteristic of cervical mucus should be recorded; including its cellularity, viscosity, Spinnbarkeit and ferning pattern when allowed to dry on the slide. A cervical score can be obtained by quantifying each of these characteristic from 0 to 3; a score of less than 5 indicating cervical hostality, greater than 10 being satisfactory and 15 maximal.

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 Prof. Kohinoor Begum, FCPS (Gynae), FICS, Professor, Department of Obstetrics and Gynaecology, SSMC and Mitford Hospital. Cervical hostality arises (though apparently normal) either poor cervical mucus or antibodies against the sperm present in the cervical mucus. Immunoglobulin A (IgA) antibody are found in the cervical mucus (identified by PCT) attached to the sperm head to be bind to mucin chain in the mucus and causes the sperm to display a characteristic 'Shaking' movement and is highly detrimental to cervical mucus penetration.

Cyclical changes of the secretion of endocervical glands occur in both Pre and Post ovulatory phases. In Pre-ovulatory phase the secretion is thin, copious which is favorable for sperm penetration and survival. But in the post ovulatory, the cervical mucus become thick, scanty due to Progesterone influence which hinders the sperm penetration. Penetration of cervical mucus by sperm has been shown to be rapid, occurring within one and a half to three minutes in the majority of women studied. This is the phenomenon for which only the motion of the sperm is responsible.

### **CERVICAL SCORING SYSTEM**

SCORE	0		2	3
Quantity	0 ml	0.1 ml	0.2 ml	>0.3 ml
Viscosity	Thick	Intermediate	Mildly viscous	Normal
Cellularity	11 Cell/HPF	6-10 Cells/HPF	1-5Cells/HPF	O Cells/HPF
Ferning	No	Atypical	10 & 2 Stems	30 to 40
	Crystallization	Pattern		Stems
Spinnbarkeit	< 1 cm	1-4 cm	5-8 cm	>9 cm

The following cervical conditions, therefore may effect the normal process of reproduction:

### ANATOMICAL ALTERATION OF THE CERVIX (CONGENITAL & ACQUIRED)

Abnormal position of the cervix pointing upwards so that it is away from the seminal pool in the posterior fornics.

*Hypoplastic cervix* which usually denotes a hypoplastic uterus due to inadequate estrogenic stimuli.

Hypertrophic cervix which usually result from old lacerations and chronic cervicitis or growth, may affect satisfactory deposition or retention of semen.

Stenosis of the OS or cervical canal as sequelae of electrocautery, cryotherapy, conization, amputation of the cervix may affect sperm migration.

Synechiae in the canal as sequelae of postpartum or post abortal curettage or infection may likewise affect sperm migration.

Laceration, scaring, distortion, congenital elongation of cervix, displacement, incompetence, acute retroversion may affect fertility.

### **Defective Endocervical Mucus**

Endocervicitis or chronic cervicitis may interfere with proper mucus production and affect sperm migration and survival.



Scanty mucus can be the result of anti oestrogen e.g clomiphen citrate or poor glandular activity of cervical endothelium as sequelae of destruction of endocervical gland with extensive electrocautery, cryotherapy, conization, ampulation, synaechiae and scarring.

**Growth of Cervix** 

Polyp or myoma may interfere with normal migration of sperm. They also tend to be infected and by keeping the canal open, may permit the development of a low grade endometritis. A poor cervical mucus is common.

### **INVESTIGATIONS**

### **Routine Tests**

- 1. History should be included a careful review of past gynaecological history (e.g. operation in the cervix, electrocautery etc.) and also a past obstetrics history (e.g. difficult forceps delivery, infection etc.).
- 2. Physical examination should take note of the position, size, structural abnormality of the cervix, cervicitis, new growth.
- 3. Probing of the cervix is also done to determine the length and course of the canal and the presence of stenosis or synaechiae or new growth.
- 4. Evaluation of the endocervical mucus at around the time of ovulation by PCT reveals a copious, watery, clear with good spinnbarkeit, hypocellular mucus, when dried, a good ferning pattered is formed. The cervical OS at this time opens. The pH of the mucus should be alkaline (7-8.2). Spermatozoa are immobilised at pH below 6.5).
- Culture and sensitivity of endocervical mucus, especially, for chlamydia and mycoplasma should be considered if there is good evidence of endocervicitis or if the ovulatory mucus has plenty of leucocytes or repeated PCT show poor result.

# 6. Special Tests Post Coital Test

This test is done at or around the ovulation time (24-48 hrs) before expected rise of basal body temperature or 15-16 days before expected mense when the oestrogenised cervical mucus is most receptive to sperm. Initial PCT performed 8-12 hours after intercourse. A sample of cervical mucus is aspirated from cervical OS and placed on a glass slide for examination under high power microscope to see - character of cervical mucus, number of motile sperm.

PCT provide information about

- a. Coital technique b. Quality of cervical mucus
- c. Quality of semen d. Ovarian function

### Sperm Cervical Mucus Compatibility Test (SCMC-T)

This in vitro cross over test is performed using mid cycle cervical mucus of the wife and semen of the husband under question and compare with donar sperm and donar cervical mucus. This is indicated if the consecutive three PCT became negative. In this test where shaking of motile sperm at the mucus interface-denotes the

presence of antibodies (IgA) either on sperm or in the cervical mucus. The site of origin can be identified by cross-over testing with donar sperm and mucus respectively. Poor sperm-mucus penetration in the absence of sperm shaking movement in SCMC-T provide evidence of non immunological cervical hostality.



# TREATMENT Congenital factors

Stricture or stenosis may be treated with dilatation of cervix under anaesthesia. Hypoplasia of the cervix and uterus require endocrine investigation prior to any therapy. Treatment consist of large doses of oestrogen given cyclically for 6-12 months, preferably, with a sequential progestin (e.g. premarin 1.25 mg from  $D_5$ - $D_{25}$  with progesterone 10mg from  $D_{16}$ - $D_{25}$  of cycle).

### Displacement

The objective is to produce a normal seminal-cervical contact as possible, trials with pessary or artificial homologous insemination (intra cervical) should first be tried before any attempt at surgery.

**Growth** These should be excised.

### **Stenosis**

Stenosis is managed by repeated gentle dilatations, preventing damage to internal OS by over dilatation, as this will result in an incompetent cervix, predisposing habitual abortion.

### Infection

Carefully obtained culture sensitivity tests should precede treatment whenever possible. Antibiotics- local or systemic, usually doxycyclin for chlamydia are given. Periodic gentle dilatations will help by promoting the drainage of infected mucus. If these are ineffective, cautery with chemicals (Silver nitrate or albothyl concentrate) is performed.

Electrocautery or cryotherapy should be last resort in resistant cases but avoid entering the endocervical canal as this may lead to stricture. Punctuate cauterization is preferable to linear type cautery.

**Synechiae** D & C may be tried but no forcible dilatation should be done.

### Lower alkalinity of Cervical mucus

One table spoonful of sodium bicarbonate in one quart of warm water as pre-coital douche will help to sperm survive.

### **Inadequate Oestrogen Stimulation**

Some times, one may see a cervix that is anatomically normal in all respect except for the scantiness of mucus at ovulation time. If destruction of gland or endocervicitis have been ruled out, this may be due to inadequate oestrogenic stimulation. This case may benefit from low dose estrogen given daily from  $D_5$  of cycle to about 2 days after rise of basal body temperature (e.g. Premarin 0.625mg).

**CONTINUED TO PAGE NO. 20** 



# MgSO<sub>4</sub> Regimens for Women with Eclampsia: Message from the Collaborative Eclampsia Trial.

### Suraiya Begum<sup>1</sup>, Syed Ershad Ali<sup>2</sup>

### **INTRODUCTION**

Eclampsia remains a rare but serious complication of pregnancy, estimated to complicate around 1 in 2000 in Europe and other developed countries (Douglas & Redman 1992) and from 1 in 100 to 1700 deliveries in developing countries (Crowther 1985). Eclampsia is associated with 10% of maternal deaths and approximately 50000 women die each year having had an eclamptic convulsion (Dully 1992).

For decades obstetricians around the world have debated the merits of anticonvulsant treatments in eclampsia. Magnesium sulphate was first used in the treatment of puerperal eclampsia in 1925. Pritchard published his initial experience with MgSO<sub>4</sub> in 1955 and this was followed by several other large observational studies. The first two randomized trials of anticonvulsant treatment in eclampsia were published in 1990. In these studies magnesium was compared with diazepam and phenytoin. One further study comparing magnesium with lytic cocktail was reported in 1994. Collectively these trials included less than 170 women. All these trials failed to reach any meaningful conclusions because of small sample sizes. In June 1995 the results of the Collaborative Eclampsia Trial was reported in the Lancet. The significance of this trial lies not just in the results which provide compelling evidence in favour of magnesium sulphate but in the fact that a study of this size involving 1687 women in nine developing countries was attempted and successfully completed. This was without doubt an awesome achievement and a tribute to the steering group and the collaborators.

ADVANTAGES OF MAGNESIUM SULPHATE (MgSO<sub>4</sub>)

In women with eclampsia it is standard practice to use anticonvulsant to control the immediate fit and prevent recurrent seizures. In 1991 only 2% of obstetricians in the U.K prescribed magnesium sulphate for seizure prophylaxis. This situation changed recently with the publication of the Collaborative Eclampsia Trial, involving nearly 1700 women with eclampsia. In this study roughly half the women were randomised to receive either magnesium sulphate or diazepam and the other half were randomised to MgSO<sub>4</sub> or phenytion. In the diazepam arm of the trial women allocated MgSO<sub>4</sub> had a 52% lower risk of recurrent convulsions than those on diazepam. In the phenytoin arm women allocated magnesium had a 67% lower risk of recurrent convulsions than those on phenytoin. There is now for the first time compelling evidence in favour of MgSO<sub>4</sub>, rather than diazepam or phenytoin, for the treatment of women with eclampsia. So the Collaborative Eclampsia Trial provides information about the advantages of MgSO<sub>4</sub> are as follows-

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Firstly, the collaborative trial provides evidence that  ${\rm MgSO_4}$  reduces the risk of recurrent seizures compared with diazepam, and phenytoin. Moreover the continued use of phenytoin in eclampsia can not be justified; not only was it found to be particularly ineffective in preventing recurrent seizures, the drug was also associated with an increase in maternal morbidity compared with  ${\rm MgSO_4}$ .

Secondly, MgSO $_4$  has effects other than inducing cerebral vasodilatation and antagonising the excitatory glutamate N-methyl-D aspartate receptor that are likely to be beneficial in eclampsia. MgSO $_4$  increases production of the endothelial vasodilator prostacyclin, inhibits platelet activation and protects endothelial cells from injury mediated by free radicals. There is also evidence that magnesium dilates human uterine arteries.

Thirdly, the use of MgSO<sub>4</sub> is not associated with detrimental effects of the neonate. Recent evidence has also suggested that in utero exposure to magnesium is associated with a reduction in the prevalence of cerebral palsy in infants born weighting less than 1500 gm.

### TREATMENT REGIMENS FOR MAGNESIUM SULPHATE (MgSO<sub>4</sub>)

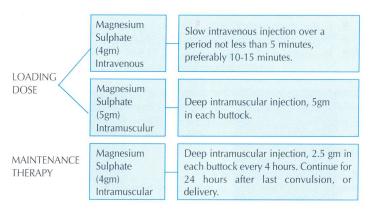
There were two separate regimens for giving  $MgSO_4$  and clinicians at each centre chose which they would use .

Both regimens were based on current recommendations and reflected clinical practice in the collaborating centres. An initial intravenous loading dose was followed by 24 hours by either an I/V infusion or regular intramuscular I/M injection.

### **Intramuscular Regimen**

This was administered as described by Pritchard & colleagues. A loading dose of 4 gm I/V (usually in 20% solution) over 5 minutes minimum, preferably 10-15 minutes was followed immediately by 5gm in a 50% solution as a deep I/M injection into the upper outer quadrant of each buttock.

Maintenance therapy was a further 5 gm I/M every 4 hrs, continued for 24 hours after the last fit.

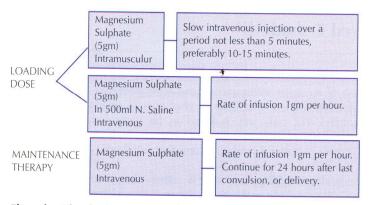


Flow chart for the intramuscular (I/M) magnesium sulphate regimen.



### **Intravenous Regimens**

The intravenous regimen was as described by Zuspan<sup>6</sup>. A loading dose of 4gm I/V was followed by an infusion of 1 gm/hour continued for 24 hours after the last fit. In most centres, the rate of infusion was controlled manually.



Flow chart for the intravenous (I/V) magnesium sulphate regimen.

### RECURRENT CONVULSIONS

In both the intramuscular and intravenous regimens, if convulsion recur a further 2-4 gm was given intravenously over 5 minutes.

There was no evidence from the <u>Collaborative Trial</u> of any difference between the intramuscular and intravenous regimens in their effects on recurrent convulsions. However intramuscular injections are painful and are complicated by local abscess formation in 0.5% of cases. The intravenous route is therefore preferred.

It is rational and sensible for clinicians to adopt the treatment regimens for MgSO<sub>4</sub> used in the Collaborative Eclampsia Trial. This has the considerable practical and economic advantage that serum monitoring is not required. Although some authors have advocated 2gm/h for I/V maintenance therapy, this should not be considered for routine practice until it has been adequately evaluated in comparison to intravenous regimens described here. It is quite plausible that higher doses will increase the hazards without any increase in the benefits associated with the use of magnesium sulphate when given as described in the trial.

### MAGNESIUM TOXICITY AND THEIR MANAGEMENT

The following guidelines were provided for management of the potential complications of MgSo4-

### 1. Respiratory arrest

To stop magnesium therapy. To give 1 gm calcium gluconate I/V -The antidote for magnesium toxicity. To intubate and ventilate immediately. Ventilation should be continued until the resumption of normal spontaneous respiration.

### 2. Respiratory depression

- To stop magnesium therapy To give 1 gm calcium gluconate I/V
- To give oxygen by mask To maintain airway and
- To nurse in the recovery position

### 3. Absent patellar reflexes

If respiration is normal, further doses of MgSO<sub>4</sub> to be withheld until the reflexes return, if respiration is depressed then management to be as in 2 above. MgSO<sub>4</sub> can be restarted if considered necessary once reflexes have returned but at a reduced dose unless there have been further convulsions.

### 4. Urine output-< 100 ml in 4 h.

If there are no other signs of magnesium toxicity, the next I/M dose of MgSO $_4$  to be reduced to 2.5 gm or the I/V infusion to 0.5 gm/h . Particular attention to be paid to fluid balance and blood loss.

### MONITORING DURING MAGNESIUM SULPHATE (MgSO<sub>4</sub>) THERAPY

MgSO<sub>4</sub> has no sedative effect, so on recovering from the post ictal phase the woman should be alert and oriented. However magnesium can depress neuromuscular transmission at the myoneural Junction, causing muscular paralysis as serum levels increase. The rationale for clinical monitoring is that loss of the patellar reflex (knee jerk) precedes respiratory depression and respiratory arrest. Frequent monitoring of the patellar reflex and respiratory rate are therefore essential if complications of therapy are to be minimised. Also magnesium is cleared by the kidney. So if renal function is impaired, less magnesium will be required. The therapeutic serum level needed to prevent convulsions is generally believed to be between 2 and 4 mmol/L. Loss of patellar reflexes occurs above 5 mmol/L and respiratory depressions at levels above 6 mmol/L. In the Collaborative Trial serum magnesium levels were not measured but data from Sibai et al. would suggest that levels were consistently less than 2 mmol/L with this regime. So to measure the serum magnesium was not essential and was not observed in the trial and the protocol for monitoring would be predominantly, clinical and to be based on ensuring that respiration is not depressed, the patellar reflexes are present and renal function is adequate. These can be monitored hourly with recourse to serum levels if there is clinical concern or if further seizures occur.

### Summary of clinical monitoring during administration of $MgSO_4$

Only to give the next I/M dose or only to continue the I/V infusion if

- \* Respiratory rate > 16/min,
- \* Urine output > 25 ml/h,
- \* Patellar reflexes are present.

### **CONCLUSION**

The Collaborative Eclampsia Trial provides compelling evidence that MgSO<sub>4</sub> is superior to diazepam and phenytoin for the treatment of eclampsia. It is rational and sensible for clinicians to adopt the treatment regimens for MgSO<sub>4</sub> used in the collaborative trial while prejudice may prevent obstetrician from evaluating magnesium but they can no longer justify not using it. It should be feasible to make it clearly and readily available for the care of all women regardless of where they live in countries until now magnesium sulphate has not been routinely used for eclampsia, there should be some regional or national strategy to ensure affordable and regular supplies.

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### **Profession Joke**

A man speaks frantically into the phone, "My wife is pregnant, and her contractions are only two minutes apart!"

"Is this her first child?" the doctor queries.

"No, you idiot!" the man shouts, "This is her husband!"

# Role of Radiology and Imaging in the Diagnosis of Acute Abdominal Conditions.

### Md. Abu Yusuf Miah

### INTRODUCTION

In our day to day practice we have to face many of the acute abdominal conditions. As we know acute abdomen means the patient complaints of an acute attack of pain in abdomen which may occur suddenly or for a period of several hours and gradually becoming worse and demands an urgent diagnosis, treatment and even surgical intervention. Early accurate diagnosis is essential for proper management. A careful history and examination findings are very very essential for the radiologists also to give a comment about the cause of the disease.

Though not all, many of the cases may be diagnosed without the help of any diagnostic tool. Some cases may be problematic. In those cases Radiology and Imaging can help a lot in determining the proper diagnosis.

### Usual radiological tools we use are

- 1. Plain film of abdomen and Chest P.A in erect posture
- 2. U.S 3. C.T.Scan (Occasionally) 4. MRI (Rarely)

### What we see in plain radiography

- (a) In most acute abdominal conditions the radiological diagnosis depends on gas patterns e.g. distribution of gases in dilated & non-dilated bowel, presence of gas inside or outside the bowel lumen.
- (b) Radiopaque shadows (c) Fluid and gas levels.

### What are the radiographic techniques

1. Supine abdomen: We can see the distribution of gas and calibre of the bowel and may show displacement of bowel gases by a mass.

- 2. Erect abdomen: To see fluid levels and free gases. Usually 3 or more small bowel fluid levels longer than 2.5 cm are abnormal.
- 3.Left lateral decubitus: Patients lying on their left side and the X-ray beam is horizontal. Patients who are unfit to sit or stand for an erect film, it is the projection of choice to show a small pneumoperitonium. In this projection free gas may be trapped between the edge of the liver and the lateral abdominal wall, or sometimes in the pelvis where it is the highest point specially in case of female.
- 4. Chest X-ray: Why?
- (a) Erect chest film is the best film to show the presence of a small pneumoperitonium.

### Dr. Md. Abu Yusuf Miah, MBBS, DMRD,

Asst. Prof. of Radiology and Imaging, DMCH, Dhaka.

- (b) A number of chest conditions which may mimic acute abdomen:
- 1. Lower lobar pneumonia 2. Myocardial infarction
- 3. Pulmonary infarction 4. C.C.F 5. Pericarditis
- 6. Leaking or dissecting thoracic aortic aneurysm 7. Pneumothorax
- (c) Acute abdominal conditions may be complicated by chest pathology: e.g. pleural effusion frequently complicate acute pancreatitis, following prolong vomiting in elderly patients in intestinal obstruction, there may be pneumonia or heart failure. Abdomen may be compared with a pandora's magic box. There are many causes of acute abdomen of which some are common which we face at our day to day practice. I want to show some of the radiological findings system wise.

### Common acute abdominal conditions found in relation with-

### G.I.Tract

(A)Acute appendicitis: Commonest acute surgical condition in the developed world. No role of radiography. But can be done to exclude other causes.

Direct visualisation by HRSG Puylaert JB graded compression technique.

The fat and the bowel loops are displaced by compression. Inflamed appendix appears to be a thick walled incompressible sausage like tube with concentric layers in transverse plane . Perifocal oedema is also present. Fluid is also seen in the lumen of appendix. It is elongated tube with one end blind. When wall thickness exceeds 6 mm it is suggestive of inflammation.



Fig. no.1-Shows inflamed appendix in transverse plane.

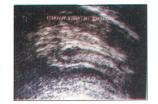


Fig. no.2-Shows inflamed appendix in long axis.

(B)Pneumoperitonium: Demonstration of small pneumoperitonium is very essential. Most of the cases the cause of the pneumoperitonium will require emergency surgery.



Fig. no.3-(a) Erect chest film-Free gas seen under both domes of diaphragm.



(b) Abdomen erect , free gas under the domes of diaphragm.



- (C) Pseudopneumoperitonium: A number of conditions which simulate pneumoperitoneum e.g.-
- 1. Chilaiditis syndrome -Distended bowel between liver and right. dome of diaphragm
- 2. Sub diaphragmatic fat-omental fat
- 3. Curvilinear pulmonary collapse





Fig. no.4- -Abdomen supine -A triangular collection of free gas in the sub - hepatic region.

Fig. no.5--A band of curvilinear pulmonary collapse with a crescent of normal lung beneath it- simulating Pseudo -pneumoperitonium.

(D)Intestinal obstruction: Dilation of bowel occurs in

- 1. Mechanical intestinal obstruction 2. Pseudoobstruction
- 3. Paralytic ileus 4. Air swallowing
- 5. Several other conditions.

Radiological differentiation depends mainly on the size, mucosal appearance and the distribution of loops of bowel. The diagnosis of intestinal obstruction depends on the demonstration of dilated loops of bowel proximally with non-dilated or collapsed bowel distal to the presumed point of obstruction.

(i)Acute gastric dilatation:

Dilatation of the stomach can be caused by 4 main groups of conditions--

(a)Mechanical gastric outlet obstruction may be a sequel of peptic ulcer or a carcinoma of the antrum.

(b)Paralytic ileus-This group conditions is frequently referred to as acute gastric dilatation.

(c)Volvulus and air swallowing are usually uncommon conditions.

### (ii)Small bowel obstruction:

Usual causes are the bands, adhesions and strangulations. Complete obstruction of the small bowel usually causes small bowel dilatation with accumulation of both gas and fluid and a reduction in calibre of the large bowel. Plain film changes in small bowel obstruction may appear after 3-5 hours if there is complete small bowel obstruction and such changes are usually marked after 12 hours. In incomplete obstruction early films may be normal.



Slide no.6--Shows acute gastric dilatation



Slide no. 7-Shows Small bowel obstruction: Multiple dilated loops and air fluid level. A very small amount of gases are noted in the large bowel.

### Differentiating points between a small and large bowel obstruction:

		Small bowel	Large bowel
1.	Distribution of loops	Central	Peripheral
2.	No. of Loops	Many	Few
3.	Volvulae connivantes	Present in jejunum	Absent
4.	Haustral markings	Absent	Present
5.	Diameter	3-5 cm	Large
5.	Radius of curvature	Small	Large
7.	Solid feces	Absent	Present

String of beads sign:

What is that: In dilated small bowel which is almost completely filled with fluid. Small bubbles of gas may be trapped in rows between the Volvulae connivanties on horizontal ray films- this is known as String of beads sign. This sign if present is virtually diagnostic of small bowel obstruction.

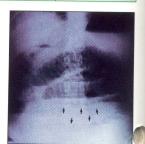


Fig. No.8- -Another slide of small bowel obstruction showing String of beads sign.

This slide shows the feature of gall stone ileus. Here you see multiple dilated loops of small bowel with a band of gas within the CBD.Gall stone ileus is a mechanical obstruction caused by the impaction of one or more gall stones in the intestine, usually in the terminal ileum and rarely in the duodenum.



Signs of gallstone ileus

Fig. No.9-Gall stone ileus.

a) Gas within the bile duct b)Features of small bowel obstruction c)Abnormal location of gallstone d)Other previous findings which coincides biliary stone.

What are the other causes of gas in the biliary tree:

a)Physiological if the sphincter is laxed. b)Following biliary surgery c)Malignant fistula d)Perforated peptic ulcer into the bile duct.

Its a case of intussusception is seen in children under 2 years of age. In children it usually commences in the ileum as the result of inflammation of the lymphoid tissue and tends to be associated with mesenteric adenitis. The enlarged lymphatic patches are forced into the ileum by peristaltic movement and acting as a tumour. So one part of the ileum is pushed into the other and causing intussusception. In adults intussusception is invariably caused by a tumour of bowel. A loops of dilated small bowel and barium enema examination is there is a soft tissue mass in the frequently required to establish a definite diagnosis and sometimes also relieves the patient.



right iliac fossa.



Fig. no. 10 (b)

Fig. no. 10 (c)

Contrast enema examination of large\*gut of a baby shows the intussusception producing a concave defect in the head of the contrast column. Sometimes contrast medium may pass beyond this, causing the well known coiled spring appearance.

(iii) Large bowel obstruction:

Usual causes are the

- a) Carcinoma -60% is situated in the sigmoid colon
- b) Diverticular disease c) Volvulus of the colon.

Key to the radiological appearance of the large bowel obstruction depends on the state of the competence of the Ileocaecal valve. The obstructed colon invariably contains large amounts of air and can usually be identified by its location and by the presence of haustral markings.

Fig. no.11-

Fig. no. 11. Shows hugely dilated large gut. Its a case of sigmoid volvulus. A haustral loop of sigmoid is seen rising out the pelvis in the shape of an inverted 'U'. Dilated haustral colons are present on the two sides of the volvulus.

When both small and large bowel dilatation are present in a case of large bowel obstruction, the radiographic appearance may be identical to those of a paralytic ileus.

Paralytic ileus causes when intestinal peristalsis ceases and as a result fluid and gas accumulates in the dilated bowel. It is frequently found in cases of peritonitis and in the post operative cases. Along with the radiological findings, history and clinical signs are helpful in differentiating between large bowel obstruction& paralytic ileus.





Fig. no.12--This film shows generalised dilatation of both small and large bowel and its a case of paralytic ileus.

Acute pancreatitis: Clinical diagnosis may be difficult in the initial stage. Other acute abdominal conditions such as perforation, acute cholecystitis, acute peptic ulcer have to be included in the differential diagnosis. A large number of radiological signs have been described, most of them are non-specific. USG and CT are the diagnostic modality.

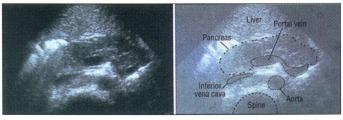


Fig. no.13--Shows the transverse scan of normal pancreas and its duct.

The normal pancreas has about the same echogenecity as that of liver but its echogenecity increase with age. When we scan the pancreas we usually identify the following anatomical landmarks:

- 1. Aorta
- 2. Superior mesenteric artery
- 3. Superior mesenteric vein
- 4. Liver etc.

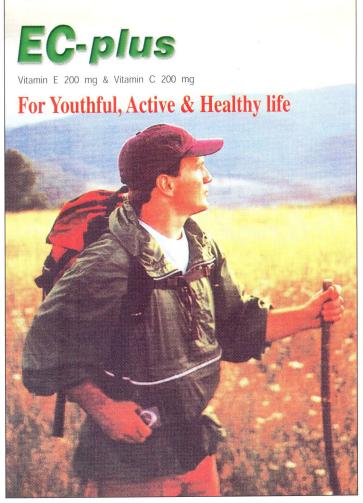
Average diameter of the head of the pancreas is 2.8 cm. body 2 cm and tail 2.5cm, duct diameter less than 2mm.

acute pancreatitis diffusely pancreas enlarged and oedematous which is hypoechogenic in comparison with the liver parenchyma. Diffusely irregularly enlarged hypoechogenic pancreas may also seen in acute pancreatitis when it is superimposed on chronic pancreatitis. C.T. is the investigation of choice for such cases.



Fig. no.14- -Shows diffusely enlarged and oedematous Pancreas

Rest of this article will be published in next issue of "The ORION".





# Fibrodysplasia Ossificans Progressvia in a Nine Year Old Boy.

# A.F.M. Ruhal Haque<sup>1</sup>, A.I. Choudhury<sup>2</sup>, Shafiqul Alam<sup>3</sup>, Md. Masum Kabir<sup>4</sup>

A nine year old boy presented with a five year history of small swellings on his back together with restriction of movements of his neck, deformity of his shoulders and elbows and restricted movement of both upper limbs. He was unable to feed himself or to manage his toilet. His Father reported that his son had developed multiple painful soft swellings over the back of his chest associated with intermittent pyrexia and pain at the age of four years. He also had congenital short great toes.



Fig -1



Fig -2

On examination, there were 2cm x 2cm and 1.5cmx1cm irregular fixed hard swellings over the inferior angle of his left scapula and the thoracic spine. The skin was healthy and free from the masses. Neck flexion was half the normal and there was no neck extension. Lateral flexion and rotatory movement in both directions was restricted to about one-third of normal. There was only 50° of passive abduction of his right shoulder and no movement between the scapula and the chest wall. Internal rotation of his right shoulder was 40° and external rotation 20°. His left shoulder had 40° of abduction and internal rotation was 50° with 5° of fixed internal rotation. Scapulo-thoracic movement was nil. Left Elbow- 90° extension lag with further flexion to 140°, pronation and supination 10° on each side; Right Elbow- flexion 0°-80° pronation and supination restricted to 5°. Wrist and finger movements were normal. All his other joints moved normally with the exception of slight restriction of movements of his thoracolumbar spine. Radiographs of neck and shoulder revealed heterotrophic bone formation. In our patients cervical radiograph shows heterotropic bone formation over the ligamental nuche (Fig. 3 Arrow). A complete blood count and blood chemistry showed no significant abnormalities.

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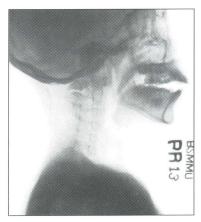


Fig -3: X-ray cervical spine

### Discussion

Fibrodysplasia Ossificans Progressvia is a rare genetic disease where ectopic bone forms in muscles, tendons, ligaments and other soft tissue.

The label of Myositis Ossificans Progressvia was changed in 1970s to Fibrodysplasia Ossificans Progressvia as bridges of bone form across the joints in a characteristic pattern. There is progressive restriction of joint movements. Fibrodysplasia Ossificans Progressvia is a disease in which the body produces extra bone that immobilizes the joints of the body. Children with Fibrodysplasia Ossificans Progressvia appear normal at birth with the exception of congenital short great toes¹. During the 1st or 2nd decade of life painful fibrous nodules appear over the neck, back and shoulders and these gradually ossify.

At present there is no specific treatment or prevention for Fibrodysplasia Ossificans Progressvia. Our patient show all the characteristic features of Fibrodysplasia Ossificans Progressvia in early childhood. The presence of short great toes at birth (Fig.1) and ectopic bone formation over the back (Fig.2) are typical. The gene or genes that are responsible for fibrodysplasia ossificans progressvia are unknown. But over expression of bone morphogenic protein 4 (BMP 4) and its messenger RNA in cells are detected from patients with Fibrodysplasia Ossificans Progressvia. The gene for BMP 4 has been located in chromosome 14q22-q23 and Fibrodysplasia Ossificans Progressvia is inherited as an autosomal dominant<sup>2</sup>.

Genetic engineering is developing fast, there is hope that such diseases which is obscure will be curable through such maneuvers which are yet to be developed.

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# Medi Image



The Mango - Poison Ivy Connection

A 27 year-old man had a pruritic and eczematous rash for three days. One week earlier, he had peeled a mango, become distracted by a telephone call, and rested his left hand on his right leg. Three days later, contact dermatitis became apparent. When much younger, the patient had been sensitized to poison oak and poison ivy; the sap of the mango rind contains oleoresins that cross-react with the oleoresins of poison ivy. The rash resolved after one week of treatment with topical corticosteroids.

# Medi Tips

Rectal sweep for hidden lesions

When performing a digital rectal examination, hook the examining finger posteriorly over the puborectal muscle and sweep the posterior lower rectum. Small tumors or polyps can be hidden in this region and may be missed. During finger insertion, ask the patient to bear down (Valsalva's maneuver). Straining relaxes the anal sphincter and puborectal muscle and allows insertion of the finger with less discomfort. A little lubricant is also helpful.

Wrestle not ....

Children often resist the administration of a topical nasal medication. However, if the medication is given while they are sleeping, there is no need to "wrestel" them.

Help parents win the bedtime battle

No matter how loving the parents, they have a limit for tolerating the whiny little voices of toddlers. Bedtime often becomes a game for children and a war for parents as little feet keep pattering down the hall. The result is always frustration, often angry words, and sadly sometimes even child abuse. A regular early bedtime is good for children-and for the parents, who need quiet time to rest, think, and regroup. Suggest a happy bedtime ritual-a bath, listening, story time, and a hug. That's it. Then, every time a youngerster gets up, the parent should whisk him or her back to bed immediately-without begging, coaxing, or a debate and certainly without more drinks, stories, or other rewards for getting up. Everyone wins with a happy bedtime routine.

No anesthetic eyedrops

Anesthetic eyedrops should not be used when removing a conjunctival foreign body. The patient should be able to feel relief after removal, thereby confirming the diagnosis. Also, because anesthetic eyedrops inhibit reepithelialization of the cornea and may lead to perforation, they should never be sent home with a patient. Eye pain can be controlled with oral analgesic medications.



# **Medi News**

### News from Internet/Journals

### **MEDICINE**

### A Fruit that Fights PMS

As many women know, <u>Premenstrual Syndrome</u> better known as PMS, is difficult to treat. But some relief may be in sight. According to a report in the January 20 issue of the <u>British Medical Journal</u>, the fruit of the chaste tree,

Vitex angus castus, proved effective in easing the sometimes debilitating symptoms of PMS. Researchers at the Institute for Health Care and Science in Huttenberg, Germany, studied 170 women diagnosed with the syndrome. Over the course of three menstrual cycles, 86 of the participants received castus extract; the other 84 received

### What is already known on this topic

- Women with the premenstrual syndrome are usually seen by primary care physicains and are a therapeutic challenge to general practitioners.
- Treatemnt of the causes is often impossible, and current treatment of the full range of symptoms is inadequate.

### What this study adds

- Agnus castus is effective in the treatment of the premenstrual syndrome.
- The effects were confirmed by women's self assessment and by the doctor's evaluation.
- Over half the women had a 50% or greater improvement in their sympotms.
- Patient acceptance was high, side effects are few and mild.

place-bos. The team assessed six symptoms-irritability, anger, mood alteration, headache, bloating and breast fullness-at the start of the first cycle and then at the end of the third cycle.

they found those women who had taken the agnus castus extract, experienced significant improvement in all the symptoms except bloating. Indeed, more than half the women had at least a 50 percent improvement in their symptoms, and side effects were few and mild. "Dry extract of agnus castus fruit," the researchers conclude, "is an effective and well-tolerated treatment for the relief of symptoms of the premenstrual syndrome."

www.bmj.com

### **New Compound Controls Weight Gain**

We've all heard scantily clad spokespeople make bogus claims about instant weight-loss supplements on latenight television. But in February 6, 2001, online edition of the *Proceedings of the* National Academy of Sciences, researchers describe what sounds like the real deal-for mice, anyway. Harvey Lodish and his colleagues of the Whitehad Institute for Biomedical Research have discovered a new compound that causes profound weight loss in mice fed an unlimited diet high in fat and sugar. The compound, called gAcrp30, is a fragment of the Acrp30 protein. Most weight loss drugs work by absorbing fatty acids in the intestine or by inhibiting the breakdown of fatty acids so that they are excreted rather than



Compound to control weight gain even after a cafeteria diet?

stored. In contrast, gAcrp30 actually causes muscle to burn fatty acids faster. Mice treated with the compound showed significantly reduced levels of free fatty acids, as well as lower glucose and triglyceride levels. Moreover, daily low doses of gAcrp30 enabled the mice to keep the weight off, despite their cafeteria diet. Though the results are promising, don't wait up nights looking for a phone number to call now. "Much further research is needed to determine whether this substance can be used in man as an aid in weight loss," Lodish remarks. "Though such a therapy is urgently needed by the many thousands of obese patients who suffer from many related health problems such as diabetes".

### **How Breast Cancer Starts and Spreads**

New research is revealing breast cancer's deadly secrets, focusing on how the disease starts and later spreads. One published in February 2, 2001, issue of the journal Nature has identified a pivotal event before breast cancer first buds. Thea Tlsty of the University of California at San Francisco and her colleagues ran cell culture studies of breast epithelial cells. The work revealed that those cells, CNRI/Photota more often than other cell types, slip past a built-in



Tharmogram showing breast cancer and its metastasis (vellow).

regulatory control on cell growth called **senescence**. And when they do escape senescence, the epithelial cells almost always develop genetic changes associated with the very beginnings of breast cancer.

The team was further able to identify molecular markers that indicate when breast epithelial cells have escaped senescence, and how far they have progressed in accumulating damaging genetic changes. Eventually these markers could be used to target cells for cancer prevention and therapy early on. "Figuring out why mutations occur—never mind what they actually are—could provide a new means for intercepting the disease before it gets started," Tlsty says.

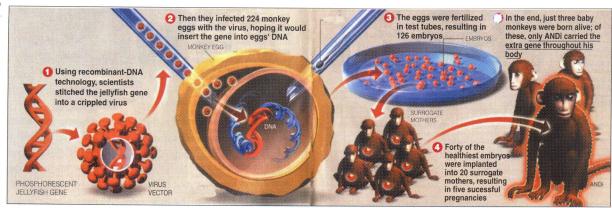
A second study from scientists at Massachusetts General Hospital appears in February, 2001 issue of *Nature Medicine* reveals a remarkable mechanism by which breast cancer spreads to the lymph nodes and lungs. Researchers long thought that the cancer reaches the lymph nodes via the lymphatic system, but exactly how the cancer got from the tumor to the lymphatic system remained unknown. The new work suggests that tumors actually develop their own internal lymphatic systems. That system then hooks up with the surrounding lymphatic vessels, providing a highway by which the tumor cells can metastasize. Important to the highway building is a protein known as VEGF-C, which encourages lymphatic vessel growth. "This could provide a new target for therapy," principal investigator Michael Detmar remarks. "By blocking the interaction of VEGF-C with its receptor on the lymphatic system we may be able to block metastasis from occuring," he concludes.

### **GENETICS**

### Team to attempt human cloning

An international group of fertility experts has announced details of their plans to be the first scientistis to clone a human being. The group, meeting in Rome, discussed their strategy for human and so-called therapeutic cloning to help tackle a range of degenerative diseases. The plan has come under heavy fire from scientific and religions camps and has been attacked as "grotesque" by the Vatican. The team includes Italian obstetrician Severino Antinori, who became famous for helping a 62-year-old woman give birth. Antinori said. "Cloning creates ordinary children. They will be unique individuals, not photocopies of individuals." Bishop Elio Sgreccia, head of the John Paul II Institute for Bioethics at Rome's Gemelli hospital, said human cloning raised profoundly disturbing ethical issues. "Those who made the atomic bomb went ahead in spite of knowing about its terrible destruction," he said before the cloning meeting started. "But this doesn't mean that it was the best choice for humanity." Dr lan Wilmut, who created Dolly, the world's first cloned sheep,

said. It took 277 tries to get it right. Other cloning attempts have ended in malformed animals and experts say the technique fails in 97 percent of cases. Antinori and his partner, U.S. scientist Panayiotis Zavos, say they plan to carry out the first operation in an unidentified Mediterranean country, starting in Octorber. Zavos, who



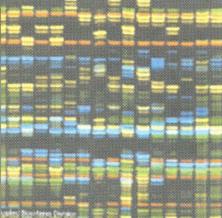
ANDi the rhesues monkey was conceived and born with an extra gene taken from a jellyfish. Here's how it was done: (modefied from Time)

announced the proposal in Lexington, Kentucky, in January, told the symposium on Friday that he had been flooded by e-mail from couples seeking to have children through cloning. "Dolly is here and we are next." he said. Last year, Britain proposed allowing human cells to be cloned for research purpose while other Europen countries, including Spain and France have banned human cloning altogether. Antinori first attracted controversy when he helped a 62-yearold woman to have a baby eight years ago by implanting an egg in her womb. In the cloning experiment, cells from an infertile father would be injected into an egg, which is then implanted in the mother's uterus for the pregnancy. The resulting child would have the same physical characteristics as his father and infertile parents would not have to rely on sperm donors. The chairman of the Human Fertilisation and Embryology Authority, Ruth Deech, said: "There are lines you should not cross. You have to consider humanity as a whole and say there are limits beyond which we should not go for the sake of future generations and for respect for the autonomy and dignity of present generations."

### The Human Genome Unravelled

The first detailed look at the human genome may have revealed few surprises to scientists, but still leaves numerous questions open as to how the sophisticated human body can be built from around 30,000 genes - a relatively low-number, only fewer than the amount in a grain of rice and only several hundred more than a mouse.

between humans and worms lies in the functions of some human genes and



This gel scan showing the arrangement of chromosomes within a cell that allows experts to take a closer look at the genetic make-up of each individual.

the proteins they control.

basis for the concept of race. Humans too, do not differ much in number of genes to worms, or even fruit flies. Researchers believe the key to the differences

Apart from an astonish-

ingly low number of

genes, the recent unvei-

ling of genetic data

showed that the biolo-

gical difference between individuals amounts to a

fraction of the three

billion letters in the

human genetic code-

proof that humans are

very much alike and that

there is no scientific

The first analysis of human genome was published a few days ago in the scientific journal *Nature* by the **Human Genome Project**, a public consortium of scientists from the United States, Britain, France, Germany, Japan and China. It can now be sighted on the net, in accordance with a similar publication by the US company Celera Genomics in the scientific journal Science.

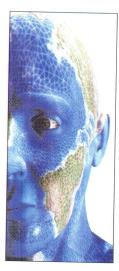
The recent unveiling is the result of a decade of hard work on discovering the myth of the human gene. However, scientists still have a long way to go on their search for curse to numerous still unfathomable illnesses, whether cancer, heart disease of addiction.

www.dw.elle.de/top story

### First Human Clock Gene Found

Late for work again? Some people have the opposite problem: on average, these morning larks fall asleep at 7:30 p.m. and wake up at 4:30 a.m. Their largely inherited and unusual sleeping pattern—one first discovered in 1999-is called Familial Advanced Sleep Phase Disorder Syndrome, or **FASPS**. And by studing a large family with the condition, researchers from the University of Utah have uncovered the first human gene that controls circadian rhythm—the roughly 24-hour-long sleep-wake cycle of many animals.

Louis Ptacek, Ying-Hui Fu and others reported in Science Express, an online advance publication of Science articles, that most of the affected family members harbor a mutation in a gene called hPer2, a clock gene that helps regulate the circadian rhythm. Alterations of the equivalent gene in fruitflies or mice makes them, too, sleep and wake earlier than normal. The mutation in the hPer2 gene changes a single amino acid in the protein,



meaning that another protein, a kinase, can no longer attach to it a regulatory phosphate group. This missing group probably leads to a more rapid accumulation of hPer2 protein in the cell and results in an advanced sleeping pattern. Of interest, a mutation in the kinase itself leads to a FASPS-like phenotype in golden hamsters.

One branch of family members in the study did not show a, mutation in hPer2. But these individuals were, on average, also less extreme "morning larks" than their affected relatives. According to Ptacek, they probably carry other genetic variations that might be common in the general population. "There are plenty of morning larks those go undetected", he says. Also, other families with FASPS do not have the hPer2 mutation, and studies of their DNA will probably reveal more genes involved in circadian rhythm

control. Further down the line, genes might surface that make people sleep longer in the morning. The proteins encoded by these genes, scientists hope, could serve as drug targets to help people with transient sleeping problems that are the result of, say, jet lag or working nightshifts.

Science Express

### **PSYCHIATRY**

### **Passing On Panic and Depression**

Okay, go ahead and blame some of your neuroses and phobias on your parents, a new study in the January 2001 American Journal of Psychiatry says. Lead author Joseph Biederman, a psychiatrist at Massachusetts General Hospital, reports that parents suffering from panic disorder, major depression or both are more likely to have children with certain types of disorders. Knowing this, he says, may help clinicians treating adults identify children at risk for psychiatric and behavioral problems. "It's a matter of being aware," Biederman notes. "Recognizing that children at a

very young age can be at high risk for emotional distress can go a long way toward doing something for them early in life."

The study looked at four sets of children: those with parents diagnosed with depression; those with parents diagnosed with panic disorder; those with parents



Go ahead and blame some of your neuroses and phobias on your parents....

diagnosed with both depression and panic disorder; and those with parents having neither condition. When they compared the groups, slightly different patterns emerged. Parental panic disorder was associated with an increased risks for panic disorder and agoraphobia in children. Parental depression was linked with increased risks for social phobia, major depression, disruptive behavior disorders and poorer social functioning among children. And parental panic and depressive disorders were associated with increased risks for separation anxiety disorder and multiple anxiety disorders in children. "The presence of depression in families," Biederman concludes, "has quite a major impact in the offspring."

Scientific American, January 03, 2001

### **NEUROSCIENCE**

### If You're Happy and You Know It ...

Just as some people appear to have selective memories or selective hearing, a new brain imaging study reveals selective emotions of a sort. In February

2001 issue of Behavioral Neuroscience, Turhan Canli and colleagues of Stanford University report that personality traits can heavily influence the brain's response to emotional stimuli. In particular, extroverted people have stronger reactions to positive emotions, whereas neurotic people have stronger reactions to negative emotions. "Depending on personality traits, people's brains seem to amplify some aspects of experience over others," says co-author John Gabrieli.

The scientsts gave 14 healthy women aged 19 to 42 years a personality test to determine their levels of extroversion (defined as the tendency to be optimistic and sociable) and neuroticism (the tendency to be anxious, worried and socially insecure). Then they placed each subject in a functional magnetic resonance imaging (fMRI) scanner, and gave them photographs to look at: some pictures showed puppies, happy couples, ice cream and other scenes planned to evoke positive emotions, whereas the rest depicted crying or angry people, spiders, guns or cemeteries.

In response to the positive images, the women who scored high on extroversion showed increased activity in the frontal cortex, amygdala and anterior cingulate-all brain regions associated with emotional control. Women who scored low on extroversion, however, showed no similar increase. And those who scored high on neuroticism displayed heightened brain activity in response to the negative images. "All of the participants saw very positive and very negative scenes, but people's reactions were very different," Gabrieli notes. "One group saw the cup as being very full while the other group saw it as very empty."

Behavioral Neuroscience

### **PSYCHOLOGY**

### **Dissecting Happiness**

Although it might be nice to have piles of money or run with the in crowe, new research confirms that neither of these will provide that universally yearned for feeling of happiness. Rather, things like self-esteem and a sense of closeness with others appear to lead to ultimate satisfaction, according to a report in the February Journal of Personality and Social Psychology.

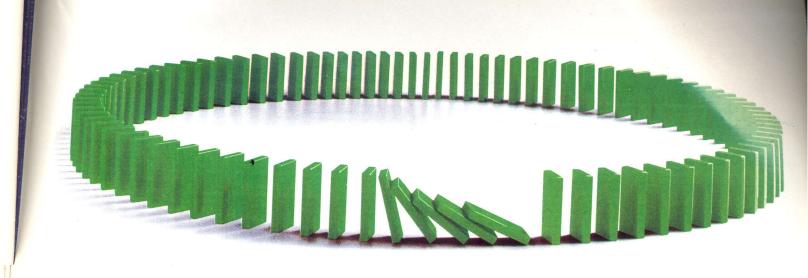
To ascertain which of the 10 basic psychological feelings people find most important, Kennon M. Sheldon, a University of Missouri-Columbia psychologist, and his colleagues conducted three studies of different groups of U.S. college students. Participants in When things go wrong people the first study were asked to describe the most may strongly wish for the safety...



personally satisfying event they had experienced during the last month. Those in the second group considered the same event, but from the last week. The third group of students reflected on the most satisflying event of the semester, and also the most unsatisfying event in that period. Results from the three groups proved fairly consistent, with autonomy, competence, relatedness and self-esteem toping the list of psychological needs.

Descriptions of the most unsatisfying event revealed that a lack of those four needs figured prominently, as did the lack of security. "It appears that when things go wrong," the authors note, "people may strongly wish for the safety and predictability that they often take for granted."

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