ept. 2003
**ACADEMY JOURNAL OF**
**APPLIED-BASIC MEDICAL SCIENCES**

**Published by :**
**ACADEMY OF APPLIED BASIC MEDICAL SCIENCES**
Corresspondence Address, Publisher/Editor : Dr. Janardan V. Bhatt, Dept. of Physiology,

Smt. NHL Mun. Medical College, V. S. Hospital Compound, Ellisbridge,
Ahmedabad - 380 006. Gujarat INDIA. Website : www.nhlmmcgym.com

**Volume 5**
**Sept. 2003** **ISSN 0972-4729**



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## INDEX

## *ATIONAL DRUG USE*


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Rational prescribing is appropriate prescribing. Appropriate prescribing is that which bases the choice of a drug on its effectiveness, safety and convenience relative to other drugs and takes cost into account only when those criteria for choice have been satisfied. When all these criteria are met with, it would be an ideal situation of 'Rational Drug Therapy'. But what is the scenario at present? About 75% of world's total consumption of drugs is in developed countries where 3/4th of world's population lives.
Millions of people suffer from lack of medicine and other millions use too many drugs. In developing countries, drug distribution system is not effective. Also there is a problem with use of drugs, both in writing a prescription and its compliance. Self-medication is also common. Prescribers are not utilizing drugs rationally and irrational drug use is far common than rational one.
Hence, knowing about 'Rational Drug Therapy' has become all the more important for medical practioners.

**v The five major questions for the Rational Use of Drugs are the following:**

1) What is it?
2) Why is it important?
3) Who are responsible?

4) How does irrationality occur?
5) What is the remedy?

**1) What is it?**
Rational Drug Therapy means the use of right medicine in the right manner (dose, route and frequency of administration, duration of therapy, etc.) in right type of patient at a right cost, i.e. the rule of 'Right'. Rational Drug Therapy also means using the drug when necessary (e.g. nitroglycerine in angina pectoris) and importantly, not using it when unnecessary (e.g. expectorant mixture in common cold). Hence the appropriate drug should be effective, safe and of acceptable quality and cost.

**2) Why is it important?**
All of us presume that, prescribers having learnt 'Pharmacology' during their M.B.B.S. course would be rational in selection and use of drugs during their practice. But, the reality is different. Irrational drug use is much more common than what we expect. Especially in third world countries like India, there are thousands of drug formulations available. There are many other factors also which account for irrationalities in the use of drugs.
To tackle this worldwide problem, 'WHO' (1985) held a meeting of experts and the problem of irrational drug use was discussed and corrective measures were suggested.

**3) Who are responsible?**

I) The prescriber
I) The producer
III) The controller
IV) The consumer

**4) How does irrationality occur?**

**I) The Prescriber-**

A) Overprescribing
B) Underprescribing
C) Incorrect prescribing
D) Irrational combinations
E) Improper diagnosis

**A) Overprescribing:** This includes prescribing more number of drugs than necessary or prescribing for longer duration or in dose higher than necessary. Polypharmacy or prescribing too many drugs is a very common practice.
**Drug categories commonly Overprescribed are:**

| | |
|---|---|
| Vitamins & tonics | Hematinics |
| Analgesics | Antispasmodics |
| Antacids | Antidiarrhoeals |
| Enzymes | Expectorants |
| Antihistaminics | Cold remedies |
| Antimicrobials | Steroids |
| Anabolics | Bronchodilators |
| Laxatives & purgatives | Sedative & hypnotics |

**Reasons for Overprescribing –**

Lack of unbiased drug information
No reorientation
Shortage of time & staff
Misguidance by industry
Fancy for "New Drugs"
Lure from Pharma Companies to prescribers.
Dictation by patients
Unethical practice and unhealthy competition

**Problems related to Overprescribing:**

1. Increased cost of therapy.
2. Poor compliance.
3. Emergence of resistant microorganisms.
4. Increased chances of drug interaction and adverse drug reaction.

**B) Underprescribing:** In developing countries this is due to nonavailability of drugs or due to inadequate stock of medicines. Hence prescriber is likely to give too little medicine and for shorter duration than necessary to each patient.

**Problems related to Underprescribing**:

1. Ineffectiveness of treatment.
2. Development of resistance to antimicrobials making it necessary to select second line drugs, which are expensive, thus increasing the cost of therapy.

**C) Incorrect prescribing:** Commonest types of incorrect prescribing are:

1. Drug is ineffective or doubtfully effective
   e.g. antimicrobials in sore throat
   (70-90 % of viral origin).
2. Drug is active but is administered in unsuitable
   circumstances. Given when not needed.
   Antimicrobials, vitamins and tonics are amongst the most misused drugs, but other drugs also are misused in this way.

**D) Irrational combinations:**
In the 12th list of essential drugs by WHO published in the year 2000, out of total 306 drugs, 'Fixed Dose Combinations' (FDCs) were only 21, while the picture is totally reversed when we look at the available market preparations. FDCs constitute 63% of drug formulations advertised in MIMS, India – March 2002. Obviously all these FDCs are not expected to be rational but are still being prescribed by the practitioners. Cough mixtures, multivitamins and analgesic mixtures are a few examples. Although correctly formulated FDCs have advantages in form of improved patient compliance (usual) improved efficacy and safety, there are many disadvantages also.

**Disadvantages of FDCs:**

1. FDCs lead to polypharmacy if all the ingredients are not necessary. This leads to increase in cost of therapy.
2. Alteration of dose of one of the active ingredients is not possible without alteration of dose of other drugs.
3. Pharmacokinetics of constituent drugs may differ which can pose the problem of frequency of administration of the formulation.
4. If 'Adverse Drug Reaction' (ADR) occurs, it is difficult to

withdraw the suspected drug alone. Sometimes the pre scriber may not be aware of all the active ingredients present in the formulation he is prescribing, which may make the situation worse.

**II) The Producer** — There is a great competition among the pharmaceutical industries for promotional activities. Drugs are promoted aggressively by many methods. There is a use of proprietary names. Inadequate quality control creates disasters; medical representatives may be giving half-correct information especially on toxicity and side effects. They give impressive handouts and persuade them. Free samples, gifts and even commissions are some of the few tactics used to allure doctors.
Advertisements in journals also play an important part in prescribing as they influence the selection of drug which otherwise should be on rational basis.

**III) The Controller** — Both the introduction of new drugs and rational use of drugs are regulated by Government agencies, Drug Controller's Office in India and Medical Council of India. But because of very poor organization and poor control over the industry, this cannot be efficiently carried out. Also there is no system of CME ('Continuous Medical Education') to educate the doctors.

**IV) The Consumer** – There are various demands of society and also of patients for a quick cure. Prescribing has a powerful placebo effect. It is prescribing which makes a clinical situation relatively medical. Health education of the consumer is poor. He has wrong beliefs that prevention can be achieved by drugs like tonics, vitamins, etc. These all are examples of plain irrationality. Because of free availability of over the counter (OTC) drugs and overpopularity of alternative medicine, self-medication with these drugs is common. There might be misinterpretation of information, which can lead to disastrous consequences.
Polypharmacy is a way of assuring that everything possible has been done. There might be a problem of communication between the patient and the prescriber or other health staff. All drugs prescribed may not be consumed and there may be poor compliance.
With growth of pharmaceutical industry and availability of large numbers of drugs having powerful effect, people throughout the world have great expectations for "**magic bullets**" or they expect "**a pill for every ill**". More the drugs, more is their misuse-which is greater in developed countries.
The main reasons of irrational prescription due to consumer factor are illiteracy, poverty, superstitious beliefs and unwanted priorities being given to useless factors.

**5) What is the Remedy?**

**Regulation**
**Education**
**Voluntary agencies**

**Ø REGULATION :**
Strict Statutory measures should be followed for malpractice. Basic condition of safety and efficacy must be fulfilled. Reregistration for practitioners should be introduced. CME ('Continuous Medical Education') is essential. Many of the drugs the practitioner prescribes were not available when he/she was as medical college student (failure of the doctor to keep up to date leads to inappropriate drug therapy). Moreover, blindly following the prescribing practices of teachers or colleagues continues this vicious circle of irrational prescribing. Hence, unbiased information about new drugs is essential to ensure their rational use. This can be in form of textbooks, drug bulletins, etc. CME programmes in form of seminars, conferences, workshops, educational TV programmes, etc. also help. With availability of computers, unbiased drug information can be available to practitioners on CD-ROM in all hospitals by a central drug information system. Prescription audit should be done. There should be a specific drug policy for achieving quality of prescriptions and marketing of drugs. Reimbursement of only the essential drugs may be carried out.

**Prescribing generic drugs:** Generic products are far cheaper than branded products. If policy of prescribing quality generic drugs is introduced at hospitals catering to poor patients, cost of therapy can be cut down drastically. Freedom of prescribing 'favoured brand' can restrict the way to generic prescribing.

**Prescribing essential drugs:** In a Report of World Health Assembly of 1975, the Director General reviewed the main drug problems facing the developing countries, to outline the possible new drug policies. The implementation of concept and use of essential drugs was one of the policies suggested to extend the accessibility and rational use of the most necessary drugs to populations, whose basic health needs could not be met by the existing supply system.
The essential drugs are those that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms. The selection of essential drugs would depend on the health needs and the on the structure and development of the health services of each country. Essential drug list can be drawn up locally and periodically updated with the advice of experts. WHO has published Model List of Essential Drugs, which has been revised several times over the last 20 years. The concept ensures both economy and rationality in the use of drugs.

**Ø EDUCATION -**
All of us know that training in pharmacology should ensure rational use of drugs in clinical practice. In addition to many factors mentioned earlier, training in pharmacology is also to some extent responsible because of its outdated nature, merely relying on rote memory and not including the training in the logical process of drug selection, the outcome of training in pharmacology is far from satisfactory. Hence, the doctor trained in this education system may not be in a position to practise rational drug therapy.
This needs to change in form of change in emphasis from basic facts only to therapeutic aspects, which includes process of drug selection, rational prescribing including instructions to the patient, etc. Experts all over the world and country have made efforts

in this direction. WHO has published "Guide to Good Prescribing" which is based on concept of 'P' Drugs. 'P' drugs are 'Personal' drugs somewhat similar to Essential Drugs at national/state level. This book describes the complete process of drug selection and prescribing in a logical manner. Teaching on these lines has started in many medical colleges, paving a way towards making future doctors who would be rational prescribers.

**Ø VOLUNTARY AGENCIES:**
Voluntary agencies can also play a role by organizing various movements by their Associations for use of rational drug therapy.

**To conclude,**
"Practicing rational pharmacotherapeutics is a part of what '**Good Doctoring**' is all about". This can be ensured by following the basic principles of 'Rational Drug Therapy' rather than deviating from them due to any reasons.

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## *A STUDY OF FUSION OF EPIPHYSES* OF ISCHIAL TUBEROSITY IN RELATION WITH AGE.


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**INTRODUCTION :**
Various works have been carried out to estimate the age from study of ossification centers and epiphyseal union in various bones, dentition etc. in India as well as in different parts of world. Very little work in this regard has been carried out in Gujarat State. Estimating age of a person, living or dead or of a bone, is a difficult, critical but important and crucial study required in various criminal and civil cases. The present study is an attempt to fill the gape in this field and provides some information about the ossification and epiphyseal union among the natives of Gujarat State.
The aims were to study the progress of union of epiphyses of Ischial Tuberosity in natives of Gujarat state of Hindu community of either sex, to study the progress of union of this epiphyses in relation to age, sex and physical development, progress of this union in relation with union of epiphyses of iliac crest.

**MATERIALS AND METHODS:**
Study was carried out at Forensic Medicine B.J.medical College, Ahmedabad. For the study students of first, second and third M.B.B.S. of both sexes were selected out of 17-18 to 21-22 year's age group.
Subjects were selected of either sex.

Subjects were selected from the Hindu community and as study was aimed to establish the age of epiphyseal union in persons from Gujarat state only those residing in Gujarat state since their birth were selected. For the date of birth of these subjects birth certificates, school leaving certificates or S.S.C. mark-sheets were considered as a documentary proof. Kuppuswamy's scale was considered for categorization of socio-economical classes.
Subjects selected were x-rayed. Total no. Of 50 students were x-rayed and examined for the study. Radiographs were studied for progress of epiphyseal union of Ischial Tuberosity.
Evaluation of epiphyseal union was carried out as follows.

0 = nonunion
+ = ¼ union
++ = ½ union
+++ = ¾ union
++++ = Complete union

**RESULTS :**
X-rays of 50 students were taken, collected and studied to estimate age from the degree of epiphyseal union of ischial tuberosity.
Table no.1 shows number of students in different known age group.
**TABLE: 1**

| **Age group in years** | **No. of boys** | **No. of girls** |
|---|---|---|
| 17-18 yr. | 3 | 2 |
| 18-19 yr. | 6 | 1 |
| 19-20 yr. | 10 | 4 |
| 20-21 yr. | 12 | 6 |
| 21-22 yr. | 4 | 2 |

**Table no.2** shows degree of fusion of epiphyses of ischial tuberosity in cases studied under different age groups.
*Here percentages are calculated for specific age group.

| **Agegroup in years** | **No. of cases studied** | **No. of cases showing various degrees of fusion** | | | | | **% of cases showing 50% or more union *** | **% of cases showing complete fusion** |
|---|---|---|---|---|---|---|---|---|
| | | O | + | ++ | +++ | ++++ | | |
| 17-18 | 05 | 2 | 2 | 0 | 1 | 0 | 20 | 0 |
| 18-19 | 07 | 2 | 2 | 2 | 1 | 0 | 42.86 | 0 |
| 19-20 | 14 | 0 | 3 | 3 | 6 | 2 | 78.57 | 14.29 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 20-21 | 18 | 0 | 0 | 3 | 7 | 8 | 100 | 44.44 |
| 21-22 | 06 | 0 | 0 | 0 | 0 | 6 | 100 | 100 |

| Age Groups | Total cases studied | [A] no. of cases showing complete fusion of ischial tuberosity | [B] no. of cases showing complete fusion of iliac crest | [C]% cases showing complete fusion of iliac crest out of [A] |
|---|---|---|---|---|
| 17-18 | 5 | 0 | 1 | - |
| 18-19 | 7 | 0 | 1 | - |
| 19-20 | 14 | 2 | 8 | 50% |
| 20-21 | 18 | 8 | 13 | 100% |
| 21-22 | 6 | 6 | 6 | 100% |

50% or more union of epiphyses of ischial tuberosity is found in all cases from 20-21 years and 21-22 years age groups.
All cases show complete epiphyseal union at the age group of 21-22 years i.e. 100%, while no case is found showing complete union of epiphyses of ischial tuberosity in age groups of 17-18 years and 18-19 years i.e. 0 %.

**Table no. 3** shows percentages of cases showing complete fusion in both sexes at different age groups.

**Age groups in years**

A - 17-18
B - 18-19
C - 19-20
D - 20-21
E - 21-22

**BOYS**

| | A | B | C | D | E |
|---|---|---|---|---|---|
| **No. of cases** | 3 | 6 | 10 | 12 | 4 |
| **% of cases50% or more union** | 0.00 | 33.33 | 70 | 100 | 100 |
| **% of cases with with 100% union** | 0.00 | 0.00 | 10 | 50 | 100 |

**GIRLS**

| | A | B | C | D | E |
|---|---|---|---|---|---|
| **No. of cases** | 2 | 1 | 4 | 6 | 2 |
| **% of cases50% or more union** | 50 | 100 | 100 | 100 | 100 |
| **% of cases with with 100% union** | 0.00 | 0.00 | 25 | 33.33 | 100 |

Here percentages are calculated for specific age group.
None of the cases in age groups of 17-18 and 18-19 years among both sexes show complete union of the epiphyses.
None of the cases in age group of 17-18 years consisting of the boys show 50% or more fusion.
All cases of age groups 20-21 and 21-22 years show 50% or more union in boys.
50% of cases of age group 17-18 years consisting of girls show 50% or more union.
All cases of age groups 18-19,19-20,20-21 and 21-22 years among girls show 50% or more union of epiphyses of ischial tuberosity.
The fusion if ischial tuberosity is found to be 100% in age group of 21-22 years.

**Table no.4** shows relation of complete fusion of ischial tuberosity with complete fusion of iliac crest at different age groups.
Out of total 50 cases studied 16 cases show complete fusion of ischial tuberosity and 29 cases show complete
fusion of iliac crest.
15 cases studied for iliac crest fusion out of 16 cases showing complete fusion of ischial tuberosity of 19-20, 20-21, and 21-22 years age groups and it is observed that all 15 cases i.e. 100%, show complete fusion of iliac crest.

**CONCLUSION:**

1: The epiphyses of ischial tuberosity show complete fusion in cases of age group 21-22 years.
2: The female shows beginning of fusion of these epiphyses earlier than those of males.
3: Complete epiphyseal union has been observed in the same age group in both sexes.
4: As far as bilateral symmetry is concerned epiphyseal union of ischial tuberosity occurs uniformly on both sides in the same individual.
5: The epiphyses of iliac crest show fusion at an earlier stage than that of ischial tuberosity.
6: It is also noted that there is no relation of socioeconomic status, weight, height or type of diet
to the process of fusion of epiphyses.

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## A Study of Cervical Smear Reports of Patients attending Gynaecology Out- patient Department of Sheth Chenoy Maternity Hospital, V.S.G.H, Ahmedabad

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**Introduction** : Cervical cancer is the most common cancer in India and ranks second among women worldwide, with almost half a million new cases each year (Ferlay et al 2000). It is the topmost cancer in the women in our country and over one lac new cases are reported annually. Screening with Cervical smear plus adequate follow up therapy can achieve major reductions in both incidence and mortality rates (Miller et al , 1990). The Papanicolou's Smear can reveal cytological abnormalities indicating presence of a pre-cancerous lesion (various grades of dysplasia, or cervical intraepithelial neoplasia), as well as cancer-in-situ or very early invasive cancer. Treatment of these early lesions is highly effective, though far more are diagnosed than will ever progress to invasive cancer if untreated.
Aims and Objectives: The aim of this study was to find out the distribution of the epidemiological factors among the women subjected to Pap smear examination of and determining some important risk factors in this community from the available Pap smear reports.

**Materials and Methods:**
This is a hospital record based study of distribution and determinants of cervical cyto-pathological abnormalities by means of examination of cervical smears in the women attending Gynaecology Out- patient Department of Sheth Chenoy Maternity Hospital, VSGH, Ahmedabad during the year 2001 (1st January to 31st December 2001). A total of 662 records of Papanicolou's Smear tests from room number 7 "Colposcopy and Cervical Smear room" of Sheth Chenoy Maternity Hospital were available for scrutiny.

**Results and Discussion:**
From a total of 662 records of Pap's Smear tests, 18 smears were found to be either unsatisfatory or inadequate which have been excluded from the analysis.

**Table1: Distribution of Cervical Cytology Reports :**

| Nr. | LESION | No. | % |
|---|---|---|---|
| 1 | Normal | 55 | 8.31 |
| 2 | Inflammatory | 43 | 65.26 |
| 3 | Squamous Metaplasia | 227 | 4.08 |
| 4 | Low grade Squamous Intraepithelial Lesions (L.S.I.L.) | 87 | 13.14 |
| 5 | High grade Squamous Intraepithelial Lesions (H.S.I.L.) | 15 | 2.27 |
| 6 | Atrophic | 15 | 2.27 |
| 7 | Carcinoma in situ (C.I.S.) | 13 | 1.96 |
| 8 | Unsatisfactory / Inadequate | 18 | 2.72 |
| **9** | **Total** | **662** | **100.00** |

Since majority (94%) were symptomatic women that come to the OPD for treatment, normal smears were just 8.3%. White discharge and lower pain abdomen together were common to over 50% of all cases. Inflammatory lesions are most common accounting for 65% of total lesions, followed by Low grade Squamous Intraepithelial Lesions (LSIL) which constitute 13%. These were previously called Cervical Intraepithelial Neoplasia grade-I dysplasia (CIN-I) High grade Squamous Intraepithelial Lesions (HSIL) or previously called Cervical Intraepithelial Neoplasia grade-II and III dysplasias (CIN-II and CIN-III) account for 2.27% cases. There was no case of malignancy detected in this sample of 662 smears . Clinical and overt cancer cases are referred to cancer hospital directly. Sometimes, advanced invasive carcinoma may present as inflammation and necrosis cytologically.

The average age of HSIL is 49 years +/- 7.92 years and that of carcinoma in situ is 48.54+/- 7.18 years in this sample as compared to 43.26 years +/– 7.82 years. This is a significant difference in age ($p<0.001$) indicating a latent period for progress of LSIL to HSIL or CIS. Therefore, early detection, prompt and adequate treatment of any lesion is essential for prevention of progress to invasive cervical cancer.

Inflammatory changes and Sq.metaplasia are more common in the relatively younger age groups in . second and third decade of life while LSIL, HSIL and CIS develop in the subsequent years. Use of oral contraceptives and Copper-T are positively associated with inflammatory changes. Atrophic changes are mostly in the post menopausal women due to hormonal deficiency. It has been observed that frequency of dysplasias and CIS significantly increased with higher parity ($p<0.05$). Spontaneous and MTP are significantly associated ($p<0.05$) with inflammatory and dysplastic changes.

**In the Screening programme for Cervical cancer in Panchmahal district of Gujarat under the aegis of National Cancer Control Programme it was aimed to test asymptomatic women. Some 15,236 women were subjected to Pap Smear examination from 1995 to 1997. In this study total 199 (1.31%) cytological abnormalities were detected which included 52 (0.34%) malignancies. LSIL constituted 69 (0.49%) cases. HSIL accounted for 69 (0.49%) cases. Additional 23 invasive cancers were detected by biopsy or clinically. Comparatively, Pap smear reports of high risk women that attended Gujarat Cancer & Research Institute**

**(GCRI) during the same period, showed that all the grades of dysplasia were ten times more common. Similarly cytologically positive cases was also 0.75% in GCRI (over 2 times more) as compared to 0.34% in the district. Atypical and suspicious for malignancy smears were also three times more in GCRI. In ICMR screening study of women over 30 years, it was observed that about 15 smears were cytologically abnormal out of every 1000 female examinees.**

| Years | A | | B | | C | | D | | E | | F | | G | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | %# | | %# | | %# | | %# | | %# | | %# | | % |
| 15-19 | 1 | 1.8 | 3 | 0.7 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 20-24 | 2 | 3.6 | 31 | 7.2 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 25-29 | 6 | 10.9 | 54 | 12.5 | 3 | 11.1 | 3 | 3.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 30-34 | 6 | 10.9 | 76 | 17.6 | 3 | 11.1 | 8 | 9.2 | 0 | 0.0 | 1 | 6.7 | 0 | 0.0 |
| 35-39 | 10 | 18.2 | 102 | 23.6 | 4 | 14.8 | 15 | 17.2 | 2 | 0.0 | 0 | 0.0 | 1 | 7.7 |
| 40-44 | 11 | 20.0 | 72 | 16.7 | 4 | 14.8 | 26 | 29.9 | 3 | 13.3 | 0 | 0.0 | 4 | 30.8 |
| 45-49 | 6 | 10.9 | 41 | 9.5 | 3 | 11.1 | 17 | 19.5 | 3 | 20.0 | 1 | 6.7 | 2 | 15.4 |
| 50-54 | 6 | 10.9 | 25 | 5.8 | 5 | 18.5 | 13 | 14.9 | 3 | 20.0 | 3 | 20.0 | 3 | 23.1 |
| 55-59 | 3 | 5.5 | 5 | 1.2 | 2 | 7.4 | 2 | 2.3 | 2 | 20.0 | 2 | 13.3 | 2 | 15.4 |
| 60-64 | 1 | 1.8 | 10 | 2.3 | 1 | 3.7 | 2 | 2.3 | 2 | 13.3 | 1 | 6.7 | 1 | 7.7 |
| 65-69 | 1 | 1.8 | 4 | 0.9 | 1 | 3.7 | 1 | 1.2 | 0 | 0.0 | 3 | 20.0 | 0 | 0.0 |
| 70+ | 2 | 3.6 | 9 | 2.1 | 1 | 3.7 | 0 | 0.0 | 0 | 0.0 | 4 | 26.7 | 0 | 0.0 |
| Total | 55 | 100.0 | 432 | 100.0 | 27 | 100.0 | 87 | 100.0 | 15 | 100.0 | 15 | 100 | 13 | 100.0 |
| Mean age | 41.6 | | 38.12 | | 44.8 | | 43.26 | | 49 | | 60 | | 48.54 | |
| SD | 12 | | 10.69 | | 11.95 | | 7.82 | | 7.92 | | 11 | | 7.18 | |

The present study of hospital records has a limitation that it cannot be projected to draw any inference to the population as only symptomatic cases are examined here.

Acknowledgement: Authors are thankful to Ms. Anushri, Ms. Ruchika, Ms. Sujata, Ms. Nili, Ms.Niharika, Ms. Meharasma and Ms. Chinmayi , students of then VII semester (2002) for assisting in compiling and analysing the data from the hospital records.

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# MPACT OF TOBACCO SMOKING ON CORONARY RISK FACTOR PROFILE

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**Abstract :**
(Atherosclerotic coronary artery disease is multifactorial disease. The tobacco smoking is the major risk factor of coronary artery disease (C.A.D.) The present study tried to determine the prevalence of all the known risk factors of C.A.D. among the tobacco smoker and compared them with non smokers. Study was designed in such a way that sixty randomized tobacco smokers who attended the "STOP SMOKING CAMPAIGN AND C.A.D. RISK PREDICTION PROGRAM" in various parts of Ahmedabad were screened from C.A.D. risk point of view. The findings were compared with age, sex, matched sixty non-smokers. The result concluded that the prevalence of all the risk factors of C.A.D. i.e Type-A personality, family history, Altered GTT (Glucose tolerance Test), Hypertriglycerideamia, Hypercholesterolaemia, low level of HDL-C, Low C/HDL-C ratio more than 5, emotional stress etc. were statistically significantly high among tobacco smokers compared to non smokers. So among the tobacco smokers the overall risk of CAD increase manifold. The study strongly emphasized that majority of risk factors are modified by mearly the simple physiological manover i.e. stopping or reduce the tobacco smoking, dietary modification, physical exercise and health education).

**Keywords :**
Tobacco smoking, Coronary Artery disease, Risk factors, Atherosclerosis.

## Introduction :

The Freminghamn study concluded that coronary Artery disease is multifactorial disease. Large number of risk factor play significant role in the development of Atherosclerosis of coronary Artery Disease (C.A.D.) Large number of MULTIPLE RISK FACTOR intervention trial suggest that the tobacco smoking is major and independent risk factor for C.A.D. The tobacco smoking is also responsible for premature development of C.A.D. young, myocardial infarction and sudden cardiac arrest and death. In India, 15.4 to 40.8% population in various parts of country consume tobacco in various forms i.e. in the form of cigarette, bidi, hukka, chilam, pipe etc. The recent study of I.C.M.R. (Indian Council of Medical Research) showed that prevalence of C.A.D. in attribution to tobacco use is significantly increased in India. The present study is designed to study the prevalence of various coronary atherosclerosis risk factors among the tobacco smoker and compared their prevalence among non-tobacco smoker.

## Method :

The STOP SMOKING CAMPAIGN AND C.A.D. RISK PREDICTION PROGRAM were arranged with a view to make the tobacco smoker aware about the coronary risk of

tobacco smoking and assess the prevalence of coronary risk factors. The total sixty (60) randomized tobacco smokers and sixty (60) non-tobacco smoker were subjected thorough clinical history & physical examination to assess the coronary artery disease. Personality type A and B was assessed by presence or absence of features like anger aggression, irritability, hurry, impatient, feeling guilty to relax. The sedentary life-style was assessed by asking the level of physical exertion at job, at home & whether the person is doing regular exercise. Emotional stress status was assessed by personal interview and by asking the level of stress at job, at home & other source of stress. Obesity was assessed by measuring body height and weight and reviewing the chart of desired weight of height for adult. Laboratory investigations carried out were, Haemoglobin % (By Sahli's method), total Serum Cholesterol, Serum Triglyceride, HDL - cholesterol, LDL - cholesterol, VLDL - cholesterol, (Enzymatic method) and post prandial blood glucose (PPBS) by oxidase method.

**Statistical test :**

The statistical test carried out here is measuring the standard error of proportion. The null hypothesis was applied and P value was calculated by normal distribution table. If the P valve was less than 0.05, it was considered statistically significant (within 95% confident interval).

**Result :**

The table No. 1 summarize the prevalence of risk factor among tobacco smoker and age sex match non-smoker. The table shows that all risk factors of coronary Artery disease are statistically significantly high among tobacco smokers compared non-tobacco smokers.

**TABLE No. 1**

Table Showing the prevalence various risk factors of C.A.D. among tobacco smokers & non-tobacco smokers.

Table shows that all the risk factors for CAD prevaled statistically significantly high among tobacco smokers compared to non-smokers. GTT Glucose Tolerance Test.

| Name of Risk factor | Among tobacco smoker in % out of 100% | Among non-smoker in % out of 100% | P Value |
|---|---|---|---|
| Symptomatic | 25% | 5% | p<0.05 |
| Positive family history | 20% | 6.6% | p<0.05 |
| Over weight | 35% | 15% | p<0.05 |
| Altered GTT | 40% | 18.3% | p<0.05 |
| Hypertension | 23.3% | 13.3% | Not Significant |
| Systolic B.P > 120 | 65% | 33.3% | p<0.05 |
| Sedentary life style | 46.6% | 40% | p<0.05 |
| Type-A personality | 63.3% | 31.6% | p<0.05 |
| Stressful life | 85% | 30% | p<0.05 |

| | | | |
|---|---|---|---|
| Hypercholesterolemia | 65% | 18.3% | $p<0.05$ |
| Hypertriglyceridemia | 45% | 20% | $p<0.05$ |
| C / HDL-C Ratio > 5 | 40% | 18.3% | $p<0.05$ |
| | n=60 | n=60 | |

**Discussion :**

Study documented the fact that prevalence of C.A.D risk factor were significantly high in tobacco smoker compared to non-smoker. In Freminghamn study, 60% of the patient with C.A.D were tobacco smokers. Tobacco smoking is major independent risk factor for C.A.D. Tobacco smoking interact with other risk factors synergistically and increase the risk of C.A.D. These risk factors are Diabetes Mellitus, Hypertension & low level of HDL-C. Further more, the tobacco smoking is associated with type A personality & excess of emotional stress which are also risk factors of C.A.D.

Study has also documented the fact that the tobacco smoking is associated with Dyslipidaemia (Increase Triglyceride increase cholesterol and decrease HDL-C level) which is atherogenic in nature. This matter lead to think the potential benefit of knowing the presence of other risk factor which are like tobacco smoking are also modifiable. As tobacco smoking interact with other risk factors, the tobacco smoker get additional benefit if these factors are diagnose and managed adequately. Incidently, many of these risk factors modification require mearly the education regarding the benefit of stopping the smoking, dietary adjustment & physical exercise. Here it should be emphasized that the tobacco smoking increase the serum cholesterol level. As there is graded relationship between raised cholesterol level & premature C.A.D. In this context, lipid lowering agents carries remarkable prospectus in tobacco smokers interact with increased serum colostral. In this context it is further emphasized that stopping of tobacco smoking result in rapid decline in risk of C.A.D. upto 50% & within 1 year the risk equal to non-smoker.

Tobacco smoke contains various substances which are Carcinogens, co-carcinogens, mutagen, toxins, Antigens, pharmacological active agents,. Recently a new group of substances is described which are known as atherogens responsible for Atherosclerosis. These are 1) Carbon Monoxide 2) Nicotine 3) Aryl Hydro Carbons 4) Hydrogen Cyanides, 5) Hydrogen Oxides 6) Antigenic glycoprotein 7) Free radicals. Out of these, carbon monoxide play crucial role in Atherosclerosis of coronary arteries disease. Carbon monoxide has direct toxic effect on endothelial cells. By producing local hypoxia, it increases the permeability of endothelial cells and ultimately the injury of Endothelium. Carbon monoxide also got the adverse effect on platelets function which produces very powerful vaso constrictor and platelets aggregating agent thromboxane A2, which produces coronary artery spasm and angina pectoris. Platelets also produces a growth factor known as Platelets Derived Growth Factor (PDGF) which stimulate the proliferation of smooth muscle cells of media of artery and enhances the migration of smooth muscle cells from media to intima of artery a important step of coronary atherosclerosis.

Nicotine of tobacco smoke has direct toxic effect on endothelial cells by raising Blood Pressure and heart rate. It increases the shear stress on vessel wall and produces the

mechanical injury to endothelial cells. Brischetto Proposed that Nicotine stimulates the secretion of Adrenaline which leads to Lipolysis by increasing the activity of Lipolytic lipase enzyme in adipose tissue. This leads to increase serum concentration of free fatty acid, Triglycerides, LDL-C, & VLDL-C. Increase LDL-C leads to increase infiltration of lipids in intima of artery. Tobacco smoke also increases the total serum cholesterol level. This raised serum cholesterol can produce direct chemical injury to endothelium. Recently it is postulated that antigenic glycoprotein of tobacco smoke produce immune mediated injury to endothelial cells. Auto antibodies are also postulated to develop against modified LDL-C.

Over all role of tobacco smoking and dyslipidaemia is described by Denial et al is summarized in following diagram.
The studies have shown that the fatty streak lesions which antidate the fibrous plaque and which actually develops under a structurally intact endothelial surface. These fatty streak lesions are precursor of Atheromatous lesions and has been demonstrated in animals (monkey and rabbits) feeding large amount of cholesterol in diet. In animal model and angiographic proved human Atherosclerosis lesions may regress their size to normal if the underlying risk factors i.e. tobacco smoking or other risk factors are removed or modified.
Conclusion & Implications

The study documented the fact that prevalence of all the risk factors of coronary artery disease are significantly high among tobacco smoker compared to non-smoker. One way tobacco smoking itself prevails among mail sex, Type-A personality and emotional stress prone persons, which are also the risk factors for C.A.D. Another way tobacco smoking interact synergistically with other C.A.D. risk factors like Hypertension, Diabetes etc. and thirdly the tobacco smoking itself responsible for dyslipidemic state which is potent Atherogenic in nature. So the overall risk of C.A.D. is increased manifold. C.A.D. risk is still higher in heavy smoker as there is strong dose response relationship. So it is strongly recommended to stop the smoking for the benefit of Cardiac health. By stopping the smoking, the benefit will be immediate one because the tobacco smoking related dyslipideaemia is reversible with stopping the smoking. The synergistic interaction with other risk factor will be stopped. In persons who have already established C.A.D., the benefits of smoking are many. Tobacco smoking itself induces the angina pectoris and stopping the smoking, the frequency of angina will be decreased. As tobacco smoking reduces the threshold of ventricular fibrillation, by stopping the smoking the risk of sudden death will be decrease. It is also recommended that if the person cannot stop smoking completely he/she should be advised to reduce the frequency of smoking, take fewer puff, inhale less smoke, inhale low nicotine cigarette, and leave a longer stub.

The study has also shown that the large number of risk factors are prevaled among tobacco smokers and many of these risk factors are like tobacco smoking are also modifiable by modern medical science. Incidently many of the risk factors are favorable modified by mearly physiological manoevers like dietary advise, physical exercise and health education. It is further emphasis that in all circumstances tobacco smoking is strongly discouraged for the benefit of cardiac health.

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Acknowledgment : Author wish to thank Dr. R. N. Rao Prof. & H.O.D. physiology & Dr. S. J. Damani Prof. & H.O.D. Cardiology Smt. N.H.L. MMC for insightful suggestions & comments during the study.

**Estimation of Mean Age at Menarche using Life table Method**

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**Abstract :**
The present study is a cross sectional study of adolescent school girls in age group 12-18 years studying in different schools in Anand District of Gujarat State. 900 girls from 22 schools were included in the study. Mean and Median age at menarche was found to be 13.95 and 14.48 Years respectively. Mean age at menarche according to various characteristics were also computed using the life table technique.
Menarche is the onset of menstruation and is one manifestation of puberty among females (Jefcoate, 1952). The onset of the first menstrual period is a qualitative event of major significance, denoting the achievement of a functional state, which involves, if not the ability to regularly conceive at least the hypothalamic control of the ovarian cycle via the pituitary gland.
The knowledge of age at menarche is very important demographically as one can consider the distribution of the age at menarche as the potential starting point of reproduction. In India particularly in rural areas in many cases, marriages are celebrated before menarche, the reproductive life of girl starts just after menarche. Thus age at menarche is an important factor affecting fertility. Knowing the mean age at menarche, the number of girls entering the reproductive cycle every year can be estimated and this can be used for planning of various health activities including family planning activities. Till date family planning activities are confined mostly to older women of society. Knowing the menarcheal age distribution, family planning activities for younger groups can be planned.
Age at menarche is an excellent overall comparative indicator of population health, timing of maturation and nutritional status. Average age at menarche is also used widely as a demographic indicator of population fecundity. More recently, the average age at menarche has been used as a measure of reproductive risk for miscarriage and unsuccessful pregnancy outcomes and as a proposed basis for Public Health Planning related to targeting sex education.
For computation of mean/median age at menarche a relatively easily performed approach would be to survey girls around the age at menarche who should have the most precise recall of age at onset. However, some will not have started to menstruate. With such incomplete data one can not simply take the average age of onset of just those who have started to menstruate. To do so would omit those who have yet to start (particularly the late maturers) and be “biased as well as inaccurate” (Chidambram; Eveleth and Tanner, 1976). Hence, life table can be used to find mean/median age at menarche which will give a fairly accurate estimate.
The specific objectives of the present study is to estimate the mean age at menarche by various characteristics using life table method.
Life table can be used for estimating the average age at menarche with certain reasonable assumptions. The assumptions of the life table model are:
1. The cohort under study is closed to migration. Its size can change only due to death of its members. In the present case the size changes because of occurrence of menarche to girls.
2. Each member of the cohort is exposed to the risk of death at each age according to the schedule that is fixed in advance and is unchanged. There is no variation in the risk of death over time and thus life table is a purely deterministic model. In the present case each member of the cohort is exposed to the risk of attaining menarche and it is assumed

that the rate at which the girls are attaining menarche remains same for the whole period of the cohort.
3. The size of the cohort is always fixed number of births of the same sex, say, 1000, 10,000 or 100,000 which is called the radix of the life table in order to facilitate comparison between different life tables.
4. The number of deaths during the year is assumed to be evenly spread over the age interval (except the first few years) especially when it is one year. In the present case it is assumed that the numbers of girls attaining menarche are evenly spread over the age interval.
The data for the present study has been obtained from a survey conducted in Anand taluka using a structured questionnaire. As per the list obtained from the District Education Officer, Nadiad, there were 49 schools in Anand taluka out of which 4 were girl schools run by Panchayats/Municipalities, 5 were boy's schools. Out of the 40 remaining co-educational schools 3 schools were English medium convent schools run by Trusts. For the purpose of the study all the 4 girls school run by Panchayat/Municipalities (Total respondents 434)and all 3 English Medium Coeducational Convent Schools run by Trusts (total respondents 64) were selected. Out of the 37 remaining coeducational schools, 15 schools having Gujarati medium of instruction were selected randomly (Total respondents 402). For the purpose of the present study, schools run by Panchayats/Municipalities are considered as government schools while schools run by trusts have been considered as private schools.
A pretested structured questionnaire was administered to 900 girl students studying in standard VII to XII standard. The data collection was done from July 1999 to August 1999. It is expected that the data regarding age at menarche and other variables have minimum errors because menarche being a recent and noteworthy event in the schoolgirls, they usually remember the dates exactly.

**Table 1.1** : Estimation of Mean age at Menarche by using Life Table Method

| **x** | **wx** | **mx** | **dx** | **qx** | **px** | **px** | **mx** |
|---|---|---|---|---|---|---|---|
| 10 | 900 | 5 | 0 | .0056 | .9944 | .9944 | 56 |
| 11 | 895 | 10 | 0 | .0112 | .9888 | .9833 | 111 |
| 12 | 885 | 94 | 8 | .1067 | .8933 | .8784 | 1049 |
| 13 | 783 | 186 | 56 | .2464 | .7536 | .6620 | 2164 |
| 14 | 541 | 363 | 59 | .5122 | .4878 | .3229 | 3391 |
| 15 | 220 | 154 | 11 | .7179 | .2821 | .0911 | 2318 |
| 16 | 53 | 41 | 2 | .7593 | .2407 | .0219 | 692 |
| 17 | 12 | 9 | 0 | .7500 | .2500 | .0055 | 164 |
| 18 | 3 | 3 | 0 | 1.000 | 0 | .0000 | 55* |

*It is assumed that M18=55 and M19=0
Mean age at menarche = 13.95 years
Median age at menarche = 14.48 years.

X Age in Completed Years
Wx Number of girls who have not started menstruation

until exact age X and are exposed to the risk of starting menstruation.

mx Number of girls who started menstruation between age X and X+1.

dx Number of girls who have not started menstruation and are aged X at the time of survey.

Qx Estimated probability of starting menstruation between age X and X+1 where

$$Qx = \frac{mx}{Wx - 1/2\ dx}$$

$$Px = 1 - Qx$$

Px Estimated cumulative probability of not starting menstruation by age X

Mx Estimated number of girls starting menstruation at age x, among an initial cohort of 10,000 girls.

$$Mx = (Px - Px+1)10{,}000$$

**Table 1.2**: Mean and Median age at menarche computed by using life table method.

| Characteristics Of respondent | Sample Size | Mean age at Menarche | Median age at Menarche |
|---|---|---|---|
| **Place of Residence** | | | |
| Urban | 446 | 13.88 | 14.45 |
| Rural | 454 | 13.99 | 14.48 |
| **Type of School** | | | |
| Girls School | 343 | 14.08 | 14.52 |
| Coeducational | 40 | 14.74 | 14.56 |
| Coeducational Convent school | 64 | 12.76 | 13.13 |
| **Religion** | | | |
| Hindus | 840 | 13.94 | 14.46 |
| Muslims | 27 | 14.36 | 14.96 |
| Christians & others | 33 | 13.72 | 14.20 |
| **Dietary pattern** | | | |
| Vegetarian | 786 | 14.01 | 14.52 |
| Non-Vegetarian | 114 | 13.52 | 14.11 |
| **Type of family** | | | |
| Joint | 287 | 14.05 | 14.58 |
| Nuclear Education of mother | 613 | 13.89 | 14.41 |
| **Illiterate** | **141** | **14.09** | **14.62** |

| | | | |
|---|---|---|---|
| Primary | 254 | 13.72 | 14.37 |
| Higher | 363 | 14.03 | 10.57 |
| Secondary Grad. & Above | 142 | 12.71 | 14.30 |
| **Birth Order** | | | |
| 1 | 345 | 13.97 | 14.48 |
| 2 | 355 | 13.85 | 14.40 |
| 3 & above | 200 | 14.04 | 14.51 |
| **Body Mass Index** | | | |
| Normal (<28.6) | 868 | 13.96 | 14.48 |
| Obese (>28.6) | 32 | 13.82 | 14.22 |

The median age at menarche found by using life table technique is 14.48 years (Table 1.1).

The analysis presented in the table 1.2, suggests that variable place of residence affects the age at menarche. The mean ages at menarche for rural area was found to be 13.99 years and for urban area was 13.88 years. Comparing the mean ages of menarche of girls studying in different type of schools it is found that the mean ages of menarche for girls studying in government run "girls school" was 14.08 years, for those studying in Coeducational School 14.74 years and for those in Convent English Medium Schools it is 12.76 years. Thus it is seen that the mean menarcheal age for girls in convent school is the lowest one. It might be due to the better socioeconomic condition of the girls studying in such type of schools.

In the case of religion it is found that Christians have the lowest mean menarcheal age of 13.72 years compared to Hindus and Muslims. Hindus have a mean menarcheal age of 13.94 years and Muslims have mean age at menarche as 14.36 years. The mean menarcheal ages for those girls who consume more fatty and protein food is 13.52 years whereas for those consuming vegetarian food it is 14.01 years. The mean ages at menarche for girls of joint family is 14.05 years, while that of nuclear family is 13.89 years. Mean age at menarche for those girls whose mothers are illiterate is 14.09 years, for those whose mothers education is upto Primary level is 13.72 years, for Higher Secondary category is 14.03 years and for those belonging to families where mothers are educated upto graduation or above the mean age at menarche is 12.71 years. The mean age at menarche for the girls belonging to birth order first is 13.97
years, for second order birth is 13.85 years and for those belonging to third or higher order births is 14.04 years.

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## CIRCADIAN VARIATION IN PEAK EXPIRATORY FLOW RATE (PEFR) IN CLINICALY NORMAL SUBJECT

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The widely used ventilatory function test are spirometry and peak expiratory flow rate that be defined as the maximum flow that can be sustained for a period of 10 mS. It has been used in various epidemiological studies in identification of chronic disease. In order to fully exploit PEFR as an epidemiological tool, we need to understand the multiple sources of variability in the measurement. This requires understanding of underlying range of biological variation within the individuals. Circadian variation is also one of the factors by which shows variation in PEFR. It is very important in case of bronchial asthama. Therefore, it is necessary to know how much circadian variation occurs in normal person. The normal values help us to to know whether circadian variation occur in subject exposed to industrial and environmental over a shift.
The present study deals with measurement of PEFR value in healthy subject in the morning hrs. and evening hrs. and
determining Circadian variation or biological variation in values.

**MATERIAL & METHODS :**
Mini peak flow meter is used in this study. For evaluation of circadian variation in values the meassurement of PEFR was done at 7 to 8 am in the morning and anbout 3 to 4 pm in the evening. In 50 clinically normal subjects. Two readings were taken and the difference in the first reading and second readings were noted.

**DISCUSSION :**
This provides an important information that there is a minimal variation in PEFR between morning and evening and this has an imporant bearing to understand the behaviour of airways in producing changes in PEFR in dust and pollutants exposed subjects. In a study conducted in cotton textile workers, the control workers showed a mean decrase of 6.0 lit. PEFR between morning and evening shift and workers in carding room showed a mean decrease of 11.0 1 lit. Therefore, the present clinically normal subjects the PEFR circadian variation is very much less than these values.
Reports indicated that the cycle of airway calibre tends to have its minimum early in the morning in normal subjects (about 4.0 am) and maximum about 12 hrs 2, 3 later. This phenomenon is probably primarily a manifestation of the normal circadian rhythm, although nocturnal phelgm build up limiting flow measured immediately upon rising, may also contribute to the morning low value.
It was suggested that the amplitude in circadian PEFR rhythm could be used as a measure

of bronchial liability. Their study suggests that those with more than 20% variability in daily PEFR should be considered asthamatics. Related to these observations is the suggestion that daily variation is related to bronchoconstrictor response.

**RESULTS :**

The PEFR value of Ist reading measured among 50 clinically normal students showed a decrease by 2.3 llit (0.51%) between morning and evening value. The second reading showed an increase of 2.1 lit (0.46%) in PEFR value. The best reading showed an increase of 2.5 lit (0.52%) in PEFR. Overall the changes in PEFR between morning and evening varies from 2.3 lit (0.51%) to +2/1 lit (0.46%).

**TABLE - I**

**CIRCADIAN VARIATION IN PEFR AMONG 50 NORMAL MALES.**

| **Reading** | **PEFR (lit/min)** | | |
|---|---|---|---|
| | morning | evening | difference |
| Ist 448.0 | 445.7 | -2.3 | |
| +81.4 | +93.6 | (0.51) | |
| IInd | 459.4 | 462.0 | +2.1 |
| +90.0 | +85.4 | (0.46) | |
| Best | 476.4 | 478.9 | +2.5 |
| reading | +85.2 | +84.1 | (0.52) |

**CONCLUSION:**

Overall changes showed an increase in PEFR between morning and evening varies between 2.3 ltr (0.51%) to +2.1 ltr (0.46%) . The best reading showed an increase of 2.5 ltr (0.52%) in PEFR. This value is less than that seen in control and occupational exposure subjects. This provides an important information that there is a minimal variation in PEFR between morning and evening and this has an important bearing to understand the behaviour of airways in producing changes in PEFR in dust and cotton textiles workers. Reports indicate that the cycle of airway caliber leads to its minimum early in the morning.

This cycle of airway caliber leads its minimum early in the morning in normal subjects (0400) and a maximum about 1200 hrs later focus sometimes placed on ‘morning dip’ in PEFR in asthamatics. This henominon is probably primarily a manifestation of the normal circadian rhythm although nocturnal phelgm build up limiting flow measure immediately upon rising may also contribute to the ‘morning dip’. Few literatures available in India suggests about circadian variation a biological variation varies in clinically normal subject.

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## PROSTATE - ASSESSMENT TO MANAGEMENTS

(Medical Aspect)
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**Introduction:**

Prostate attract the attention of medical professionals because carcinoma of Prostate is the most common malignancy in man. Some people consider it as a counter part of female breast in man, as prostate Cancer is also hormone dependent.

However, the vast varieties of disorders of prostate are associated with significant morbidity and mortality in man. Many men with carcinoma of prostate do not die due to Carcinoma Prostate but due to associate other medical condition with Ca - Prostate as an incidental finding.

Benign prostate hyperplasia (BPH) is a universal phenomenon. It begins with the age of 45 as a second growth spurt.

The most interesting aspect of the prostate is that both benign and malignant tumors are hormone / androgen dependent. As these disorders are common in elderly people; assessment and management of prostate is the important aspect in geriatrics practice and attract research in gerontology.

In the 8th decade 90% of the man have BPH however it is not pre-malignant condition. Amongst the medical professionals, the question always remains in context to prostate whether lesion is benign or malignant* in this study and article we have discussed our observations and how to sort out whether the lesion is benign or malignant in context to recent and latest literature available.

* Whether the person is symptomatic or asymptomatic.

**Material and Method:-**

132 patients suspected with prostate lesion had undergone prostate biopsy. Usual Hysto pathological routine i.e. Paraffin wax etc. were carried out. The tissue was stained with Hematoxyline and Eosin, PAS and retic stains. The slides Were examined under light microscope to label tissue as a benign or malignant. Cyto diagnosis was also carried out.

Our observation was compared with the observations of similar study done by other research workers.

**Observations:-**
Total 132 all male patients (age range 38-80) presented to out institute for histopathological diagnosis of prostate lesion between January 2002 - December 2002 were included in our study. The results are summarized in following table.

| Lesion | Number | Percentage |
|---|---|---|
| BPH | 124 | 93.94% |
| Adeno Carcinoma | 8 | 6.06% |
| Total | 132 | 100.00% |

BPH was more common among age range from 38 to 63 while adenocarcinoma was more common among age range 53 - 80 years. (P £ 0.05)
The other inflammatory lesion i.e. prostatitis uretheritis metaplasia etc. were associated with BPH.
All the malignant lesions were adenocaranoma (6.06%)

**Discussion:-**
Benign Prostate hyper plasia is the most common prostate lesion our study (93.94% n= 124)
Comparative study

| | Our Study | | D. Javan B.etal | | Arun Chitale | |
|---|---|---|---|---|---|---|
| | Number | % | | Number | | % |
| Bph and other Begingn L | 124 | 93.94 | 820 | 83 | 6357 | 89 |
| Malignant | 8 | 6.06 | 231 | 17 | 0790 | 11 |
| **Total** | **132** | **100** | **1.51** | **100** | **7165** | **100** |

From the above table, it is evident that the benign lesions i.e. BPH is the most common lesion among the Prostate disorders.
Sung J.C. et al studied the prostate biopsy among the men aged more than 70 years. They found malignancy among 56.8% and when the age range selection was > 80 years, 81 persons had malignancy. They followed the all the cases for many years and found in follow up that majority of them died due to unrelated causes irrespective of stage of prostate cancer.
It has been found that cancer of prostate may be present among asymptomatic individuals.
It can be present in the prostate label as BPH. There are no symptoms and signs specific for prostate cancer in clinical set up. Prostate cancers it is difficult to predict which cancer will be slow growing and which will be the aggressive one. Therefore, it remains the rule of thumb just like other cancer to detect early stage and it aggressively irrespective of stage.

American Cancer society recommend Digital Rectal Examination (DRE) to be carried out among the man age > (greater than) 40 years every year and to measure prostate specific antigen (PSA) is to be measured every year among the man age greater than 50 years for the early detection of prostate cancer. Incidentally prostate specific antigen is insensitive (35% False -ve) and non-specific (raised level in BPH 65%) for the detection of Ca Prostate. Therefore, there is no general rule but it is recommended that
(a) It DRE is negative and PSA<(less than) 4ngm/litre the annual follow up is required.
(b) If the PSA is greater than 10ngm/litre, or DRE Is abmormal trans-rectal ultrasonic guided prostate biopsy is indicated (TRUS).
(c) If the DRE is negative and PSA is in the range of 4.1-10 ngm/litre the situation is controversial but majority recommended TRUS aspecially when the sonography of prostate is abnormal.
In this context, Kamoi K et al found that instead of PSA, several PSA related index is highly sensitive. Such indexes include,
(a) Correctng absolute PSA level with Prostate volume.
(b) PSA density for patient's age (Age reference PSA).
(c) Free PSA
(d) Free PSA bound PSA ratio.
(e) Transitional zone PSA.
These indexes are highly sensitive for Ca-Prostate.
In certain instances, serial analysis of PSA and rate of rise of PSA is also useful. PSA is also used in staging the Carcinoma, assessing, the response to therapy and detecting the relapse.
In this set up sonography, C T scan, MRI scan, are useful for the early detection and assessing the stage of the tumor and the gland and use the guideline for the biopsy. They are also useful for the staging. In this context, Baver J J et al have studied the Prostate biopsy under 3D computer visualization of the prostate at the time of biopsy. They found, that the lateral plane biopsy including apex yield better than the core-biopsy.
FNAC of Prostate is also evaluated for the detection of Prostate cancer with advantage and disadvantages and does not appear superior to Traditional biopsy. Large number of other biological markers have been are for the revolution for the cytodiagnosis of prostate cancer including immunohistology flow cytometry, ultra structural study, cytogenetic study, receptor analysis and molecular biology. William J. A. et al found, DNA topo isomerase IInd alpha. In immuno histochemical staining as a marker of prostate cancer.
Ornstein D. K. et al found intracellular free form of PSA as a highly valuable Cancer marker.
Arenas M. I. et al found certain glycoconjugates of proteins highly valuable in detecting prostate cancer.
D. Amico A. V. et al found gleasons score from biopsy study very helpful in guiding the therapy of choice and predicting the outcome of prostate Cancer.
Zlotta A. et al found other biological marker i.e. HK2 and tissue Kallikrein.
Krishan A. et al found flo cytometry for androgen receptors expression in both malignant and benign tumors.
Other cytomarkers of prostate cancer are Lewis antigen, tumor toxin, Immunotoxin.
- M. A. b B - 3, Pseudomonas Endotoxin
C-Kit

k.t. Ligand
Stem. Cell factor, expression of mutant P. 53c - My, intracellular Prostate Specific Acid Phosphatase. Low molecular weight keratin Lew - 7 epithelial membrane Antigen. Antigen antibody 3u B E 12 identities in basal cells in Prostate. It has diagnostic value for benign lesion and absent in Adeno carcinoma. Such markers increase sensitivity up to 90% or more.
Management Perspectives:-
If the lesion is malignant one and is in operable stage, (early stage) all patients should undergo Radical prostatectomy (Never sparing) with pelvic Lymphadenactomy with the hope of cure of cancer. As the surgery is associated with significant morbidity, and usually done in elderly persons who had usually have associated medical condition to prevent radical surgery radiation therapy as a primary treatment for prostate cancer is under evaluation. However, at present, the radiation is less curative than surgery, Radiation is done in the form of external beam (6000 - 7000 reds). Recently local implantation of radioactive sheets of Iodine 125 I, Gold 198 Au, Palladium 103 Pa, Irridium 192 Ir are also associated with encouraging result of primary care of cancer. The only hazard is impotency . Radiation is also indicated for secondary metastasis e.g. bone. Cancer chemotherapy is reserved for hormone insensitive tumors.Majority of the surgery done today are palliative one for the relief of bladder neck obstructive symptoms i.e. (hesitancy, incomplete emptying residual urine, dribbling, Dysuria, frequency & urgency, obstructive uropathy, etc.). These surgeries include open prostatectomy or trans-urethral resection (TUR)*. Recently other palliative measures i.e. hyperthermia, cryosurgery LASER, coils stands are also available and claim to be associated with less post-operative morbidity and complication. Their superiority is under emulations.
*Irrespective of whether the lesion is BPH or malignant.
- Pharmacological Maneuvers :-
Alpha - one, Adrenergic receptor blocker i.e. terazosin……. relax the the bladder neck smooth muscle and relieve the obstructive urinary symptoms and improve the urinary flow.
- 5 Alpha reclutase inhibitor Finasteride :
It inhibit the conversion of testosterone into Di-Hydroxy-testosterone is indicated in BPH as the BPH is androgen dependent.
As more than, 95 percent of prostrate cancers are hormone / androgen dependent large number of medical and surgical methods have established for development of androgen deprivation i.e. both surgical and medical.
Prostrate: Both the surgical
In addition, medical methods are available for androgen deprivation theory. The surgical methods are Orchiectomy and adrenalectomy as both are the source of androgen in man. Hypophysectomy is also a form of surgery. However, these surgeries are rarely indicated in elderly people due to associate significant morbidity. Besides significant number of effective medical methods of androgen deprivation are also available and preferable. This includes (a) Inhibition of pituitary Gonadotropines by Estrogens i.e. Diethylstilbestrol - 3 mg per day leads to decrease secretion of testosterone. This therapy was used largely in past and today also. (b) Recently L HRH analogues such as Leuprolide or Buserelin are introduced and inhibit the LH secrection and leads to decreases secretion testosterone. This compounds have safe cardiovascular profile and can be used safely in elderly people

(Better than Estrogens) (c) The third medical method of androgen deprivation is the inhibition of androgen synthesis by testis and adrenals i.e. (I) Medical Adrenalectomy by high dose of exogenous glucocorticoids for a long period (ii) A compound aminoglutethemide androgen synthesis inhibitors (iii) Androgen receptors blocking anti-androgens which inhibit the binding of androgen to cytoplasmic acceptor protein. i.e. Cyproterone, Bicalutamide, Flutamide or Nilutamide. Exceptionally certain prostate cancer express DCL2 gene and become androgen independent and certain mutation of genes leads to loss of specificity for legand. Therefore, the receptor can respond to hormones such as progesterone. They overall prognosis of prostate cancer is depending upon the stage, the grade of malignant cells. (Gleason's scale) Capsular penetration and invasion to perineal structures i.e. Seminal resides, urinary bladder , etc. metastasis of Lymph nodes, distance metastasis, androgen dependency and response to therapy. But overall medical therapy is significantly beneficial,n addition, medical methods are available for androgen deprivation theory. The surgical methods are Orchiectomy and adrenalectomy as both are the source of androgen in man. Hypophysectomy is also a form of surgery. Though this surgeries are rarely indicated in elderly people due to associated with significant morbidity. Besides significant number of effective medical methods of androgen deprivation are also available, preferable acceptable to the patient. This includes (a) Inhibition of pituitary Gonadotropines by Estrogens i.e. Diethylstilbestrol - 3 mg per day leads to decrease secretion of testosterone. This therapy was used largely in past and today also. (b) Recently L HRH analogues such as Leuprolide or Buserelin are introduced and inhibit the LH secrection and leads to decreases secretion testosterone. This compounds have safe cardiovascular profile and can be used safely in elderly people (Better than Estrogens) (c) The third medical method of androgen deprivation is the inhibition of androgen synthesis by testis and adrenals i.e. (I) Medical Adrenalectomy by high dose of exogenous glucocorticoids for a long period (ii) A compound aminoglutethimide androgen synthesis inhibitors (iii) Androgen receptors blocking anti-androgens which inhibit the binding of androgen to cytoplasmic acceptor protein. i.e. Cyproterone, Bicalutamide, Flutamide or Nilutamide. Exceptionally certain prostate cancer express DCL2 gene and become androgen independent and certain mutation of genes leads to loss of specificity for legand. Therefore, the receptor can respond to hormones such as progesterone. They overall prognosis of prostate cancer is depending upon the stage, the grade of malignant cells. (Gleason's scale0 Capsular penetration and invasion to perineal structures i.e. Seminal resides, urinary bladder , etc. coma metastasis of Lymph nodes, distance metastasis, androgen dependency and response to therapy. Overall, medical therapy alone is associated with good prognosis.

Conclusion and Implication:

The study documents the fact that the majority of the prostate lesions are begin one, though all the efforts should be made to rule out the malignancy in every individual, with the hope of cure of cancers by early detection and radical prostatectomy and Lymphadectomy or by intensive curative radiation therapy. In last two decades, large number of imaging techniques has been evolved to detect prostate lesion in early stage. I.e. CT MRI, etc. The recent method i.e. computerized 3-D-imaging followed by histopatholpgical biopsy gives the best result; through it is available in few centers. Similarly, large number of immuno-histo-cyto chemical studies are under evaluation and associated with 80 percent - 90 percent sensivity in diagnosis to cancer cells prostate

lesions. Newer cytological and biological markers of prostate cancers are also on way and will be available for clinical utilization. Meanwhile it is worth to consider the recommendation of American Cancer Society for the early detection of prostate cancer even in asymptomatic individiuld i.e. (a) Digital Rectal Examination every year in the male age greater than 40 and
(b) yearly assessment of PSA among the male age greater than 50 years.
Though PSA is not specific for prostate cancer, PSA related indices and ultrasonogralhy guided trans Rectal Prostate Biopsy are the primary steps for the assessment and management of prostate lesion in day to day practice at present.

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# STERILIZATION AND DISINFECTION

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Microorganisms cause infection, contamination and decay. So it becomes necessary to remove or destroy them, from the material or from areas. This is the object of sterilization.
Sterilization is defined as a process by which an article, surface or medium is freed of all living microorganisms including bacteria, fungi. Spore and viruses.
Disinfection means the destruction or removal of all pathogenic organisms by chemical disinfectants e.g. aldehyde, Halogens, alcohols, surfactants.
Cleaning of the material is necessary prerequisite for sterilization of disinfection.

**Choice of method of Sterilization and Disinfection**. :
All instruments and apparatus to be sterilized should be first thoroughly cleaned by washing and scrubbing. The same applies to areas for fumigation as the presence of organic matter reduces the efficiency of chemical disinfectants.
Autoclaving is the method of choice for sterilizing all the theatre appliances that will withstand it. Those which cannot withstand autoclaving are sterilized by chemical methods; Lysol, chloroxylon or iodophor for surgical blades and scissors; formaldehyde o0r gluteraldehyde for endoscopes and specialized rubber equipment; and ethylene oxide for heart-hung machines. Syringes are sterilized by autoclaving, hot air sterilization or gamma radiation. Diabetics are commonly advised to keep their syringe and needle permanently immersed in spirit and to boil them once a week. Gamma radiation is now increasingly used to sterilize many types of disposable articles on a massive scale so that they can be had ready for use.
Autogenously and some types of synthetic grafts seed in cardiovascular surgery are sterilized with anti biotics. It is customary to sterilize the air in operation theaters with ultra-violet radiation or with iodophor spray. Ultraviolet radiation is also used to sterilize the air inside sterile dispensing cabinets. Solutions of biological material such as sera and antibiotics which cannot be sterilized by heat are often sterilized by filtration. Though a few vaccines will withstand sterilization by steam at 100 degrees C. Laboratory glassware is ordinarily sterilized in a hot air oven after thorough preliminary cleaning. Wards, theaters and sick rooms and the contaminated furniture can be swabbed with formalin or iodophor solution, fumigated with g aseous formaldehyde or sprayed with iodophor solution or with a commercial mixture containing glutaraldehyde, chemically bound formaldehyde and benzalkonium chloride (Bacillocid). Books and bedding can be fumigated with gaseous formaldehyde or ethylene oxide. Cotton clothing and rubber mattresses can be autoclaved. Cotton mattresses, however, cannot be autoclaved and have to be exposed to sunlight and fresh air. If heavily soiled they are best destroyed by incineration. Incineration is the method of choice for soiled dressings, pathological materials and animal carcasses. If facilities for incineration are not available they are best disinfected with Lysol or iodophor. Lysol and iodophor can also be used for, disinfecting the excreta of patients with infectious diseases before disposing them into the toilet. The skin, especially its deeper layers, cannot be sterilized. The best method for reducing the bacterial count on the skin is thorough scrubbing and washing, followed by the

application of a suitable antiseptic. For preoperative preparation of the skin, the preferred antiseptics are tincture of iodine (mitis) aqueous iodophor (2%) solution and a 2% solution ofhibitane in alcohol. Alcohol or spirit is commonly applied to the skin before an inspection. Acryflavin and chloroxynol are the popular wound anticeptics, though heavily infected wounds are best treated with systemic antibiotics. Although Condy's lotion (0.1% aqueous solution of potassium permanganate) is still the favorable for bladder washes, 1% aqueous solution of acetic acid and silver nitrate are far more effective for this purpose.

Chloroxylenol is a popular and effective disinfectant for hand washing by attendants and for sick room swabbing. Feeding utensils of patients with communicable diseases are best kept separate, washed and finally washed with boiling water. Soiled bed linen and clothes of patients treated at home should be soaked in a disinfectant such as chloroxylenol and then washed. After recovery of the patient, bed linen and clothes are best loundered and heavy articles such as mattresses exposed to sunlight.

Swimming pools and water supplies are generally disinfected by chlorination, whereas potassium permanganate is a convenient domestic disinfectant for water, fruits and vegetables.

## MALARIA VACCINE

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**What is the basis of development of vaccine against malaria?**

- The strategy for malaria vaccine development is based on the identification and characterization of those parasite antigens, which specifically stimulate protective immune response.
- interest is focused on the extra-cellular forms (sporozoites and merozoites), which come into direct contact with the immune system and also on the sexual stages, which develop within mosquitoes and could be possible targets of vaccines capable of blocking transmission of the disease.
- After identification of the major sporozoite surface protein, the circumsporozoite protein (CS protein) and the elucidation of the deduced amino acid sequences of several CS proteins, most efforts are focused on producing protective antibodies against the central repeat region of CS proteins.
- T-cell responses elicited by the CS protein and other malaria pre-erythrocytic antigens can definitely protect against malaria.

**What are the difficulties in the development of the vaccine against malaria?**

- The complex structure and life -cycle of the malaria parasite and the nature of its interaction with its human host prelude any rapid solution to the vaccine problem.
- The protozoan parasite of the genus Plasmodium undergoes a multi stage development cycle, part of which takes place in the vertebrate host and part in the mosquito vector.
- Changes in both morphology and antigen expression occur during the cycle.

- The parasite confronts the host with a large number of antigenic components, each developmental form of the parasite, containing distinct, stage-specific antigens.
- Only a small proportion of the many antigens present, however are likely to stimulate protective immune responses. The rest are either irrelevant to protection or may induce undesirable host responses. Vaccination using whole parasite is therefore not feasible.
- Malaria parasites cannot be obtained in sufficient quantities or in sufficiently pure form.
- Cloning of genes for the protective antigens or antigenic structures requires high tech genetic engineering research.

**Ref. Menace of Malaria by the same Author**

## NTERESTING FACTS ABOUT AMYGDALA CIRCUIT

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An almond shaped neurostructure about 1inch inside each temple in the brain a part of, the brains limbic system. It coordinate the action of the autonomic and endocrine system and is involved in emotions. Unpleasant odors activate the amygdala and the Cortex in temporal lobe (insula). Its gray matter involves mediating the evolutionary ancient chemical nervous system represented today by our blood stream. After its surgical removal angry voices and other negative sign may loose their meaning and become incomprehensible.

Brain circuit coursing through the amygdala holds promise as target for treating anxiety disorders obsessive compulsive disorders post traumatic stress disorder phobias etc. Because its strategic location between inputs from the senses and memory and physiologic and behavioral outputs. Amygdala is hub in a wheel of fear. It can quickly activate almost every system in the body to fight like the or also run like crazy. Not accurate just fast meanwhile it helps brain to learn and form new memories Cortex calms amygdala down. Anxiety disorders can be due to over active amygdala or under active prefrontal Cortex.

Circuits involving the central nucleus of the amygdala appear to process conditioned fear responses to specific stimuli circuits involving a closely related area be bed nucleons of the stria testminalis handle non conditioned anxiety. Both circuits in turn connect to the hypothalamus brainstem and other brain areas mediating specific signs of fear and anxiety. The central nuclear pathway may thus play a role in disorder involving specific stimuli such as phobias while the stria terminalis circuit may underlie the more free floating symptoms of generalized anxiety disorders. If confirmed this could prove to be an important information in the development of treatments for anxiety disorders. If there are biochemical differences between the 2 nuclei one might be able to design medications with enhanced specificity.

A woman who had a defective amygdala was shown series of faces but trouble picking up faces that display fear. This shows fear holds in amygdala.

In intact brain it was found by brain scans and MRI

1. Amygdala of overanxious young children were on an average much larger compared to other children.

2. Brain cells using most oxygen and nutrients therefore signal in the amygdala appears to be more active in
those with post traumatic stress disorder then in those
without.
3. The stress of a building collapse could turn a normal
amygdala into an over active one.
4. Amygdala is very active in depressed points even when
they are sleeping. Dopamine is not the only neurotrans
mitters involved in Schizophrenia serotonin has been implicated also the amygdala is supposedly the loca
tion of the malfunction as this would explain the pres
ence of auditory visual and olfactory hallucination. Cur
rent research suggests that Dopamine be involved in
brains reward circuit for this reason dopamine is strongly
implicated in connection with highly addictive sub
stances.
The mesolimbic system is the one that includes the internal reward system. This system terminates in nucleus llubean. It also has connection with amygdala, which is involved, in memory processing. The combination of these elements emotional responding memory and the internal reward system results in a circuit this increases the probability that whatever behavior triggers activities in it will be repeated

## CLINICAL TIPS FOR HIV

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HIV is – Human Immuno deficiency Virus
AIDS IS – Acquired Immune Deficiency Syndrome
In infection with HIV the cells that defend the body against the disease are killed. When more and more of these cells are damaged, the body finds it difficult to fight this infection and the person develops AIDS.
- HIV infection is detected by blood examination. These
tests do not detect the virus in the blood but they detect
the antibodies that the body produces as a relation to
HIV infection. Antibodies develop in 6-12 weeks after
HIV infection.
- There are two types of HIV – HIV 1 & HIV 2 & they
mutate.
- 1st December is WORLD AIDS DAY.
- Red ribbon with Fish born is the symbol of AIDS awareness.
- HIV is no longer limited to high risk groups.

**- INTERPRETATION OF A HIV ANTIBODY NEGATIVE TEST :**

A negative test means :
a. The individual has been infected but not yet produced antibodies to virus.

b. The individual is not infected with the virus.
c. After Virus enters human body it usually takes 4-8 weeks for the detection of the antibodies. In the serum samples. This period is referred to as "WINDOW PERIOD"

**HIV SPREADS THROUGH:**

1. Using unsterile contaminated needle for injecting, tattooing and shaving with contaminated blade.
2. Sharing contaminated needles and syringes.
3. Transfusion of HIV contaminated blood.
4. Infected women to her baby during pregnancy par turition of breast feeding.
5. Sexual intercourse with an infected person.

**HIV DOES NOT SPREAD THROUGH:**

1. Urine of faeces 2. Sweat or tears
3. Cloths 4. Saliva
5. Insects – mosquitoes or bed bugs.
6. Using same toilet. 7. Water or food
8. Air. Coughing or sneezing.

**SUSPECTS AIDS:**

1. Tuberculosis 2. Kaposi's sarcoma
3. Esophageal condidiasis, dysphasia
4. Oral Candidiasis 5. Prolonged fever
6. Chronic Diarrhoea
7. Weight loss of more than 10% of body weight.

## PROTECT YOUR SELF WITH UNIVERSAL PRECAUTION :

1. Wash Hands, Wear Gloves.
2. Wear Mast, Gown and protective eye wear
3. Do not recap needles or mouth pipette.
4. Incinerate the infected material.
5. Protect broken skin against spills of blood and body fluids.
6. Dispose infected material in double bagged waste basket with closed lids.
7. Always prepare fresh hypochlorite to put gloves clothes etc.
8. Add ¼th cup of bleaching powder to 1 bucket of cold water put the gloves and cloth and close the lid for 30 minutes.

## DIABETES AND INFECTION

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Diabetes is one of the oldest diseases known to mankind. The ebers papyrus of 1500 BC mentions its symptoms and suggests treatment. In the same way infections related to diabetes are also known for long. The fateful association of diabetes mellitus and tuberculosis has been known for nearly one thousand years. At the turn of the century many diabetic patients still represent an important issue. Infection tends to occur with greater frequency and severity in diabetic patients than in non-diabetic. The occurrence of infection in a diabetic patient perpetuates a vicious cycle in which infection results in uncontrolled hyperglycemia which in turn causes further aggrevation of infections. Diabetics are more prone for infections as compared to normal. Uncontrolled diabetes rapidly promotes infection. There is a typical association of infection with diabetes, as sugar is a good media for rapid and abundant growth of organisms and at the same time infection itself disturbs the blood sugar levels and may precipitates ketoacidosis. Such infections are responsible for complications and morbidity more frequency than would be anticipated in normal individuals. However, now-a-days due to improvement in the greater health and better understanding diabetes and with the development of most effective diagnostic techniques, earlier intervention with newer human insulins as well as availability of broad spectrum antibiotics with better tolerability, have made the results are more favorable and hence the death rates due to infections had gone down from 17.6% in preinsulin era to 8.5% in insulin era. Let us hope still some better data will come out in recent future.

**WHY DIABETICS ARE MORE PRONE FOR INFECTIONS**

It is said in diabetics there are certain factors which play part in this direction. Increased susceptibility to infection is in this way multifactorial. The main effect f hyperglycemia and additional immune disturbance in type I diabetics do play role. The impairment of wide range of functions in neutrophils and macrocytes (Macrophages) including chemotaxis and adherence phagocytosis and intracellular killing of microorganisms is brought by hyperglycemia. In diabetes the movement of phagocytic cells may be generally impaired.

The W.H.O. has included diabetes in its classification of secondary immunodeficiency diseases. The development of secondary immunodeficiency seems to be determined by alterations involving at generally including polymorphonuclear granulocytes and/or lymphocytic subsets activity.

Polymorph nuclear granulocytes represent the host's first defense barrier against bacterial agents. Alternation in chemo taxis, phagocytosis, immunoglobulin production and complement functions do occur in diabetic patients. Polymorph nuclear granulocytes, cells from diabetics have a reduced chemo taxis especially when the diabetes is poorly controlled. There are two stages of phagocytosis adhesion and ingestion of microorganisms into intracytoplasmic vacuoles. An increase in sialidase enzyme secretion together with a corresponding reduction in cell membrane sialic acid may play part along with defective lactin receptors losing their capacity to recognize target and fail

to initiate phagocytosis. The critical step of intracellular killing is mediated by the intracellular release of toxic free radicals, super oxides and hydrogen peroxide. This respiratory burst which is impaired in diabetics correlates with intracellular killing. This whole process is dependent on nicotinamide adenine dinucleotide phosphate (NADPH). The NADPH is normally generated by the metabolism of glucose through the hexose monophosphate shunt and in diabetes more glucose enters the phatogocytes and is metabolized by the polyol Pathway. Aldose reductase, the rate limiting enzyme of this process requires NADPH and this is consumed when flux through polyol pathway increase. This competition for NADPH is thought to account for the reductions in the respiratory burst and in intracellular killing.

The metabolic disturbances associated with diabetes are probably important in impairing the function of polymorphonuclear cells. Once phagosome and lysosome fusion has taken place. Killing is carried out by lysosomal enzymes. A decrease in the killing capacity of polymorph nuclear granulocytes associated with high blood sugar may come to normalization within 48 hours after correction of blood sugar levels.

Several immunoglobulin levels IgG and IgA have been reported to be reduced in diabetics as compared to normal. As well as a significant reduction in the quantity and functional activity of complement components may occur in diabetic patients. Above all these local factors like underlying susceptibility to infection, vascular disease, nerve damage and increase in blood sugar may aggravate the process. This may call upon decrease circulation, hypoxia and reduction in absorption of antibiotics and proliferation of bacteria.

In type I or IDDM, genetics predisposition to infections also plays part. Along with all above factors which are abnormalities of aspects of phagocyte functions – mobilization and chemo taxis, adherence phagocytosis and intracellular killing with bactericidal activities, micro vascular circulations abnormality may result in decreased tissue perfusion. Hyperglycemia per say reduces oxidative killing capacity because of increased glucose Metabolism through polyol pathway depleting NADPH which is necessary for generation of super oxide free radicals.

In type I or IDDM, there is alteration in some lymphocyte subpopulations, a reduction in ‘T’ lymphocytes and under specifically in the number of CD4 phenotype. (‘C’ helper ‘T’ Lymphocytes) and reduction in CD4/CD8 ration serum immunoglobulin levels IgG and IgA have been reported to be reduced in diabetics compared to normal. As well as significant reduction in the quantity and functional activity of complements may occur in Diabetic patients. An underlying susceptibility of target tissues due to hyperglycemia, vascular disease and nerve damage is proved with the relative tissue hypoxia may cause proneness to infections. A reduction in antibiotic absorption due to microangiopathy may lead to persistence of infections. A reduction in antibiotic absorption due to microangiopathy may lead to persistence of infection. About 25% of IDDM subjects have this.

**WHAT EFFECT INFECTION PRODUCES ON METABOLISM:**

The major cause of hyperglycemic crisis is infection. It is the most common precipitation of Ketoacidosis in diabetics and it accounts for 30% of cases. Due to increase secretion of counter regulatory hormones such as glucagons, cortisol, growth hormone and catecholamine, gluconeogensis is stimulated and blood glucose levels are increased and

insulin secretion is inhibited. This results in relative or absolute insulin deficiency. In NIDDM due to insulin resistance significant hyperglycemia may persist as glucose uptake in liver and skeletal muscles is impaired. The elevation of counter regulatory hormones and insulin deficiency in diabetes with infection leads to diabetic ketoacidosis and creates an emergency which should be dealt with immediately considering condition itself and infection too.

The underlying mechanism has still to be determined, but increases in circulating cortisol concentrations and in certain cytokines, secreted by immune cells in response to infection, may contribute amongst the latter are the interleukins and tumor necrosis factor a, which impair insulin action by inhibiting the tyrosine kinase activity of the insulin receptor. Here the requirement is to keep blood sugar near normal levels.

**DIFFERENT INFECTIONS IN DIABETICS**

**1. RHINOCEREBRAL MUCORMYCOSIS**

The four genera which affect the humans are Absidia, Mortierella, Mucor, and Rhizopus. This relates to a fulminant fungal infection. Pulmonary and alveolar variety are also very common and less common are cutaneous, gastrointestinal (more of esophagus and fugal diarrhea) and other disseminated form.

This fulminant variety is now-a-days seen commonly and frequently, if brain does not know eyes do not see and brain does not record. Here the route of entry is nasopharynx and may extent upwards causing severe headache and involvement of Para nasal sinuses may lead to bloody discharge. When orbital structures are involved, it may lead to proptosis and loss of vision with a bad prognostic value. The diagnosis is done by

culture of biopsy of affected mucosae. Most important complications are meningoencephalitis, thrombosis of internal carotid arteries and cavernous sinuses. Tissue biopsy show characteristic hyphae. Rhinocerebral mucormycosis can presents as a painful soft tissue periorbital and perinasal swelling with induration and

discoloration with blood nasal discharge. Patients may come with diabetic ketoacidosis.

The treatment consist of human insulin to get normal blood sugar, intravenous fluids and aggressive surgical management, especially when it extents to the orbits, then radical debridement is necessary, here the progression is rapid (in hours to a few days) and out come is usually fatal if not dealt with aggressively. It may lead to exophthalmus, opthalmoplegia and cranial nerve palsies and meningoencephalitis. Patients may require reconstructive surgery. Mortality remains as high as 50%.

Tc agents, Tc hexamethylporpyleneamineoxine (HMPAO) is becoming increasingly common for white cell scanning. Recently Tc-anti-Nca-90fab'-fragment was used. In patients with soft tissue and abdominal infection this form of imaging has a diagnostic accuracy upto 100%. In prosthetic infection focal infection and in acute and chronic osteomyelitis it gives accurate results. It also throws some light on successful antibiotic

therapy while comparing 99Tc infection Scan before & after treatment with antibiotics. Pulmonary mucormycosis is also known and it mimics any chest infection, presenting with cough, fever, pleuritic pain and haemoptysis and it should be suspected in any refractory pneumonia in diabetic patients.

## 2. MALIGNANT EXTERNAL OTITIS

This condition occurs in elderly uncontrolled diabetics and is caused by a chronic infection of external auditory meatus and leads to destruction of surrounding tissue due to pseudomonas aeruginosa. It is also known as progressive invasive of necrotizing otitis external, high index of suspicion in diabetics, not responding for otalgia and otorrhoea by common drugs will help, in 50% of cases. There is involvement of facial nerve. When there is extension of infection to jugular foramen of in hypoglossal canal, the involvement of 9th, 10th, 11th, and 12th cranial nerves is quite possible. It may end up in meningitis where MRI may help in diagnosis. Standard antibiotics like penicillin (carbenicillin) plus an aminoglycoside for a pretty long time may help with surgical debridement monotherapy with ceftazimide as well as ciprofloxacin may work well. Involvement of temporal bone and back of skull is common – The overall mortality in the condition is 20% and others may land up with permanent disability.

In my department still nine patients are coming with good diabetics control along with very good control of this condition.

Therapy consists of surgical debridement and a combination of carbenicillin with an amynoglycoside continued for upto six weeks and at least one week after negative cultures to ensure no recurrence.

## 3. EMPHYSEMATOUS PYELONEPHRITIS

This may follow a severe bacterial urinary tract infection. Pyelonephritis presents with loin pain, fever and systemic upset and urinary tract symptoms often with severe disturbance of glycemic control. Most likely definition of this entity includes a requirement for the presence of gas within the renal parenchyma which may enter the perinephric space by extension. This is a necrotizing infection with gas production in and around the kidney. Gas may occur in calyces, collecting system of in bladder. A plain x-ray film and CT- scanning without contrast may show a motted renal parenchyma with the gas bubbles and often a radial distribution. Usual causative organism is typical urinary pathogens like E.coli, K. pneumoniae, B. urinabillis and E.aerogens. After giving proper antibiotics like third generation cephalosporin of ciprofloxacin and other fluroquinolones for a sufficient period of time, if it does not respond then nephrectomy is necessary. Intravenous insulin infusion is often required for control of hyperglycemia.

## 4. EMPHYSEMATOUS CHOLECYSTITIS

This predominantly occurs in diabetics more common with the type II diabetics involving both the sexes equally. It is a rare complication of acute cholecystitis in which air is found in the lumen and in the wall of gall bladder with the possible extension in the pericholecystic space. In 80% of the cases diabetes is detected. Here perforation and gangrene takes place in the gall bladder and mortality is increased. Here the presentation is the same as pain in the right upper quadrant, nausea, vomiting and fever. During the next 48 hours gas develops in the gall bladder lumen and wall, and then extension of gas occurs. This is revealed on radiological examination. Here the response is well with broad spectrum parentral antibiotics and early cholecystectomy before gangrene in the gall bladder appears.

**5. ACUTE NECROTIZING FASCITIS**

This is soft tissue infection which is necrotizing and spreads along the fascial tracts of planes and causes the problem. This is also known as acute dermal gangrene. It is severe & progressive and leads to necrosis of subcutaneous tissues down to the level of the muscle fascia but usually sparing the muscles. In North Western Europe a sharp increase in the number of cases have taken place with invasion by group streptococci, other Meleney's gangrene which advances very slowly affection the skin is also known.

Involvement of the perineum and external genitalia by group A b - hemolytic streptococci of various serotypes-most common is M1 is primarily responsible but may act together with staphylococci aureus and epidermidis of anaerobes, including enterobacteriae.

With proper control of diabetes with perfect dose of human insulin, high dose of intravenous antibiotics, benzylpenicilline and clindamycin work well. Along with the early and extensive surgical debridement with hyperbaric oxygen therapy may work.

**6. INFECTION CAUSED BY THERAPEUTIC INTERVENTIONS**

Now-a-days with new devices of insulin injections, the problems of boiling the needle and syringes have gone away and the occurrence of finger bed infection and abscess have decreased, when patients take insulin by themselves and with newer devices like disposable insulin syringes and Novopen, and Humapen, occurrence of infection and abscess formation have gone down and occurs in few cases.

Impotency is higher in the diabetics than their counter parts non diabetics. Along with other therapies penile prosthesis are very common. The chances of infection are seen as early as 2 week of as late as 2 years after implantation, staphylococcus epidermidis is the infection organism in 40 to 50% of the cases. Immediate therapy consists of the removal of prosthesis and therapy with broad spectrum antibiotics and the post operative drainage.

As compare to non-diabetics the infection rate is higher among diabetics undergoing organ transplantation e.g. kidney, heart transplantations.

Continuous ambulatory peritoneal dialysis is all increasingly common modality of therapy in end stage renal disease in patients with diabetes. This also carries a risk of infection like any indwelling foreign body in the diabetics. Also many diabetics with end stage renal disease undergo heamodialysis through subclavian or femoral catheter kept in situ for days or months. These are also prone for infections. Arterio venous grafts can also be infected by haematogenous spread of microorganism form a distant site of infection, staphylococcus aureus is estimated to cause 80% of infection. All above infections need proper antibiotics for adequate time period. Occasionally a surgical approach is required.

**"Shape the Future of Life: Healthy Environment for Children."**
**World Health Organization - 2003**

(Dr. Jay K. Sheth – Assistant Professor, Dept. of P&SM)

World Health Day is celebrated every year by the World Health Organization on 7th April with one World Health Day Theme to focus attention of international community on a specific aspect of public health issues of worldwide concern to mark the importance of health for productive and happy lives. World Health Day 2003 is a global advocacy activity dedicated to environmental health issues with particular emphasis on child health with the theme “Shape the Future of Life: Healthy Environment for Children.”

The burden of disease from environment-related diseases is great and falls disproportionately on children. Every year over 5 million children ages 0 to 14 die, mainly in the developing world, from diseases related to their environments - the places where they live, learn and play. Almost one third of the global burden of disease can be attributed to environmental risk factors, over 40% of this burden falls on children under 5 years of age, who constitute no more than 12% of the world’s population. Air pollution from the inappropriate combustion of fossil fuels for cooking and heating causes respiratory infections, which are responsible for up to 20% mortality in children under five years of age. Diarrhoeal diseases kill around two million children under the age of five every year, and are almost entirely related to unsafe drinking water and the lack of sanitation and hygiene.

Every child has the right to grow up in a healthy environment. The future development of our children – and of their world – depends on their enjoying good health now. Children are particularly vulnerable to environmental hazards. Their immune, reproductive, digestive and central nervous systems are still developing and they spend their time closer to the ground where most dust and chemicals accumulate. They explore their surroundings through hand-to-mouth behaviour and are unaware of potential risks. Children are not “little adults” - they are particularly vulnerable because they are in a dynamic state of growth and their ability to detoxify and excrete toxins differs from that of adults. Their characteristics such as natural curiosity and lack of knowledge, are aggravating factors. Exposure to environmental risks at early stages of development can lead to irreversible damage. they are more susceptible at the same time they are also more exposed at an early age and for a prolonged period of time. Therefore, they develop diseases with long latency periods. Children have a unique vulnerability. As they grow and develop, there are “windows of susceptibility”: periods when their organs and systems may be particularly sensitive to the effect of certain environmental threats. Some environmental diseases result in physical or mental long-term disability; others cause more immediate and short-term effects. Many environmental threats to children’s health are aggravated by persistent poverty, conflicts, natural and man-made disasters, and social inequity.

For the children although their personal world is often small, but there too lies the risk and these risks are increasing. Generations of children have suffered from certain ‘basic’ risks existing in their environments. These are unsafe drinking water, inadequate sanitation, indoor air pollution, insufficient food hygiene, poor housing and inadequate waste disposal. Today’s ‘modern’ risks result from the unsafe use of dangerous chemicals, the inadequate disposal of toxic waste and other environmental hazards, noise and industrial pollution. Unsafe chemicals in toys and household products may also harm children. ‘Emerging’ potential environmental threats to health include global climate change, ozone depletion, contamination by persistent organic pollutants and chemicals and other hazards, and emerging diseases.

Children are often exposed not just to one risk factor at a time but to several simultaneously. They frequently live in unsafe and crowded settlements, in underserved rural areas or in slums on the edges of cities which lack access to basic services such as water and sanitation, electricity, or health care. They are likely to be exposed to industrial and vehicle pollution as well as to indoor air pollution and to unsafe chemicals. Children are also likely to suffer from unintentional injuries (accidents) and poisonings associated with unsafe housing and consumer products. They are more likely to be undernourished, causing them to be more vulnerable to environmental threats.

The suffering of children because of environmental hazards is not inevitable. There are solutions; most of the environment-related disease and deaths can be prevented. The economic burden of environment-related disease is enormous. But when environmental risks are reduced, the financial gains are considerable. We will have to ensure that through our actions they will inherit a world free of the indignity and indecency occasioned by poverty, environmental degradation and patterns of unsustainable development.

For most of these prioritizing risks, security, stability, emergency preparedness and economic development are key to overcoming them. While experience shows that even in underdeveloped economies, these risks can be significantly reduced, experience also shows that, in higher income societies, the overall burden of environmental diseases in children decreases - at the same time as the relative priorities change. Therefore, regions and countries will have to set their specific priorities to complement these global ones.

The physical, social and intellectual development of children from conception to the end of adolescence requires an environment which is both protected and protective of their health. Prevention of exposure is the most effective means of protecting children … and of strengthening the potential of countries. The mission of the WHO Task Force for the Protection of Children's Environmental Health is to prevent disease and disability in children associated with such environmental hazards and acknowledging the importance of social and psychosocial factors.

We all know what we have to do. Strategies have been developed to combat these threats to children's health. They need to be implemented on a national and global scale. By working together on many fronts, by building on existing programmes, and by adapting concrete actions to local needs, every country can make a difference. Together, we are better able to confront the environmental health issues faced by communities, countries, regions and sectors all around the world.

To conclude, in words of executive director of United Nations Environment Programme "Human rights cannot be secured in a degraded or polluted environment. The fundamental right to life is threatened by various types of environmental pollution. Environmental conditions clearly help to determine the extent to which people enjoy their basic rights to life, health, adequate food and housing, and traditional livelihood and culture. It is time to recognize that those who pollute or destroy the natural environment are not just committing a crime against nature, but are violating human rights as well."

## PILEPSY: MANAGEMENT ASPECTS

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**Definition**

**Convulsion** is ”An intense paroxysm of involuntary repetitive muscular contraction.”
While, **Seizure** (Latin-to sacire- to take possession of) is defined as “A paroxysmal event due to abnormal, excessive, hyper synchronous discharges from an aggregate of central nervous system neurons.”
Approximately 5 to 10 % of the population will have at least one seizure during their lifetime, with the highest incidence occurring in early childhood and late adulthood.
**Epilepsy** (Greek- to seize upon or taking hold of) is “A group of CNS disorder, characterized by paroxysmal cerebral dysrhythmias, manifesting as disturbance of consciousness or body movements or sensory or psychic phenomenon.”
It is a condition in which a person has recurrent seizures due to a chronic underlying process; Refers to a clinical phenomenon rather than a single disease entity.
Using a practical definition of epilepsy as two or more unprovoked seizure, the incidence is approximately 0.3 to 0.5 % in different population throughout the world and the prevalence of epilepsy has been estimated at 5 to 10 persons per1000.
**Epilepsy syndrome** are “The disorders in which epilepsy is a prominent feature, and there is sufficient evidence to suggest a common underlying mechanism.”
1. Partial seizures
2. Adult onset epilepsy
3. Any abnormality in neurological examination
4. Interactable refractory epilepsy
5. Patients presenting with status epilepticus.

… MRI has been shown to be superior to CT in the scanning for the detection of cerebral lesions associated with epilepsy.
… Functional imaging procedures such as PET and SPECT are also used to evaluate certain patients with medically refractory seizures

**Management**

@ Almost always a multi-modal approach
@ Includes
… Treatment of the underlying conditions that cause or contribute
… Avoidance of precipitating factor/s
… Suppression of recurrent seizure by prophylactic therapy
… Addressing a variety of psychological and social issues.
@ Treatment plans must be individualized for each patient.

**TREATMENT OF UNDERLYING CONDITIONS**

If the sole cause of the seizure is metabolic disturbance; the treatment is aimed at reversing the problem and preventing the recurrence. (No AED required generally)
If the apparent cause was a medication or illicit drug use, and then appropriate therapy is avoidance of the drug.
Seizures caused by a structural lesion of CNS, may not recur after appropriate treatment of the underlying lesion. However, this is a high-risk group and hence most patients are

maintained on AED for at least 1 year and an attempt is made to withdraw medication only if the patient has been completely seizure free.

**AVOIDANCE OF PRECIPITATING FACTORS**

Unfortunately little is known about the specific factors that determine precisely when a seizure will occur in a patient with epilepsy. Some of the patients can identify particular situations that appear to lower the seizure threshold, these situation are to be avoided.
Ex- sleep deprivation
Alcohol intake
Stress
Rarely, specific stimuli such as video monitor, music or individual's voice (reflex epilepsy)

**ANTI-EPILEPTIC DRUGS**

It is the mainstay of the therapy. The overall goal is to completely prevent seizures without causing any untoward side effects, preferably with a single medication and a dosing schedule that is easy for the patient to follow.

**When to initiate?**

AED should be started in any patient with recurrent seizures of unknown etiology or a known cause that cannot be reversed.
@ In a case of first unprovoked seizure in a child:
Start onlywith a repeated attack or there is abnormal neurological examination.
@ In a case of first unprovoked seizure in an adult:
Start only if- abnormal neurological examination,
Presenting as status epilepticus,
Postictal Todd's paralysis,
Abnormal EEG, or
Structural epileptogenic CNS lesion.
@ Risk of recurrence:
…EEG normal & CTSCAN normal — 24 % in next 2 yrs.
…EEG abnormal & CTSCAN normal — 48 % in next 2 yrs.
…EEG normal & CTSCAN abnormal — > 70 % chance of recurrence

**Principles**

(As described by International League Against Epilepsy)
1. Identify precipitating factor, if any.
2. Explain the patient /relatives about the AED.
(Rx/limitations/duration/regularity/side effects)
3. Start with small dose of a single drug.
Gradually increase if seizures continue and if S/E do not occur.
4. If seizures continue with a maximum tolerated dose of a single drug, reconsider the diagnosis and etiology.
5. If still inadequate response, add another first line of drug-Gradually built the dose and withdraw the initial agent.

6. Adjust the dose of drug to optimum level Based on sei
zure response and side effects.
7. If still inadequate response, think of two drug combina
tion therapy.
8. If seizures, replace with one of the second line AED.
9. Withdraw the initial agent.
10. If the seizures still continue, use one of the newer AEDs.

**Monitoring**

Monitoring of serum AED level can be very useful for establishing the initial dose schedule. However, the therapeutic ranges are only approximate guide. The key determinants are the clinical measure of seizure frequency and presence of side effects, not the laboratory values.

**Selection of AED**

@ Depends on Type of the seizure
Efficacy
Relative convenience of the dosing schedule
Potential side effects

| First line | Second line |
|---|---|
| Partial Carbamazepine | Lamotrigine |
| Phenytoin | Gabapentin |
| Valproic acid | |
| Generalized Phenytoin | Lamotrigine |
| Valproic acid Carbamazepine | |
| Phenobarbital | |
| Absence Ethosuximide | Lamotrigine |
| Valproic acid Clonazepam | |
| Atypical absence, Valproic acid | Lamotrigine, |
| Myoclonic, Clonazepam | |
| Atonic Felbamate | |

**When to discontinue?**

It seems reasonable to attempt withdrawal of AED in a child after 2 yrs and in adults 2-3 yrs of seizure free period. It is preferable to reduce the dose gradually over 2-3 months and then withdraw- especially with barbiturates, benzodiazepines, vigabatrin & carbamazepine.

@ Chances of recurrence are high if:
1. Abnormal EEG,
2. Partial seizures,
3. LG syndrome or JME,
4. Longer duration of epilepsy,
5. Patient on poly therapy,
6. Patients with difficult to control seizures,
7. Abnormal neurological examination and
8.CNS structural lesion

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## NEW DRUGS

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**Emend (aprepitant)**, a P/neurokinin 1 (NK1) receptor antagonist, is an antiemetic medicine used to prevent and control nausea and vomiting caused by chemotherapy treatment. It is always used in combination with other antiemetic agents.
Emend capsules for oral administration contain either 80 mg or 125 mg of aprepitant. Unlike other chemotherapy-induced side effect treatments, it has little or no affinity for serotonin (5-HT3), dopamine, and corticosteroid receptors.
In addition, animal and human studies using Positron Emission Tomography (PET) have shown that it crosses the blood brain barrier and occupies brain NK1 receptors. It also augments the activity of the 5-HT3-receptor antagonist ondansetron and the corticosteroid dexamethasone.
USFDA approval of Emend was based on several clinical studies. Treatment with aprepitant was compared with standard therapy in subjects receiving a chemotherapy regimen that included cisplatin > 50 mg/m2. Results showed Emend, in combination with ondansetron and dexamethasone, prevented acute and delayed nausea and vomiting associated with highly emetogenic chemotherapy including high-dose cisplatin.
In studies, a statistically significantly higher proportion of subjects receiving aprepitant had a complete response, compared with subjects receiving standard therapy. A statistically significant difference in complete response in favour of the aprepitant regimen was also observed.
The most common chemotherapeutic agents used in the studies were etoposide, flourouracil, gemcitabine, vinorelbine, paclitaxel and doxorubicin.
The aprepitant-treated subjects ranged from 14 to 84 years of age, with a mean age of 56 years. 170 subjects were 65 years or older, with 29 subjects being 75 years or older.
Commonly observed side effects-
Asthenia,dehydration ,dizziness ,diarrhea ,hiccups and dizziness.

**Fuzeon (enfuvirtide)** is an HIV fusion inhibitor that helps block the viruses' ability to infect healthy T- cells. This drug does not cure HIV infection or AIDS and must be taken as part of a combination antiretroviral regimen.

Fuzeon in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.
The drug is given under the skin by injection in the upper arm, upper leg or stomach two times a day. The recommended dose of is 90 mg (1 ml) twice daily.
Fuzeon blocks HIV's ability to infect healthy CD4 cells. When used with other anti- HIV medicines, Fuzeon can reduce the amount of HIV in the blood and increase the number of CD4 cells. This may keep the immune system healthy, so it can help fight infection.
The active ingredient, enfuvirtide, interferes with the entry of HIV-1 into cells by inhibiting fusion of viral and cellular membranes. Enfuvirtide binds to the first heptad-repeat (HR1) in the gp41 subunit of the viral envelope glycoprotein and prevents the conformational changes required for the fusion of viral and cellular membranes
USFDA approval of Fuzeon was based on data from two 24-week phase III pivotal studies of approximately 1,000 subjects, TORO 1 (T20-301), conducted in North America and Brazil, and TORO 2 (T20-302), conducted in Europe and Australia. These studies showed that treatment-experienced subjects receiving Fuzeon as a part combination regimen of anti-HIV drugs, experienced greater immunologic improvements and were twice as likely to achieve undetectable plasma levels of HIV compared to subjects receiving an anti-HIV regimen alone.
Commonly observed side effects :
Local injection site reaction, pain and discomfort, induration, erythema nodules and cysts, pruritus, ecchymosis, diarrhea, conjunctivitis and pancreatitis) :
Amevive (alefacept) is an immunosuppressive dimeric fusion protein that reduces lymphocyte counts (T-cells) thus treating the cause of psoriasis. It is indicated in patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy
Amevive is available in either intramuscular injection (15-mg alefacept) or intravenous injection (7.5-mg alefacept) formulations.
Amevive (alefacept) is an immunosuppressive dimeric fusion protein that consists of the extracellular CD2-binding portion of the human leukocyte function antigen-3 (LFA-3) linked to the Fc (hinge, CH2 and CH3 domains) portion of human IgG1. Alefacept is produced by recombinant DNA technology in a Chinese Hamster Ovary (CHO) mammalian cell expression system.
Amevive reduces immune cell counts, which could increase the chance of developing infection or malignancy. Amevive interferes with lymphocyte activation by specifically binding to the lymphocyte antigen, CD2, and inhibiting LFA-3/CD2 interaction. Activation of T lymphocytes involving the interaction between LFA-3 on antigen presenting cells and CD2 on T lymphocytes plays a role in the pathophysiology of chronic plaque psoriasis. The majority of T lymphocytes in psoriatic lesions are of the memory effector phenotype characterized by the presence of the CD45RO marker[1], express activation markers (e.g., CD25, CD69) and release inflammatory cytokines, such as interferon y.

**Amevive** also causes a reduction in subsets of CD2+ T lymphocytes (primarily CD45RO+), presumably by bridging between CD2 on target lymphocytes and immunoglobulin Fc receptors on cytotoxic cells, such as natural killer cells. Treatment

with Amevive results in a reduction in circulating total CD4+ and CD8+ T lymphocyte counts. CD2 is also expressed at low levels on the surface of n) :
Iressa is an anticancer drug that inhibits an enzyme (tyrosine kinase) present in lung cancer cells, as well as other cancers and normal tissues that appears to be important to the growth of cancer cells. It is taken alone, not with other atural killer cells and certain bone marrow B-lymphocytes.
Amevive was evaluated in two randomized, double blind, placebo-controlled studies in 726 adult subjects with chronic plaque psoriasis. In both trials, Amevive or placebo was administered once a week for 12 weeks. In total 77% of subjects had previously received systemic therapy and/or phototherapy for psoriasis. Response to treatment was defined as the proportion of subjects with a reduction in score on the Psoriasis Area and Severity Index (PASI) ³ of at least 75% from baseline at two weeks following the 12-week treatment period. In the study,onset of response to Amevive treatment (at least a 50% reduction of baseline PASI) began 60 days after the start of therapy.
Commonly observed side effects-
Serious infections, malignancies, lymphopenia, sore throat, dizziness cough, nausea, itching ,muscle aches ,chills, injection site pain, inflammation and accidental injury .

**Iressa (gefitinb) :**
The recommended daily dose of Iressa is one 250 mg tablet with or without food. Higher doses do not give a better response and causes increased toxicity.
Gefitinib is an EGFR tyrosine kinase inhibitor. It works by binding to the intracellular enzyme (tyrosine kinase) of the EGFR to directly block signals turned on by triggers outside or inside the cell.
The activity of epidermal growth factor and its receptor, the EGFR, have been identified as key drivers in the process of cell growth and replication. Heightened activity at the EGF receptor, whether caused by an increase in the concentration of ligand around the cell, an increase in receptor numbers or a decrease in receptor turnover or receptor mutation, can lead to an increase in the drive for the cell to replicate. There is now a body of evidence to show that the EGFR-mediated drive is increased in a wide variety of solid tumours, including non-small cell lung cancer, prostate cancer, breast cancer, gastric cancer, colon cancer, ovarian cancer and tumours of the head and neck.
Gefitinib is an anilinoquinazoline with the chemical name 4-Quinazolinamine. The mechanism of the clinical antitumor action of gefitinib is not fully characterized. Gefitinib inhibits the intracellular phosphorylation of numerous tyrosine kinases associated with transmembrane cell surface receptors, including the tyrosine kinases associated with the epidermal growth factor receptor (EGFR-TK). EGFR is expressed on the cell surface of many normal cells and cancer cells.
USFDA approval of Iressa was based on a phase III trial. The multicenter clinical trial in the U.S. evaluated the tumor response rate of Iressa 250 and 500 mg/day in 216 subjects with advanced non-small cell lung cancer whose disease had progressed after at least two prior chemotherapy regimens including a platinum drug and docetaxel. Iressa was taken once daily at approximately the same time each day. Subjects received Iressa, 102 (47%) and 114 (53%) receiving 250 mg and 500 mg daily doses, respectively. In addition, 41% of the subjects had received two prior treatment regimens, 33% three prior treatment regimens, and 25% four or more prior treatment regimens.

Results showed that the overall response rate for the 250 and 500 mg doses combined was 10.6% (95% CI: 6%, 16.8%). Response rates appeared to be highly variable in subgroups of the treated population:
5.1% (4/79) in males, 17.5% (11/63) in females, 4.6% (5/108) in previous or current smokers, 29.4% (10/34) in nonsmokers, 12.4% (12/97) with adenocarcinoma histology, and 6.7% (3/45) with other NSCLC histologies. Similar differences in response were seen in a multinational study in subjects who had received 1 or 2 prior chemotherapy regimens, at least l of which was platinum-based. In responders, the median time from diagnosis to study randomization was 16.7 months (range 8 to 34 months).
Commonly observed side effects Diarrhea, rash, acne, dry skin, nausea, vomiting, pruritus, anorexia and asthenia.

**Oxytrol (oxybutynin transdermal system)**, is a transdermal patch designed to deliver oxybutynin continuously and consistently over a 3- to 4-day interval after application to intact skin. Oxytrol is available as a 39-cm2-patch system containing 36 mg of oxybutynin. Oxytrol is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.
The dose of Oxytrol is one 3.9 mg/day system applied twice weekly (every 3 to 4 days). Oxybutynin is an antispasmodic, anticholinergic agent. The active ingredient is dissolved in the thin layer of adhesive that sticks the patch to the skin. Oxytrol delivers the medicine slowly and constantly through the skin and into the bloodstream, bypassing initial metabolism in the liver and the gastrointestinal tract
Patients who have urinary retention, gastric retention, uncontrolled narrow-angle glaucoma or hypersensitivity to oxybutynin or other components of Oxytrol should not use Oxytrol.
USFDA approval of Oxytrol was based on the efficacy and safety evaluated in patients with urge/urinary incontinence a phase III controlled study. The study was a randomized, double blind, placebo-controlled study, comparing the safety and efficacy of Oxytrol at dose levels of 1.3, 2.6, and 3.9 mg/day to placebo in 520 subjects. Results showed that subjects experienced a significant reduction in weekly incontinence episodes, urinary frequency, and urinary void volume in active treatment groups versus placebo.
Commonly observed Side Effects-
Diarrhea, dysuria headache, dry mouth, flatulence, nausea abdominal pain, application site pruritus, erythema and vesicles.

**Meningitis Vaccine for infants older than two months:**
Chiron Corporation announced that the UK's Medicines Control Agency (MCA) and the Irish Medicines Board have approved its meningococcal C conjugate vaccine Menjugate™ for immunizing infants aged two months and older against meningococcal disease caused by Neisseria meningitidis serogroup C.
This approval extends the indication for Menjugate to now include active immunization of children from two months of age and up. Menjugate was previously approved for children older than 12 months, adolescent and adults in the UK.
The vaccine has now been included as part of the UK and Ireland's extensive immunization program. The UK initiated a vaccination program and, according to the Department of Health, the program has reduced the number of meningococcal C cases in

immunized groups by 70 percent. The Republic of Ireland has also launched its vaccination campaign.
In published studies analyzing the effective response of infants and children, Menjugate was shown to be well tolerated, capable of stimulating a robust immune response and producing a sustained protective effect against the bacterium after vaccination.

**Once-Weekly Fosamax (Alendronate):**
The United States Food and Drug Administration (USFDA) has approved a new dosage strengths of Merck & Co., Inc.'s Fosamax® (alendronate sodium), 'once-weekly tablets' — 70 mg for the treatment of postmenopausal osteoporosis.
Fosamax is the first and only oral medication approved for the treatment and prevention of postmenopausal osteoporosis in a once-weekly dosing regimen.
Patients and their health care professionals now have the opportunity to choose between once-daily and once-weekly alandronate.
Fosamax once-weekly regimen is therapeutically equivalent to once-daily regimen.
The most common gastrointestinal (GI) adverse experiences were abdominal pain, indigestion, acid regurgitation and nausea. There were no statistically significant differences between the two dosing regimens in upper GI adverse experiences that resulted in discontinuation of the drug.
To assist patients in following the dosing regimen for the once weekly dosing of Fosamax, a patient-friendly blister package containing a four-week supply has been developed. Patients can select a day of the week that works best for them to take the once-weekly dose of Fosamax. If a dose of Fosamax once weekly is missed, patients should take that tablet the morning after it is remembered. Patients should not take two tablets on the same day, but should return to taking one tablet once a week as originally scheduled on their chosen day.
Apart from the dosing frequency, the dosing administration instructions for the once-weekly and once-daily formulations are the same. Fosamax, like other bisphosphonates, should be used with caution in people with certain stomach or digestive problems. In addition, Fosamax should not be used in patients with severe kidney disease or low levels of calcium in their blood, in patients who are allergic to Fosamax or in patients who are pregnant or nursing.
Fosamax now provides physicians and health care providers with the option to prescribe the once-weekly regimen at the same catalog price as a week's worth of the daily regimen.

**Monthly Injectable 'Combined' Contraceptive Injection:**
The Pharmacia Corporation announced that the U.S. Food and Drug Administration (FDA) approved Lunelle™ Monthly Contraceptive Injection (medroxyprogesterone acetate and estradiol cypionate injectable suspension), Lunelle, a combined hormonal injectable contraceptive method, has contraceptive benefits similar to the pill yet offers women the convenience of once-a-month dosing.
"Lunelle is more than 99 percent effective when administered as scheduled, offering women a reliable and convenient new birth control option."
Lunelle was approved based on data from a pivotal clinical study of 1,103 women that compared the efficacy, safety and patient acceptability of Lunelle versus Ortho-Novum

7/7/7®, a leading oral contraceptive, at 42 sites in the U.S. The data reported no unintended pregnancies among the 782 women taking Lunelle versus two unintended pregnancies among the 321 women using the oral contraceptive after 15 cycles of use. The person can be out of the health care provider's office in less than 15 minutes once a month. It is recommended that Lunelle be administered every month by a health care provider, not to exceed 33 days, as a single, small 0.5ml monthly intra-muscular injection. The estrogen in Lunelle is metabolized to 17 beta-estradiol - the body's natural estrogen - and at peak levels does not exceed a woman's natural cyclic levels of estrogen. Lunelle Monthly Contraceptive Injection provides monthly menstrual cycles and unlike long-acting progestogen (Medroxyprogesterone)-only, leads to a quick return to ovulation, usually within two to four months. More than 50 percent of the users became pregnant during the first six months following discontinuation of Lunelle.
Adverse reactions were common as with other combined contraceptives.

**Lescol XL (Fluvastatin), Extended Release :**
The data on the entirely synthetic Fluvastatin originated from small studies until Novartis Pharmaceuticals Corporation announced approval by the U.S. Food and Drug Administration for Lescol® XL (fluvastatin sodium) 80 mg, an extended-release tablet formulation of fluvastatin.
The reformulated extended-release Lescol XL 80 mg tablet provides patients with a higher dose of medication, while maintaining safety. With this slow release delivery form of the drug, availability of the statin to the liver is increased while minimizing the risk of systemic exposure to high drug doses throughout the body.
In addition, fluvastatin is not predominantly metabolized by the cytochrome P450 3A4 pathway, thus minimizing the potential for interactions with drugs that patients commonly take on a daily basis that are metabolized through this pathway.
The USFDA approved Lescol XL 80mg based on their review of data from five controlled clinical trials that were four to 24 weeks in duration in more than 900 patients with Type IIa or IIb hyperlipoproteinemia. A pooled analysis of pivotal trials and phase III trials showed significant LDL-C reductions ranging from 35-38 percent in patients with dyslipidemia. Lescol XL 80 mg produced a median reduction in TG of 19 percent in patients with dyslipidemia and 25 percent in patients with primary mixed dyslipidemia (Fredrickson Type IIb). Thus, slowing the progression of A.S. in patients with coronary ischaemic heart disese.
In addition, Lescol XL 80 mg produced HDL-C increases ranging from 0-15 percent (25th -75th percentile: median 7 percent) in patients with dyslipidemia and increases ranging from 3-20 percent (25th-75th percentile: median 11 percent) in patients with primary mixed dyslipidemia (Fredrickson Type IIb). These trials confirmed that a daily dose regimen of Lescol XL 80 mg provides significantly improved efficacy with a similar safety profile when compared to Lescol 40 mg.
Health authorities in Austria, Brazil, Portugal, Switzerland, Thailand, and the United Kingdom also have approved Lescol XL 80 mg.
The current formulation of Lescol is marketed in more than 90 countries Lescol has been studied in more than 25,000 patients.
In Phase III clinical trials, the overall incidence of adverse events for Lescol XL was similar to Lescol 40 mg, and no cases of myopathy or rhabdomyolysis were observed in

these trials.
Lescol XL should not be used by pregnant or nursing women and in patients who currently have liver disease or unexplained increases in liver enzyme levels. It is recommended that liver function tests be performed before the initiation of therapy and at 12 weeks following initiation of treatment or elevation in dose. Treatment with Lescol XL should be discontinued if myopathy or rhabdomyolysis are diagnosed or suspected.