Contents

Correspondence

Recent advances

Deschooling Medical Education in India

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"Students are schooled to mistake medical treatment for health care, social work for the improvement in community life, police protection for safety, military poise for national security, and the rat race for productive work."

Ivan Illich

Wise people learn from their own mistakes; wiser people from the mistakes of others. Indians being the wisest of the lot should learn from the mistakes that the western audits have discovered in our present modern medical interventions and in the scientific basis of modern medicine.[1] It would be too late to learn from our own mistakes as we do not audit what we do in medicine anyway! Ever since the first three medical colleges were set up by the East India Company in 1857, based on Macaulay's ideas, we promoted rote learning, students being taught by indifferent faculty resulting in mediocrity. There are exceptions, though. Mediocrity is competing with others, while excellence is competing with oneself, the latter being absent in our system. We punished original thinking and failed to create thinking, humane doctors. We have been pushing students into parallel coaching institutions before they get into medical schools to rote learn the premedical subjects to pass the "so called" entrance tests, again throttling their thinking capacity. Aptitude of the entrants to become healers is never tested. The earlier this system dies the better for us as our entire education system was intended to make us rote learning robots of the western thoughts in the first place. The following extract from the speech of Thomas Babington Macaulay in the House of Commons on the 2nd February 1835 says it all. ""I have traveled across the length and breadth of India and I have not seen one person who is a beggar, who is a thief. Such wealth I have seen in this country, such high moral values, people of such calibre, that I do not think we would ever conquer this country, unless we break the very backbone of this nation, which is her spiritual and cultural heritage, and, therefore, I propose that we replace her old and ancient education system, her culture, for if the Indians think that all that is foreign and English is good and greater than their own, they will lose their self-esteem, their native self-culture and they will become what we want them, a truly dominated nation."(Italics mine)

What ails our present medical education?

The MBBS degree that was introduced by the London University syllabus of 1857 continues even after 60 years of political independence with minor tinkering here and there. Time has come to see if this is relevant to our present day needs. Progress in science has shown us that the scientific basis of modern medicine is very shaky-more about it below. The course is overburdened with information and the student is left with very little time to study sick human beings where, in fact, the student should get all his education. Bed side medicine, the core of medical education, is all but dead in the present scenario.[2] The faulty theory, based on statistical science, and not pure science, is being dinned into the students head with a top heavy curriculum which leaves much to be desired, resulting in the student having no choice but to rote learn the textbook stuff to the exclusion of real learning of medicine on the bed side. Basic doctor does not need such detailed instructions in sub-specialties that we teach now. Basic doctor needs to be a humane healer with adequate basic knowledge of the subject, mainly the fundamentals of clinical medicine for all age groups with some principles of surgery. Basic doctor also needs to know that there are possibilities to help the patient in desperate situations out with the modern medical boundaries in alternate systems that have been in existence for centuries, where there are scientifically proven

healing methods. The present curriculum does not allow that laxity while in the west teaching alternate medicine is mandatory for the basic doctor.[3]

Deep down modern medical science is very shallow-The conventional research in medicine is only a statistical research; there is no hard science in that area. We have been using the wrong mathematical basis for research in medicine. Whereas the human body is dynamic and follows the non-linear mathematical model, we use the linear model of deterministic predictability of Newtonian science. This has resulted in most, if not all, our data, to date, being questionable.[4] We have been predicting the unpredictable future of humans by routinely screening the apparently healthy and declaring them to be unwell while time evolution in any dynamic system depends on the *total initial knowledge* of the organism.[5] The latter, in the case of human beings, depends on their mind (consciousness), body and the genes. Routine screening, at best, could measure only a few parameters of the body. Audits now show that all kinds of screening measures have resulted in misery for mankind while helping the medical and drug industry to earn plenty of profits.[6] We have been trying to medicalise the whole population. If one looks at the following data one will be convinced. Almost 90% of the population, by the age 40, will have at least one "so called" risk factor qualifying for drug therapy. With the drugs that we have for this purpose and the recent expose of the nefarious designs of the drug companies the future of mankind looks really bleak unless we quickly deschool medical education.[7] Jeremy Laurance, health editor of The Independent, London wrote on the 27th February 2008 issue thus: " The pharmaceutical industry came under assault from senior figures in medical research yesterday over its practice of withholding information to protect profits, exposing patients to drugs which could be useless or harmful." Most drugs come under this category. David Eddy, a professor of cardiac surgery at Stanford converted mathematician, has now come up with a soft ware encompassing 10,000 differential equations (non-linear mathematics) by name archimedesmodel, which is a virtual human body with all its physiology, where one could test to audit interventions of any kind.[8] This has thrown up shocking data that most of what we have been doing has done more harm to mankind than good. Medical science needs to change from its time honored reliance on conventional science of linearity to that of the new science based on consciousness, non-linearity and CHAOS, a futuristic science in the making.[9] I have been working on the non linear functioning of the heart for the last three decades and have come up with excellent data about a very good new diagnostic and prognostic test in HRV (heart rate variability) which will eliminate most of the common mistakes that are made on the surface ECG where scalar measures are used to derive vector analysis![10]

Sad demise of humane bedside medicine-Medicine had been practised on the bed side, with emphasis on the art of medicine, from time immemorial up until the birth of the first *clinic:* then came *the hospital*.[11] It is only in the last 50 odd years that medicine started riding piggy-back on technology which has now resulted in medicalising the whole population. Doctors have succeeded in schooling the population to believe that health depends on medical intervention alone; while the truth is that the health of the society does not depend on doctors and hospitals. In fact, recent audits have shown, in a fourteen industrialized countries study, that those countries with a higher doctor-patient ratio and bigger bed strength had worse health status of the population and shorter life expectancy![12] While trillions of dollars had been spent in the last quarter of a century in the west for medical intervention only 3% of the life expectancy increase has been attributed to medical interventions including vaccinations. Rest of the improvement came from nutrition, sanitation, education, better mode of living and affluence.[13] Time honored doctor-patient relationship, on which depended relief from illnesses in the past, has all but vanished what with doctors practising medicine based on the array of scopes, shadows and laboratory reports rather than on the suffering human being's bedside. This scenario has brought American medicine to its

nadir. The recent movie SICKO by the celebrated US film maker, Michael Moore, and an editorial in a recent issue of the *Texas Heart Institute Journal* entitled Hyposkillia, document all that there is for the common man to know about the sad state of the medical world in that country.[14]

Future medical education scenario-Medical education in the future must be totally changed for the good of patients and doctors as well. Change is life and change is the heart of true science. Science could be defined as "making models, mostly mathematical constructs, which with verbal jargon are supposed to work." In that case the mathematical basis of medicine must be strong and it should naturally come from non-linear mathematics. With the understanding of consciousness in physics, medicine could take advantage to scientifically fathom the mind, which does not reside in the brain alone but, does so in every human body cell at its sub-atomic level. With the understanding of the mind better patient care could be planned.[15]Mind is at the root of most, if not all, diseases from common cold to cancer. Healing also needs the help of the mind of the hapless victims of illnesses. With the recent discovery of the most powerful *expectation effect (EE)* the role played by the doctor on the bedside assumes greater significance. It is the strong expectation effect that boosts the immune system of the body that alone helps healing.[16] EE depends, to a great extent, on the faith and confidence that the patient has in his/her doctor. Consequently, future medical education should revolve round this summit where two human beings meet; one with an illness or an imaginary illness and, the other in whom the first has confidence. All teaching and learning should be on the bedside and clinical research should replace laboratory research to a great extent. Clinical research is simply having a problem on the bed side and going as far away from the bed as one could to get an answer. The latter could include all the laboratories and research facilities including the library. Unfortunately, in the present system research goes in the opposite direction, where laboratory results are thrust on the patient and the interventions are based on those results rather than on clinical indications! With the governmental funds drying up, medical research now depends more and more on pharmaceutical and technology company funds.[17] "Experts criticised the stranglehold exerted by multinational companies over clinical trials, which has led to biased results, under-reporting of negative findings and selective publication driven by the market, which was worth £10.1bn in the UK in 2006, amounting to 11 per cent of total NHS costs" notes a report in the Independent, London, on its February 27th, 2008 issue. Medical education of the future must have two clear cut compartments-first four year course, after class 12, to train a basic family physician, the only breed that has been shown to be useful to society in recent studies. And another slot of four years for those that expect to specialize after the first course. The second slot comes after a couple of years of practice as a family doctor preferably in a remote village. One does not become a specialist at the end of second four year course, though. S/he gets his license to be trained as a specialist after the second four year certification based mostly on, an on going on the job evaluation but not based on an end year examination of rote learning and information recall. Real skill is learnt after one gets a license to be a specialist. Learning stops only at the grave for any specialist. A good surgeon is one who knows how to operate, a better surgeon is one who knows when to operate and the best is the one that knows when NOT to operate. At that last stage only one becomes a true specialist, rest of them are only impersonators.[18]

Undergraduate course of study-The first four years are all done on the bedside, most of it in the community where the true phase of diseases is seen. The present big teaching hospitals delude the student to believe that the filtered patient population of the tertiary care teaching hospital is the true incidence in society. The common minor illness syndromes that form the bulk of the disease load in the world on a given day with significant sick absenteeism in the industry are excluded from the teaching hospitals. The new system, "problem based learning," will encourage better interaction between the teacher and the taught with both having equal curiosity to learn in a new atmosphere. The student is exposed to patients from day one in any medical school. This will

make his ego get boosted to learn better.[19] Very little of human anatomy, except the bare minimum, need be taught at this stage along with solving each patient's problems and so are the other preclinical and Para-clinical subjects taught with reference to the patient at hand. That is what makes the teacher as curious as the student. The teacher will have to learn these subjects along with his/her pupils. In depth study of the relevant pre and Para clinical subjects are taught in the second four year course only for those that hope to become specialists. Investigation reports and their genesis are all learnt along with the problem on hand. At the end of the four years a student will have been exposed to the whole spectrum of illnesses. Another advantage is that the student gets better trained in the common illnesses that are commoner than one thinks they are.Another lacuna in the present system is that the student does not get exposed to true public health needs, the health of the public. Clean drinking water supply, nutritious food, overall sanitation systems like toilets for every house, economic empowerment of poor women, educating the girl child in the villages up to, at least, the age 20 to reduce the fertility rate, avoiding the deadly carbon monoxide laden cooking smoke from coming into the village houses, necessity to let the villagers use the mosquito nets, importance of taking care of the need of specially enriched diet for the pregnant mothers to avoid still births as also to avoid the killer diseases in the child in its later life, judicious vaccinations using safe vaccines, disaster management systems for remote villages, dangers of alcohol and tobacco use, and the importance of poverty as the mother of most illnesses, the need to teach patients to be tranquil for better health need to be stressed in the course of four years to make the end product a responsible citizen of the community in which s/he lives. Inkling into pharmaco-economics would teach the future doctor to be parsimonious in prescribing drugs and ordering tests at the behest of the industry.[20]Having learnt about the illnesses in detail the student is then exposed in the final year to the healing methods available in many of the complementary systems that have been authenticated by hard scientific studies of which there are many. There is a new journal, the Journal of the Science of Healing Outcomes (JSHO), with great scientists on its editorial board, trying to publish the authenticated wheat in all those systems rejecting the chaff by hard scientific methods and not using the statistical science of RCTs (randomised controlled studies).[21] RCTs have been discredited lately.[22] This will achieve two fold advantages. This teaching will make the student aware of the possibilities of proven healing methods in many other systems when modern medicine fails, as also does that remove the holier-than-thou attitude that the present modern medical doctors have towards the gems in those systems, many of whom have been useful to mankind for centuries and some of them are very much Indian like Ayurveda, Siddha, Unani, Acupressure, Yoga, Meditation, Massage therapy, Reiki, Pranic healing etc.[23, 24].When the basic family doctor qualifies after four years study s/he could be interned with a good family physician in society for a year to follow the footsteps. Second year could be spent as a family doctor in a village. At the end of all those six years the student gets registered to be a specialist family physician in his/her own right to be let loose on the gullible public. The watch dog bodies that are built into the Indian system like the MCI etc. could be made to keep a careful watch on the ethical and moral standards of medical practice in the country rather than breathing down the necks of medical schools as it happens now. If they wish they could have an exit examination to screen the good from the bad doctors that have passed out of the colleges rather than measuring the class room size and the staff bio data as it is done today. Bad institutions will die a natural death if the majority of their graduates do not make their grade in the exit examination. Education institutions will then depend on the buyers market. The license raj will not improve the standards of education at all.

Postgraduate course-All the good medical schools and the larger well staffed hospitals could be selected to train postgraduates if they have the necessary infrastructure. Any basic doctor that wishes to train as a specialist should first qualify to get a junior position job in the above mentioned institutions for a year. At the end of that year he/she

will sit an on line all India entrance examination to join the next three years of pyramidal growth as a specialist in those institutions that have adequate educational and patient material infrastructure. Those who fail the examination will have one more chance after three months to re-sit the examination. Failure for the second time will disqualify the student from going further unless he does the first year work again before re-sitting the examination.The last three years are spent for hands on experience. Every student must be employed by the institution on a reasonable salary for maintenance in a residential capacity with staff quarters. Those that do not make the grade in certain difficult specialties could be eliminated by yearly evaluation in addition to the on going evaluation based both day to day performance and the log book details of the work that the candidate has done. This will ensure that the final year has much less crowd of students for the rest to get better hands on experience. Those that get thrown out of the pyramid in one specialty could try another specialty by sitting a simple entrance test for that new specialty when there is a vacancy. The job evaluation done by the teachers could be counterchecked by a senior censor who has not supervised the candidate. There could be designated senior specialists to do the job in their own region. Hopefully, this system will eliminate most of the corruption that goes on despite all the rules in the field of postgraduate education today. It might also bring out better quality specialists to be further trained either in the country or abroad if they so wish. This would also bring respect to Indian PG degrees as there will be uniformity of standards across the country with identical evaluation.

Continuing professional developmental courses, (CPDs)-These are not only mandatory but must be the responsibility of the institutions that have offered the degree in the first place. Regular on line self assessment scores must be accumulated to give 50% credit for the ten yearly recertification in all specialties excluding family practice where the recertification should only be recommendatory and not mandatory. A good human being with minimal training for six long years should make an ideal family physician. His theory knowledge is of secondary importance although it is advantageous to have family physicians also to have recertification less frequently. Education of doctors by drug companies, as is done now, through the multitude of "so called" conferences could be put an end to as most of them are used to buy favours from doctors by the drug companies. Out of the thousands of delegates only a few will attend the "scientific lectures" while the rest, along with their families, would be enjoying a well paid holiday at the cost of the drug companies. Doctors are wined and dined lavishly in these meets where, in addition, the drug companies bring their "thought leaders" from abroad to lecture and pontificate on their behalf in the guise of guest lectures most of which are company material being fed to the gullible doctors. Future doctors should understand the new science of CHAOS as the human body follows only this science.[25]

Conclusions-Medical education in India is crying for reforms. We need to first educate society about the ills of the present system and then introduce a saner, more relevant and a humane educational system that, hopefully, will bring out good human beings who are adequately trained to "cure rarely, comfort mostly but console always."

"The art of progress is to preserve order amid change, and to preserve change amid order."

Alfred North Whitehead

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Integrated Disease Surveillance in India - a New Initiative

Commentary

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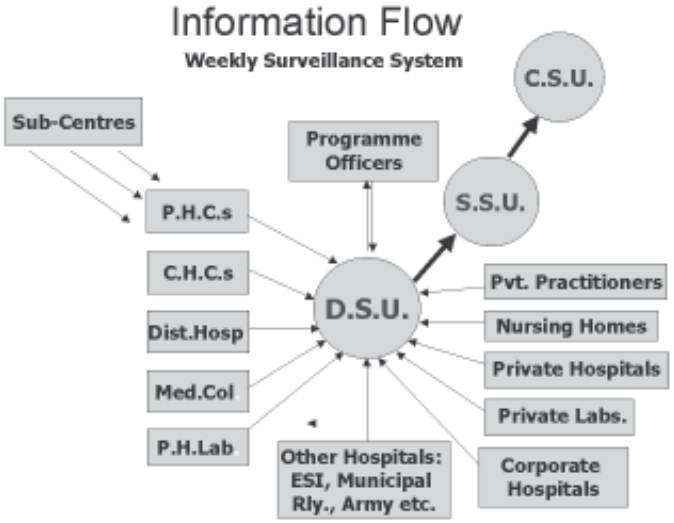
Surveillance is defined as the ongoing systematic collection, collation, analysis, and interpretation of data and dissemination of information to those who need to know in order that action is taken. It is important for early detection of outbreaks and epidemics to reduce mortality and morbidity, monitor effectiveness of prevention and control measures, early detection of emerging (new) or re-emerging (resurgent) infectious diseases and to monitor the trend of diseases occurring in the community. The existence of an effective surveillance system did not get the attention of our Health Planners until the occurrence of a number of outbreaks (plague 1994, 2002, malaria 1995, dengue hemorrhagic fever 1996, and chikungunya fever 2006) which led not only to loss of human life but also a huge economic loss. These outbreaks underlined the need for an early warning system so that outbreaks are detected early and appropriate preventive and control measures are applied timely to minimize the impact of the outbreak. On the basis of recommendations of various expert committees, National Surveillance Programme for Communicable Diseases (NSPCD) was launched by the Centre in 1997-98 in five pilot districts of the country and over the years extended to cover 101 Districts in the country in all 35 states and UTs in the country. This programme was based on outbreak reporting (as and when outbreaks occur) with weekly reporting of epidemic prone diseases directly from Districts (including nil reporting) to the Centre.NSPCD significantly improved the capacity of these districts and states to detect, investigate and respond to outbreaks, yet it was not case based reporting and did not give a complete picture of disease burden in the country especially in respect of epidemic prone diseases. Thereafter NSPCD was discontinued and Integrated Disease Surveillance Project (IDSP) was conceptualized with the objectives of establishing a decentralized district-based system of disease surveillance for timely and effective public health action, to improve the efficiency of disease surveillance for use in health planning, management and evaluating control strategies and to integrate existing surveillance activities so as to avoid duplication and facilitate sharing of information across all disease control programmes and other stake holders, so that valid data are available for decision making at district, state and national levels. The project was formally launched by Union Minister of Health and Family Welfare on 8th November 2004.

Under surveillance system the following three methods of data collection will be followed; Routine surveillance, Sentinel surveillance and Periodic surveys. Core Conditions under surveillance in IDSP for regular surveillance include Malaria, Acute Diarrhoeal Disease (Cholera), Typhoid, Jaundice, Tuberculosis, Acute Respiratory Infection, Measles, Polio, Road Traffic Accidents, Plague, Yellow fever Menigoencephalitis/ Respiratory Distress, Hemorrhagic fevers and other undiagnosed conditions. For Sentinel Surveillance HIV, HBV, HCV, Water Quality and Outdoor Air Quality have been included. For assessing NCD Risk Factors, regular periodic surveys will be done. In addition certain state specific diseases will also be included. The list will be reviewed and modified according to the needs of surveillance at least once in two years.Depending on the level of expertise and specificity, disease surveillance in IDSP will be of following three categories:

- **Syndromic –** Diagnosis made on the basis of clinical pattern by paramedical personnel and members of the community.
- **Presumptive –** Diagnosis made on typical history and clinical examination by Medical Officers.

- **Confirmed** – Clinical diagnosis confirmed by an appropriate laboratory test.

The administrative structure consists of a surveillance committee and a surveillance unit each at central, state and district level. The district level is the focus for integrating surveillance functions. Since a major chunk of patients reports to private practioners, their involvement has also been ensured in the programme. In addition the Medical Colleges will also be involved in disease surveillance, training and monitoring of the programme.The frequency of reporting for regular surveillance is weekly with nil reporting. The emphasis will be on completeness and timeliness of data. The flow of information under IDSP has been shown in the Figure below.



For reporting of data three types of forms are there.Form S for Suspect Cases will be filled by Health Workers at Sub Centre level, Form P for Probable Cases will be filled by Doctors at PHC, CHC and Hospitals and Form L for Lab Confirmed Cases will be filled at the Laboratories. Frequency of reporting will be weekly. Currently S and P forms are being simplified and Software for data handling & analysis is being developed.

Any surveillance system is incomplete without analysis of data and the action taken thereon. Ideally data should be analysed at all levels but the District surveillance officer (DSO) will be the main person responsible for data analysis under the programme. At this level the analysis will be limited to study the occurrence of disease in time, place and person. This will help the DSO in identifying outbreaks/Potential outbreaks. A Rapid Response Team consisting of a Physician/Paediatrician, Microbiologist and a Public Health Person will be constituted at the district level, which will investigate the outbreak and recommend control measures. Depending on the magnitude of the outbreaks, various trigger levels will be activated as follows:

- Trigger-1: Response Health Workers
- Trigger-2: Outbreak Inv. & Response (PHCs/ CHCs)
- Trigger-3: Outbreak Inv. & Response (District Surveillance Unit)
- Trigger-4: Epidemic Response (State Surveillance Unit)
- Trigger-5: Disaster Response (Central Surveillance Unit)

The project was scheduled to be implemented in 3 phases. Different states included in these three phases have been shown below:

- Phase – I (2004-05): Tamil Nadu, Kerala, Karnataka, Andhra Pradesh, Maharashtra, Madhya Pradesh, Uttaranchal, Himachal Pradesh & Mizoram (nine states)
- Phase – II (2005-06): Chattisgarh, Goa, Gujarat, Haryana, Rajasthan, West Bengal, Manipur, Meghalaya, Tripura, Chandigarh, Pondicherry, Delhi;
- Phase – III (2006-07): Uttar Pradesh, Bihar, Jammu & Kashmir, Jharkhand, Punjab, Arunachal Pradesh, Assam, Nagaland, Sikkim, A & N Island, D & N Haveli, Daman & Diu, Lakshwadeep.

Presently 88% of districts in Phase I states (183 out of 210 districts) 62% of districts in Phase II states(117 out of 189 districts) are reporting data to Central Surveillance Unit. There has been a steady improvement in Data reporting. Timeliness of reporting has also improved. Still

a lot needs to be done.Some of the achievements and certain new initiatives which have been introduced in the project are:

- Restructuring of IT network
- A 24X7 Call Centre (Tel-1075) made functional in Feb 2008
- Decentralization of office and lab equipment
- Base line assessment of all district level labs done
- States have identified to strengthen 1-2 district labs to make them functional immediately (50 priority labs)
- Additional training requirements allowed to all States
- 14 focus States identified to be visited and monitored by designated officers
- Convergence with NVBDCP initiated-MF 11 form of NVBDCP modified to capture all acute febrile illnesses which may cause outbreaks;District Surveillance Officer and District Malaria Officer will share data
- Process initiated to simplify IDSP weekly reporting forms (S, P, L) and include these forms into NRHM integrated Form
- Strengthening of CSU -7 Epidemiologist;2 Microbiologists; 2 IT programmers
- Avian Influenza component included under IDSP

Although much work has been done in implementation of the project, yet there are areas which need strengthening. The States need to realize the importance of the programme and its monitoring at a high level. Coordination between DHS and DME should be improved. There is need for Dedicated State and District Surveillance Officers.

Public Health Capacity should be increased at State/District levels. For success of the project it is vital that the doctors record diagnosis in OPD registers. The Private Sector Participation is critical for the success of the project as about 70% of patients are being managed there. There should be regular interaction between DSO and Private Doctors. An evaluation of IDSP in Bellary, Karnataka showed that the involvement of private sector in the project was not there at all. This further strengthens the need to give attention to this area of vital importance. The Data generated in the programme should be compiled, analyzed and used at all levels and a regular feedback should be provided. For surveillance in urban areas the coordination among various agencies is extremely important since a number of agencies are involved in provision of health care services. There is also need for Strong and effective convergence with other National Health Programmes and ICMR.

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3

Commentary

National Programme for Control of Blindness-an Update

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National Programme for Control of Blindness [NPCB] was launched in the year 1976 as a 100% Centrally Sponsored scheme with the goal to reduce the prevalence of blindness from 1.4% to 0.3%. As per Survey in 2001-02, prevalence of blindness is estimated to be 1.1%. Main causes of blindness are as follows: - Cataract (62.6%) Refractive Error (19.70%) Corneal Blindness (0.90%), Glaucoma (5.80%), Surgical Complication (1.20%) Posterior Capsular Opacification (0.90%) Posterior Segment Disorder (4.70%), Others (4.19%) Estimated National Prevalence of Childhood Blindness /Low Vision is 0.80 per thousand.

Objectives of the programme

- Reduce the backlog of blindness through identification and treatment of blind
- Develop Eye Care facilities in every district,
- Develop human resources for providing Eye Care Services;
- Improve quality of service delivery;
- Secure participation of Voluntary Organizations in eye care.

Programme activities

- Identification and treatment of cataract
- Detection and correction of refractive errors including school eye screening
- Eye screening of persons in blind school
- Community Awareness [IEC]
- Eye Banking and cornea collection
- Procurement of equipments and consumables
- Infrastructure development and technological advancement
- Training of health personnel
- Teleophthalmology
- Maintenance of equipments
- Monitoring and evaluation
- Surveillance

Budget- Allocation and expenditure of NPCB is as follows:

Year	Budget Allocated	Expenditure
2002-03	85.00	84.62
2003-04	86.00	85.62
2004-05	88.00	87.20
2005-06	93.32	92.84
2006-07	111.87	111.53
2007-08	165.20	164.95

Achievement:s

Cataract surgery: Performance of Cataract Surgery has been steadily increasing as indicated below:

Year	Target	Achievement	% IOL
2002-03	4000000	3857133	77
2003-04	4000000	4200138	83
2004-05	4200000	4513667	88
2005-06	4513000	4905619	90
2006-07	4500000	5040089	93
2007-08	5000000	5404406	94

School Eye Screening Programme:

Year	Teachers Trained	School Children Screened	Children Detected with Refractive Errors	Poor Children provided free glasses
2002-03	35267	9736805	506663	98697
2003-04	88317	19260984	552963	184305
2004-05	97310	26862932	572691	283070
2005-06	126163	29737168	771901	385403
2006-07	203221	35429289	963168	456634
2007-08	193629	27676430	1126985	512020

Donated Eyes Collected

Year	Total no. of eyes Collected
2003-04	23741
2004-05	23553
2005-06	28007
2006-07	30007
2007-08	38596

Collection and Utilization of donated eyes- In the year 2007-08 we were able to collect nearly thirty eight thousand eye balls. Hospital cornea retrieval programme is the main strategy for collection of donated eyes, which envisages motivation of relatives of terminally ill patients, accident victims and others with grave diseases to donate eyes. Eye donation awareness fortnight is organized from 25th August to 8th September every year to promote eye donation/eye banking. Gujarat, Tamilnadu, Maharashtra, Delhi, Chandigarh Andhra Pradesh, Kerala and Karnataka are leading States in eye collection/cornea retrieval activity.

Training of Ophthalmic Surgeons - Eye surgeons working in public sector in different states are given training in various sub-specialties of ophthalmology in selected 27 institute in government and public institutions and the expenditure in borne directly by the Government of India. The area of training include ECCE/IOL, SICS, Phaco emulsification, low vision services, glaucoma management, pediartric ophthalmology, indirect ophthalmology, medical retina and laser technique, vitreo retinal surgery, eye banking & corneal transplantation, oculoplasty, strabismus diagnosis and management.

Year	No. Of eye surgeon trained
2002-2003	176
2003-2004	229
2004-2005	350
2005-2006	250
2006-2007	250
2007-2008	300

IEC Activities- IEC activities are undertaken at Central, State and District Blindness Control Societies level. Special campaigns for mass awareness are undertaken during Eye Donation fortnight (25th August to 8th September) and World Sight Day (2nd Thursday of October). A innovative strategy for community awareness on eye donation has been initiated by involving not only Eye-banks but also Blood Banks with the popularization of slogan "Jeete Jeete Rakt Daan, Mritue ke Uprant Netra Daan". At the Central level, prototype IEC material is produced and disseminated to the States. Guidelines and training manuals are also prepared centrally and disseminated. A quarterly newsletter has been started since July 2002.

Support to Voluntary organization- VOs/NGOs play an important role in implementing various activities under the programme. District Blindness Control Societies (DBCS) have been established

throughout the country under the Chairmanship of District Collector/Deputy Commissioner. Till date, 604 DBCSs have been established. The Blindness Societies have been merged with Health Societies both at State and District level under National Rural Health Mission [NRHM]. Under the scheme a non-recurring grant a maximum of Rs.25.00 lakhs is granted for expansion/up gradation of Eye Care Units for tribal and backward rural areas. Also Rs. 10 lakh is granted for up gradation of Eye Banks as non-recurring assistance and Rs. 1000 is provided per pair of eyes as recurring assistance for registered eye banks and a sum of Rs. 25,000 is provided for setting up of vision centres. So far [2007], 80 NGOs have been assisted under this scheme with one time non-recurring grant. Till date 45 eye banks in voluntary sector were assisted to promote collection of donated eyes.

New Initiatives proposed under XIth five year [2007-12] plan period-A budget of Rupees 1250 [one thousand and two fifty] crores have been earmarked for NPCB in the XIth five year plan period. This includes continuation of Xth plan period activities and proposed new activities:

- Construction of dedicated Eye Wards and Eye Operation theaters in Districts and Sub Districts Hospitals in North-Eastern States, Bihar, Jharkhand, J&K, Himachal Pradesh, Uttaranchal and few other States as per demand.
- Appointment of Ophthalmic Surgeons and Ophthalmic Assistants in new districts in District Hospitals and Sub District Hospitals.
- Appointment of Ophthalmic Assistants in PHCs/ Vision Centers where there are none (at present ophthalmic assistants are available in block level PHCs only)
- Appointment of Eye Donation Counselors on contract basis in Eye Banks under Government Sector and NGO Sector.
- Grant-in-aid for NGOs for management of other Eye diseases other than Cataract like Diabetic, Retinopathy, Glaucoma Management, Laser Techniques, Corneal Transplantation, Vitreoretinal Surgery, Treatment of childhood blindness etc of Rs. 750 per case for Cataract/ IOL Implantation Surgery and Rs.1000 per case of other major Eye Diseases as described above.
- Special attention to clear cataract backlog and take care of other eye care ailments from North Eastern States by organizing and mobilizing team of ophthalmologist from Central government and NGO hospital.
- Development of mobile ophthalmic unit in hilly/ underserved states and initiation of Telemedicine in Ophthalmology {Eye Care Management Information and Communication Network} on pilot basis
- Provision of latest equipment to RIOs, medical colleges, District/Sub district hospital, CHC, Vision centres.
- Strengthening of low vision services by providing training of health personnel and low vision aid to Regional Institute of Ophthalmology [RIO] and selected medical colleges
- Provision of exclusive budget for maintenance of equipment
- Involvement of Private Practitioners.

Acute Limb Ischemia

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Acute limb ischemia has been defined by the Transatlantic Inter-Society Consensus (2000) as 'any sudden decrease or worsening in limb perfusion causing a potential threat to extremity viability'. It is a relatively common surgical emergency and estimates suggest that 30–40 cases will present annually to the average district general hospital. Unfortunately, the threat is not only to the limb, but these patients are also at high risk for death. Limb hypoperfusion results in systemic acid-base and electrolyte abnormalities that impair cardiopulmonary and renal function. Successful reperfusion may result in the release of highly toxic free radicals, further compromising these critically ill patients. Therapeutic choices are often few and patient expectations are not always realistic. The management of acute limb ischemia requires a thorough understanding of the anatomy of the arterial occlusion and the open surgical and percutaneous options for restoring limb perfusion. Priorities for the diagnosis and effective management of these critically ill patients are provided.

Clinical presentation-The classical description of the features of acute limb ischaemia is the "six Ps": pain, parasthesia, paralysis, pallor, pulseless, and perishingly cold. However, the severity of the symptoms and signs of acute ischaemia is not proportional to the degree of ischaemia. Initially there is spasm of the distal arterial tree with an associated pallor. Over the next few hours there is some vasodilatation and the deoxygenated blood gives a mottled purple appearance that blanches. As ischaemia progresses this turns darker in colour and becomes fixed. Symptoms and signs of acute limb Ischaemia are- Pain, Parasthesia, Paralysis, Pallor, Pulseless, Perishingly cold

Aetiology-The majority of acute limb ischaemia is caused by acute thrombosis in a vessel with pre-existing atherosclerosis (60%). Emboli account for a further 30% of acutely ischaemic limbs. The management and outcome of these two broad categories is different and thus distinguishing between them is essential. Other causes include aortic dissection, trauma, iatrogenic injury (arterial cannulation), peripheral aneurysm and injury caused by extreme cold. Important differentials may be intra-arterial drug administration and venous gangrene.

Causes of acute limb ischaemia-Thrombosis, Embolus (usually atrial fibrillation or cardiac source), Aortic dissection, Trauma, Iatrogenic injury, Thrombosed aneurysm (popliteal), Thromb-osed bypass graft, Injury caused by extreme cold, Intra-arterial drug administration, Venous gangrene, Prothr-ombotic states

Embolism-Most emboli (80%) have a cardiac cause and arise from the left atrium in patients with atrial fibrillation or following acute myocardial infarction. Less common cardiac sources include prosthetic valves, valve vegetations in endocarditis, "paradoxical" embolus (a venous embolism from a deep venous thrombosis passes into the systemic arterial circulation through a congenital communication between the right and left cardiac circulation), and atrial myxoma. Arterial aneurysms account for a further 10% of emboli and may be in the aortoiliac, femoral, popliteal, or subclavian arteries. In some patients no source is found. Most emboli lodge at bifurcations of arteries as the diameter of the vessel suddenly reduces here. The commonest site of embolic occlusion is the femoral bifurcation. Other sites that emboli lodge at are the brachial, popliteal, and aortic bifurcations. (An embolus lodged in the latter site is known as a saddle embolus.)

Thrombosis-In most cases thrombosis is secondary to pre-existing atherosclerosis. Predisposing factors are dehydration, hypotension, malignancy, polycythaemia, or inherited prothrombotic states. Clinical features suggestive of thrombosis are a previous history of intermittent claudication, no source for emboli, and reduced or absent peripheral pulses in the contralateral limb (Table-1).

Table-1, Differentiation of embolus from thrombosis		
	Embolus	Thrombosis
Onset	Sudden (minutes)	Hours
Severity	Complete (no collaterals)	Incomplete
Embolic source	Yes	No
Previous claudication	No	Yes
Contralateral pulses present	Yes	No
Upper limb affected	Commonly (25%)	Rarely
Multiple sites affected	Sometimes (15%)	No

Assessment -Patients who present with an ischaemic limb often have widespread arterial disease. Particular attention should be paid to pre-existing coronary, cerebrovascular, and renovascular abnormalities. General assessment of the patient requires a clear history and examination with particular regard to identifying the underlying cause of limb ischaemia. Assessment of the limb requires a judgment of the severity of ischaemia.

Classification of ALI-An ad hoc committee of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery created a classification for acute arterial occlusion. Three general classes are recognized:

- Class I: Non-threatened extremity; elective revascular-ization may or may not be necessary.
- Class II: Threatened extremity; revascularization is indicated to prevent tissue loss.
- Class III: Ischemia has progressed to infarction and salvage of the extremity is not possible.

Table-2, Clinical Categories of Acute Limb Ischemia				
Category	**Sensory Change**	**Motor Change Arterial**	**Doppler Signals Venous**	
Viable	None	None	Audible	Audible
Threatened	Rest pain	Moderate	Inaudible	Audible
Irreversible	Anesthetic	Paralysis	Inaudible	Inaudible

Immediate management - Patients who present with limb ischaemia are potentially seriously ill. Remember to go through the ABC of resuscitation. Give 100% oxygen. Get venous access and start slow intravenous infusion (a litre of normal saline over 8 hours, unless the patient is very dehydrated in which case it should be faster). Withdraw blood for full blood count, measurement of urea and electrolytes, glucose in diabetics, cardiac enzymes, clotting, and group, and save. A thrombophilia screen and lipid profile are also useful. Get a chest radiograph and an electrocardiogram, and if the patient is in atrial fibrillation arrange for cardiac monitoring. Insert a urinary catheter to monitor resuscitation if the patient is dehydrated. Prescribe opiate analgesia if the patient is in severe pain, and call for senior help.

Subsequent management - This will depend on the assessment of the severity of the ischaemia. There are three broad categories:

Class I: Non-threatened extre-mity; elective revascular-ization may or may not be necessary.

Class II: Threatened extremity; revascularization is indicated to prevent tissue loss.

Class III: Ischemia has progressed to infarction and salvage of the extremity is not possible.

This assessment can only be made by an experienced surgeon and will dictate further treatment. In the last category amputation is inevitable and often a pressing need as delay may result in death from the systemic sequelae of muscle necrosis (hyperkalaemia, acidosis, acute renal failure, and sepsis). In the at risk and viable limb category, management usually involves initial intravenous heparinisation to prevent propagation of thrombus and prompt angio-graphy to plan further intervention. If there are no contraindications (eg aortic dissection, multiple trauma, head injury) give an intravenous bolus of 5000 units of heparin and start an infusion of 1000 units per hour. Recheck the activated partial thromboplastin time (APTT) in 4-6 hours, and aim for a time 2-2.5 times the normal range. The acutely threatened group needs expert vascular input. Thrombolysis, angio-graphy, angioplasty, embol-ectomy, or urgent arterial bypass may be required depending on the individual circumstances.

Management Options-In the 1960s and the 1970s, balloon catheter thrombectomy, first introduced by Fogarty et al became the cornerstone of therapy. Interestingly, this marked the beginning of catheter-based endovascular therapeutic options that introduced the concept of remote, rather than direct, open surgical intervention for management of occlusive vascular disease. While improvements in open surgical techniques have diminished the rate of limb loss associated with ALI, the mortality rate remains unacceptably high. In fact, patient survival has not changed dramatically since the report of Blaisdell and colleagues more than 20 years ago. The discordance of limb salvage and patient survival is explained by the specific factors controlling the two events. While mortality occurs as a result of concurrent medical comorbidities and the fragile baseline medical state of patients presenting with ALI, limb loss is related to an unsuccessful revascularization procedure. As such, the rate of amputation has diminished over the decades, presumably because of improvements in surgical technique. Open surgical techniques for salvage of an ischemic limb include: 1) balloon catheter thrombectomy 2) bypass procedures to direct blood flow beyond the occlusion 3) endarterectomy with or without patch angioplasty 4) intraoperative isolated limb thrombolysis. The search for less invasive revascularization strategies has been ongoing, with the goal of lessening the morbidity of the procedures without compromising the quite satisfactory rate of limb salvage that has been achieved with contemporary surgical procedures. Pharmacologic thrombolysis and, more recently, percutaneous mechanical thrombectomy (PMT) hold potential in this regard. Both techniques can effect clearance of the occluding thrombus from a peripheral artery in a minimally invasive fashion, restoring blood flow to the extremity and allowing the identification of any underlying lesion that was responsible for the occlusive event. The unmasked culprit lesion can then be addressed in a directed manner with angioplasty, stenting, or a limited operative procedure performed electively in a well prepared patient.

Conclusion-Acute limb ischaemia is both life and limb threatening. It requires prompt assessment. Consider the underlying causes and arrange investigations as a matter of urgency. Atherosclerosis, the major cause of limb ischemia, is a global phenomenon. As such, attention should be directed not only to the limb at risk but to the patient as whole. Hence, modification of systemic risk factors must play an important role in the long-term care of these patients. While thrombosis in an artery with preexisting disease is commoner in the Western literature, embolism remains more frequent in India. The heart remains the commonest source and arterio-arterial embolism is now being recognized more frequently due to better imaging with CT or MR angiography.Thrombolysis is a good option in carefully selected patients. However, when ischemia is severe, thrombolysis may not be the preferred therapy since the revascularization is slow. Finally, when limb viability is in doubt, the muscles should be assessed for viability through a fasciotomy. Revascularization should be done only if the muscles are viable. Attempts to restore circulation to dead muscles will result in hyperkalemia, lactic acidosis and myoglobinuria.

5

Review Article

Evaluation of Peripheral Vascular Disease

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Initial patient evaluation plays a very important role in detection and management of Peripheral Vascular Disease (PVD).Though many modern and sophisticated investigations are available today, none can replace the role of a detailed history recording and a thorough clinical examination.Initial evaluation is important in all branches of medicine and it is vital in PVD because of two main reasons. Firstly, this will decide about the urgency of the situation. In other words, all cases of acute ischemia are mostly diagnosed by history and physical examination. Sophisticated tests have a limited role in diagnosing acute ischemia. Therefore, a good clinical history and careful physical examination allows forming a clinical impression, upon which all other tests are based. Secondly, clinical evaluation determines the eventual therapy in most of the patients. Arteriography helps in planning revascularization once the vascular specialist decides to intervene with endovascular or open surgery.The process of diagnosis and treatment of peripheral vascular disease (PVD) involves-Reaching a presumptive diagnosis on clinical grounds; Using non invasive diagnostic measures to either confirm the diagnosis or grade the functional severity of the condition; Angiography or other invasive/more advanced tests only if intervention is planned, confirming the diagnosis and the extent and degree of involvement.

Symptoms of PAD

Claudication (limp)– considered "functional" and does not usually require intervention. It consists of pain or heaviness in the muscles, is produced by exercise and relieved by rest. It is reproduced by the same degree of exercise. It is considered disabling if interferes with daily activities, which varies with patient's age and occupation. Claudication can be classified as follows

Type	Site of Pain	Level of occlusion
1. Leg/calf claudication	Pain in the calf	Femoral\ popliteal occlusive disease.
2. Buttock and thigh claudication	Pain in the buttocks and thigh	Aorto iliac artery occlusive disease.
3. Foot claudication	It is very rare, pain over Fore foot; it is of cramping type on walking.	Infra popliteal occlusive disease or crural pedal artery disease.
4. Upper limb claudication	Pain in the upper limb.	Subclavian artery, Brachial artery, axillary artery occlusive disease.

Differential Diagnosis

- **Chronic compartment compression syndrome**- Pain over the calf muscle on exercise and does not subside with rest.
- **Neurospinal compression**- Numbness, weakness over buttocks and thigh produced by standing rather than just ambulation and it is not relieved by stopping unless the patient sits down with upper body bent forward and straightens out the lumbar spine.
- **Venous Claudication**- Bursting type of pain on walking associated with leg swelling; usually occurs in the latter part of the day, relieved by prolonged rest and leg elevation.
- **Arthitic or inflammatory process involving the foot** - RA, Plantar fascitis, metatarsalgia

Rest pain-It is present at rest as the name implies and indicates critical limb ischemia (CLI),

which nearly always requires intervention to prevent limb and at times, loss of life. It is typically a nocturnal pain over the fore foot (can be localized to an ischemic ulcer or gangrene toe). Pain not relieved by substantial doses of narcotics and patient sleeps with the foot dependent either dangling it over the side of the bed or resting it on a chair.

Non healing ischemic ulcer/ gangrene-Indicates severe ischemia. Its onset, duration, the extent of tissue loss and presence or absence of secondary infection has to be documented. It is usually associated with rest pain; but can be painless in a neuropathic foot. Non-healing ulcers for more than 3 weeks, have grayish granulation tissue base with surrounding skin pale or mottled, painful, not bleeding.Note: CLI is the term applied only to CHRONIC critical limb ischemia.

History of associated risk factors and contributing factors -Tobacco consumption in any form, Diabetes Mellitus, Hypertension, Cardiac Illness, Cardiovascular accident/ Transient ischemic attack, Dyslipidemia, Renovascular disease, Collagen vascular disease/Arthiritis, Family history of atherosclerosis, Any H/o abortions, Any drugs usage, Past history of any surgery, Any history of allergy

General & Physical Examination-Complete physical exam is mandatory.

Systemic examination-Cardio vascular(Look for cardiac murmurs), Respiratory (Associated pulmonary complication or COPD), Abdomen(For any palpable mass or pulsatile mass, bruit),Central Nervous System(Any motor or sensory deficits)

Examination of extremities-Coldness, Pallor/rubor(Pallor on elevation of limb to 90 degree point, termed Buergers angle, Angle < 30 – severe ischemia), Skin mottling, Hair loss, Atrophy (skin changes), Brittle Nails, Tissue loss/ulceration, Absent capillary filling, Oedema, Subcutaneous atrophy changes(Discolo-uration/Pigmentation, Erythema/cellulites),Motor system examination

Examination of all peripheral pulses -Carotid, Subclavian, Axillary, Brachial, Radial Artery, Ulnar arteries, abdominal aorta, Femoral, Popliteal, Anterior tibial, Posterior tibial and Dorsalis pedis arteries; Grading of pulsation(0- Not palpable, 1- Barely palpable/weak, 2- Normal, 3- Prominent, 4- Aneurysmal); Auscultate for bruit over carotid, abdominal aorta and femoral arteries.

In upper limb ischemia-Along with the above mentioned physical examination examination has to be done for any supraclavicular mass/pulsatile mass by the following tests

Elevated arm test- For thoracic outlet syndrome, abduct the shoulder to 90 and rotate the upper limb externally, open and close the fist for 5 minutes. This induces pain in patients with TOS.

Tinnel's sign- Tenderness over the brachial plexus in the supraclavicular, some times seen in TOS.

Adsons sign- Obliteration of radial pulse and hand parasthesia produced by rotating the head to the ipsilateral side and deep inspiration.

Investigations

Non Invasive- Ankle brachial index, Segmental pressures, Plethysemography, Transcutaneous oximetry, Arterial Doppler study.

Invasive- Angiogram (DSA), CT Angiogram, MR Angiogram.

Ankle brachial index-

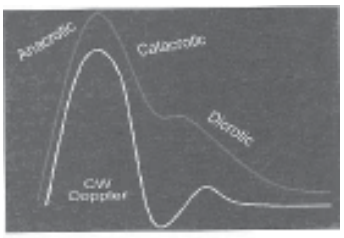
- The blood pressure cuff is placed just above the ankle. Listen to the DPA or PTA arterial signals with a Doppler; inflate the blood pressure cuff until the Doppler signal disappears; slowly deflate the cuff. The pressure at which the signal reappears is the ankle pressure.
- The highest ankle pressure of DPA or PTA divided by the highest brachial pressure obtained with Doppler gives ABI.ABI > 0.95 – Normal; > 0.50 - < 0.95 – minimal to moderate arterial insufficiency (claudication range); < 0.50 – severe arterial insufficiency associated with rest pain or tissue loss)
- ABI improvement of > 0.15 after intervention indicates successful revascularization.Calcified vessels are difficult to compress hence give falsely elevated ABI. In this situation toe pressure has to be checked. Normal toe pressure is 20-40 mm Hg less than Ankle pressure and the normal toe brachial index is 0.75.

Segmental pressures - It is performed to identify specific segments of arteries involved, determine multilevel segment disease or single segment involvement. Test is done using 4 cuff method, where in cuffs are placed- Around the thigh at groin level; Around the thigh just above knee; Around the calf below the knee; At ankle level. And segmental arterial pressures are recorded placing Doppler probe at the ankle for arterial sounds and inflating the above cuffs sequentially and it is divided by brachial pressure.

- Thigh pressure >Brachial pressure by > 30 mm/hg - Normal
- Thigh pressure < Brachial Pressure by 30 mm/hg – Aorto Iliac disease/ iliac-femoral artery occlusive disease
- Difference of pressure between any two adjacent or parallel cuffs of more than 20-30 mm/hg, indicates disease at the level of cuff and between the 2 cuffs. Use of a cuff that is relatively small compared with the size of the limb results in false high pressure reading

Air plethysmography (Air PPG)-Device record changes in volume. Air PPG devices utilize pneumatic sensor cuffs to measure blood volume changes in segments of the upper and lower extremities with plethysmographic pressure transducers convert cuff pressure into an analog waveform.Gives same information as the Doppler study, but interpretation of the wave form is different. It is useful in patients with non compressible vessel (such as in diabetes mellitus) since volume changes drive the test machines.Normal PPG waveform characteristics

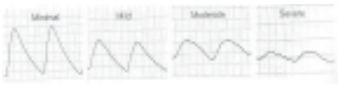
- Brisk systolic upstroke-typically within a fifth of a second, and sometimes referred to as the anacrotic limb.
- Sharp systolic peak.
- Gradual down stroke component also known as the catacrotic limb.
- Dicrotic notch-the result of a reflected wave from the peripheral during diastole, indicating normal, high peripheral resistance.



Red colored wave form: PPG wave form

The primary distinction between normal limbs and extremities with arterial occlusive disease is absence of the dicrotic notch. With progressive disease severity there is a decline in amplitude of the wave form.

As illustrated below, characteristics of abnormal plethysmographic waveforms that accompany increased disease severity include: a prolonged upstroke, rounding of the systolic peak, and a waveform down stroke that bends away from the baseline. A rounded systolic peak accompanied by a major delay in systolic upstroke is indicative of a hemodynamically significant stenosis or occlusion proximal to the recording sire. Subjective waveform descriptions for amplitude reduction include diminished, blunted, rounded, elongated and flat.



Photoplethysmography (PPG) -Photoplethysmography is based on the principle that light is attenuated in proportion to the quantity of blood that is present in cutaneous tissue. The major component of PPG is the photocell, consisting of an infrared light-emitting diode (LED) and phototransistor.Due to its small size, simplicity and sensitivity, the use of PPG is a more simplified method for obtaining qualitative venous and arterial flow measurements in cutaneous vessels.PPG technology can be used to record toe pressures. While the big toe is the standard site for obtaining a toe pressure and toe-brachial index (TBI) additional digital pressures may be recorded based on symptoms.

Transcutaneous oxygen tension(TcPo2)- Measurement of intracutaneous oxygen tension by placing the probe over the skin surface Normal – 40-70 mmHg. At foot level – TcPo2 < 20 mmHg in measured with severe rest pain, ischemic ulcers or gangrene.

Handheld Doppler - Continuous wave, non directional device meets most of the requirements for audible interpreta-tion. Normal peripheral Doppler signals are biphasic or triphasic. Arterial signals are obtained despite absence of palpable pulses.Distal to stenosis or occlusion - flow signals are typically low pitched and monophasic. Absence of distal Doppler signals, in case of proximal occlusion, is uncommon in chronic ischemia, but important finding in acute ischemia.Signals from proximal to the occlusion is of – "to and fro" or thumping quality.

Duplex scan-Frequency of sound(or light)emitted by a moving source is shifted up if the source is moving toward the receiver and down if the source is moving away from the receiver.Combining Doppler with ultrasound and color is added instantly to the blood flow. In the clinical setting, pulsed Doppler system with real time B-mode component of the duplex scanner is commonly used.

Qualitative Analysis- Normal wave form is triphasic Velocity increases rapidly in early systole reaches a peak, and then drops almost equally as rapidly, reversing in early diastole. In late diastole, the velocity tracing again becomes positive, before returning to the zero flow baseline.In Stenosis – Loss of reverse flow, with progression of stenosis wave forms – Progressively dampened

Quantitative Analysis- Peak to peak pulsating index - peak to peak frequency difference of the Doppler wave form – divided by mean frequency. Normal PIpp – Increases from proximal to distal portions.In stenosis or occlusion PIpp value below the involved segments tend to decrease.

Clinical examination and non invasive physiological testing is adequate to come to an early and accurate diagnosis in nearly all vascular patients. They can also determine the need for intervention and further invasive or advanced testing. They are also extremely useful in following patients either on medical therapy or after intervention. Angiography is performed when intervention is planned. Options available include conventional angiography, digital subtraction angiography, CT angiography and MR angiography.

Aneurysm

An aneurysm is the dilatation of an artery full of spiritous blood. **Fernel** (1591). Considerable attention has been given throughout ancient and modern history to the cause and treatment of aneurysms. One of the earliest texts known, by the **Ebers Papyrus** (2000 B.C.), contains a description of traumatic peripheral arterial aneurysms. **Galen** (131-200) defined an aneurysm as a localized pulsatile swelling that disappeared on pressure and wrote, "if an aneurysm be wounded, the blood is spouted out with so much violence that it can scarcely be arrested". The first elective operation for treatment of an aneurysm was reported by the most famous surgeon in Greek antiquity, **Antyllus,** in the second century. His recommendation for aneurysm repair was named Antyllus method. "An operation for aneurysm whereby is applied two ligatures to the artery, cut between them and evacuating its contents" remained the basis of direct arterial operations for next centuries. He was also first to recognize two forms of aneurysm – the developmental caused by dilatation and the traumatic following wounding of an artery. In the seventh century, details of operative repair of an arterial aneurysm were rewritten by **Aetius** of Amida in his book De Vosorum Dilatatione ("On the Dilation of the Vessels"). Aetius also recognized the difference between true degenerative aneurysms and traumatic false aneurysms. Aetius also believed Galens teachings that no wound heals properly without the formation of pus, brought about by the application of dried herbs (incense).**Ambrose Pare** (1510-1590), who mainly contributed to the principles of proper wound care, also applied his observations to aneurysm operations. He described the death of a patient, whose brachial artery aneurysm had been treated by application of a caustic, resulting in a torrential fatal hemorrhage. In 1590, **Peter Lowe** (1550-1612), personal physician to King James VI in Scotland, reported that one of the highest ranking officers in the Spanish Regiment presented with a peripheral arterial aneurysm.

6

Review Article

Venous Thromboembolism

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Venous thromboembolism (VTE) incorporates two inter-related but distinct clinical conditions, deep vein thrombosis (DVT) and pulmonary embolism (PE). Quoted as a major health problem and one of the most common preventable causes of hospital deaths in the western world, it has rarely evoked such consideration in India. Not surprisingly, a Pubmed search of "Deep vein thrombosis + India" yields just 8 articles. The true incidence of VTE is hard to get because of the often silent nature of the condition. In the western world, the incidence is one case of DVT and 0.5 cases of PE per 1000 population/year [1].Hospitalised patients are especially at risk for VTE as most have multiple risk factors. Autopsy studies have shown the incidence of VTE in hospitalised patients to be as high as 34.7% with fatal pulmonary embolism in 9.4% [2]. Table-1. shows the absolute risk of VTE in hospitalised patients[3].

Most studies from India have looked at specific patient groups like postoperative orthopaedic patients [4, 5] and there is no data on the overall incidence of VTE in the general population. The prevailing belief that VTE is less in the Asian population has essentially been disproved [6, 7, 8, 9] and there appears no reason to believe that it should be any different in India.

Pathophysiology and risk factors-Virchow's far-sighted observation on the triad of factors leading to venous thrombosis has, with some refinement, stood the test of time. The triad of change in blood flow, change in blood constituents and change in vessel wall has now been refined to venous stasis, hypercoagulability and venous endothelial injury. Venous thrombi are intravascular deposits made up of fibrin, red cells, platelets and leucocytes. Typically these thrombi are believed to start in areas of slow or turbulent venous flow such as large venous sinuses or venous valve cusps and also in areas of direct venous trauma. Activation of the coagulation pathway is the crucial step in the initial formation of venous thrombi and this is believed to happen due to local injury or remote release of mediators. Activation of the pathway alone is inadequate in formation of a full fledged venous thrombus as inhibitors of thrombosis such as antithrombin and thrombomodulin-protein C and S, tissue factor pathway inhibitor (TFPI) along with the fibrinolytic pathway would clear the clot. Hence, it is persistent activation due to endothelial stimulation along with poor flow failing to clear the activated factors that results in an imbalance in the pro and anti-thrombotic pathways which ultimately leads to progression of the thrombus.Heit and colleagues have listed the following conditions as major risk factors for developing VTE: increasing age, male gender, surgery, trauma, confinement in hospitals or nursing homes, malignancy, neurologic disease, central venous catheter, prior superficial vein thrombosis and varicose veins [10] . Pregnancy, oral contraceptive pill use and hormone replacement therapy are independent risk factors in women.The surgical patient has all three Virchow's factors present in the peri-operative period. They

Table-1, Absolute risk of venous thromboembolism in hospitalised patients

Patient Group	VTE Prevalance (%)
Medical patients	10-20%
Cardiac Patients	15-40%
Major Gynaecological Surgery	15-40%
Major Urological Surgery	15-40%
Neurosurgery	15-40%
Stroke	20-30%
Hip and Knee arthroplasty	40-60%
Major Trauma	40-50%
Spinal Cord injury	60-80%
Critical Care Patients	10-20%

have venous stasis due to immobilisation and surgical positioning. Direct venous injury or remote release of mediators of coagulation due to tissue trauma also increases the risk of venous thrombosis. The risk factors for a surgical patient developing VTE have been extensively studied and the important determinants appear to be age, type of surgery, length of procedure and duration of immobilization. Hull et al [11] have categorised post operative patients into low, moderate and high risk for VTE on the basis of these characteristics (Table-2).

vessel lumen which is mediated by leukocyte infiltration and cell mediated thrombolysis. In animal models the recanalisation process has been found to begin within a few days of the initial thrombosis and complete recanalisation of the vessel lumen is the most common outcome. Re-thrombosis would naturally impede with the recanalisation process and recurrent thromboembolism of up to 47% has been reported in patients inadequately anti-coagulated in the first 3 months after an initial proximal DVT [12]. The clinical

proximal iliofemoral DVT tend to cause more acute and chronic complications than distal calf vein DVT. Calf DVT tends to recanalise faster than proximal ones. Pulmonary embolism is the most dangerous complication of acute DVT. As with acute DVT, this usually remains clinically silent. 25-50% of all patients with documented DVT and absent pulmonary symptoms have been shown to have evidence of PE on lung perfusion scans [13]. Symptomatic pulmonary embolism is strongly associated with inadequately treated DVT

Table-2, Stratification of patients based on their risk for developing venous thromboembolism

Category	Characteristics
Low	Age < 40 yr, no other risk factors, uncomplicated abdominal/thoracic surgery Age > 40 yr, no other risk factors, minor elective abdominal/thoracic surgery < 30 min
Moderate	Age > 40 yr, abdominal/thoracic surgery > 30 min
High	History of recent thromboembolism Abdominal or pelvic procedure for malignancy Major lower extremity orthopaedic procedure

Natural History-Acute DVT is followed by a complex process of attempted recanalisation of the

behaviour of acute DVT depends on the location of thrombosis. In the lower limb,

and underlying poor cardio-pulmonary reserve of the patient. The mortality rate of PE is 11%

Table -3, Clinical model to assess pre-test probability of deep vein thrombosis

Clinical feature	Score
Active cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilisation of the legs	1
Recently bedridden for more than 3 days or major surgery within 4 weeks	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling by more than 3 cm compared with the asymptomatic leg (measured 10 cm below the tibial tuberosity)	1
Pitting oedema (greater in the symptomatic leg)	1
Collateral superficial veins (non-varicose)	1
Alternative diagnosis as likely or wider than that of deep vein thrombosis	-2

Low probability: score of 0 or less; Moderate probability: 1-2; High probability: 3 or more

within an hour of presentation and a further 30% among survivors if not recognised [14].

Diagnosis-The clinical diagnosis of DVT is generally inaccurate, especially in the inpatient setting. Of patients undergoing duplex ultrasound "to rule out DVT", only about 15% are found to have DVT [15]. In order to better select patients for screening, Wells et al [16] have suggested the following clinical model to assess pre-test probability of DVT (Table- 3).

The value of a clinical probability score along with D-dimer assessment is useful to eliminate the possibility of DVT. Plasma D-dimers are derivatives of fibrin degradation products and are found to be raised in patients with thromboembolism. Plasma D-dimer assay has very high sensitivity but poor specificity for venous thrombosis and hence a patient with low probability of DVT with a negative D-dimer test has almost no probability of having venous thrombosis. Duplex ultrasonography has replaced venography as the investigation of choice in diagnosing DVT. It is cheap, easily available and non-invasive. However it does have some disadvantages that need to be kept in mind – diagnosis of isolated calf vein DVT and evaluation of iliac veins are often dependant on operator experience, patient habitus and the clinical situation. Despite these limitations, a negative report from a single, technically adequate ultrasound examination is sufficient grounds to withhold anticoagulation therapy. A complete ultrasound performed by trained sonologists with a proper protocol, resulted in only 4 (1.1%) instances of misdiagnosis in more than 400 patients [17]. CT pulmonary angiography is the most useful test for detecting a pulmonary embolus. It can be combined with CT venography as a single scan to diagnose both PE and DVT.

Treatment-Once the diagnosis of DVT has been established, treatment involves anticoagulation to encourage clot lysis and recanalisation and prevent re-thrombosis and embolization. Traditionally, this involved a continuous infusion of unfractionated heparin followed by oral anticoagulation with warfarin for a period of 3-6 months. Unfractionated heparin consists of a heterogeneous mixture of olysaccharide chains and hence, its therapeutic action can be extremely variable. This necessitates the need to monitor therapy using either activated partial thromboplastin time (aPTT) or heparin blood levels and titrating the dose based on these. Low molecular weight heparins (LMWH) are derivatives of unfractionated heparin formed by depolymerisation. The advantage they have over unfractionated heparin is that the anticoagulant response to a standard dose of LMWH is consistent and predictable and hence does not require monitoring during therapy. Also, the half life of these drugs is longer and once-daily dosage is possible. Several trials have shown that LMWH are atleast as effective as unfractionated heparin in the treatment of DVT [18, 19, 20, 21] and the risk of bleeding related complications appears to be less [22]. Continued anticoagulation is usually maintained using oral warfarin. The major complication of anticoagulant therapy is bleeding. Heparin can also result in an immune mediated thrombocy-topenia called Heparin Induced thrombocytopenia (HIT) syndrome which can result in wide spread arterial and venous thrombosis. If HIT syndrome is diagnosed then heparin in all forms has to be stopped and anticoagulation using other agents such as hirudin and argatroban will have to be instituted.There is considerable debate about the indication for catheter-directed thrombolysis in the management of acute DVT. Current research suggests that thrombolysis may beneficial in patients with impending venous gangrene and patients with extensive iliofemoral venous thrombosis who will invariably develop post-thrombotic syndrome if managed with anticoagulation alone. The indications for thrombectomy are identical. Thrombectomy is not widely accepted because it is invasive and therefore thrombolysis is preferred choice.The Sixth ACCP Consensus Conference on Antithrombotic Therapy has made the following recommendations for duration of anticoagulation: patients with reversible or temporary risk factors for VTE may be treated for 3-6 months, while patients with irreversible risk factors such as thrombophilic states and malignancy are to be treated indefinitely [23].

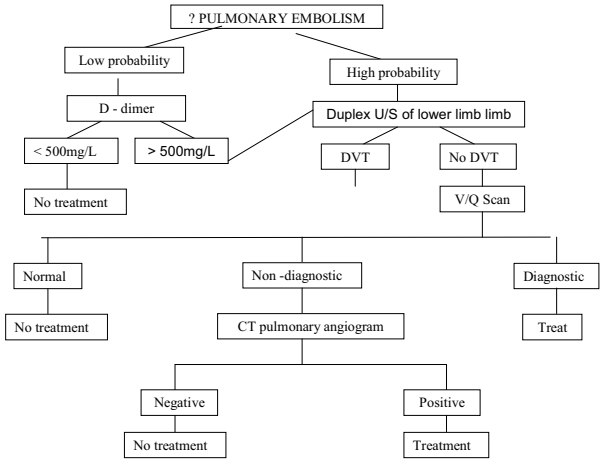
Prophylaxis-There are 2 ways in which pulmonary embolism, the most serious complication of DVT can be prevented - primary

prevention of the initial DVT and secondary prevention by early detection and treatment of DVT. Given the poor sensitivity of clinical diagnosis of DVT, primary prevention has become the preferred mode of prophylaxis. Methods of primary prevention include early and persistent mobilisation, pharmacological agents like unfractionated heparin and low molecular weight heparin (LMWH) and mechanical means like intermittent pneumatic compression and graduated compression stockings.Patients at low risk should be encouraged early mobilisation and do not require prophylaxis. Patients with moderate risk should have additional pharmacological prophylaxis. Patients in the high risk group require pharmacological and mechanical prophylaxis. In patients undergoing surgery in which minor haemorrhage may be critical to the outcome, such as neurosurgery, ophthalmic surgery and spine surgery, mechanical prophylaxis is recommended. In surgical patients, the prothrombotic state begins intraoperatively and hence prophylaxis should ideally commence before induction of anaesthesia. Trials have shown that initiating prophylactic anticoagulation 2 hours prior to surgery is both safe and effective in decreasing the risk of fatal PE [2, 24]. If prophylaxis cannot be started peri-operatively because of the risk of bleeding, there is still a beneficial effect in starting it postoperatively. Prophylaxis in the postoperative period is generally maintained till the patient is discharged. However in high risk orthopaedic procedures such as hip replacements, extended prophylaxis up to 30 days is indicated.

Prophylactic anticoagulation in the setting of regional neuraxial anaesthesia poses the risk of a spinal hematoma which can potentially lead to permanent neurological impairment. Specific risk factors for this happening are prolonged epidural analgesia, traumatic introduction and females over the age of 75 yrs. Specific guidelines on the usage of prophylactic anticoagulation, in this setting, have been outlined by the American Association of Regional Anesthesia Consensus Conference [25]. Among the various pharmacological agents, meta-analyses have shown that LMWH and unfractionated heparin have equal efficacy in preventing VTE in general surgical patients. However the group on unfractionated heparin had a higher incidence of minor bleeding episodes such as wound hematomas [26, 27]. Intermittent pneumatic compression alone is a useful method of thromboprophylaxis in surgical patients at high risk of bleeding. However it is limited by patient compliance and ease of use. Graduated compression stockings are simple to use and moderately effective. They have been shown to increase the velocity of venous blood flow. They are recommended in patients at low risk for VTE and can be combined with pharmacological prophylaxis in patients at medium to high risk. Its usage is contraindicated in patients with peripheral vascular disease.

Fatal PE is the most dramatic effect of VTE and remains the most common preventable cause of death in hospitalized patients. The best strategy is prevention by adequate prophylaxis for VTE. Early detection is essential for improved out come and requires a high degree of suspicion, when post operative patients have- Unexplained trachycardia, Unexplained fever, Chest pain, Dyspnea, Hemoptysis

The diagnostic strategy for the investigation of suspected pulmonary embolism is [28]



Treatment of PE is decided by the cardiovascular status of the patient. If the patient has circulatory collapse then he is best managed by catheter directed thrombolysis or thrombectomy. If the patient is stable then adequate anticoagulation is sufficient.

Vena cava filters- Vena cava filters can be placed in the IVC to prevent emboli from the legs reaching the lungs. There are many devices available, varying from permanent, optional retrievable or temporary filters. The advantage of a temporary filter is that it protects the patient during a high-risk situation, but can be removed once this risk is over. There are five absolute indications for filter placement

- Patients with VTE and absolute contraindication to anticoagulant therapy
- Patient with recurrent VTE while on adequate anticoagulation
- Patients who develop major bleeding complication requiring cessation of anticoagulants
- Patients with VTE and left to right shunt
- Patients who undergo surgical thrombectomy for chronic thromboembolic PE

Although the incidence of complication from vena cava filters is reported to be around 5-10%, death directly related a filter is rare [29]. Serous complication include -Insertion site thrombosis,Filter migration, Caval thrombosis, Caval penetration.

Editor's note- This is a detailed and simplified review of a very complex subject. It is important for all medical practitioners to be aware of the possibility of venous thromboembolism in their patients. Hospitalization is a risk factor for this entity with the incidence being 1000 times more compared to community.

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John Hunter

John Hunter performed perhaps the most famous operation for an arterial aneurysm. Hunter had observed that the blood supply to the horns of deer changed under different conditions. A rich blood supply was present when the crest was full, but the blood vessels decreased in number and size when the horns shed. Hunter inferred that reserve vessels, now termed "collaterals", might develop in humans if obstruction occurred in their arteries. In December 1785, a beer delivery man was admitted to St. George's Hospital with a pulsatile mass in the popliteal fossa, possibly secondary to repetitive trauma against the coachman's seat while driving on rough streets. The patient had been symptomatic for 3 years, he complained of leg pain on walking and rested frequently presumably owing to arterial occlusion distal to the aneurysm. Standard treatment at that time entailed above-knee amputation. Hunter's previous experiments, however, suggested that collateral vessels have formed around the obstruction or the leg would have developed gangrene. Thus, he incised above the knee at a location now known as "Hunter's canal" and tied four ligatures around the artery. Four sutures were used to avoid sawing through the vessel. After a bout of local infection, the patient survived and was discharged fully ambulatory. Later, Hunter performed four similar operations and three were successful; the fourth patient died 26 days postoperatively.

Peripheral Vascular Injuries

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Early detection and management of vascular injuries remains crucial for limb salvage in trauma patients. The prompt control of hemorrhage and restoration of circulation by repair can avoid death, amputation in some situations. Ligation of the injured vessels was a common procedure in the past to stop the bleeding but that resulted in amputations to the tune of 50% in World War II. The prompt of the repair of vascular injuries can reduce the amputations to less than 2% as seen in civilian injuries.[1] The diagnosis and management of vascular trauma continues to be challenged by changing policies such as mandatory exploration of all suspected injuries, selective evaluation and non-operative management of minimal injuries. We often treat lower extremity vascular injuries following road traffic accidents in our hospitals. More than one third of the vascular injuries are noted in the upper limbs and they are not as challenging as those in the lower limbs. If the vascular injuries are not adequately treated, complications such as thrombosis, delayed bleeding, arteriovenous fistulae, false aneurysms are likely to occur. Early repair of vascular injuries may be much simpler than the delayed repair of the complications like arteriovenous fistulae or traumatic false aneurysms. Even today, there are many critical issues in the management of vascular injuries and they are:

- When to consider a primary amputation?
- What is optimum use of angiography?
- What is the ideal management of injuries which are angiographically called "minor"?
- What is the optimal sequence of repair of artery, vein, nerve and bone?
- The choice of durable graft when primary end to end repair is not possible?

Types of Injuries and immediate care-Penetrating vascular injuries due to low velocity bullets, sharp instruments and gun shot wounds are common in some western urban cities. But blunt injuries to vessels are more common in the rural areas and also road traffic accidents. Hospitalized patients (6.5%) with orthopedic injuries are known to have associated vascular injuries.[2] The extremity vascular injuries are often associated with both bone fractures of the forearm, leg and dislocation of the knee. The severity of the crush associated with vascular injury determines the out comes of the vascular repair.The incidence of amputation is higher after blunt and crush injuries than after wound from sharp instruments or low velocity missiles. The amputation rates can be as high as 26% when there is a combination of vascular injury and skeletal trauma compared to the vascular injury alone (0.6%).[3] At the same time amputation rates in vascular injury patients were not significantly influenced by the associated venous trauma. Initial management of trauma patient is very important (Air way, breathing, circulation - ABC) before attention can be given to the bleeding area in the leg. Control of bleeding along with resuscitation of the patient with replacement therapy saves the patient. Local pressure is preferable to the routine use of tourniquets to control the bleeding as they can compromise the circulation through the collaterals to the ischemic limb. It is better to avoid applying traumatizing clamps blindly if there is a vessel in the depths of the wound since they may damage the adjacent important nerves or tissues. Life threatening bleeding from the major veins should be controlled along with arterial using local compression. After attending to the immediate problems, one should concentrate on getting the history from the patient or his relatives who were at the scene of the injuries. One should note the amount of blood loss, mechanism of injury, symptoms of circulatory, sensory and motor

insufficiency. It is important at this stage to exclude the possibility of intra cranial, intra thoracic and intra abdominal injuries. During physical examination of the extremity with vascular injury base line observations should be recorded about the volume of the pulses, filling of the veins, speed of capillary refilling, color, temperature, neurological functions of the extremity.

Signs of arterial injury in the extremity-The signs of arterial injury to be noted are classified to - hard signs and soft signs. When there are hard signs to be noted it becomes mandatory to consider exploration of the wounds. The urgency to repair depends on the number and severity of associated injuries, bleeding, distal ischemia and critical site of injury. The hard signs are-distal circulatory deficit (ischemia, pulses diminished or absent), Vascular Bruit, Expanding or pulsatile hematoma, Arterial bleeding. The soft signs are-Small or moderate size stable hematoma, Adjacent nerve injury, Shock (unexplained by other injuries), Proximity of penetrating wound to major vascular structure. The need for mandatory exploration of all wounds with suspicion of vascular injury has come down with better clinical examination and judicious use of investigations such as color Doppler test and angiography. Presence or absence of arterial pulse distally in the extremity would not always exclude or confirm the possibility of vascular injury. In some patients local hematoma, dislocations, fractured ends may be compressing the artery with intervening soft tissues and give an impression as though the vessel is damaged on the clinical appearances. If the compression is relieved then the pulse can be felt in the distal part of the limb. The pulse may be also diminished in patients with shock or hypotension. At the same time the presence of pulse may not exclude the proximal arterial injury.[4] If the vessel is partially severed there can be a palpable pulse distally in 61% of patients.[5] Snyder et al noted that in 56% of the subclavian artery injuries and 16% of the popliteal artery injuries the pulses are palpable.[6] Sirinek and associates noted that routine exploration of all wounds with suspected vascular injuries is associated with 5% morbidity and 0.4% mortality and no injury in 64% of patients.[7]

Investigations-Arterial Pressure Index (API) less than <0.9 is found to be indicative of vascular injury. Duplex scanning can be informative and useful in the hands of an experienced operator. Angiography is the gold standard for the detection of vascular injury. The arteriogram can establish, localize the injury and help in planning the operation. The angiographic findings of obstruction, extravasations, early venous filling, arteriovenous fistula, wall irregularity, filling defect, false aneurysm are important to confirm the diagnosis of vascular injury. But these findings will be seen only when an accurate angiography is done otherwise there is a possibility to miss the hard signs of vascular injury in angiograms too. The need for venograms is not well defined in the literature. Intra operative angiograms (single shot) can be very helpful to define the concomitant distal arterial injuries and completed successful repair.

Primary amputation and Non operative treatment - The attitude that vascular reconstruction is always indica-ted is inappropriate and may result in serious morbidity. If there is extensive crush with nerve injury, muscle injury, skeletal injury in addition to vascular injury, it would better to consider primary amputation to avoid the morbidity and secondary amputations. Different types of injury severity scores have been introduced to assess the risk of amputation. MESS score has been shown to be very effective in predicting the out comes in these patients. However the final decision about limb salvage or primary amputation should be made under ideal circumstances, that is in the operation theatre. Patients with soft signs are followed carefully with non operative therapies. But it should be noted that there is a possibility that these patients with soft signs of vascular injury may also need interventions if there is progression to the next stage or appearance of new hard signs. Such patients may need repeat studies and close monitoring.

Vascular repair: technical considerations- Good anesthesia (GA is preferable to regional) with adequate precautions to meet the intra operative blood losses. The patient and limb should be properly positioned. The donor site for harvesting autogenous vein graft should also be prepared and draped simultaneously. Longitudinal incisions are made to expose the vessels to get an access proximal and distal to

the site of injury. The arterial segments proximal and distal to the site injury should be dissected and isolated outside the hematoma and taped. If it is necessary one can also consider intra operative angiogram to define the vascular injury at this stage. Intra arterial shunts are rarely used to maintain the distal circulation while other procedures are done. A Fogarty catheter can be used for thrombectomy from the arterial tree in the proximal and distal arterial segment. Irrigation of the distal arterial tree with heparinized solution or ringer lactate washes any residual thrombi in the distal bed. Similarly any thrombus on venous side is also washed out and removed. Adequate debridement of the dead tissues in the wound is important.

Which one to be repaired first artery, bones, vein or nerve-If there is adequate distal flow then probably the sequence of repair is personal preference, but if there is distal ischemia or venous hypertension artery and vein should be repaired first. If a major vein is injured then it would better to repair it to avoid venous hypertension and to increase benefits of good flow through the repaired artery. Bone fixation by the orthopedic surgeon is usually done after the vascular repairs by the vascular surgeons in ischemic patients. It is also important for the vascular surgeons to be available during the orthopedic procedures as there is a fear of damage to the reconstructed vessels. In their series Synder WH et al found that in 10% of the cases of popliteal artery repair the later orthopedic manipulations disturbed the vascular repair. A good initial debridement is very important after repair of the vessels and fixation of the fractures.

Methods of Repair - The method of vascular repair depends on the type of vessel injury and extent of debridement required during the procedure. Minor lacerations and puncture wounds in the large vessels can be probably repaired by the lateral repair. But the same lateral repair in similar type of injuries in medium or small vessels may result in narrowing or stenosis. Some kind of local repair of vessel (vein patch angioplasty) may be required to close the wounds without compromising the lumen in medium or small vessel when they are important.

The primary repairs such lateral repair, end to end anastomosis are less often possible in the lower extremities following blunt injuries in the road side two wheeler accidents with fractures of long bones. Some times mobilization of the proximal and distal arterial segments after excision of the devitalized segment makes it possible to approximate the two ends for primary anastomosis. These arterial ends are spatulated to avoid anastomotic stenosis. Non absorbable suture such as prolene 4 -0, 5-0, 6-0 are used in these patients. The vein grafts are usually are best taken from the opposite limb to avoid compromising the venous return in the injured leg. The proximal part of the long saphenous vein is better suited for the larger vessel reconstructions and it is better to preserve it for a later use. The saphenous vein at the level of the ankle can be used for patches, short segment bypass in the brachial, popliteal and tibial vessel bypass operations. A good vein should be at least 4 mm in diameter to be used in the bypass operations. The vein grafts can be distended and gently dilated

Type of injury	Type of vessel	Type of repair
Clean cut injury or small laceration	In large vessel	Lateral repair or end to end repair
Clean cut injury or small laceration	Medium or small vessel	Vein patch angioplasty
Gunshot wounds	Blood vessels after debridement	Vascular bypass with vein graft in medium sized vessels and with Synthetic graft in large vessels.
Blunt and crush injuries of the extremities	Debridement and excision of the crushed vascular segment	Bypass with vein graft

using heparinized blood with pressure not more than 150 -160 mm of Hg and avoid injury to the endothelium by excessive distention. If the size of the saphenous vein graft is not matching the vessel to be bypassed then a panel, spiral graft constructed with the saphenous vein.

Prosthetic grafts- Synthetic grafts are used when the suitable vein grafts are not available. When a synthetic graft is used on the contaminated wounds one should be cautious about the infection of the grafts. However the incidence of anastomotic disruption seems to be more with venous graft anastomosis than with the synthetic graft anastomosis in the studies. Use of the prosthetic graft may save some time in the emergencies as there is no need to harvest the vein graft in patients who very critical under anesthesia. Whenever there is contamination of the wounds it is better to choose the anastomosis far away from the infected wounds and in the healthy areas. The anastomosis should be covered with healthy tissues and preferably neighboring viable muscle can used to cover and protect the anastomosis. The type of suturing continuous or interrupted depends on the size of the vessels. When the vessels are larger than 5 mm, continuous suturing is convenient and in vessels smaller than 5 mm interrupted sutures are preferred to avoid stenosis. The important veins are also similarly repaired when they are injured. The smaller veins can be ligated when the venous return is not compromised.

Soft tissue coverage and fasciotomy after vascular repair-The repaired vessels should be covered by healthy viable tissues to avoid infection, necrosis and hemorrhage. Sometimes it may necessary to take the help of the plastic surgical procedures to give good skin and muscle coverage to the repaired vasculature. Compartmental pressure may increase after reperfusion of the ischemic extremities and jeopardize the microcirculation and result in the thrombosis of the vascular grafts. Wide fasciotomies are done and muscle compartments are decompressed. The edematous muscles bulge out after the fasciotomies. Perifibular fasciotomies are preferred by some times for adequate decompression of all the four compartments of the leg (Anterior, lateral, Superficial and deep posterior compartments).

Post surgical complications after vascular repairs- Thrombotic re-occlusion and hemorrhage are the common complications after vascular repair. A completion angiogram, adequate excision of the contused arterial segment, adequate mobilization of the proximal and distal arterial segments before stretching them, adequate anticoagulation in the perioperative period, properly selected and harvested vein graft with minimal trauma will certainly reduce the number of vascular thrombotic and hemorrhagic complications. Reperfusion injury due to delayed revascularization is also going to result in rethrombosis, muscle necrosis and renal failure due to myoglobinuria. This can be avoided by adequate hydration, diuresis and debridement of the dead muscles in the perioperative period. Delayed complications such as secondary hemorrhage, arteriovenous fistulae can be managed by explorations and infection is a common accompaniment in such patients. Broad spectrum antibiotics and anti staphylococcal agents are to be used in adequate doses in the post operative period to avoid infections.

Conclusion-The adequate management vascular injuries can save the limbs and life in the modern world. The suspicion and early detection of the vascular injuries can certainly reduce the morbidity and mortality in the patients with musculoskeletal trauma secondary to road traffic accidents. Adjuvant therapies such as anticoagulation, antibiotics, debridement, adequate muscle cover, healthy and suitable vascular grafts, close peri-operative monitoring for reperfusion injury, adequate fasciotomy, adequate training of the surgeons will improve the limb salvage after vascular trauma in our patients.

Thoraco-Abdominal Aortic Aneurysm (TAAA)

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Although infrarenal abdominal aorta is the commonest site of aortic aneurysm, TAAA contributes to a small percentage of aneurysms which pose extreme technical and surgical challenge in management.

Classification of TAAA-Modified Crawford classification

Type	Proximal	distal extent
I	Distal to left subclavian A	Above renal A
II	Distal to left subclavian A	Below renal A
III	6th intercostal space	Below renal A
IV	12th intercostals space	Below renal A
V	Below 6th intercostal space	Above renal A

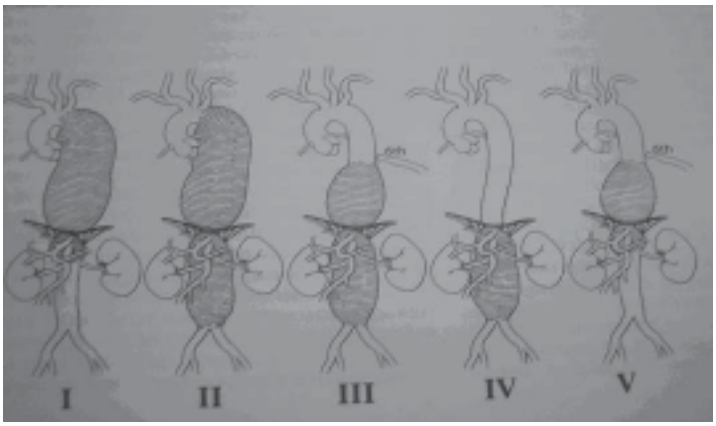

Fig-1, Schematic representation of Classification of TAAA-Modified Crawford classification

Adopted from Rutherford's textbook for Vascular surgery 6th ed.

Natural history-Incidence of TAAA is 10.4 cases per 100,000 person years with mean age of 59-69 years (age of onset is a decade late for females) and male to female ratio is 3:1. Untreated TAAA has 5 year survival of 39%. 70% Of TAAA patients have diagnosed HT, 26% have CAD,10% have CVA, almost all are Smokers and 32% have COPD. Commonly, TAAA are detected incidently (asymptomatic). Symptomatic TAAA presents with bachache. First presentation of 10-20% of TAAA is rupture. Most common cause of death is rupture of aneurysm. Most important risk factor for rupture is aneurysm size (then rate of expansion). 1 year rupture rate of 8cm aneurysm and life time rupture rate of untreated aneurysm are 80%. Average rate of expansion of aneurysm is <4mm/year and expansion >1cm/ year indicates impending rupture. The main factors affecting aneurysm size and rupture rates are systemic hypertension (particularly diastolic HT), smoking, COPD-FEV1 <60% (increased collagenase activity), gender (females have greater risk of rupture), age (relative risk of rupture increases by factor of 2.6 per decade of age). Aneurysm related factors like saccular type and false aneurysms have higher rupture rates and warrant early intervention.

Mega-Aorta-refers to extensive aortic aneurysm involving ascending, arch and thoracoabdominal aorta. It is associated with Marfans syndrome, Chronic aortic dissection (40% develop aneurysm in 4 years) Note-25% TAAA are associated with chronic aortic dissection

Etiology-Degenerative-commonest;Chromosomal disorders- Marfans syndrome 20%TAAA –first degree relatives affected and familial clustering is seen; Infective- septic embolism or contiguous spread. Organisms involved include Salmonella, H influenzae, Staphylococcus,M tuberculosis, Treponema pallidum

Syndromes associated with TAAA-1. Marfans syndrome-Fibrillin -1(FBN1) gene on chr 15- autosomal dominant; Turners syndrome-gonadal dysgenesis-45X and mosaic; Ehlers Danlos syndrome-types 1-X; Polycystic kidney disease-chr 16p, 4q

Clinical presentation-Most common presentation of TAAA is incidental detection (asymptomatic). Commonest symptom is ill defined chronic backache Acute changes in character of pain means sudden expansion or impending rupture. TAAA can present with

- **compressive symptoms/ signs-** Hoarseness of voice (left recurrent laryngeal N / Vagus with vocal cord palsy), Dyspnoea (Tracheo-bronchial tree), Pulmonary HT (Pulmonary artery), dysphagia (Esophageal), Early satiety/weight loss (Duodenal), hemoptysis /hematemesis (Erosion to TB tree/ esophagus)
- **thromboembolic symptoms-** Paraparesis/paraplegia (acute occlusion of intercostals/spinal artery) OR distal thrombo-emb-olism.

History and Examination focused to other vascular beds like coronary, carotids, mesenteric vessels, renal and femoropopliteal segment should be done.

Diagnostic imaging

- CT Angiography is the investigation of choice. It can be done fast, detects calcification, thrombus and outlines the lumen clearly.
- Transesophageal echocardiography: can be used in patients with impaired renal function or in a hemodynamically unstable patient.
- Selective aortography can be performed to identify patent artery of Adamkiewicz (used in some centers) or to identify aortic branch occlusive disease
- Magentic resonance angiography with gadolinium.

Other investigations include- Blood biochemistry, blood counts, coagulation profile, Cardiac (ECG, ECHO, CAG), Pulmonary- CXR, PFT; Renal- Sr creatinine, renal vessel imaging ;Carotids-duplex scan

Treatment options-Watchful waiting for <5cm aneurysm with control of risk factors and monitoring of rate of expansion and diameter ; Surgical management; Endovascular-TEVAR

Size threshold for intervention - 6cm for type I to III TAAA; 5cm for Type IV, those with Marfan's syndrome, chronic dissection, young age.

Surgical techniques -Emergency surgery rate for ruptured TAAA is about 6.8% . Elective surgery is performed under General anesthesia using a double lumen endotracheal tube to permit single lung ventilation. Large bore central line is placed for rapid transfusion. Arterial line and Swan Ganz catheter are placed for monitoring. Lumbar CSF drainage is done to reduce the risk of spinal cord damage. CSF pressure is kept below 10 mm Hg till the third post operative day.

Operative management - Position: Right semi-lateral decubitus position(Stoney's position) with access to both groins; Incision: Full thoraco-retroperitoneal 6th rib excising diaphragm splitting incision; Preclamp anticoagulation is done with 1mg/kg of Heparin, sequential clamping, distal aortic perfusion via a biomedicus pump is established. No 9 F Pruitt catheters are used for perfusion (flow rate of 450ml/mt) and cooling of renal/ Visceral vessels. Gelatin or collagen coated Woven Dacron graft is preferred for replacement with reattachment of lower intercostals and visceral vessels as Carrel patch.

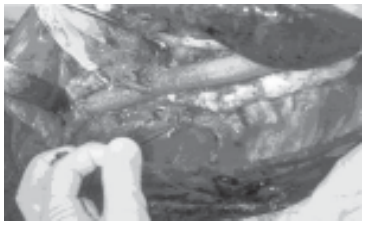

Figure- 1 TAAA repair with pre-coated Dacron graft, left renal artery carrel(arrow head) and visceral vessels carrel (double arrow)seen

Complication	Remarks	Prevention
Paraplegia & delayed neurological deficits	3.3% for TAAA repair 10% for type II TAAA Predictors of poor results- • acute dissection • Type II TAAA • Renal insufficiency	Reimplant intercostals A MAP >90 mm of Hg Hb >10gm% Cardiac index >2L/m CSF drainage to <10 mm of Hg for 72hrs
Renal failure	4-29%, 15% of which needs hemodialysis risk factors- preop creatinine>2mg/dl direct left renal A revascularistionsimple cross clamp technique	Cold blood perfusion-300-600 ml/mtReduce renal O2 useMaintain O2 deliveryReduce direct renal tubular injuryFenoldopam-dopaminergic agonist
Visceral	Risk of intraoperative bleed with hepatic dysfunction	Perfusion to liver and bowel via celiac or SMA cannulation
Cardiac	31% association with CAD, 12% mortality raterisk factor for early mortalityventricular dysrhythymias at temp <32 deg C	Left atrial to femoral bypassAfter load reduction by nitrates
Pulmonary	20-50%risk factors- advanced age, aortic cross clamp time>60mts,blood transfusion, smoking	Keep central tendinous part of diaphragm intact,Preserve phrenic N

Outcome-Mortality- 15% Normal risk, 50% high risk (age>79,DM,CCF); Mortality+Morbidity-30% 5 year survival rate is 60-70%; negative predictors of long term survival(Advanced age, Type II TAAA, Renal failure, Emergency surgery, Cerebrovascular disease, Active smoking)

Conclusion- TAAA open repair is extremely stressful for the patient and is an extreme challenge to the operative team. With regular focused team for TAAA open repair will help improve the results.

Editor's note-TAAA repairs can be performed with acceptable risks in centers with experience in this surgery. Use of visceral perfusion helps to reduce morbidity and mortality. Newer techniques use stent grafts for endovascular repair. Two modalities are under use now. Hybrid procedures- Bypasses are performed to visceral arteries and then the aneurysm is excluded using a stent graft; Use of fenestrated stent grafts to reperfuse the visceral arteries.

9

Review Article

Abdominal Aortic Aneurysm

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Abdominal aortic aneurysm (AAA) is defined as a focal dilation of the aorta involving an increase in diameter of at least 50 percent as compared with the expected normal diameter[1]. The incidence of AAA is found to be progressively increasing from 12.2 per 100,000 in the year 1950 to 36.2 per 100,000 during the year 1980 to 350 per 100,000 in the year 2000. This increase in incidence can partly be attributed to increased life expectancy and improved screening modalities. There is 2-6 times higher incidence in males, who also tend to develop the disease at a younger age compared to women.

Pathogenesis - AAAs are commonly a result of degenerative process occurring in the aorta. Aortic wall contains elastin and collagen- the matrix proteins- along with the vascular smooth muscle cells. Elastin is the principle load-bearing element in the aorta while collagen is important to prevent rupture after the formation of the aneurysm. Elastin is found to have a half-life of 40-70 years. There is a progressive reduction in the number of elastin layers from the thoracic aorta to the infra-renal aorta associated with decrease in the proportion of elastin in relation to collagen. Long-standing hypertension also leads to medial disintegration. These are said to be the factors involved in the causation of degenerative infra-renal aortic aneurysms. Since degenerative aneurysms are associated with widespread atherosclerotic changes, they are also called as atherosclerotic aneurysms. The other factors implicated in the causation of AAAs include – Infections (Staphylococcus aureus, Tuberculosis), Arteritis, Connective tissue disorders (Marfan's syndrome, Ehler Danlos Syndrome), Trauma, Pseudoaneurysm from anastamotic disruption. Degenerative aneurysms account for approximately 90% of AAAs.

Risk Factors- Prevalence of AAAs in a given population is associated with the following risk factors

- Smoking: Risk ratio(RR) - 5
- Male gender: Risk ratio(RR) – 5.6
- Age : Risk ratio(RR) – 1.7 for every 7 years
- Family history: Risk ratio(RR) – 12 for first degree relatives
- Hypertension
- Hypercholesterolemia

Natural history of AAA- The natural history of aneurysm is to enlarge and rupture. There is no evidence for regression of aneurysms- spontaneous or secondary to conservative therapy. Aneurysms enlarge at an average rate of 0.4cm / year. Enlargement rates are found to be directly proportional to hypertension, COPD, family history and increased aneurysmal thrombus.

Clinical features- most of the patients who have AAA have their diagnosis made during routine clinical examination or while being radiologically investigated for an unrelated disorder. Most of the aneurysms become symptomatic when they either expand at a rapid pace (stage of sudden expansion) or rupture. Patients then present with severe abdominal pain or back pain radiating to flank or groin. Ruptured aneurysms classically present with a triad of severe abdominal pain, hypotension and pulsatile abdominal mass, though all three features are present only in 26% of patients with ruptured aneurysm. 80% of aneurysm rupture is into the retroperitoneum, and due to the tamponade that ensues, patients have a higher chance of presenting to the hospital and undergoing successful repair. 20% of aneurysm rupture is into the free peritoneal cavity which due to lack of tamponade leads to massive hemorrhage and circulatory collapse.

AAAs can also present with symptoms not related to acute expansion or rupture, but to distal thrombo-embolism in less than 5% of the patients.

AAAs also present with symptoms related to local

pressure effects like early satiety and vomiting due to duodenal compression, urinary symptoms due to pressure on the ureters or encasement of the ureters in case of inflammatory aneurysms, deep vein thrombosis due to compression of IVC

Diagnosis- Physical examination detects only 29% of AAAs less than 4cm in size, 50% of AAAs between 4-4.9cm in size and 75% of AAAs more than 5cm in size, even in focused examination. Ultrasonography is the least invasive, least expensive and widely available investigation, particularly for initial confirmation in cases of patients suspected to have AAA or subsequent follow-up and also for purposes of screening. However, ultrasound cannot reliably tell the anatomic extent, visualization may be obscured by bowel gas and rupture may not be detected by ultrasonography. Inter-observer variation of up to 5mm in size is noted.

Computed Tomography (CT), though more expensive and requiring contrast injection for delineation, is more reliable in assessing the anatomical extent, images the iliac arteries, and detects rupture. CT gives the exact position of the renal and other visceral arteries in relation to the aneurysm. Presence of layered thrombus in CT is the definitive sign for diagnosis of AAA. Inter observer variability is less than 5mm. CT can also detect other abdominal pathologies not detected by clinical means or other investigations. At present CT is considered the gold standard investigation for AAA.

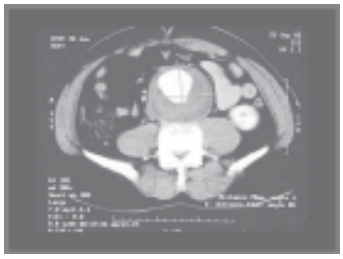

Fig-1,CT scan showing an aneurysm in the infra-renal segment of the aorta with layered thrombus

MRI though comparable to CT in terms of assessing the anatomical extent, size and rupture, is not widely used due to the cost involved and lack of widespread availability of MRI. But MRI is useful in patients who require contrast study, but have renal failure. Arteriography may not depict the true size of the aneurysm as the thrombus in the aneurysmal cavity is not imaged but only the luminogram is seen. But arteriography is useful to evaluate the condition of vessels in patients with concomitant occlusive disease in aorto-iliac segment, or with anomalies like horse-shoe kidney or pelvic kidney.

Evaluation of the patient- As most of the patients with AAA are elderly, and due to frequent involvement of vasculature of other systems in the disease process, evaluation of the patient's cardiac, renal and other systems is paramount in deciding the mode of therapy for an individual patient. Treatment for patients with AAA is not usually denied on chronological age alone as endovascular treatment of AAA is a relatively safe and effective procedure. Cardiac status is the most important predictor of post-operative morbidity and mortality in patients with AAA undergoing intervention. As history and physical examination may not always predict the true cardiac status, patients are usually subjected to other investigations which may include echocardiography, coronary angiogram and cardiac scintillation scans. Patients found to have significant coronary artery disease may require catheter based or surgical cardiac revascularization prior to aneurysm repair. Renal functional status may influence the mode of investigation used for evaluation and pulmonary function test has to be optimized prior to surgical intervention to avoid post-operative pulmonary complications.

Treatment options-Medical management: is recommended in patients with aneurysm with low risk of rupture which include patients with aneurysm less than 4.5cm with no symptoms. Smoking cessation and aggressive control of hypertension form the basis of medical management. As ultrasonography routinely underestimates aneurysm size by 4-5 mm CT is the ideal mode of investigation for initial assessment followed by serial ultrasound monitoring. Recent reports suggest that tetracyclines may delay progression of the aneurysm

Surgical Treatment- Aneurysmal surgery has evolved from the initial methods of aneurysm ligation, wrapping, inducing thrombosis of the aneurysm to the present day management of

intraluminal graft placement with aneurysmorraphy as popularisd by Stanley Crawford.

Pre operative beta-blockade has shown to reduce the post-operative myocardial ischemia due to reduction in oxygen demand. General anesthesia supplemented by epidural analgesia is the anesthetic mode of choice. AAA repair is done usually through the anterior midline trans-peritoneal route which gives excellent exposure but may be associated with post-operative pulmonary complications. Alternative approaches include transverse abdominal and retro-peritoneal exposure. Operative steps include thorough exploration of the abdomen to exclude other pathology and then division of ligament of Treitz to allow rotation of small bowel to the right. Aneurysm is exposed by incising the peritoneum from the inferior border of pancreas to the level of the iliac vessels to the left of the base of small bowel mesentery. The normal aorta just above the aneurysm and the common iliac arteries are clamped after dissecting. Heparin anticoagulation is used just prior to clamping. The aneurysm is opened longitudinally and the thrombus is evacuated. Back bleeding from the lumbar vessels is controlled by suturing the ostia. Proximal anastamosis of the graft [usually pre-clotted woven Dacron or coated knitted Dacron graft] to the aorta is done after obtaining hemostasis in the aneurysmal sac. Distal anastamosis can be either proximal to the aortic bifurcation or to the common iliac vessels or the femoral vessels depending on the aneurysm morphology. Anastamosis is done using polypropylene sutures.

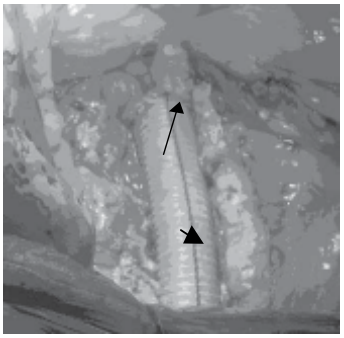

Fig-2 Dacron graft (short arrow) in place after proximal and Distal (long arrow) anastamosis for repair of Infra renal AAA

Patient will have to receive adequate intra-venous fluids, mannitol and bicarbonate correction prior to declamping to prevent the occurrence of hypotension, acidosis and renal failure (declamp syndrome).

IMA will have to be re-implanted onto the graft if the back-bleeding from the ostium is brisk or there is significant SMA disease so as to prevent mesenteric ischemia. The upper anastamosis and the graft are to be isolated from the peritoneal cavity by suturing the aneurysmal sac over the graft and re-approximating the peritoneum to the left of the base of the mesentery. The small bowel and other abdominal viscera are to be inspected to rule out ischemia prior to closure of the abdomen.

Complications of AAA surgery- Cardiac complications: commonly occur within 48 hours after surgery. Reducing heart rate and control of hypertension thereby reducing myocardial oxygen demand, correction of anemia and control of pain will help in significant reduction in the incidence of peri-operative MI.Other complications include hemorrhage, renal failure, renal ischemia, pulmonary complication, mesenteric ischemia, paraplegia, distal embolism, pseudoaneurysm, graft infection, graft thrombosis, aorto-enteric and graft enteric fistula and sexual dysfunction.

Ruptured abdominal aortic aneurysm-The most dreaded and devastating complication of aneurysms is rupture. The devastating nature of this complication is highlighted by the fact that 50% of patients with ruptured AAA die prior to reaching the hospital and of the patients who undergo surgery peri-operative mortality of 40-50% is noted. Rupture of aneurysm can occur into the following four locations-Free peritoneal cavity, Retroperitoneum, GIT commonly duodenum or jejunum, Inferior vena cava. Of these sites, retroperitoneal rupture of the aneurysm carries the best prognosis with the peri-operative mortality of around 50%. This is due to the fact that the rupture can be contained in the retroperitoneum and hemodynamics of the patient can be successfully maintained until surgery.The differential diagnosis for patients with ruptured abdominal aortic aneurysm (RAAA) include renal colic, pancreatitis, GI hemorrhage, inferior wall MI, diverticulitis and GI perforation, of which RAAA

has the worst prognosis. Emergency ultrasound abdomen is the cheapest and the fastest way to confirm the presence of aneurysm in patients with suspicion of RAAA, but cannot detect extra-luminal blood. C T is the most accurate method to detect RAAA and is also helpful in delineating the anatomy and identifying associated disorders. But due to the possible delays in obtaining a scan it may be prudent to shift the patient to the operating room rather than scan room.

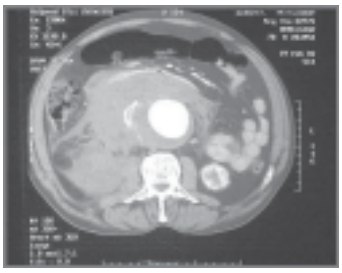

Fig-3, CT scan showing aneurysmal aorta with indistinct anterior margin and extravasation of blood into the surrounding areas suggestive of contained rupture

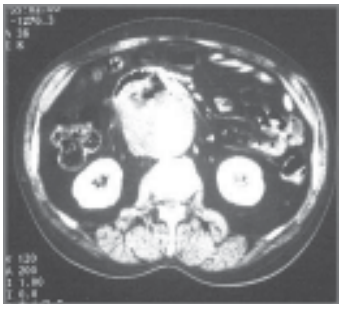

Fig-4, CT scan showing gas in the aneurysmal aorta in a patient with history of melena suggestive of primary Aorto-enteric fistula

Operative Management- At present operative management is the standard treatment for RAAA, though endovascular repair by placing a stent across the aneurysm is increasingly popular especially in the western countries. At least 6 units of cross-matched blood should be available at hand prior to induction.Though a variety of approaches are described most surgeons prefer the standard anterior midline approach because of the rapidity and ease of exposure and easy access to supra-celiac aorta if necessary for control of hemorrhage. After obtaining proximal control of the aorta-either in the supra-celiac segment or infra-renal segment-, the anesthetists are given time for effective resuscitation. The aneurysm sac is opened and the clot evacuated. Retrograde bleeding from lumbar and IMA is controlled, and proximal anastamosis is either done to the infra-renal neck or to the proximal aneurysmal sac if sufficient infra-renal segment is not found for anastamosis.

If an aorto-caval fistula is found at the time of surgery, vena cava is compressed both above and below the fistula and the fistula is suture closed from within the aneurysm sac with care being taken not to allow air or thrombus or debris to enter the venacava. Distal anastamosis is done either proximal to aortic bifurcation, or the iliac arteries or the femoral arteries as the anatomy of the aneurysm necessitates. Endovascular repair is being increasingly practiced where a stent is placed across the aneurysm but use is limited due to cost involved and lack of facilities and expertise. Complications include post operative bleeding due to coagulopathy secondary to massive transfusion and hypothermia, lower limb ischemia, colonic ischemia, paraplegia and paraparesis due to supra-celiac or thoracic aorta clamping to obtain proximal control, cardiac events, respiratory failure, renal failure, irreversible shock, liver failure and MODS. AAAs is an ever increasing problem due to demographic transition. Management of the abdominal aortic aneurysms has placed increased burden on healthcare delivery system due to the predominantly elderly population with this disease and associated co-morbidities. Introduction of endovascular repair has simplified management though at present the use is limited due to the costs involved, limited expertise and lack of long term results. Early detection, follow-up and elective repair of aneurysms is desired as it carries only 4% risk of peri-operative mortality as compared to repair in an emergency setting which is associated with a peri-operative mortality of 40-50%.

10

Review Article

Mesenteric Ischemia

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In the earlier days the surgical treatment of mesenteric ischemia was removal of infracted bowel before the patient was moribund. Klass, in 1951 was the first surgeon to focus on restoration of arterial supply to salvage the gut and performed the first SMA embolectomy. In the next two decades, many more reports of mesenteric revascularization came in but mortality remained high, to the tune of 70 – 90%.Presently with improved surgical and endovascular techniques and improvement in anesthesia and critical care, morbidity and mortality still remains high. Delay in diagnosis remains the greatest obstacle to the reduction of morbidity and mortality surrounding this disease.

Anatomy-Three major branches from the abdominal aorta supply the GI tract. Celiac artery arises at level T12-L1 and divides into common hepatic, left gastric and splenic arteries. The superior mesenteric artery arises at level of L1 and branches into inferior pancreaticoduodenal, middle colic and jejunal and ilieal branches. The inferior mesenteric artery arises at level of L3 and divides into left colic and sigmoidal branches. The splanchnic circulation is characterized by a wide network of collateral blood pathways that impart redundancy and resultant protection from ischemia or infarction. The celiac axis and SMA are connected by the superior and inferior pancreaticoduodenal arteries and the SMA and IMA by the marginal artery of Drummond.

Pathophysiology-Splanchnic blood flow can range from 10 to 35% of cardiac output. The increase occurs in response to food intake. Two of the three mesenteric arteries must be significantly diseased to cause symptoms of chronic mesenteric ischemia (CMI) and SMA must be one of them. Sudden occlusion of SMA alone can cause acute ischemia.

Acute mesenteric ischemia-It can be due to emboli to SMA or thrombosis of SMA. Most emboli are cardiac in origin and sometimes are from proximal aorta. Sudden onset of abdominal pain in a patient with cardiac disease must alert the clinician to the possibility of mesenteric embolism. Thrombosis usually occurs on pre-existing chronic disease.For diagnosis, a clinical suspicion is mandatory. Patient with cardiac disease, sudden onset of severe, continuous abdominal pain, often accompanied by diarrhea or vomiting must alert the clinician. There is accompanying leucocytosis. Other lab parameters and x-ray findings are seen only later in the course of the disease once bowel is infarcted. Elevated levels of intestinal fatty acid binding protein may offer some promise as a diagnostic tool.Duplex scan requires the presence of a trained vascular radiologist, a fasting patient and bowel bereft of gas: a combination nearly impossible to achieve in an emergency setting. Multi-slice CT scan can demonstrate occluded vessels (upto second generation branches), bowel wall edema, stranding in the mesentery. In addition, other pathologies could also be easily detected.A high index of suspicion followed up by multi-slice CT on emergency basis is likely to provide the best chance of diagnosis and an opportunity for revascularization.On angiography, SMA is found occluded at or near origin in case of thrombosis and affects the entire bowel from ligament of Treitz to mid transverse colon. In contrast, an embolus lodges at a branch point and the proximal jejunal branches are often spared.

Treatment-Initial management includes correction of fluid and electrolyte imbalances, baseline cardiac assessment, broad spectrum parenteral antibiotics

and anticoagulation. Endovascular therapy with fibrinolysis should not be attempted since there is a very high risk of ongoing bowel damage during the period of lysis.Surgery is the mainstay of treatment and begins with a complete exploratory laparotomy and assessment of bowel viability. Lower limbs must be included in draping for vein harvesting. In case there is extensive bowel infarction incompatible with life, it is appropriate to close with no further intervention. Revascularization is done either by SMA embolectomy or superior mesenteric artery bypass, usually from the infra-renal aorta. Bowel viability must be re-assessed after restoring blood supply and appropriate resection done. When there is doubt about bowel viability, re-look laparotomy is done after 12-36 hours.

Chronic mesenteric ischemia- It is a life-threatening problem that can result in death due to inanition or bowel infarction. The underlying pathophysiology is the failure to achieve post-prandial hyperemic blood flow. While atherosclerosis is the leading cause for CMI, other etiologies include Takayasu's disease, aortic dissection, fibromuscular disease, SLE, Rheumatoid arthritis and drugs like cocaine and ergot.A typical patient is cachectic, middle-aged, with history of smoking who presents with post-prandial abdominal pain and weight loss. The pain is usually epigastric and causes patients to avoid certain foods or eating altogether (food fear). Most patients often undergo extensive GI checkup before someone suspects CMI. Gastric ulceration or gastroduodenitis are often seen due to ischemia.A Duplex ultrasound is a good screening modality. Angiography is diagnostic and helps in planning revascularization strategies.

Treatment-All patients with CMI should be taken up for revascularization even if co-morbid factors increase risk of surgery. While long term total parenteral nutrition has been considered an option in high risk patients, it is practically inconvenient, carries risk of catheter related infections and does not alleviate the risk of bowel infarction. Revascularization options include angioplasty and stenting and mesenteric artery bypass. There is no clear cut agreement in literature as to which is the better option and as to how many vessels should be revascularized. Synthetic grafts or femoral veins are best conduits for mesenteric bypass. Inflow may be taken from supraceliac aorta, infra-renal aorta or an aortic graft. All patients are maintained on anti-platelet agents and statins.

Median arcuate ligament syndrome-The median arcuate ligament of the diaphragm compresses the origin of celiac axis which is augmented by full expiration in a large number of individuals. Its contribution to CMI is uncertain and it is unlikely to be able to produce CMI on its own. It is a diagnosis of exclusion. Surgical therapy may offer relief in patients who are females, have postprandial pain, weight loss more than 8 kgs, absence of drug abuse or psychiatric history and angiographic confirmation of celiac axis compression with post-stenotic dilatation. Effective treatment includes relief of compression and mesenteric bypass. Another option could be laparoscopic division of the ligament followed by angioplasty of celiac axis.

Non-Occlusive Mesenteric Ischemia (NOMI)-NOMI is caused by primary splanchnic vasoconstriction and has high mortality. It is associated with shock state, cardiopulmonary bypass and use of vasoactive drugs like digoxin, vasopression and á-adrenergic agents.

Management- Early arteriographic diagnosis and subsequent intervention offer the best chance for better outcome and survival. Pain out of proportion to physical findings and normal radiographic findings are suggestive of early ischemia and should prompt consideration of immediate diagnostic arteriography. Other biochemical and radiological findings as seen in acute ischemia, are indicative of bowel infarction. Arteriographic criteria for diagnosis of NOMI include narrowing origins of multiple branches of SMA, string of sausage sign, spasm of mesenteric arcades and impaired filling of intramural branches.

Treatment includes immediate management of precipitating

factors like shock and cardiac events and use of vasodilators that diminish cardiac preload and afterload. Definitive treatment is selective intra-arterial infusion of papaverine into the SMA. It is best to start with 30 mg/hr. Arteriography is repeated once pain resolves and infusion is continued for 24 hours. One needs to be vigilant for signs of bowel infarction and intervene appropriately.

Mesenteric venous thrombosis -It is a rare disorder with a wide range of clinical presentations. It usually involves the superior mesenteric and splenic veins and may involve inferior mesenteric and portal veins.One should suspect this diagnosis in patients with acute abdomen with history of previous thrombotic episodes or known thrombophilia. Others may present pain and loss of appetite, often of a few days duration, diarrhea, occult GI bleed and occasionally bowel infarction and peritonitis. There may be mild leucocytosis and slightly elevated LDH. Diagnosis can be confirmed by venous phase of CT scan or with contrast enhanced MR venography. Color Doppler can often show presence of thrombi in the veins.Treatment is usually conservative with life-long anticoagulation. Aggressive management with surgery or thrombolysis can be done in selected patients. Any associated hypercoagulable state must be appropriately treated.

History of vascular surgery

On June 12, 1906, **Jose Goyanes** of Madrid excluded a luetic popliteal aneurysm by proximal ligation. In addition, he mobilized the adjacent vein and used it as an in situ interposition graft between the proximal femoral artery and the distal popliteal artery by means of end-to-end anastomoses. Six months later in December 1906, **Erich Lexer** resected an axillary artery pseudoaneurysm and restored continuity by using the great saphenous vein. In 1913, **Pringle** also reported removal of popliteal and brachial aneurysms and bridging of the defect by saphenous vein graft. Unfortunately, these important contributions, which had a good outcome, remained largely ignored until many years later. The first clinical transplantation of a homologus artery from one human to another was performed by **Pirovano** in 1910. **Halstead** was the first to successfully combine ligation with resection of subclavian artery aneurysm in 1892. In 1916 Halstead reported 27 cases of a cervical rib in association with subclavian aneurysm and hypothesized the rheologic mechanism leading to post stenotic dilatation and aneurysm formation. Subsequent successful reports of aneurysm repair by **Matas, Lexer** and **Pringle** at the turn of the twentieth century confirmed the feasibility of arterial suture and led to the development of modern vascular surgery.The introduction of anticoagulants, especially heparin (discovered in 1916 by **Maclean**, animal experiments in 1918 by **Howell**, chemical purification in1933 by **Charles** and **Scott** and first clinical application by **Crawford** in 1935), made it possible to control thrombosis. This was the magic key to reconstructive vascular surgery.A technique of wrapping abdominal and peripheral aneurysms in cellophane was introduced by **Rea** in 1948. He also attempted this to the abdominal aortic aneurysm of Albert Einstein, but failed.In 1952, **Voorhees** introduced Vinonyn –N, the first fabric prosthesis. Other prosthetic grafts such as PTFE by **Edwards** in 1957, Polyester by **Debakey** in 1960 and e-PTFE by **Soyer** in 1972 also helped and expanded the available options for interposition grafting. The first case of arterial reconstruction by homograft for a subclavian aneurysm was described by **Schein** and colleagues in 1956.In 1934, **Lewis and Picknerg** described the much more frequent occurrence of upper extremity thromboembolic complications associated with aneurysms. Crutch induced blunt trauma producing pseudoaneurysm of axillary artery was first described by **Rob** and **Steandven** in 1956. The ulnar artery can be aneurysmal in the dominant hand due to repeated blunt trauma. This entity was first reported by **Guattani** in 1772 and the term 'Hypothenar hammer syndrome or aneurysm' was coined by **Conn** in 1970.

Peripheral Arterial Occlusive Disease

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Peripheral arterial occlusive disease is one of the common problems treated by a vascular surgeon. At the onset, we should understand that PAOD is a manifestation of a systemic disease, whether autoimmune or atherosclerotic. The usually seen entities include atherosclerosis, Takayasu's arteritis and Thromboangitis obliterans. This chapter is a brief summary on evaluation and management of PAOD to provide a basic understanding of the disease.

Presentation - In current practice, atherosclerotic arterial disease is the commonest. Symptoms depend on the artery affected and include claudication, rest pain, digital gangrene, non-healing ulcer. Femoral and popliteal arteries are involved in about 80-90% of cases, aorto-iliac segments in about 30% and the tibial arteries in 50% of patients with lower limb arterial disease.

Risk factors-Risk factors are similar to coronary artery disease and include tobacco use, DM, hypertension, hyperlipidemia, increasing age, and thromb-ophilic factors like hyperfibrin-ogenemia, hyperhom-ocysten-emia and presence of anti-cardiolipin antibodies.

Some definitions

Claudication- this refers to pain or discomfort, usually in the calf, brought on by exercise and relieved by a few minutes of rest. Symptoms are reproduced by the same degree of exercise.

Rest pain- As the name suggests, pain is present at rest, usually in the foot or digits or around an ulcer. Patients often keep the limb dependent, resulting in edema.

Critical ischemia- This indicates an endangered limb and is manifested by rest pain, tissue loss, and ankle pressure less than 50 mm of Hg.

Evaluation of patients-As for all patients, a good history and physical examination are invaluable. These provide an indication to the etiology, extent and severity of disease.

Non-invasive vascular lab- This provides a more objective assessment of the physiological state of disability produced by the disease and can also be used to assess outcomes after intervention and during follow up. Commonly performed investigatons are hand-held Doppler examination, recording of segmental blood pressures and pulse volumes and digital plethysmography. **Ankle-brachial index** is calculated by dividing the systolic ankle pressure by the systolic brachial pressure. The normal value is more than 0.95. In diabetic patients, the value may be abnormally high due to calcification of tibial arteries and calculation of **toe-brachial index** is a good alternative.

Color Doppler is an excellent tool to define the extent of disease in the femoro-popliteal segment. It has some limitations when it comes to aorto-iliac and calcified tibial arteries.

Angiography is performed only when intervention is planned in the form of surgery or endovascular procedure. Occasionally, it is done to confirm the diagnosis of Takayasu's arteritis. Options include conventional angiography, digital subtraction angiography, magnetic resonance angiography and CT angiography. Most of our patients now undergo MR or CT angiography for diagnosis and planning revascularization.

Treatment planning -Treatment is always individualized and based on the patient profile, symptomatology, patient expectations, risks of various interventions / surgery and expected benefit in terms of relief of symptoms and prevention of future

complications. A Vascular Surgeon is best suited to choose the management option since he is the only specialist trained to provide all forms or therapy viz. medical, surgical and interventional. The flow chart shows the broad guidelines for managing a patient with peripheral arterial disease. Risk factor modification is an integral part of all modalities. In addition, antiplatelet agents and statins are used for all patients with the aim of improving overall cardiovascular health and reducing the risk of cerebrovascular and coronary events. The aim of treatment is to improve the overall quality of life of the patient and enable him or her to carry on with a normal lifestyle.

Medical therapy - It is indicated in intermittent claudication. The aim is to improve the pain free walking distance and maximum walking distance. Drug therapy is combined with exercise, usually walking. While supervised exercise programs are more effective, they are often not practical for our patients and setting targets for them to follow works very well. In addition to risk factor modification, drugs like Cilostazol and l-carnitine are useful in improving pain-free and maximal walking distance.

Surgery or endovascular procedures are best for patients with critical limb ischemia or with disabling claudication. The choice of procedure depends on knowledge of natural history of disease, patient's requirements, feasibility, short and long term efficacy, safety and of course, the costs. Needless to say, continuing risk factor modification is important for these patients too.All patients must remain in regular follow up for surveillance of the surgical or endovascular procedures since it is easier to tackle failing procedures rather than failed ones and to continue risk factor modification.

History of vascular surgery

In 1804, **Antonio Scarpa** (1752-1832) wrote a definitive treatise on the forms and diagnosis of arterial aneurysms. The first surgical ligation of a femoral artery aneurysm was performed in 1808 by **Astley Paston Cooper** (1768-1841). Although he is remembered for his contributions to inguinal hernia and female breast anatomy, his most famous operation was performed for a leaking iliac artery aneurysm in 1817. Cooper also cautioned that patients who present with one aneurysmal disease should be evaluated for the coexistence of others, an advice that is equally applicable today.

In 1810, **Dominique Anel** described Anel's operation "Ligation of an artery immediately above and on proximal side of an aneurysm". The 18th century can be characterized as the era of arterial ligation for treatment of aneurysms, with surgeons such as **Brasdor** and **James Wardrop** defending the merits of different sites of ligation in relation to the aneurysms. The first attempted surgical correction of a subclavian artery aneurysm was performed in 1818 by **Valentine Mott**, who ligated the artery. About this time, several ingenious treatments were also introduced. **Giovanni Monteggia** (1762-1815) unwis-ely attempted to cure an aneurysm by injecting a sclerosant into it, which predictably failed because of rapid blood flow. Unsuccessful attempts to thrombose aneurysms by passing an electric current between needles stuck into the vessel were done in 1832. **Charles Hewitt Moore** (1821-1870), at Middlesex Hospital in London, introduced obliteration of aneurysms by inserting steel wires in 1864, once using 26 yards of the material .

A better method of treatment of peripheral aneurysm had been developed in 1888 by the **Rudolph Matas** (1860-1957). His technique of endoaneurysmorrhaphy, involved clamping above and below the aneurysm, opening it, ligating branches from within and buttressing the wall with imbricated sutures. By 1906, he had performed 22 obliterative operations and 7 restorative operations (preserving the arterial lumen) with no recurrences. Matas endoaneurysmorrhaphy prestaged the current prevailing of "Internal" or intrasaccular reconstruction conceived by **Oscar, Creech** and **Michael Debakey.** In 1913, Matas reported 225 cases of endoaneurysmorrhaphy repair, and seven of these were subclavian aneurysms .

Anterior Segment Involvement in Diabetes Mellitus

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Diabetes is termed as the epidemic of the new millennium. The primary driver of the epidemic of diabetes is changing lifestyle, change in dietary pattern, and decreased physical activity due to modernization. 'Fast food culture' and 'Sedentarinism'. It has been projected that 300 million individuals would be affected with diabetes by the year 2025. India leads the world with the largest number of diabetic subjects earning the dubious distinction of being termed as the "*Diabetic Capital*" of the world. According to the Diabetic atlas 2006 the number of people with Diabetes in India is currently around 40.9 million and is expected to rise to 69.9 million by the year 2025[1-2]. India is prone to be the diabetic capital because of peculiar Asian Indian phenotype which includes increased insulin resistance and greater abdominal adiposity[3].

Type-1Diabetes affects young and lean people, these are insulin dependent and always need insulin. Type-2 Diabetes tend to affect older obese people and the abnormality found is partial insulin deficiency, insulin resistance or both. The disease presents itself as macro vascular and micro vascular disease. The macro vascular disease leads to coronary artery disease, peripheral vascular disease stroke, while the micro vascular involvement leads to nephropathy and retinopathy. People with Diabetes Mellitus are 25 times more likely to get blindness, 17 times more prone to get kidney disease and 30-40 times more prone to get amputations[4]

Diabetes and eye-Diabetes produces variety of ocular changes. Both anterior and posterior segment of eye is involved. Although cataract and retinopathy are responsible for most of the sight threatening conditions, many ocular structures are affected by diabetes as well. We shall review the anterior segment involvement in diabeties

Lids and conjunctiva

- **Recurrent stye, chalazion and blephroconjunctivitis-** Increased blood sugar levels predispose the patient to develop these recurrent lesions
- **Xanthelesma**-a fatty deposit in the subcutaneous tissue of lids is associated with hyperlipidemia which is frequently associated with Diabetes Mellitus

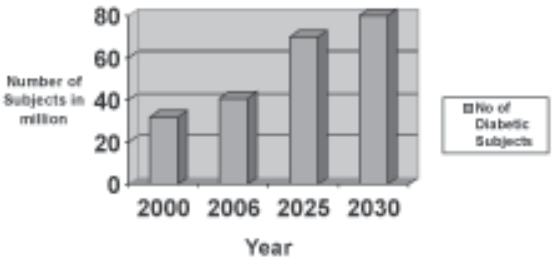

Fig.-1, Estimated number of diabetic subjects in India. (2, 3)

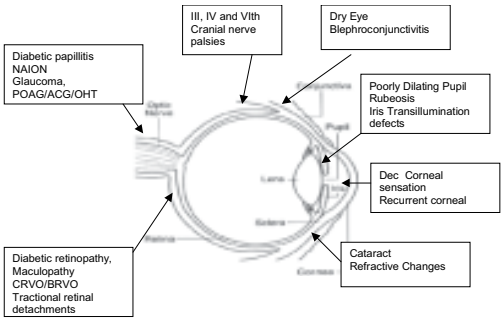

Figure-2, Common eye abnormalities in diabetes

- **Dry eye** - Diabetes Mellitus is frequently associated with keratoconjunctivits sicca and dry eyes . The mechanism responsible for dry eyes is unclear, but autonomic dysfunction may be responsible. Aldose

reductase, the first enzyme of the sorbitol pathway, may also be involved[5].

- **Ptosis of the upper lid** -Due to oculomotor nerve palsy can be a presenting feature of Diabetes Mellitus. This is due to microvascular infarction of the oculomotor nerve.

Cranial nerve involvement- Diabetes is the underlying cause of III IV and VI nerve palsy in 30% of cases with age > 45 years

- **Diabetic 3rd nerve palsy-**It is painful in 20 % of the cases and the pupil is spared in 80% of the cases. In cases in which pupil is involved the effect is subtle with the anisocoria of less than 1mm rather than the fully dilated unreactive pupil found in compressive lesions[6]. Ischemic III nerve palsy spontaneously resolves in 12 weeks although they may recur later
- **IV and VI nerve palsies-** These are also seen in Diabetics. In older patient with vasculopathic age group a presumptive diagnosis of micro vascular palsy must be borne in mind. This too usually clears in 12 weeks but may recur. MRI is indicated in the event of progression or failure to resolve. It is important to note that diabetes rarely causes multiple involvement of more than one cranial nerve. If multiple cranial nerves are involved, there is a presence of focal neurological signs or deterioration is seen then compressive lesions should be looked for in the patient

Corneal involvement in diabetes -Corneal involvement in diabetes is known as diabetic keratopathy. Diabetic keratopathy comprises several symptomatic corneal conditions including superficial punctuate keratopathy, punctate corneal erosion syndrome, and corneal ulceration[7]

It is important to analyze the reason for Diabetic Keratopathy. Subclinical abnormalities which are noted in the cornea before development of corneal complications is

- Decrease in epithelial barrier function[8-9]
- Abnormalities in shape of epithelial cells[10-14]
- Pleomorphism and Polymegathism of endothelial cells[10-14]
- Basement membrane thickening[15-16]
- Decrease in corneal sensitivity

Epithelial defects and recurrent corneal erosion syndrome have been associated with Diabetes Mellitus

Corneal damage is often encountered after intraocular surgery in patients with Diabetes Mellitus. Based on this finding fragility of the cornea in patients with diabetes has been suggested[17-19]. Recovery from corneal edema in contact lens wearer is slower in diabetics than in non diabetic subjects[20-21]

Soichi et al[22] found increase in corneal thickness one month after surgery which was significantly higher in diabetic group than in the non diabetic group. The cornea has been reported to be thicker in eyes of diabetic subjects by some authors[23-24] but shown dissimilar by others[23,25]

Roszkowska et al[24] demonstrated that the cornea in diabetic patients is significantly thicker than the cornea in non-diabetic subjects, speculating that the pump function of the corneal endothelium is decreased, resulting in edema against osmotic pressure in eyes of diabetic patients

Goebbels and Spitznas[26] reported no difference in endothelial permeability between diabetic and non diabetic subjects before cataract surgery. The endothelial permeability increased 4 days after surgery in both the groups but recovered in 3 weeks in non diabetic subjects and in 6 weeks in diabetic subjects. This result is in consistence with delayed recovery of endothelial function in the cornea of diabetic subjects

Theories of Corneal Keratopathy

One theory which explains the fragility of the corneal endothelium in eyes of diabetic patients is **polypol osmotic theory**. Firstly, an increase in the polyol metabolism in the corneal epithelial cells is reported as a mechanism of diabetic keratopathy[27-28].There is a strong similarity in the spatial distribution of aldose reductase, an enzyme entry into polyol pathway and the target organs affected by typical diabetic pathology including kidney and blood vessels[27-28]. There is also report of the accumulation of

polyol and the expression of aldose reductase in the corneal epithelium and endothelium[27] These data are consistent with the clinical findings that the corneal epithelium and endothelium are targets of diabetic complications.

Inhibition of aldose reductase activity using aldose reductase inhibitor (ARI) ameliorates corneal changes in diabetic models. In these models, ARI was effective in inhibiting the loss of corneal sensation,[29] delaying corneal epithelial wound healing[30], enlargement of epithelial and endothelial cell size[11-12, 31],breakdown of corneal epithelial barrier function[32], and accumulation of sorbitol [33]

Decrease in corneal sensations and loss of nerve derived trophic factors have been postulated as causative factor for diabetic keratopathy. Nakamura et al have revealed that insulin-like growth factor 1 (IGF-1) and substance P, a neuropeptide present in sensory nerves, accelerate corneal epithelial wound healing[34]. In addition, the authors showed that topical application of substance P and IGF-1 accelerated the corneal epithelial wound healing process in diabetic animals. These studies help to strengthen the potential pathogenic link between decreased corneal sensation and diabetic keratopathy

Advanced glycation end products (AGEs) have been implicated in the development of diabetic keratopathy and may explain some of the changes. AGEs deposit in the basement membrane of the corneal epithelial cells of diabetic patients.[35] molecular structure of basement membrane components changes and they lose adhesive property. The corneal epithelial cells lose attachment on the basement membrane and predispose to corneal erosions Thus potentially Diabetic Keratopathy provides a model to shed light upon complications in other organs

Iris Involvement in Diabetes Mellitus

Retinal ischemia due to Diabetes Mellitus leads to production of Vascular Endothelial Growth Factor (VEGF) which diffuses into the anterior segment of eye and causes neovascularization of the iris. Early neovasularization of the iris appears as small tuft of blood vessels along the pupillary margin (NVI) or in the angle of anterior chamber (NVA). Pan retinal photocoagulation is generally required to induce regression. This is a precursor to Neovascular Glaucoma (NVG)

There is a los of iris pigmentation in diabetic subjects leading to increase in iris transillumination

Pupillary Involvement in Diabetes Mellitus

Size of the pupil is under control of parasympathetic system which innervates the sphincter muscle and the sympathetic system which innervates the dilater pupillae muscle.

There are a number of similarities between senile miosis and diabetic miosis. In comparison with that of healthy young people the pupil in both groups fails to dilate in darkness and is differentially more sensitive to phenylephrine than to hydroxyamphetamine. The action of cocaine is reduced in the elderly pupil, which suggests that a reduction of sympathetic activity occurs with age due to a degenerative process that is accelerated in diabetes[36]

In diabetics the resting pupils are smaller than in healthy subjects, characterized by failure to dilate in darkness, the possible cause being autonomic dysfunction partially denervating both sphincter and dilator muscle.(Diabetic Autonomic Neuropathy, or DAN)

One pupillary manifestation of DAN is small pupil size but the mechanism for this is unclear despite a number of previous studies that have assessed pupil function in diabetic patients using both static and kinetic methods[37]. The small pupil is supersensitive to phenylepherine[36]. This super sensitivity, which is also found in Homer's pupils is evidence in favor of a neuropathic rather than a myopathic etiology in the miotic pupil of diabetes[38,40]

Small pupil size in diabetes may be due to the fact that there is damage to the pupillary parasympathetic supply of diabetic patients which occurs before the pupillary sympathetic pathway is affected. This draws from the fact that there is a denervation hypersensitivity to dilute pilocarpine seen in these cases[39] .

It is a common clinical impression that the pupil in patients with diabetic neuropathy is difficult to dilate for fundal inspection or catatact surgery. The agents which used are homatropine, cyclopentolate, and tropicamide. These normally work by paralyzing the parasympathetic constrictor drive, allowing the sympathetic input to the dilator to dominate. The loss of sympathetic tone in patients with diabetic neuropathy would thus limit the usefulness of the anticholinergic mydriatics. Addition of a directly acting sympathomimetic, to which the pupil is supersensitive ,improves the mydriasis in these cases[41].

Glaucoma in Diabetes

Diabetes mellitus has been suggested as one of the risk factors for primary open angle glaucoma (POAG). The inclusion of diabetes in this list is controversial. Although numerous studies have addressed this question, early studies came to differing conclusions regarding the presence of an association with some upholding[42-43] and some refuting[44-46] the presence of a link between the two diseases.

Diabetic patients have higher intraocular pressures than the normal population, especially those treated with insulin[47]. In Blue mountain study the authors found a significant and consistent association between diabetes and glaucoma, which appeared independent of the effect of diabetes on IOP, suggesting that there is a real association between these two diseases[47].

The Baltimore eye disease the largest case-control study in the literature1failed to find any association apart from that explained by referral bias[48]

The Beaver dam study however reported the presence of open-angle glaucoma is increased in people with older-onset diabetes[49]

The prevalence of diabetes or a positive glucose tolerance test has also been shown to be higher in patients with POAG[51]

Diabetes also appears to influence the nature of field loss in patients with COAG with a prevalence of inferior field loss of 64.4% versus 36.4% in diabetics Vs non diabetics respectively[52]

Lens and Diabetes

There is a fluctuating change in refraction when there are major fluctuations in the blood sugar levels. The essential feature is that the changes of refraction come on suddenly and bilaterally and the myopic trend is associated with the rise and a hypermetropic trend with fall of blood glucose levels

Fumiki Okamoto et al reported transient hyperopia associated with rapid correction of hyperglycemia is highly dependent on the rate of reduction of the plasma glucose level. A reduction of refractive index in intraocular tissues, especially in lens, appears to be responsible for this hyperopic change in their study

Many authors, who investigated the effect of acute changes in plasma glucose level, have reported that decreasing plasma glucose levels causes hyperopic change. It was also reported that a hyperopic change occurred regardless of whether the plasma glucose level increased or decreased. Some investigators have observed both myopic and hyperopic changes in diabetic eyes.

Duke Elder postulated that the changes of refraction come on suddenly and bilaterally and the myopic trend is associated with the rise and a hypermetropic trend with fall of blood glucose levels, and the hypermetropic trend occur not as an initial phenomenon but following a myopic shift. He postulated that due to rising glucose concentration there is a hydration of the cortical layer of the lens relative to the nucleus. The tissue swells and is deformed. The curvature is increased and refractive index is increased and the eye becomes myopic. Reverse occurs in decreasing blood sugar levels in which hydration of the nucleus takes place. An onset of sudden myopia should alert the physician of rising blood sugar levels and an onset of hypermetropia should alert the physician of too rigorous treatment

During intensive hypoglycemic treatment in the hospital, some diabetic patients complain of disturbance of vision such as difficulty in reading and blurred vision with their own glasses because of refractive changes. If a new prescription for glasses is

made at that time, there is a possibility that the new glasses will soon become inadequate. This phenomenon occurs with transient hyperopia due to acute changes in plasma glucose levels

Diabetic Cataract

There is a three to fourfold increase in prevalence of cataract in patients with diabetes under 65 years and up to a twofold excess prevalence in patients above 65 years according to the data from the Framingham and other eye studies. The risk is increased with the duration of diabetes and in those with poor metabolic control

The most frequently seen type of cataract in diabetics is the age-related or 'senile' variety, which tends to occur earlier and progresses more rapidly than in non-diabetics. Caird concluded that diabetes causes a more rapid maturation but may not affect initiation of cataract. A special type of cataract known as snowflake cataract is seen in young type 1 patients and tends to progress rapidly. Initially a large number of fluid vacuoles appear underneath the anterior and posterior capsule which is soon followed by appearance of bilateral snow flake white opacities in the cortex Cataracts may be reversible in young diabetics with improvement in metabolic control

Pathogenesis of Diabetic Cataract

Sorbitol, aldose reductase and the osmotic hypothesis

The key biochemical feature in diabetic cataract is aldose reductase which is a sorbitol pathway enzyme which converts excess sugar in the lens to sugar alcohol (glucose sorbitol and galactose ducitol). This only occurs at high sugar levels. This alcohol is not metabolized and is not able to escape from the lens. It accumulates making the cytoplasm markedly hypertonic. Water moves into the lens causing swelling and destroying the lenticular structure and formation of foci of interfibrillar and intracytoplasmic light scattering with resultant opacification

Auto oxidation of sugars

The possible role of auto oxidation of sugars in etiopathogenesis have been suggested by many workers

Non enzymatic Glycosylation

There is non enzymatic glycosylation of lens proteins plays an important role in sugar induced cataract.

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13

Review Article

Hydatid Disease of Liver

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Hydatid disease is a parasitic infestation by a tapeworm of the genus *Echinococcus*[1, 2]. Human echinococcosis is a zoonotic infection. Human infection is acquired from ingestion of the parasite eggs from infected animals and represents a dead end of the life cycle of the parasite. 4 species of Echinococcus are known to infest Humans. These are *Echinococcus granulosus,* causing cystic echinococcosis; *Echinococcus multilocularis,* causing alveolar echinococcosis. Amongst the rare ones are *E vogeli* & E. oligarthrus, which are mainly restricted to areas of Central and south America. *E Granulosus* is the most common of all. *E multilocularis* is rare but is the most virulent.The word "Echinococcosis" is derived from the Greek phrase meaning "hedgehog berry". In Latin "Hydatid" denotes a watery vesicle.Majority of the cases of Hydatid Liver disease may remain symptom-free for as long as the rate of growth of the cyst is exceedingly slow, approximately 1 cm/year[4]. Symptoms usually appear once the cyst size exceeds more than 5 cms which may be in the form of vague Rt upper quadrant pain with or without a palpable lump[5]. Once the complications set in, the symptoms become more severe but they still remain non-Pathognomic. The complications that can result are usually due to rupture or infection of the cyst. These occur when the intracystic pressure crosses 80 cm H_2O, or are subcapsular in location, or if the cyst is located in the left lobe of liver. The presentations that follow the complications may manifest as follows: Cholestatic jaundice, Cholangitis, Pancreatitis, Secondary ecchynococcosis, Systemic immunological reactions: urticaria, asthma, anaphylaxis, Membranous nephropathy, Fistulae formation-External(cutaneous); Internal(Biliary-bronchial/pleural fistulae, Biliary-enteric fistula),Infective-Liver abscess,Peritonitis, Empyema, Lung abscess, Mediastinitis

Investigations

Serology - Using various immunodiagnostic methods specific serum antibodies or circulating antigen pertaining to the cestode can be detected to aid in diagnosis.

- **ELISA-** Employing hydatid fluid antigen for detection of echinococcal antibodies (lgG) in the serum is the most widely used[6]. With its Positive predictive value of 97% it is considered the most sensitive and specific amongst others. However positive test can occur in normal persons from endemic areas and in those with other parasitic infections. Therefore it needs confirmations by the arc-5 immunoelectrophoretic (IEP) test, this test does not cross-react with noncestode parasites, but it cross react with T. solium infestation, sensitive for active disease only.
- **Casoni intradermal test-** Sensitivity 65-70%, Sepcificity 40%[8]
- **Indirect Haemagggluti-nation** - Ini-tial Latex agglutination, Useful for screening
- **Complement Fixation Test -** Useful test for post op monitoring
- **Indirect Fluorescent Antibody test-** Sensitivity 78%. This test remained positive 2-3 years after eradication of hydatid disease in an individual patient.
- **Dot immunobinding assay** - (HA-DIA – Echino-strip) Considered an office procedure[7] can be used for a large scale screening of populations in developing countries.

Serological tests have limitations in monitoring patients after surgery, percutaneous drainage or drug therapy. The antibody titers rise following surgery and percutaneous drainage. The titers start falling at 3 months and become negative in period of 12-24 months.

Molecular diagnosis

DNA Hybridization Techniques and PCR - The scope of immune diagnosis of Echinococcosis has been expanded by an extraordinary new tool, the Polymerase Chain Reaction. It is diagnostic. The sensitivity of the E. multilocularis PCR corresponds approximately to the DNA content of one single Echinococcus egg.

Imaging of Echinococcosis

Ultrasound Abdomen- Ultrasound has become the imaging modality of choice because of the following features it offers:

- Non-invasive imaging which is readily available and cost effective.
- New generation high resolution scanners have a real time 3-dimensional scanning capability and are portable[8].
- Ultrasound has a specificity of upto 90%. The visualization of **Hydatid sand**, daughter cysts and movement of echogenic sand within cyst-diagnostic. However sub-centimetric and subcapsular cyst may be missed.

Based on the US findings of the complexity of the cyst various classification systems have been devised for management.

Hassen Gharby, 1981

Type I-Pure fluid collection

Type II-Fluid collection with a split wall

Type III-Fluid collection with septa

Type IV-Heterogenous appearance

Type V-Reflecting thick walls

Lewall & McCorkell

Type I-Simple fluid filled cyst

Type I-R-Lesion with undulating membrane

Type II-Daughter cysts and/or echogenic material

Type III-Densely calcified cysts

Intra-Operative Ultrasound (IOUS)-The sensitivity is increased to more than 95%. IOUS is particularly useful in delineation of extensions of cysts located close to major ducts and portal vein radicles- the "mapping" of the Hydatid cyst. It offers high sensitivity of cystobiliary communication in the form of:

- Presence of hydatid material in biliary tree
- Sign of 'loss of continuity' of the bile duct wall
- Gas in the hydatid cyst

Computerised Tomography- It has an advantage over ultrasound for better localization of daughter cysts and its distribution within the liver parenchyma and it's the segmental anatomy.

MR Cholangiography- It's the diagnosis of choice in cases where there is a suspicion of rupture of the cyst into the Biliary tree causing either of these: obstruction in distal CBD, cholangitis, pancreatitis or biliary stricture

ERCP-This invasive modality has its specific indications. It should not be used as a diagnostic tool but preferably as an interventional modality. This is indicated in

- History of Jaundice, cholangitis, passage of 'grape skins' in stools
- Post operative setting: Hydatid debris in CBD, Post op biliary fistula sclerosing cholangitis.
- Therapeutic: Endoscopic papillotomy & drainage of CBD cysts with or without stenting.

Radionuclide Scanning- Today its application is quite limited. However HIDA scan demonstrates the following:

- Assessment of the function of the rest of the liver
- Non functioning 'cold' spots which are non specific indicators of hydatid cysts.

Differential Diagnosis-Though having a high positive predictive value of the ultra sound and CECT abdomen in diagnosing Hydatid cyst of live, there are situations when other possibilities have to be ruled out, like- Liver abscess, AmoebicPyogenic, Cortical cyst, Policystic disease, Haemangioma

Medical Management-As a primary modality in cases of Inoperable primary liver echinococcosis; Adjunct to surgery for prevention of secondary echinococcosis; Concomitant therapy for PAIR. Benzimidazoles are broad-spectrum antihelmintics active against parasites of both human and veterinary importance[9]. Mebendazole and albendazole are the benzimidazoles that have been used extensively to treat human echinococcosis. Mebendazole produces many biochemical changes in the susceptible

organisms e.g.: inhibition of parasite-specific fumarate reductase, reduced glucose transport and uncoupling of oxidative phosphorylation. However Albendazole should be considered as the drug of choice for medical treatment of cystic echinococcosis. The characteristics of the cysts that are useful for prediction of response to medical treatment are:

- Size-Smaller cysts, which are younger and have a thinner wall, show a more favorable response to chemotherapy [9, 10].
- Site-The best results seen with hepatic, pulmonary and intraabdominal cysts.

Dosage

- Mebendazole is given in doses of 40-50 mg/kg/day, usually in three divided doses for duration of treatment is 3 months. Treatment (up to 6 months) may be more effective and should be considered in cases predicted to be poorly responsive to therapy.
- Albendazole is given in daily dose of 10-15 mg/kg/day. It is given in an intermittent treatment schedule with 4-week courses of therapy separated by drug free intervals of 2 weeks to decrease the incidence of adverse effects[11].
- Praziquentel: given at a dose of 40 mg/kg once a week concomitantly with benzimidazoles. The drug is useful in cases of cyst content spillage during surgery. The drug is not recommended for children below 4 years of age.
- Ivermectin: Ivermectin is a macrocyclic lactone (avermectins) produced by the actinomycete *Streptomyces avermitilis*. Is has been used as a scolicidal agent for percutaneous treatment of cystic echinococcosis in animal models[12].

Per cutaneous Aspiration injection and Reaspiration (PAIR)-Ultrasound guided percutaneous treatment of cystic echinococcosis: was first introduced in 1986 by Mueller in Germany. It is indicated cysts that are deep seated and have ultrasound characteristics of Gharbi type I to III. It involves ultrasound guided puncture of the cyst using a fine needle, aspiration of the cyst contents, injection of scolocidal agent and re-aspiration (PAIR)[12]. After 9-18 month following successful PAIR, 76 to 90% of patients reported to became seronegative, but the late appearance of these responses and their unclear correlation with viability makes use of serology for follow up of the patients difficult.

Scolicidal agents-Hypertonic (15-20%), Saline Formalin 2%, Hydrogen peroxide10%, Hypertonic saline 15-20%, Chlorhexidine, Absolute alcohol, Cetrimide 0.5%, Silver nitrate 0.5%, Povidone Iodine, Ivermectin

Adverse events - Allergic reactions, Fever & infection, Dissemination and local recurrence, Biliary fistulas, Caustic sclerosing cholangitis

Contraindications- PAIR is currently considered to be contraindicated for inaccessible or superficially located hepatic cysts, inactive or calcified cysts, and cysts with dominant non-drainable material and those cysts with communications with biliary tree or with multiple septations. It is also contraindicated in early pregnancy.

Surgical Management- The decision to operate for liver hydatidosis depends on the condition of the patient and the cyst characteristics. An ideal candidate for surgical management would be young, fit patient with a large cyst prone to trauma. There is consensus that uncomplicated, large peripherally located viable hydatid cysts require operation as do all complicated cysts. Small deeply placed parenchymal cysts less than 4 cms in diameter can be observed on serial ultrasonography till they reach a subcapsular position.

Principles of Surgical management

- Elimination/Prevention of spillage
- Removal of all cyst elements
- Closure of biliary communications
- Sterilisation of cavity
- Closure

Pre-operative preparation-Preoperative albendazole at the prescribed dosages have been proven to be of benefit in ensuring minimal recurrences and adequate cyst sterilization. It also results in significant reduction of intracystic pressure,

which facilitates surgical removal and percutaneous aspiration. An effective protocol to follow is to use 4 weeks of pre-operative chemotherapy with albendazole and follow up with 8 weeks of post op therapy, if no spillage has occurred during surgery. However the latest recommendation of therapy commencing 4 days prior to surgery; then 1 month postoperatively as adjunct is as effective.

Per-operative preparation-The principle of sage decompression during surgery is to prevent uncontrolled rapid decompression into the peritoneal cavity. To ensure this the following measures are adopted:

- Use of green or blue drapes so that the pale white cyst wall may be seen against a dark contrast.
- Packing off the rest of the operative field with drapes soaked in scolicidal solution.
- Use of separate 'sump' suction devices for the cyst contents.
- Decompression by aspiration of the cyst before injection of the scolicidal agent.

Use of Cones- Saidi in 1971 and Aarons in 1983 proposed the use of double walled cone devices that attach by suction to the cyst wall in order to avoid spillage of cyst contents during surgery. The problems encountered with these devices were inadequate space to access the cyst contents, failure of suction in remote locations and these lead to the gradual disuse of these devices.Two main surgical approaches are in use:

- Drainage procedures, and the obliteration of the cyst cavity after evacuation of the cystic content. The various procedures available are simple marsupialisation, evacuation of cyst contents and capitonage, cyst evacuation and omentoplasty.
- Radical operations, such as hepatectomy, resection of the cyst or pericystectomy. Cysts located peripherally, and pedunculated cysts can be excised entirely. Such operations have a higher morbidity and mortality rates and can be considred radical procedures for such a benign disease. Hepatic resection should especially be considered for Echinococcus alveolaris cases which are located on one hepatic lobe.

The hydatid cyst in the liver is different from other liver cysts because the cyst does not collapse after evacuation due to the presence of the lining ectocyst. This gives rise to a residual cavity, which is managed with either direct suture closure or with omentoplasty. The cavity may at times communicate with intra hepatic biliary radicles, which are primarily sutured under vision. However in the presence of significant cyst-biliary communication, the cyst can be drained internally, usually by a Roux-en-Y cysto-jejunostomy, or Cystogastrostomy. Majority of the cysto-biliary communications close by itself if there is no distal obstruction. In case of distal obstruction due to impacted cystic contents in CBD which were not picked during the surgery can be managed endoscopically. If during surgery, the cystic contents are observed in a normal caliber CBD, choledochotomy with evacuation of cystic content and debris from biliary tree and irrigation with 0.9% NACI solution preferably without T-tube drainage of the CBD. If CBD is dilated, with hydatid content in it, choledochoduodenostomy is preferable. Roux and Y hepaticojejunostomy have been reported for the treatment of bile duct stricture associated intrabiliary rupture.

Laparoscopy in the management of hepatic hydatidosis - Laparoscopic surgery has added a new dimension to hydatid cyst surgery and provides and alternative to open surgery in well-selected patients. The laparoscope provides adequate visual inspection, and it is possible to inspect the entire cavity, especially in cysts placed high on the right lobe, which may not always be possible in open surgery. Use of two-suctin method, in which a separate power-suction device for evacuation of the cyst contents is suitable for all types of hepatic hydatids including multilocular lesions without peritoneal contamination.

Follow up-Postoperatively adjuvant chemotherapy is continued for 1 month. ELISA or Indirect Hemaglutination are carried out at 3, 6, 12, and 24-month post-op.

Current trends and future directions-The recommended management of uncomplicated **Gharby** type I, II and some type

III lesions is PAIR + Chemotherapy. Open surgical procedures are best suited for the complicated cysts. Superficial type I & II cysts can be best managed Laparoscopically[13]. Vaccine (EC-90) is still in its experimental stage. However works are on to define its efficacy for primary prevention and post op disease free survival. With increase in the awareness of the disease causation, presently more emphasis is being laid on various preventive measures, like proper offal disposal, chemoprophylaxis in form of Praziquantel (5 mg/kg) for dogs, control of the dog population, regulation of livestock butchering.

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Management of a 50 Years Old Diabetic Patient with Epistaxis in Emergency

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Epistaxis is defined as bleeding from inside the nose. It is a common condition presenting in 7% to 14% of the general population each year. Most patient who develop epistaxis do not seek medical attention because the bleed is minor and usually stop quickly. The incidence appears to be higher in males than females and more frequent in the winter months than the summer months. In elderly people incidence of nose bleeding is almost equal in both sexes.There are two types of epistaxis. First one is anterior nose bleeding which is by far more common in child or young adults, whereas the other one posterior epistaxis is more often seen in older adults with hypertension or arteriosclerosis. Anterior epistaxis accounts for 90% to 95% of all episodes.

Salient findings in history

This may be spontaneous or due to trauma of the nasal septum by fingers or nasal sprays. Usage of regular nasal sprays, usually local corticosteroid sprays, may induce intermittent epistaxis by the force of the spray creating damage to the epithelium of the nasal septum. This epithelium may crust and bleed when this crust is either removed or falls off. Deviation of the nasal septum may aggravate the incidence of bleeds because the septal deflection will often crust and removal of the crust by a finger or excessive nose blowing may stimulate a bleed. If the removal of crust becomes habitual, continuous trauma may cause a septal ulcer to form. This cane result in a reduction of the blood supply to that area of septal cartilage and may result in a septal perforation. A foreign body in the nose can be an usual cause of epistaxis and is usually seen in small children or mentally retarded patients. These patients present with a bloodstained foul-smelling unilateral discharge. Nasal tumors may cause intermittent epistaxis. In young male teenagers, juvenile angiofibroma should be excluded, and in elderly patient, malignancies of the nose, sinuses, or postnasal space must be excluded. In rare cases, tumors located in the middle ear (glomus tympanicum) can present with intermittent epistaxis.The commonest associated systemic disorder associated with the development of epistaxis is hypertension. This is followed by alteration of clotting abilities of the patients caused either by anticoagulation medication or liver dysfunction. Drugs implicated in epistaxis include aspirin, clopidogrel, nonsteroidal anti-inflammatory drugs, and warfarin. In patients with hypertension and epistaxis, it is thought that increasing age induces fibrosis of the tunica media of the arteries. This may prevent adequate vasoconstriction after rupture of the blood vessel, requiring intervention to stop the bleeding. Recently, Nakada et al. showed there was increased apoptosis is an attempt by the body to cause regression of the thickened arterial walls.Inherited bleeding diatheses are also associated with epistaxis. The most common of these is hemophilia A with a reduction of the procoagulant portionj of clotting factor VIII followed by von Willebrand disease with a reduction in von Willebrand factor (vWF). The procoagulant factor and vWF together form factor VIII. Hemophilia B is less common and is caused by a deficiency of factor IX. These diseases result in a prolongation of the partial thromboplastin time (PPT) and sex-linked, occurring only in males. Desmopressin can be given preoperatively to increase the levels of vWF and factor VIII. In addition, cryoprecipitate may be given intraopoeratively if needed. Other diseases that may also affect the clotting cascade include hematologic disorders and malignancies, liver disease, renal disease, and malnutrition. Telangiectasia in the nasal mucosa may be a manifestation of hereditary hemorrhagic telangiectasis. This is an autosomal dominant inherited condition known either as

hereditary hemorrhagic telangiectasia (HHT) or as Osler-Rendu-Weber disease. These patients develop telangiectasia in all their mucosal surfaces as well as on their skin. In addition arteriovenous malformations can be found in the brain, lungs liver, and gut. The telangiectasias have thin fragile vessel walls with absent smooth muscle and often group together forming a lesion that, if seen in the brain, gut, or lungs, may form an arteriovenous malformation. In the nose, these lesions form raised lesions on the nasal septum, lateral nasal wall, and floor of the nose. Their increased fragility may result in spontaneous epistaxis without any obvious precipitating incident.Other systemic factors that can predispose to epistaxis are liver disease (commonly cirrhosis) and renal disease (renal failure). Both of these systemic diseases can lead to the development of clotting disorders. In the case of liver disease, clotting factors manufactured in the liver may be deficient and in renal disease a high urea may affect platelet function. Moreover diabetes mellitus can cause epistaxis by either aggravating arteriosclerosis or contributing to hypertension or predisposing nasal mucosa to opportunistic infections and thus making it inflamed.

Clinical findings-If the patient's general condition is good and nasal bleeding is mild to moderate it is always prudent to identify the bleeding site. After a brief history, patient's general examination should be done to look for pallor, lymhadenopathy, icterus, clubbing and pedal edema. Patient's blood pressure and temperature should be recorded. A thorough examination of skin and extremities should be done to find any evidence of bleeding disorders. Local examination of nose should be done by anterior rhinoscopy, posterior rhinoscopy and flexible and/or rigid nasendoscopy to visualize bleeding site, to know condition of nasal mucosa (inflamed, uncleared or crusted), to see any deviated nasal septum or perforated septum, to see presence of fungal spores, to visualize any growth in nasal cavity or to rule out any other nasal pathology.

Investigations - Following investigations should be done:

- Routine hemogram including hemoglobin, total count and differential count.
- Complete coagulation profile including bleeding time, clotting time, platelet count, prothrombin time and activated partial thromboplastin time.
- Blood glucose levels (fasting and postprandial).
- Culture and sensitivity for fungal growth from nasal scrapings if fungal infection of nose suspected.
- X-ray paranasal sinuses (Water view).
- X-ray nose lateral view (for nasal trauma)
- Diagonostic endoscopy
- CT Scan nose, paranasal sinuses and nasopharynx
- Carotid artery angiography, if needed.
- Liver function test and renal function test

Differential diagnosis

Local

- Trauma (digital, nasal fractures, nasal sprays);
- Anatomic deformities (e.g., septal spur/deflection/ perforation)
- Foreign bodies
- Intranasal tumors
- Chemical irritants
- Nasal O_2, CPAP (continuous positive airway pressure)
- Nasal surgery/nasal intubations
- Inflammatory diseases (Viral upper respiratory infections, bacterial sinusitis, allergic rhinitis, Polygenic granuloma, Granulomatous diseases (Wegener's granulomatosis, tuberculosis, sarcoidosis, syphilis)
- Environmental irritants (cigarette, **cocaine, snuff, heroin** and chemicals, pollution)
- Tumors/vascular malformations (Angiofi-broma, Aneurysms, Epider-moid carcinomas, Nasal papilloma, Adenocarcinoma, Encephalocele, Esthesioneuroblastoma, Hemangioma)

Systemic

- Coagulation deficits
- Thrombocytopendia
- Acquired coagulopathies
- Congenital coagulopathies
- Vitamin A,D,C,E, or K deficiency
- Liver disease/Renal failure/ Chronic alcohol abuse/ Malnutrition

- Polycythemia vera
- Multiple myeloma
- Anticoagulant drugs (asprin, nonsteroidal anti-inflammatory drugs, heparin, Coumadin)
- Leukemia
- Arteriosclerotic
- Collagen abnormalities
- Hereditary hemorrhagic telangiectasia
- Cardiovascular conditions that increase venous pressure (congestive heat failure, mitral valve stenosis)
- Hypertension
- Infections

Suggested management

- Observation (especially in pediatric patients)
- Pharmocologic (Hemostatic, antibiotics, antiseptic cream and barrier ointment)
- Nasal packing (traditional anterior pack, Nasal sponges, Gelfoam, Traditional posterior pack, nasal balloon)
- Cautery (Silver nitrate, Endoscopic electrocautery, Laser-photocoagulation)
- Embolization
- Ligation, Transantral ligation of the internal maxillary artery, External ligation of the ethmoid arteries, Endoscopic ligation of the sphenopalatine artery)
- Surgery (Septoplasty, Septal dermoplasty)

Clinical Procedures

Minor Hemorrhage-Most episodes of epistaxis are minor and stop spontaneously. Antiseptic creams are thought to work by reducing vestibulitis and mucosal inflammation as well as by moistening the mucosa and preventing drying and crusting. Barrier ointments are thought to work by preventing crusting of the septal mucosal, which may help reduce mucosal friability and decrease the frequency of minor epistaxis. Although antiseptic creams and barrier agents are often considered first choice for the treatment at the first consultation, Silver nitrate cautery may be used if, on examination of Little's area, a large dilated blood vessel is seen that is thought to be the likely cause of the recurrent epistaxis. Frequent use of nasal sprays and septal deflections may aggravate mucosal friability in Little's area. Repeated removal of crusts from the anterior nasal septum may also result in recurrent mucosal damage and friability. Education about stopping crust removal and correct positioning of nasal sprays may reduce the incidence of minor epistaxis. Minor epistaxis can also be treated by the placement of a local nasal pack.

Exsanguinating Hemorrhage-Exsanguinating Hemorrhage usually occurs after major trauma. Anterior skull base fractures may cause damage to the anterior and posterior ethmoidal arteries, whereas fractures of the maxilla may result in hemorrhage from the internal maxillary artery or one of its branches. If the sphenoid is involved with fractures traversing the internal carotid artery, catastrophic bleeding may result. Patients with major hemorrhage are resuscitated in the emergency room. If major hemorrhage continues, a postal space Balloon catheter (Foley catheter may be used instead) is inserted into the nasopharynx and inflated with 15mL saline and allow a platform onto which the ribbon gauze can be tightly packed. The nose can then be packed with ribbon gauze. The gauze is layered and tightly packed providing pressure to the mucosa of the nasal cavity. Should bleeding continue, the patient should be taken to the operating room and examination of the nose performed under general anesthetic. Bleeding from the region of the sphenopalatine artery can be managed by an sphenopalatine artery ligation. If this fails to control bleeding, then the external carotid artery should be ligated in the ligation of the anterior ethmoidal artery and the posterior ethmoidal artery if necessary. Massive hemorrhage from the sphenoid region usually indicate an internal carotide injury. If the patient is under general anesthetic, the blood pressure should be lowered by the anesthetist to allow grater visibility for the surgeon and to facilitate the placing of packing against the anterior face of the sphenoid sinus. If possible, an sphenoidotomy can be performed and packing placed into the sphenoid to gain control of the hemorrhage while a muscle plug is harvested from the sternomastoid muscle in the neck. This muscle is placed against the carotid artery in the sphenoid and a pack placed on top of the muscle thereby obtaining control before the patient is sent for arteriography. If this fails to control the

hemorrhage, a temporary vascular clamp can be placed across the common carotid artery in the neck while a sphenoidotomy is performed and the muscle and pack placed in the sphenoid on the carotid artery. This clamp should be removed as soon as possible to limit cerebral ischemia and the possibility of the stroke. At arteriography, if the lesion is in the vertical portion of the carotid in the sphenoid, then a stent may be placed, but if it is in the region of the carotid siphon, then balloon occlusion of the carotid may be necessary and embolization of the internal carotid may be the only solution for saving the patient's life. The major risk of carotid occlusion is cerebral ischemia, hemiplegia, and in some cases, death.

Emergencies in exsanguinating epitaxis

Step 1- Airway and circulatory support and general anesthesia.

Step 2- Anesthetist rapidly lowers blood pressure to allow surgeon to localize site of bleeding. If bleeding still uncontrolled, a neck incision is made and first the external carotid is clamped with a vascular clamp. If bleeding continuous, the internal carotid is clamped with a vascular clamp for a short period of time to establish the site for bleeding in the nose.

Step 3- If superior in the nose, local pack is placed followed by anterior ethmoidal ligation.

If posterior, establish if from sphenoid or sphenopalatine area. If sphenopalatine area, perform sphenopalatine ligation. If from sphenoid, a ribbon gauze pack is placed in the sphenoid (if necessary a sphenoidotomy may need to be performed for access), muscle is harvested from the sternomastoid muscle, the nasal pack is removed, the muscle packed into the sphenoid followed by another ribbon gauze pack. The vessels in the patient's blood pressure.

Step 4- the patient is taken to the interventional radiology suite and an angiogram is performed. If possible, an endovascular stent is placed over the site of injury; if this is not possible, occlusion of the internal carotid at the site of injury may need to be considered.

Major Hemorrhage

A patient with major hemorrhage may present actually to the emergency room with epistaxis or present to the specialist with a history of recurrent trips to the emergency room for the management of epistaxis. For the patient who present with active epistaxis, the first step is to ensure adequate intravenous access and resuscitation of the patient before attempting to gain control over the epistaxis. Acute epistaxis will in almost all cases be from one side only. A history of which side started bleeding first will indicate the site of bleeding. As that nasal cavity fills with blood clot, blood may track around the posterior aspect of the nasal septum and bleeding will come from the opposite nostril. A history of the amount of blood lost is also valuable in the initial assessment of the patient. Standard emergency room protocols should be followed with assessment of the patient. Standard emergency room protocols should be followed with assessment of pulse rate, blood pressure, and hemoglobin and appropriate resuscitation with intravenous fluids.If the patient is actively bleeding, the patient is given a bowl and paper towels and told to blow all the blood clots out of his or her nose. Once both nostrils are clear, the patient is instructed to lean forward and to let the blood drip into a bowl. The surgeon should be appropriately clothed with protective clothing, mask, and headlight. The patient is asked to tilt the head back while a speculum is placed in the nose and the nasal cavity thoroughly sprayed with a combination of lidocaine, epinephrine (or adrenalin), and saline. This allows some decongestion and anesthesia of the nasal cavity. The patient then bends forward again letting the blood drip into the bowl. The surgeon now uses a rigid nasal endoscope and suction to clear the nasal cavity of any residual blood clots and attempts to identify if the bleeding is coming from anterior and high up in the nose or if it is coming from the posterior nasal cavity. Anterior septal bleeders can usually be dealt with by using a combination of chemical or electrical cautery and local nasal packs. Anterior bleeders are usually from Little's area and are usually venous. Chemical cautery will in most cases be sufficient to control hemorrhage. Posterior or high anterior bleeders that are easily visible can be treated by either chemical or electrical cautery.Most cases of major hemorrhage occur in the posterior region of the nasal cavity and the exact site is not visible in t he emergency room. The presence of a significant septal deflection can pose

significant difficulties. In these patients, it is preferable to slide a narrow expandable nasal pack into the nasal cavity around the septal deviation rather then attempt ribbon gauze. Packing. These expandable packs are made from either hydroxylated polyvinyl acetate (Merocel) or polyvinyl alcohol (Expandacell and Rhinorocket). The blood soaks the pack, which expends and fills the nasal cavity. If this fails to stop the bleeding, the pack is removed and a posterior nasal space catheter is placed. The nasal cavity is then packed with ribbon gauze soaked in bismuth iodoform paraffin paste (BIPP) or petroleum gauze coated with pulse oximetry. The anterior ethmoidal artery is ligated if the bleeding is anterior and high and the sphenopalatine artery is ligated if the bleeding is posteriorly located. No nasal packing is placed in the nose after arterial ligation and the patient is discharged from hospital within 6 hours of the procedure. This patient should be admitted; if after a further 12 hours here is no further bleeding, then the balloon can be deflected. If bleeding does not reoccur, the nasal pack can be removed after a further 12 hours. If bleeding reoccurs, the patient is repacked and arterial ligation is performed. Should arterial ligation fail, embolization is performed.

Surgical procedures

- Anterior Ethmoidal Artery Ligation can be done with/ without endoscope.
- Endoscopic sphenopalatine artery (SPA) ligation is the procedure of choice for uncontrolled posterior epistaxis.
- Transantral Ligation of the maxillary Artery-Until recently, this was the procedure of choice, but it is rarely used today because SPA ligation is easier, has less complications, and is more effective at controlling epistaxis.
- Management of Hereditary hemorrhage Telangiectasia (HTT) Management of HHT is regular laser treatment of all telangiectasia. Lasers that are currently used are the potassium titanyl phosphate (KTP), neodymium: yttrium-aluminum-garnet (Nd:YAG), argon, argon plasma coagulation laser, and more recently the pulse dye laser. If there is an associated septal perforation, silastic septal splints are placed over the perforation and held in place with a transseptal suture for 1 to 2 weeks before they are removed. This allows the mucosa around the septal perforation to heal without crusting from turbulent airflow.
- Alternatives include septodermoplasty, in which skin grafts are placed on the nasal septum.
- Recently, the use of systemic tranexamic acid and topically applied tranexamic acid has been described for patient with sever HHT.

Complications of epistaxis management

Complications	Avoidance
Septal perforation, reabsorption	Limited cautery, proper [ack size/balloon inflation
Alar rim, columella necrosis	Proper pack size and balloon catheter stabilization without contact with alar or columella
Apnea, Hypoxia	Proper posterior pack size and placement, monitor oxygen saturation, avoid bilateral packs because bleeding is usually unilateral
Hyprovolemic shock	Intravenous fluids as needed
Aspiration of packing	Adequate placement and securing of nasal packs
Recalcitrant bleeding	Identify the bleeding site, inadequate pack, or missed diagnosis
Infection	Prophylactic oral and topical antibiotics
Neurovascular insult	Careful evaluation of etiology and cautions technique

Conclusions

- Before examining the nose of a patient with epistaxis, ensure that doctor should have protective clothing, local anesthetic spray, rigid endoscope, suction, cautery, nasal packs, and packing forceps. After clearance of blood clot, attempt to localize the site of bleeding. If it is accessible, then local cautery may suffice; if the exact site is uncertain, determine if bleeding is high in the nose or posterior. Place a nasal pack (on a balloon catheter if necessary). If posterior, consider ligation of the sphenopalatine artery, and if high and anterior, consider ligation of the anterior ethmoidal artery. Recent study suggest that the optimal management for patients requiring admission to hospital for sever epistaxis is arterial ligation.
- Consider embolization if arterial ligation fails to control the bleeding.
- Manage patients with coagulation disorders conservatively, considering their life-long challenge of future recalcitrant epistaxis. Escalate treatment as dictated by their lack of response to simpler measures.
- Patients with hereditary hemorrhagic telangiectasia are best managed by intermittent laser treatment.
- The placement of posterior nasal packs with the occlusion of the nasal airway may predispose patients to apnea, hypoxia, and arrhythmias that may be life-threatening. Careful monit-oring of these patients is mandatory.
- Be aware of the potential complications of the treatments for epistaxis when considering management of these patients.

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Alexis Carrel

Modern techniques of aneurysm repair were made possible by **Alexis Carrel** who demon strated arterial replacement and successfully anastomosed blood vessels. In 1890, Alexis Carrel was admitted to the Medical School of Lyon, where he developed interest in blood vessel repair and did intensive research on vascular surgery. This interest was precipitated by an unsuccessful portal vein injury repair of the French president M. F. S. Carnot in 1894. With **Charles Claude Guthrie**, he wrote in 1906: "The vessels must be handled very gently and the endothelium must be protected from drying by isotonic saline. No dangerous metallic forceps are used. Great care is exercised to obtain accurate and smooth approximation of the endothelium of the vessels without invagination. Sutures should be made with very fine needles while the wall is somewhat stretched. Stenosis or occlusion only occurs as a result of faulty technique" - which is still valid 100 years later. In 1910, he demonstrated that blood vessels could be kept in cold storage for long periods before transplanting them. Carrel won the noble prize for his work in 1912 "in recognition of his work on vascular suture and the transplantation of blood vessels".

Correspondence

'Two stage procedures in septic peritonitis following principle's of damage control technique'— our retrospective clinical experience with 143 patients in last 8 years

Damage Control Procedure needs no introduction. It regulates dramatic surgery, percolates rationality to prevent heroic surgical procedure. It drops mortality and minimizes morbidity too. An aphorism goes "operation is successful but the patient is dead" this becomes true if the principles of damage control surgery are ignored. 'Trauma to the tissue' is dramatic, be it is mechanical, bacterial, viral or carcinogenic in origin. Onset of a vicious cycle of 'three' inter related changes occur in patients with neglected tissue assaults-Metabolic acidosis (pH<7.35), Severe Hypothermia, Coagulopathy. Therefore mini-mal invasion yields maximum benefit to the patient as well as to the team of attending doctors. This is life saving.There is definite life saving benefits in applied procedure of putting an intra peritoneal drain prior to the laparotomy when the patient stands unfit for general anaesthesia but peritonitis is suspected. 'Bacterial trauma' is buffered by the drainage of intra peritoneal fluid load and countering the 'abdominal compartment syndrome'. Metabolic changes occur when the patients are left untreated for 24 to72hrs after 'trauma' to the abdomen. Diseased state, diabetes, and other co morbid factors jolt the condition. At this stage definite surgery without preparation with time is life killing.

Pathophysiology-Simulate the iatrogenic 'Tension pneumoperitoneum' in laparoscopic surgery in a patient with bacterial hydro peritoneum leading to Abdominal compartment syndrome (>25cm H_2O or 18mm of Hg.)Toxic fluid load + pneumoperitoneum-increase systemic vascular resistance (SVR), increase sympathetic output from absorption of CO_2, H2S and NO—increase myocardial wall tension to set myocardium to high O_2 demand. Abdominal organs like liver, kidney & spleen are compensated. Raised intra abdominal pressure (IAP) hinders venous return through IVC and decrease preload and cardiac output by 40-60%.Cephalic diaphragm shift and associated supine position, bacterial load, oedematous gut with translocated fluid add more metabolic derangement in this type of neglected patient. Low muscle tone in these patients (end expiratory abdominal muscle tone) decrease respiratory efficiency.

Methods-We operated upon these neglected patients by introducing Foley's catheter in the Right or Left flank or in both to drain the intra peritoneal contaminated fluid load and to minimize the severity of 'abdominal compartment syndrome'. We managed 143 patients (1999-2007) by putting drain initially for 2 to3 days prior to the definite surgical intervention in a stable condition. The drains were put under local infiltration of lidocaine 1% in patients with intestinal perforation (n=123), Typhoid & roundworm perforation, (n=8). Ruptured intestine due to RTA, stab, elephant knock & blast injuries (n=8) and intraperitoneal abscesses (4).We monitored the patients under a team of surgeon, Anaesthetist and Pathologist.

'Damage control surgery aimed at cleaning the peritoneal cavity, so-called peritoneal toilet' contaminated fluids and particulate matter is best removed from the cavity in the earliest possible time. Scientific evidence co relates with positive outcome with peritoneal lavage. Again it is also evident that leaving saline or Ringer's solution in the peritoneal cavity may drop the peritoneal defenses by

'diluting the macrophages'- bacteria swim perhaps better than macrophages.[1] peritoneal irrigation with antibiotics is not also advantageous. Despite the dictum that it is impossible to effectively drain the peritoneal cavity, drains are still commonly used and misused. E.coli is thought to be a blood-borne agent infecting the peritoneum and affecting the system in neglected perforative peritonitis. Therefore systemic control with hydration, hypoxia control and prophylactic intra venous antibiotics may optimize the patient before definite surgery.

Philosophy of management is simple: - Control of source and Damage control. Initial management of neglected perforated peritonitis was resuscitation and analgesia. Optimization, then definite procedure - laparotomy. A small incision around umbilicus is sufficient to put a laparoscope primarily to do peritoneal lavage and locate perforation[2]. Damage control includes abbreviated laparotomy and temporary closure. Definite procedure is best to follow when the patient is stable and organ function is maintained, usually 48 to 72 hours after initial minimum operative procedure as a life saving benefit[3]. Response to surgery is modulated both by the neuro-endocrine system and inflammatory mediators, acute phase response; Hypoxia; hypercarbia or pH changes adversely affect surgery. Correction with time is life saving.[4] 3 patients died after laparotomy (2.09%) and procedure after initial 2-3 day conservative approach with intra peritoneal drain, intra venous antibiotics, metronidazole, analgesic and PPIs. Complications came out as intestinal fistulae in 1 patient (0.69%). Burst abdomen in two (1.39%), post operative pain & adhesions in five (3.49%) and. Six patients did not turn up in the post operative follow up (4.19%).

Conclusion- the patients were treated with conservation as they were initially unfit for general anaesthesia. After 2-3 days conservative management with intra peritoneal drain they were treated with definite procedure. Procedure may be evaluated as life saving procedure in neglected 'trauma'. Continuous monitoring per and post operatively by Anesthetist with Pathological & Biochemical study of blood & peritoneal fluid helped us to keep the patient metabolically stable. It is the management under a team that was all that necessary for the life saving measure than the procedure of individual surgery.Laparostomy is the modern procedure in otherwise unfit patients in the current day surgical management. We approached with our technique as the infra structure was not sufficient. Randomized control trial is necessary to get the true picture. However we managed to save 140 lives in our set up.Laparoscopy might be the procedure when the patient is stable.

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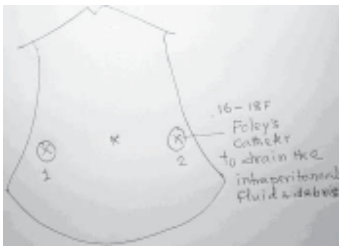

Gamut of Radiological Findings in Pulmonary Aspergillosis

Aspergillosis is a mycotic disease caused by a dimorphic fungus belonging to the Aspergillus species, usually A fumigatus. A flavus, A niger, A glaucis and a variety of other genus are occasionally pathogenic. Aspe-rgillus is an intensely antigenic soil fungus; its conidiophores are ubiquitous in the atmosphere and human exposure inevitable. In the airways it is capable of multiplying into the hyphal form, under favourable conditions. The histologic, clinical, and radiologic manifestations of pulmonary **aspergillosis represent a spectrum** determined by the virulence of the organisms and the patient's immune response [1] (Table 1). We discuss the radiological manifestations of aspergillosis encountered in four patients.

IMMUNE STATUS			
HYPERSENSITIVE ⇩	NORMAL ⇩	MILD IMMUNOSUPPRESSION ⇩	SEVERE IMMUNOSUPPRESSION ⇩
ALLERGIC ASPERGILLOSIS	SAPROPHYTIC ASPERGILLOSIS	CHRONIC NECROTIZING ASPERGILLOSIS	INVASIVE PULMONARY ASPERGILLOSIS

Discussion-Allergic bronchopulmonary aspergillosis is caused by a complex twofold immunologic reaction comprising an acute type I immediate hypersensitivity reaction mediated by IgE and a delayed immune complex type III reaction mediated by IgG, in response to *Aspergillus* antigens. The fungi proliferate in the tracheo-bronchial tree, constantly releasing surface antigens into the airways. With protracted infection, immune complexes and inflammatory cells are deposited in the bronchial mucosa, producing necrosis and eosinophilic infiltrates (type III reaction) with bronchial wall damage and bronchiectasis [2]. Excessive mucus production and abnormal ciliary function lead to mucoid impaction. Many patients cough up thick mucous plugs in which hyphal fragments can be demonstrated at culture or histologic analysis. In the acute setting, areas of consolidation may be seen on the chest radiograph, ranging in distribution from sub-segmental to lobar with upper lobe predilection. Tram line shadows representing edematous bronchial walls may also be encountered. Pathologically the alveoli are filled with eosinophils, and the walls of smaller bronchi show eosinophilic infiltrates. Radiologic manifestations in the chronic stage include homogeneous, tubular, finger-in-glove areas of increased opacity in a bronchial distribution, usually predominantly or exclusively involving the upper lobes [3]. These shadows are related to plugging of airways by hyphal masses with distal mucoid impaction and can migrate from one region to another (Fig-1). CT findings in allergic bronchopulmonary aspergillosis consist primarily of mucoid impaction and bronchiectasis involving predominantly the segmental and subsegmental bronchi of the upper lobes (Fig-2). In approximately 30% of patients, the impacted mucus has high attenuation or demonstrates frank calcification at CT (Fig-3). ABPA is treated with chest physiotherapy and inhaled or systemic corticosteroids. **Saprophytic aspergillosis** (aspergilloma) is characterised by Aspergillus infection without tissue invasion. It typically leads to conglomeration of intertwined fungal hyphae admixed with mucus and cellular debris colonizing a pre-existent pulmonary cavity or ectatic bronchus. Such cavities are usually due to tuberculosis, sarcoidosis or histoplasmosis; rarer causes include pulmonary sequestration, bronchogenic cysts and pnematoceles [4]. Saprophytic **aspergillosis manifests** on the chest x-ray as a mobile, dependent nodular opacity located within a pre-existing cavity (Fig-4). As on the radiograph, the most

characteristic finding of an aspergilloma on CT consists of an ovoid or round soft tissue attenuation, intra-cavitary mass that usually moves when the patient decubitus is changed (Fig-5, 6) [5]. Aspergillomas are often associated with thickening of the cavity wall and adjacent pleura. Pleural thickening may be the earliest radiographic sign before any visible changes are seen within the cavity. Reversibility of the pleural thickening corresponding to the resolution of intra-cavitary fungal material has been demonstrated at follow-up radiography. Approximately 10% of mycetomas resolve spontaneously. This reversibility suggests that the thickening of the cavity wall and pleura are due to a hypersensitivity reaction[6]. The imaging differential diagnosis of saprophytic aspergillosis includes ruptured echinococcal cyst, Rasmussen aneurysm in a tuberculous cavity, lung abscess, bronchogenic carcinoma, hematoma, and *P carinii* pneumonia [7].

Chronic necrotizing aspergillosis (semi-invasive aspergillosis) is characterised at pathologic examination by the presence of tissue necrosis, granulomatous inflammation and fibrosis resembling post-primary tuberculosis. Many patients have co-morbid conditions like chronic obstructive airway disease, corticosteroid therapy, diabetes mellitus, malnutrition and chronic alcohol intake. Clinically the patients manifest with chronic productive cough and fever, hemoptysis has been reported in 15% of affected patients [8]. Radiologic findings initially consist of unilateral or bilateral upper lobe consolidation and nodular opacities (Fig-7). Progressive cavitation develops as a result of necrosis of the consolidated lung parenchyma [9]. Adjacent pleural thickening is commonly seen. The radiological picture typically progress slowly over months or years.

Invasive aspergillosis is a serious pathologic condition caused characterised by vascular invasion, arteriolar thrombosis and ischemic tissue necrosis which is invariably seen in immunocompromised patients. Clinically, patients develop cough, pleuritic chest pain, fever, dyspnea, and tachypnea. An early diagnosis is essential because a delayed or improperly treated infection has a 65%–90% mortality rate. Clinical findings may mimic thromboembolic disease and microbiological diagnosis may be difficult because sputum cultures are positive in only 10% of patients [10]. Therefore, more invasive diagnostic approaches, including bronchoscopy with transbronchial biopsy, percutaneous needle aspiration biopsy, or open lung biopsy, may be required. The radiographic pattern consists of peripheral wedge shaped nodules or single or multiple areas of consolidation (Fig.8). At computed tomography (CT) a characteristic finding in early invasive aspergillosis consists of a halo of ground glass attenuation surrounding a soft tissue nodule. This "halo sign" is related to presence of hemorrhage surrounding the central necrotic nodule (Fig-9) [10]. The CT halo sign is also encountered in other pulmonary infections such as Candida, Herpes simplex and Cytomegalovirus and in malignant conditions like Kaposi's sarcoma and hemorrhagic metastases. The hyphal form of the fungus invades the pulmonary vasculature resulting in pulmonary hemorrhage, arterial thrombosis, and eventual infarction. Over time, with retraction of the infarcted center and peripheral reabsorption of necrotic tissue by leukocytes, a central cavity of devitalized tissue is formed. The air crescent sign results when air fills the space between the devitalized tissue and surrounding parenchyma. An opaque rim of hemorrhagic tissue peripheral to the radiolucency makes visualization of the air crescent possible Treatment is with intravenous amphotericin B, the case fatality is high despite intensive therapy.

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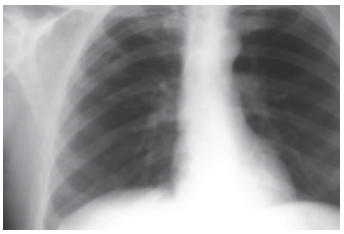

Fig-1, Chest x-ray shows tubular areas of increased opacity in a bronchial distribution and cystic lucencies with opaque cuffs, representing bronchoceles and bronchiectasis respectively.

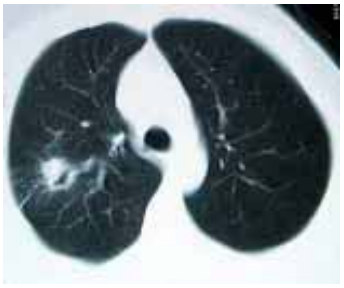

Fig-2, Spiral chest CT shows mucoid impaction (finger-in-glove sign) of dilated bronchi in the right upper lobe.

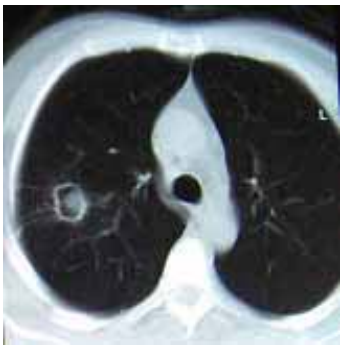

Fig-3, HRCT shows ectatic bronchi with thickened walls filled with hyperdense mucus in the both upper lobes.

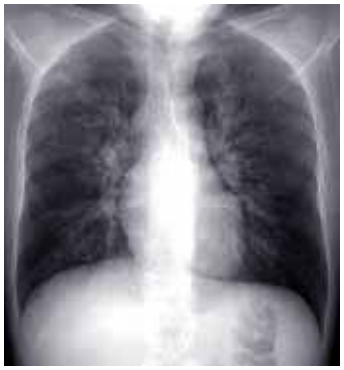

Fig-4, Chest x-ray shows a smooth walled tubercular cavity in the right upper zone with a dependent nodular shadow (fungal ball).

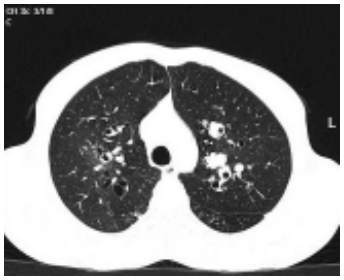

Fig -5, Axial CT scan through the upper chest shows a thin walled cavity in the right upper lobe containing a soft-tissue density mass in contact with the medial wall.

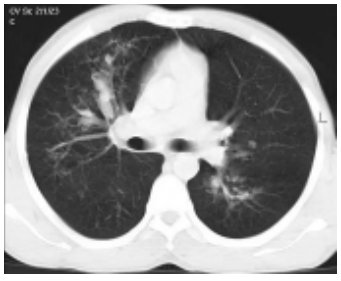

Fig -6, Chest CT with the patient in the right lateral decubitus position shows the fungal ball resting along the lateral wall of the cavity indicating mobility.

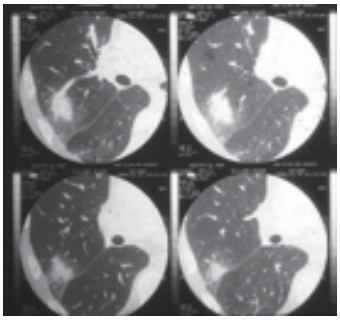

Fig-7, Chest CT shows an irregular airspace opacity in the posterior segment of the right upper lobe (semi-invasive aspergillosis confirmed by FNAC).

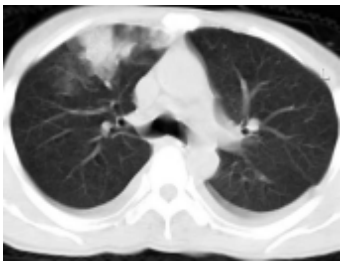

Fig-8, Spiral CT through the upper chest reveals a pleural based wedge shaped infarct in the anterior segment of the right upper lobe.

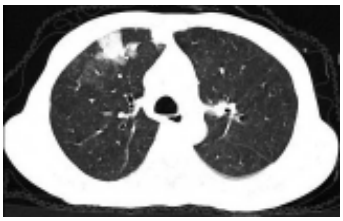

Fig-9, HRCT reveals a halo of ground glass haze surrounding the wedge shaped opacity (infarct)

The present & future of vascular surgery

One of the major developments in vascular surgery over the past years has been the introduction of endovascular repair of aneurysms. In 1967, **Dotter** did canine experiments and was credited for first arterial stent designed for remote arterial insertion. In humans, this was initially described for aortic aneurysms by **J.C. Parodi** in 1991. This technique uses an endoprosthesis, which is delivered through the femoral arteries, to exclude an aneurysm from the circulation. In 1993, **May** and colleagues from Australia reported the first transluminal placement of a prosthetic graft stent device for treatment of subclavian artery aneurysms. Endovascular repair has several theoretical advantages over conventional surgery, and early evidence suggests that endovascular surgery is better for patients with coexistent disease, who would be at high risk for conventional surgery. Endovascular stenting should be considered in the treatment of carefully selected patients with difficult and dangerous aneurysm. Currently, Cragg endopro system developed by **Rousseau** in 1996, Wallgraft (Schneider Minneapolis, Minn.), a self-expanding wallstent by **Krajcer** in 1997, Palmaz stent and Corvita stent-graft are established grafts for treatment of peripheral arterial aneurysms. Now the guidelines for the development and use of endovascular prosthesis and their reporting standards have been published in 1995, but they have unique complications and unresolved issues, especially long-term durability. This modality is under rigorous prospective evaluation with randomized trials and comparative studies to know about late and long term results.Direct compression therapy as reported by **Kronzon I.** in J Am Soc. Echocardiogr 1997 and ultrasound guided percutaneous injection of thrombin as described by **Liau** and colleagues in 1997, are only for iatrogenic femoral and other pseudoaneurysms. These two modalities have some success in management of the fresh, uncomplicated, catheter-induced pseudoaneurysms, but are unlikely to succeed with infected and complicated aneurysms.

The history of vascular surgery is very extensive. Many other advances in asepsis, anaesthesiology, blood transfusion, coagulation, angiography, radiology, improved instrumentation and simplification of flow and pressure measurements helped to achieve the current status. Regardless of aetiology and site, the principle for aneurysm repair is still the same. The life threatening lesions should be addressed first, followed by the limb threatening lesions. The aneurysm must be excluded from the circulation and arterial circulation restored.

16

Monoclonal Antibodies

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Recent Advances

Monoclonal antibodies are antibodies that react with specific molecular target. The idea of 'magic bullet' was first proposed by Paul Ehrlich at the beginning of the twenty century. The advent of hybridoma technology to produce mAB was a major advance in immunology. Since the discovery of the methods for fusing mouse myeloma cells with B-lymphocyte, it has made possible to produce a single species of antibody that recognizes a specific antigen. Presently, several mAB have received FDA approval for malignancies and some other special disorders. Paul Ehrlich, postulated that if a compound could be made that selectively targeted to a disease-causing organism, than a toxin for the organism could be delivered along with the agent of selectivity.In the 1970s the B-cell cancer myeloma was known, and it was understood that these cancerous B-Cells all produce a single type of antibody.The invention of mAB production involving human-mouse hybrid cells was initiated in 1975 by George Kohler, Cesar Milstein and Niele Kaj Jerne (Nobel Prize Winners-1984) The key idea was to use a line of myeloma cells that had lost their ability to secrete antibodies, come up with technique to fuse these cells with healthy antibody producing B-cells, and be able to select for the successfully fused cells. In 1988 Greg winter and his team pioneered the techniques to humanize mAB, removing the reactions that mAB caused in some persons.

Polyclonal Vs Monoclonal Antibodies

Both polyclonal and monoclonal antibodies are used for prevention and treatment of organ transplant rejection. Polyclonal antisera are generated by repeated injections of human thymocytes (anti-thymocyte-globulin) or lymphocytes (antilymphocyte-globulins) into animal such as rabbits, goats; sheep's or horses and purifying the immunoglobulin fraction. Although highly effective these preparation vary in efficacy and toxicity from batch to batch.It is now possible to make essentially unlimited amounts of a single antibody of a defined specificity. These monoclonal reagents have overcome the problems of efficacy and toxicity seen with polyclonal products but they are more limited in their target specificity.

Generation of Monoclonal Antibodies

Monoclonal antibodies are produced by hybridoma technology. Basically, hybridoma technique consists of fusing two different cell lines, a myeloma cells and B-lymphocytes capable of producing an antibody that recognizes a specific antigen. They may be part mouse (murine), part human (termed chimaric or humanized antibodies) or fully human.In the initial step, mice are immunized with desired antigen, then lymph node or spleen is harvested and B cells separated. These B cells are fused with B-ce3ll myeloma, taken from myeloma cell culture. The fused hybrid cells are called hybridoma, and since they are derived from cancer cells, are immortal and can be grown indefinitely. The hybrid cells expand in culture supplemented with HAT (hypoxanthine; aminopterin and thymidine). Selected cells are subjected to recline. The murine mAB thus obtain can be used directly or freeze for future use but have limitation of brief action and induce a human anti-mouse antibody immune response. The human immune system recognizes mouse antibodies as foreign, rapidly removing them from circulation and causing systemic inflammatory effects. These days, recombinant antibody engineering involves the use of viruses or yeast to create antibodies, rather then mice. The

technologies referred to as repertoire cloning or phase display. These techniques rely on rapid cloning of immunoglobulin gene segments from which antibodies with desired specifications can be selected.

Nomenclature

The name of all representative are ended with –'mAB', that denote monoclonal antibodies, e.g. Abciximab. The nomenclature adopted for naming mAB is to terminate the name in – ximab for chimeric antibodies e.g. Infliximab, Retuximab, and –umab for humanized antibodies such as Declizumab, Gemtuzumab etc.

Modification and Types

Monoclonal antibodies are more limited in their specificity. The conventional mAB as synthesized, are generally 'free' and termed as mAB, e.g. basilximab, palvizuman etc. These days mAB may be ENGINEERED to produce immuno-conjugates by combining the antibody with some conjugate such as toxin, as immunotoxins e.g. denileukin-diftitox or combined with a radioactive isotopes, as radio-immunoconjugate e.g. 90 Y ibritumomab. Other conjugates are immunocytokine (mAB & cytokine) and immunoliposome (mAB & liposome). Recently, antibodies have been engineered to contain a second specificity, known as bispecific antibodies, like an antibody with specificity to B-cell lymphomas and to CD3, which bind to and activate normal T-cells, may enhance T-cell mediated lyses of lymphoma cells. mAB raised against the immunoglobulin idiotype on B-cell lymphoma represent another therapeutic strategy.

Pharmacodyanamics & Pharmacokinitics

A variety of mechanism(s) of cell killing have been described for mAB like antibody-dependent cellular cytotoxicity (adcc), complement-dependent cytotoxicity(CDC) and direct induction of apoptosis, but the clinically relevant mechanism remain uncertain.The action of mAB is directed against T and B lymphocytes, tissue narcosis factor Alfa (TNF Alfa) and interleukins (IL). Addition of some active compound as conjugates mAB can provide targeted specificity to cytotoxic actions, thus mAB can be used as therapeutic missiles to target specific tissues.The most preferred route of delivery is intravenous. As general, distributaries volume is small therefore penetration to tissue is limited. mAB may persist is circulation for two days to two weeks, depending upon their types.

Therapeutic Indications

These days, mAB are used in various medical conditions like cancer and graft rejection. One possible treatment for cancer involves mAB that bind only to cancer cell specific antigen and induce an immunological response against the target cancer cell. These antibodies deliver lethal drug delivery. Such mAB could also be modified for delivery of a toxin, radioisotope, and other active conjugate. Role of some agents are will established while other are under clinical trail.

- **Cancer** - B-cell Leukemia (Alemtuzumab, Retuximab); Relapsed AML (Gemtuzumab, ozogamicin); Nonhodgkin lymphoma (Retuximab, Infliximab); Brest Cancer (Cetuximab, Trastuzuman); Lung Cancer,non-small cell (Trastzumab, Bevancizumab); Colorectal Carcinoma (Bevacizumab, Cotuximab)
- **Acute organ transplant rejection**-Basiliximab, Daclizumab, Efalizumab.
- **Rheumotoid arthritis**-Infliximab, Adalimimab, Etanercept,
- **Inflammatory bowel disorder (Crohn's diease)** – Infliximab, Etanercepet.
- **Dermatological disorder (Psoriasis)**-Eflalizumab, Enfliximab.
- **Anti-Platelets** -Abciximan (to prevent restenosis after angioplastry).
- **Others**-Apart from well known therapeutic utility, some mAB are under clinical trails for disease like diabetes mellitus and asthma etc.

Diagnostic Implications

Once mAB for a given substance have been produced they can be used to detect the presence and quantity of that substance". This principle is used in several diagnostic procedures, for instance in a Western blot test (to detect a protein on a membrane)

or an immunofluorescence test (to detect a substance in a cell). They are also useful in immunohisttochermistry which detect antigen in fixed tissue sections. mAB can also be used to purity a substance with techniques called immunoprecipitation and affinity chromatography.

Toxicity

Administration of majority of mABs can result infusion related toxicity. Hypersensitivity and bone marrow suppression are other common adverse reactions, some other reported side effects are cardiomyopathy, pulmonary haemorrrhage, arthalgia and gastrointestinal perforation etc.Individual antibodies can show some of unique adverse impact, like rituximab can result severe pancytopenia, opportunistic infection andeventlly death, particularly in patient who received purine analog. Cardiac dysfunction is potentially erious side effect of trastuzumab and bevacizumab. The incidence of skin rash is significantly greater in cetuximab that other mab. Gemtuzumab – ozogamicin can result serious hepatic toxicity and fatal veno-occlusive disease.

Conclusion

Monoclonal antibodies are immunoglobulins produced by single clone of cell. The advent of genetic engineering have made possible to prodfuce various monoclonal antibodies like named, conjugated and bispacific. These ae highly selective in nature and employed for targeted drug delivery. Monoclonal antibodies play an important role in medicine and used both for therapeutic as well as diagnostic purposes. These days, number of monoclonal antibodies have been generated and approved for cancer, auto immune and some other specific disorders.

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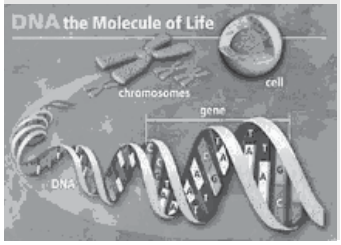
Discovery of the helix structure of DNA

Rosalind Franklin is most associated with the discovery of the structure of DNA. At 26, after she had her PhD, Franklin began working in x-ray diffraction - using x-rays to create images of crystallized solids. She pioneered the use of this method in analyzing complex, unorganized matter such as large biological molecules, and not just single crystals.

Franklin made marked advances in x-ray diffraction techniques with DNA. She adjusted her equipment to produce an extremely fine beam of x-rays. She extracted finer DNA fibers than ever before and arranged them in parallel bundles. And she studied the fibers' reactions to humid conditions. All of these allowed her to discover crucial keys to DNA's structure. Maurice Wilkins, her laboratory's second-in-comm-and, shared her data, without her knowledge, with **James Watson and Francis Crick**, at Cambridge University, and they pulled ahead in the race, ultimately publishing the proposed structure of DNA in March, 1953.



National Cancer Control Programme (NCCP)-an Update

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Cancer is a broad term used for identifying a large number of diseases. Perhaps the only common features of these diseases are the ability of uncontrolled cell proliferation that cannot be checked by the normal cell kinetics regulators. A normal cell suddenly turns into rogue cell and start dividing continuously without a check leading to development of solid lumps [tumors] or an abnormal rise in the number of dispersed cells like the blood corpuscles. Cancer can occur in any part of the body and in any organ or tissue. Even though most of the cancers are generally associated with old age, no age group is immune to this disease. Cancer originates in our own cells, but several factors, both intrinsic and external to the body, which influence our daily life can add to the life time cancer risk. While cancer as such is not infectious however some infections can act as stimulus to induce and promote cancer. In addition, environmental pollutants like many chemicals, industrial effluents, some therapeutic drugs, and mutagenic agents including ionizing radiation, extensive use of tobacco and alcohol can increase the risk of cancer.[1,2,3,4]

Global burden-According to estimate for the year 2000, world wide over 10 million new cases of cancer occurred (approximately 5.3 million men and 4.7 million women) and over 6 million people died from cancers.[5] By the year 2020, there will be 20 million new cancer cases with 12 million deaths. Even though high incidence of cancer is reported from developed countries [North America, Europe, Japan and Australia] developing countries bear half of the global cancer burden as 75% of the world's population lives in these countries.[6] This proportion is likely to increase further in the next twenty years because of population growth, increase life expectancy, urbanisation/ industrialisation, changing dietary habits, better control of infections, and increase tobacco consumption etc.[7] In developed countries, cancer is the second most common cause of death, and epidemiological evidence points to the emergence of a similar trend in developing countries. [8]

Magnitude of disease burden in India-Cancer is an important public health problem with 8 to 9 lakh cases occurring every year. At any point of time, it is estimated that there are nearly 25 lakh cases in the country with nearly 4-lakh death occurring annually due to cancer. Cancer incidence in India is estimated to be around 70-90 per 1,00,000 population.[9] From the population-based registries in India covering 28–30 million population from different parts of the country, the age adjusted incidence rates vary from 44 to 122 per 100,000 population in males and 52 to 128 per 100,000 females. [10, 11, 12] Cancer registry has also highlighted that more than 60% of cancer in male & 70% in female occur in the age group of 35-64 and 3.5%-4.5% in childhood thereby suggesting the impact of cancer as a major public health problem in most productive age group. It has been found out that 34% of the cancers in the country are related to tobacco use (48% of cancers in men and 20% of cancers in women. Data from population based registries indicate that the leading sites of cancer among men are cancer of oral cavity, lungs, oesophagus & stomach whereas among women it is cancer of uterine cervix, breast and oral cavity. Oral, breast, and cervix cancer constitute 40-50% of the cancer burden in India. Over 70% of patient report for diagnostic and treatment services in advanced stages of the disease, resulting in poor survival and high mortality rates. [13] Moreover,

for many of the cancers affecting humans there exist limited treatment protocol thus leading to prolonged suffering and death.[14, 15]

National Cancer Registry Programme [NCRP] -To provide a comprehensive picture of the magnitude and patterns of cancer in the country, National Cancer Registry Programme [NCRP] that includes database of cancer cases both at the level of population and hospital was initiated by Indian Council of Medical Research [ICMR] in 1982. The Population-based cancer registries takes the sample population in a geographically defined area while the Hospital-based cancer registries take the data from patients coming to a particular health institution. Currently, there are 21 Population-based registries and 6 Hospital-based registries all over the country. In 2001, data from all cancer registries and all medical colleges were collated for the "Development of an Atlas of Cancer in India" (www.canceratlas.india.org) to have an idea of patterns of cancers in several other parts of the country, including those not covered under NCCP.

Milestones under NCCP- National Cancer Control Programme [NCCP] was launched during the year 1975-76 with various schemes to strengthen cancer control activities in the country with priorities given for equipping the premier cancer hospital/ institutions. However, the strategy was revised during 1984-85 and stress was laid on primary prevention and early detection as per the objectives envisaged under the programme. To broaden the reach of the programme, District Cancer Control Programme [DCCP] was started in selected districts near the medical college hospitals in the year 1990-91. As the programme did not make a significant impact in the community, evaluation of NCCP was done by National Institute of Health & Family Welfare, New Delhi during 2002 and based on the recommendation it was revised further.

Goals & objectives of NCCP

1. Primary prevention of tobacco related cancer,
2. Secondary prevention of cancers amenable to early diagnosis such as cancer of uterine cervix, breast and oro-pharynx.
3. Strengthening of cancer treatment facilities including palliative care in terminal stage

Schemes under National Cancer Control Programme (NCCP)[16]

- **Regional Cancer Centres** (RCCs)-are envisaged for providing comprehensive cancer treatment services, undertaking IEC and outreach activities for enhancing community awareness & reducing the geographical gap in terms of service availability, offering specialized training of health personnel and conduct of research. New RCC are provided one-time grant of Rs. 5.00 [five] crores and existing RCCs with Rs.3.00 [three] crores to further strengthen the cancer care services. The approved list of equipment under the scheme are cobalt unit; linear accelerator; mammography machine; radiotherapy simulator; treatment planning system; mould room equipment, CT scan; radiation monitoring equipment; ultrasound; fibre optic endoscope; x-ray machine; gamma camera and other nuclear medicine equipment; pathology and cytology microscope and other related equipments, and other units for operation theatre/aneasthesia.
- **Development of Oncology Wing-** Government medical colleges & hospitals are providedwith a grant of Rs. 3.00 [three] crore for the development of Oncology Wing for purchase of equipments and construction.
- **District Cancer Control Programme-**The DCCP has been designed with a focus on prevention of cancer, early detection, minimal treatment of common cancers and provision of supportive care including palliation of patients in advanced stage. It is to be implemented through a nodal agency, which may be a Regional Cancer Centre [RCC] or Government Medical college or hospital

with a provision of radiotherapy facility and a cluster of 2-3 districts are attached to the nodal institute identified by the respective states. A grant-in-aid of Rs. 90.00 lakhs spread over a period of 5 years is provided per DCCP proposal.

- **NGO Scheme-** NGO provide an effective interface with the community and the people for any disease control activities. They play a very critical role in view of their better reach at the grass root level because of trust and relationship building, empathy & flexibility in approach. Under the scheme a grant of Rs. 8000/- [eight thousand] per IEC camp is provided to NGOs through identified nodal agency.

Achievements till 2007-08

- **Schemes under NCCP**: As of now, there are 27 Regional Cancer Centres, including 6 NGOs, providing comprehensive cancer care services (list of RCCs annexed). Support has been given to 82 institutes including government medical colleges and hospitals for development of oncology wing. The current position with regard to availability of treatment facility in the country is as follows: Cobalt units [265]; Liner Accel-erators [70]; Brachy-therapy [120]; Treatment planning units [140]; Simulators [80]; Radiotherapy centres [165 with 128 in urban areas]; Radiation Oncologists [650]; Medical oncologists/unit [110/32]; and Surgical oncologist/units [150/45].
- Nearly 28 districts have been covered under the scheme DCCP. On the IEC [information, education and communication] front the programme supports activities of health magazine 'Kalyani' and telecasted by Prasar Bharti targeting especially those living in the most populous States. It is an interactive programme that provides an interface to the people with experts on various health and social issues including cancer. Kalyani is telecasted in 9 capital Doordarshan stations i.e. Bhopal, Bhubaneshwar, Dehradun, Guwahati, Jaipur, Lucknow, Patna, Raipur, Ranchi and 12 sub-regional stations i.e. Gorakhpur, Varanasi, Bariely, Mau, Allahabad, Indore, Gwalior, Jagdalpur, Daltonganj, Bhawanipatna, Sambalpur & Muzaffarpur. IEC materials in the form of audio-video spots, posters, leaflets, flipcharts etc. have been developed. Advertisements are given in the leading dailies for creating awareness about cancer among general masses.
- **National Cancer Awareness Day**: The birth anniversary of Nobel Laureate Madam Curie is observed as National Cancer Awareness Day since 2001, with a focus on cancer awareness.
- **Onconet-India:** National Informative Center [NIC] has prepared the Detailed Project Report [DPR] for Operationalization of Onconet in India. Under the project RCCs will be linked with each other and also each RCC would in turn be linked to 4 peripheral centres thus facilitating telemedicine services and continued medical education. Under telemedicine, services like tele-consultations, tele-referral, telepathology etc. will be provided and the budget provided for the project is Rs.13.25 crores, which will be carried out in 2 phases.
- **Membership of IARC:** International Agency for Research on Cancer [IARC] is a specialized agency of WHO to coordinate International Cooperation in Cancer Research. India has become a member of IARC at the 48th Session of the governing Council of IARC held in May 2006 at Lyon, France, which shall provide a fillip to cancer research in the country. IARC has provided technical and financial support to projects related to cancer research and prevention in India.

Budget allocation of NCCP- The programme has been strengthened in the successive five-year plans with low but substantial financial allocation. The amount allocated for NCCP has been 11.5 crore, 20 crore, 80

crore, 195 crore, 266 crore during the period 1980-85, 1985-90, 1992-97, 1997-2002, 2002-07 respectively. Expenditure Finance Committee proporsal for the X1th five year plan period [2007-12] budget allocation is under process.

Challenges, Issues and Concerns- [17] The three modalities of treatment namely, surgery, radiotherapy and chemotherapy are grossly inadequate in the country both in terms of personnel and equipment especially in semi-urban and rural areas. This has forced the rural population to seek treatment in the urban area, which is geographically and financially inaccessible to them. To reach such facilities they are constrained to spend huge amount of money mostly beyond their reach that further impoverished them. On an average 50-60% of the patients are treated with radiotherapy, 20% with surgery and 25-30% with chemotherapy [as primary treatment or in combination]. Multidisciplinary therapy, tissue conservation, protocol driven treatment of supportive care are only available to 5% of cancer patients treated in designated centres.

- **Radiotherapy**-Taking into consideration the requirement of one Teletherapy machine for 1 million population, India will need just over 1100 machines and there is a considerable shortfall with 345 machines at present.
- **Medical Oncology**- Chemotherapy is an important treatment modality in cancer. Unfortunately many drugs used in chemotherapy are at present very expensive and there is an urgent need to make these drugs affordable.
- **Surgical Oncology-** availability of surgeons trained in oncology is grossly inadequate. Surgical oncology training may be provided to general surgeons during their training as well as to those in practice as majority of cancers cases are likely to present themselves to a surgeon in the first instance. Affordability of the newer advances in surgical management is another area of concern.
- **Diagnostic facilities for cancer -** Cytopathology forms an important par to diagnostic techniques along with various other recent advances in diagnosis like MRI, CT scan, and PET. Trained experts like cytotechnicians, cytotechn-ologists, and pathologists are also inadequate.
- **Palliative care-** Pain relief and palliative care are important requirements as majority of the cancers present in advanced stages to a cancer treatment facility. Oral Morphine tablets has been made available from 1991 and currently available to cancer patients in few parts of the country. Awareness regarding concept & management of cancer related pain is lacking in health professional, community and patients. There is further limitation of manpower professionals and NGO in providing palliative care.
- **Research-** Data regarding cancer has been available in India for a long time since the introduction of the National Cancer Registry Programme. However, large areas of the country are not adequately represented in the current registry programme which is further compounded by the fact that there is also lack of public health oriented research in the country.
- **Information, Education and Communication [IEC] -** Inspite of being an important component of NCCP, the programme addresses this issue to a limited extent only. Promotion of breast self-examination, cervical screening etc. is being carried out at some places only and yet to receive wider acceptance. There is no education on risk factors, early warning signals and their management. Cancer screening is not practiced in an organized manner in any part of India. There is a huge scope for strengthening of IEC through the programme.
- **Monitoring and Evaluation -** National Institute of Health and Family Welfare

[NIHFW] carried out evaluation of the programme in 2002 and based on the recomme-ndation the programme was revised in December 2004. However, monitoring system under NCCP is poor and needs to be established.

- Lack of integration & poor coordination within health department and absence of linkage with other department, organizations and NGOs.
- Cheap bidi's which are equally harmful as cigarettes available in plenty [In India, nearly 40% of adults are smokers]
- Pan masala introduced during the last 20 years has caught up as a habit across the community including children.
- Poor implementation of Indian tobacco act and related legislation compounded by poor political commitment.
- No sustainable human resource development efforts of different category

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2. Manuscript : Manuscripts can be submitted in a CD (compact disc) in MS Word (in addition ton to one hard copy). Typescript should be sent to the Editor, NBE Journal of graduate Medical Education, Training & Research, National Board of Examinations, Ring Road, Ansari Nagar, New Delhi-110029 (India)

Manuscripts should be presented in as concise a form as possible, typewritten in double space on one side of a good quality bond paper (21.0x29.7 cms). Pages should be numbered consecutively and the contents arranged in the following order : - Title; Name (s) of the author (s); Department(s) and Institution(s); Abstract; Key words; Introduction; Material & Methods; Results; Discussion; Acknowledgement; and reference. Abstract, Tables and Legends for Figures should be typed on separate sheets and not in continuation of the main text.

Title : Title of the article should be short, continuous (broken or hyphented titles are not acceptable) and yet sufficiently descriptive and informative so as to be useful in indexing and information retrieval.

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Results : Only such data are essential for understanding the discussion and main conclusions emerging from the study should be included. The data should be arranged in unified and coherent sequence. Data presented in tables in and figures should not be repeated in the text. Only important observations need to be emphasized or summarised.

Discussion : the discussion should deal with the interpretation of results without repeating information already presented under Results. It should relate new findings to the known ones and include logical deducations. It should also mention any weaknesses of the study. The conclusions can be linked with the goals of the study. All hypotheses should, if warranted, clearly be identified as such; recommendations may be included as part of Discussion, only when considered absolutely necessary and relavant.

Acknowlegdgment : Acknowledgment should be brief and made for specific/technical assistance and financial support only and not for providing routine departmental facilities and encouragment or for help in the preparation of the manuscripts (including typing or secretarial assistance)

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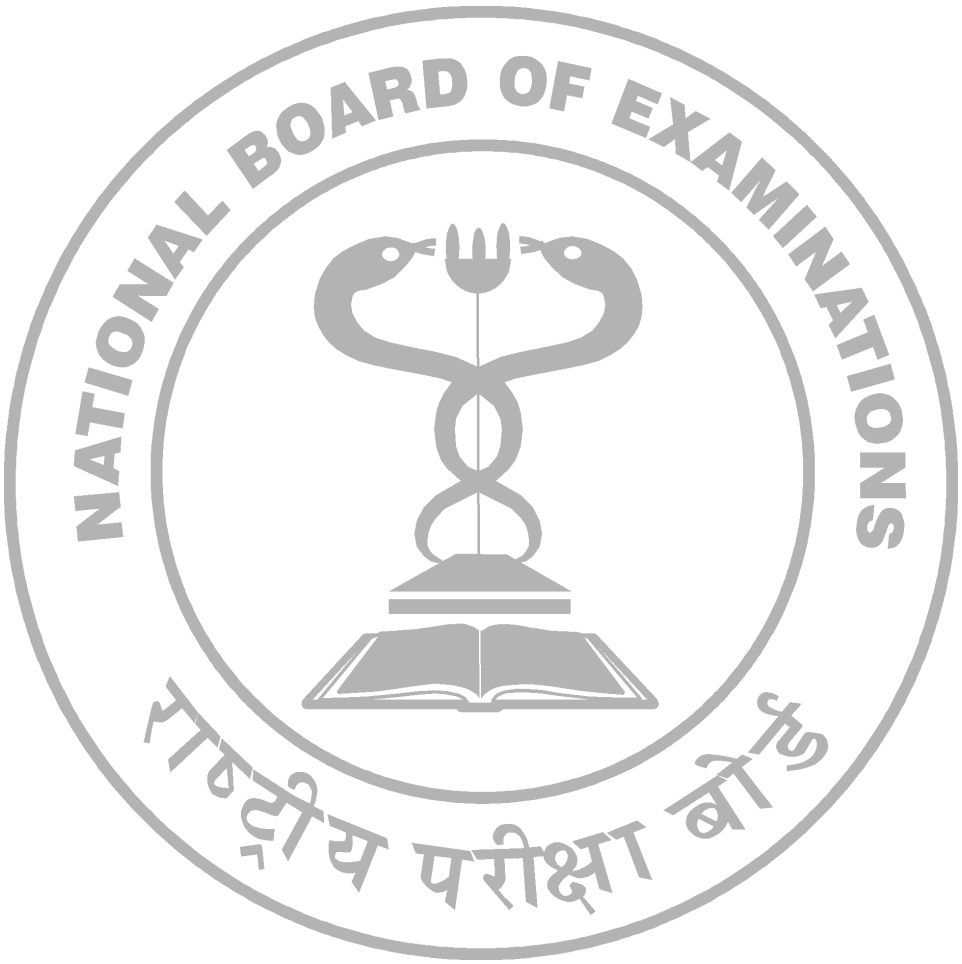
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